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ACC/AHA PRACTICE GUIDELINES

ACC/AHA Guidelines for Coronary Angiography

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Coronary Angiography)

Developed in collaboration with the Society for Cardiac Angiography and Interventions

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This document is available on the websites of the ACC (www.acc.org) and the AHA (www.americanheart.org). Reprints of this document (the complete guidelines) are available for $5 each by calling 800-253-4636 (US only) or writing the American College of Cardiology, Educational Services, 9111 Old Georgetown Road, Bethesda, MD 20814-1699. Ask for reprint No. 71-0164. To obtain a reprint of the shorter version (executive summary and summary of recommendations) published in the May 4, 1999, issue of *Circulation*, ask for reprint No. 71-0163. To purchase additional reprints (specify version and reprint number): up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 214-706-1466, fax 214-691-6342, or e-mail pubauth@heart.org

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 states. 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 have a favorable effect on 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 production of such guidelines in the area of cardiovascular disease since 1980. This effort is directed by the ACC/AHA Task Force on Practice Guidelines. Its charge is to develop and revise practice guidelines for important cardiovascular diseases and procedures. Experts in the subject under consideration are selected from both 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. Patient-specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or

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therapies are considered as well as 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 yearly and as changes occur.

These practice guidelines are intended to assist physicians in clinical decision making by describing a range of 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 all of the circumstances presented by the patient.

The executive summary and recommendations are published in the May 4, 1999, issue of *Circulation*. The full text is published in the *Journal of the American College of Cardiology*. Reprints of both the full text and the executive summary and recommendations are available from both organizations.

These guidelines have been officially endorsed by the Society for Cardiac Angiography and Interventions.

James L. Ritchie, MD, FACC
Chair, ACC/AHA Task Force on Practice Guidelines

I. INTRODUCTION

The ACC/AHA Task Force on Practice Guidelines herein revises and updates the original "Guidelines for Coronary Angiography," published in 1987 (1). The frequent and still-growing use of coronary angiography, its relatively high costs, its inherent risks and the ongoing evolution of its indications have given this revision urgency and priority. The expert committee appointed included private practitioners and academicians. Committee members were selected to represent both experts in coronary angiography and senior clinician consultants. Representatives from the family practice and internal medicine professions were also included on the committee.

The English-language medical literature was searched for the 10 years preceding development of the guidelines. The searches yielded >1,600 references that the committee reviewed for relevance. Evidence relative to the use of coronary angiography was compiled and evaluated by the committee. Whereas randomized trials are often available for reference in the development of treatment guidelines, randomized trials regarding the use of diagnostic procedures such as coronary angiography are rarely available (2). For development of these guidelines, when coronary angiography was a necessary procedure in describing a clinical subset or in choosing a course of treatment and that therapy was shown to have an advantage for the patient, especially in the context of a randomized trial, then the indication for angiography was given greater consideration than indications cited in less-rigorous evaluations of data.

This document uses the ACC/AHA classifications of Class I, II, or III. These classes summarize the indications for coronary angiography as follows:

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

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

- **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 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: The presence of multiple randomized clinical trials.

Level of Evidence B: The presence of a single randomized trial or nonrandomized studies.

Level of Evidence C: Expert consensus.

This document was reviewed by 6 outside reviewers, 3 nominated by the ACC and 3 by the AHA, as well as by reviewers nominated by the Society for Cardiac Angiography and Interventions (SCAI), the American College of Physicians (ACP), and the American Academy of Family Physicians (AAFP). The document will be reevaluated two years after the date of publication and yearly thereafter and considered current unless the task force publishes a further revision or withdrawal.

Recommendations concerning the staffing and equipment of cardiac catheterization laboratories are beyond the scope of this report and can be found elsewhere (3). Statements concerning the use and safety of ambulatory and outpatient cardiac catheterization procedures and the performance of cardiac catheterization in laboratories without on-site cardiac surgical backup are available (3).

This report is not intended to provide strict indications or contraindications for coronary angiography because, in the individual patient, multiple other considerations may be relevant, including the family setting, occupational needs, and individual lifestyle preferences. Rather, the report is intended to provide general guidelines that may be helpful to the practitioner.

For these guidelines, coronary angiography is defined as the radiographic visualization of the coronary arteries after direct opacification with contrast media. After a discussion of general considerations regarding coronary angiography, the applications of coronary angiography in specific disease states are presented and discussed in the body of this report. Recommendations are made for appropriate use of coronary angiography in these conditions. After the body of the guidelines, appendices are presented that include a discussion of special considerations regarding coronary angiography; a discussion of alternative imaging modalities, including intravascular coronary ultrasound, intracoronary Doppler ultrasound, and coronary angioscopy; definitions of angiographic coronary anatomy and the Canadian Cardiovascular Society (CCS) classification of angina; and the desired elements of a coronary angiographic report.

II. GENERAL CONSIDERATIONS REGARDING CORONARY ANGIOGRAPHY

A. Definitions

Coronary angiography is defined as the radiographic visualization of the coronary vessels after the injection of radiopaque contrast media (4,5). The radiographic images are permanently recorded for future review with either 35-mm cine film or digital recording. Percutaneous or cutdown techniques, usually from the femoral or brachial artery, are used for insertion of special intravascular catheters. Coronary angiography further requires selective cannulation of the ostium of the left and right coronary arteries and, if present, each saphenous vein graft or internal mammary artery graft to obtain optimal selective contrast injection and imaging. Numerous specialized catheters have been designed for this purpose. Physicians performing these procedures must be technically proficient in all aspects of the procedure and have a complete understanding of the clinical indications and risks of the procedure and of coronary anatomy, physiology and pathology. It is also important that these physicians understand the fundamentals of optimal radiographic imaging and radiation safety. Coronary angiography is usually performed as part of cardiac catheterization, which may also involve angiography of other vessels or cardiac chambers, and hemodynamic assessment as needed for a complete invasive diagnostic evaluation of the individual patient's cardiovascular condition.

Coronary anatomy varies, and several nomenclatures have been used to describe the anatomy and extent of disease. Currently, the most commonly used is that described in the Coronary Artery Surgery Study (CASS), recently modified by the Bypass Angioplasty Revascularization Investigation (BARI) Study Group (6,7). These schemes acknowledge three major coronary arteries: the left anterior descending (LAD), the circumflex, and the right coronary artery, with right-dominant, balanced, or left-dominant circulations. A diagram and description of the coronary anatomy are shown in Appendix A. In this nomenclature, the coronary tree is divided into 29 segments with the ability to account for anatomic variations, such as a large branching obtuse marginal of the circumflex. The extent of disease is usually defined as one-vessel, two-vessel, three-vessel, or left main disease, with significant disease taken to mean the presence of a stenosis of $\geq$50% diameter reduction, although many angiographers define a significant stenosis as being narrowed by $\geq$70% diameter reduction. Other methods to quantify the extent of disease, such as an obstructive coronary artery score or myocardial jeopardy score, have also been used and have been shown to be predictive of long-term outcome (8–10). Although coronary lesions that reduce luminal diameter $<$50% are considered hemodynamically insignificant, they are not clinically benign. These lesions may progress either acutely or chronically, and patients with nonsignificant obstructions have significantly more cardiovascular events during follow-up than those with truly normal coronary angiograms (11).

B. Purpose

The purpose of coronary angiography is to define coronary anatomy and the degree of luminal obstruction of the coronary arteries (4,5). Information obtained from the procedure includes identification of the location, length, diameter, and contour of the coronary arteries; the presence and severity of coronary luminal obstruction(s); characterization of the nature of the obstruction (including the presence of atheroma, thrombus, dissection, spasm, or myocardial bridging), and an assessment of blood flow. In addition, the presence and extent of coronary collateral vessels can be assessed.

Coronary angiography remains the standard for assessment of anatomic coronary disease, because no other currently available test can accurately define the extent of coronary luminal obstruction. Because the technique can only provide information about abnormalities that narrow the lumen, it is limited in its ability to accurately define the etiology of the obstruction or detect the presence of nonobstructive atherosclerotic disease. A more detailed description of the limitations of coronary angiography and the use of alternative imaging modalities is contained in Appendices B and C. Despite these and other limitations, coronary angiography is the only method currently available for defining the details of the entire coronary endoluminal vascular anatomy, and it provides the reference standard against which other tests are compared. The procedure is associated with a small but definable risk (Table 1) and is relatively expensive. As such, the physician must make reasoned decisions on its use based on the anticipated clinical benefit versus the risks and costs of the procedure.

Coronary angiography is principally used in three clinical situations (12): first, to determine the presence and extent of obstructive coronary artery disease (CAD) in a setting in which the diagnosis is uncertain and CAD cannot be reasonably excluded by noninvasive testing; second, to assess the feasibility and appropriateness of various forms of therapy, such as revascularization by percutaneous or surgi-

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Table 1. Risk of Cardiac Catheterization and Coronary Angiography (No. of Patients = 59,792)

	%
Mortality	0.11
Myocardial infarction	0.05
Cerebrovascular accident	0.07
Arrhythmia	0.38
Vascular complications	0.43
Contrast reaction	0.37
Hemodynamic complications	0.26
Perforation of heart chamber	0.03
Other complications	0.28
Total of major complications	1.70

Modified with permission from Noto et al. (13).

cal interventions; and finally, as a research tool for the assessment of treatment results and the progression or regression of coronary atherosclerosis.

C. Morbidity and Mortality

Although the incidences of significant morbidity and mortality are low, coronary angiography may cause serious complications and, thus, the benefits must justify the risks. A 1990 survey by the SCAI indicated that the total risk of all major complications from coronary angiography is <2% (Table 1) (13). Although serious complications are rare, certain groups of patients are at higher risk. The stability of the patient before the procedure significantly influences outcome, with the highest risk associated with patients who undergo the procedure in an emergency setting. Patients with critical left main coronary stenosis have a >2-fold higher risk of complications from coronary angiography, and care is required when procedures are performed on patients in whom left main lesions are suspected (14). Another study from the SCAI registry database identified 12 predictors of major complications after cardiac catheterization (Table 2) (15). Patients in a moribund condition before the procedure had the highest risk (10-fold), and shock, acute myocardial infarction (MI), renal insufficiency, and cardiomyopathy increased the risk of complications. Despite the higher risk of complications in these patients, the risk-benefit ratio may still favor performance of coronary angiography, because the information obtained may be invaluable in making appropriate decisions about therapeutic interventions. Although age is not shown in Table 2, it is generally considered to be a significant factor related to cardiovascular mortality after coronary angiography. The skill and experience of the operator, the catheterization laboratory staff, and the preprocedure and postprocedure staff are also important factors in reducing complications. Operator experience is clearly related to lower complication rates. This fact has led one national organization to recommend a minimum operator volume of 150 diagnostic catheterizations per year (16). This is also true for coronary angioplasty facilities. Recent studies have suggested that

Table 2. Multivariate Predictors of Major Complications of Coronary Angiography (No. of procedures = 58,332)

Variable	Coefficient	Odds Ratio (95% CI)
Moribund	−1.90	10.22 (3.77, 27.76)
Shock	−1.09	6.52 (4.18, 10.18)
Acute MI <24 h	−0.98	4.03 (2.61, 6.21)
Renal insufficiency	−0.43	3.30 (2.39, 4.55)
Cardiomyopathy	−0.79	3.29 (2.23, 4.86)
Aortic valve disease	−0.36	2.72 (2.02, 3.66)
Mitral valve disease	−0.30	2.33 (1.76, 3.08)
Congestive heart failure	−0.32	2.22 (1.71, 2.90)
New York Heart Association Functional		
Class I		1.00
Class II		1.15 (0.94, 1.41)
Class III		1.32 (0.92, 1.51)
Class IV		1.52 (1.16, 1.74)
Hypertension	−0.38	1.45 (1.22, 1.73)
Unstable angina	−0.24	1.42 (1.16, 1.74)
Outpatient/inpatient	0.34	0.63 (0.52, 0.76)

Moribund indicates a patient who responds poorly due to a life-threatening condition; MI, myocardial infarction; major complication, any adverse event listed in Table 1. Modified with permission from Laskey et al. (15).

laboratory volumes of >200 angioplasty cases per year and 75 cases per operator are necessary to minimize complications and maximize success (17–19). A recent ACC expert consensus document discusses the issue in more detail (19). Many catheterization laboratories are located in hospitals without on-site cardiac surgery facilities. Although there is no evidence that outcomes are worse in these laboratories, if ad hoc angioplasty is anticipated, or the patient is likely to need urgent or emergency surgery after angiography, transfer to a hospital that can provide both diagnostic and therapeutic procedures should be strongly considered.

D. Relative Contraindications

There are no absolute contraindications for coronary angiography. Commonly accepted relative contraindications are shown in Table 3. Although these contraindications are widely used, few data exist as to the inherent risks of performing the procedure when these problems are present.

Of the known relative contraindications to coronary angiography, renal insufficiency has been the most extensively studied (20–29). The reported incidence of significant worsening of renal function after angiography ranges from 10% to 40% in these patients. The risk increases with the severity of preexisting renal insufficiency (24). In patients without preexisting renal insufficiency, the risk of developing a significant reduction in renal function is 0% to 0.5%. More than 75% of patients who develop renal insufficiency recover completely, but permanent impairment of renal function that requires dialysis can occur in up to 10% of patients who develop this complication. Baseline creatinine, male sex, diabetes, and volume of contrast are independent predictors of the development of renal insufficiency after

Table 3. Relative Contraindications to Coronary Angiography

Acute renal failure
Chronic renal failure secondary to diabetes
Active gastrointestinal bleeding
Unexplained fever, which may be due to infection
Untreated active infection
Acute stroke
Severe anemia
Severe uncontrolled hypertension
Severe symptomatic electrolyte imbalance
Severe lack of cooperation by patient due to psychological or severe systemic illness
Severe concomitant illness that drastically shortens life expectancy or increases risk of therapeutic interventions
Refusal of patient to consider definitive therapy such as PTCA, CABG, or valve replacement
Digitalis intoxication
Documented anaphylactoid reaction to angiographic contrast media
Severe peripheral vascular disease limiting vascular access
Decompensated congestive heart failure or acute pulmonary edema
Severe coagulopathy
Aortic valve endocarditis

PTCA indicates percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft.

contrast injection. Diabetic patients with preexisting renal insufficiency are particularly prone to develop renal failure (22). In patients at risk for renal failure, pretreatment with intravenous fluids or mannitol or with intravenous furosemide after angiography, as well as the use of nonionic contrast media, has been beneficial in some studies (20,23,28). However, in a recent randomized study, intravenous hydration with 0.45% saline was the most effective means of preventing worsening renal failure in high-risk patients, reducing the risk of worsening renal failure from 40% with furosemide and 28% with mannitol to 11% with intravenous hydration (20). It is also critical that the volume of contrast be minimized to reduce the chance of contrast-induced renal failure.

Major reactions to angiographic contrast medium are rare, but in patients with a known anaphylactoid reaction to contrast media, the risk of subsequent reaction may be as high as 50% (30,31). Patients with a known cardiovascular disorder who are taking a beta-blocker are at increased risk for contrast reactions (31). Observational studies suggest that pretreatment of a reaction-prone patient with a corticosteroid and/or a H_1 and H_2 histamine blocker can reduce this risk to an acceptable level when the indications for the procedure justify its need (30–33). However, only one randomized trial of corticosteroids has been conducted. In that study, a two-dose corticosteroid regimen (before and after angiography) significantly reduced the incidence of anaphylactoid reactions (34). In addition, the use of nonionic contrast may reduce the incidence of subsequent anaphylactic reactions (32,34).

The presence of uncompensated congestive heart failure increases the chance of major complications after coronary angiography. Although limited data are available to accurately define its risk, treatment of the heart failure before coronary angiography is advised. In addition, it is advisable to limit contrast volume and use nonionic contrast media in patients with poor left ventricular function to reduce the adverse hemodynamic effects of contrast media.

It should be recognized that most of the relative contraindications may be temporary or reversible, and therefore if the procedure can be safely delayed, risks may be lowered. In high-risk patients and patients with relative contraindications, the procedure should not be performed in an outpatient setting. The guidelines for outpatient cardiac catheterizations are described in more detail in the "ACC/AHA Guidelines for Cardiac Catheterization and Cardiac Catheterization Laboratories" (3).

E. Utilization

In 1993, cardiac catheterization was the second most frequently performed in-hospital operative procedure in the U.S. and the most frequently performed procedure in patients older than 65 years of age (35). In that year, ≈1,078,000 inpatient cardiac catheterization procedures were performed (36). It is estimated that an additional 668,000 patients received cardiac catheterization as outpatients (John Goodman and Associates, 1996, personal oral communication). There are no similar data specific for use of coronary angiography, but in adult patients, cardiac catheterization includes coronary angiography in most cases.

Approximately 48% of cardiac catheterizations are now performed in the elderly, who are defined as ≥65 years of age (35). Men are more likely to have cardiac catheterization than women. There are also racial differences in use of coronary angiography in the U.S. In 1993, cardiac catheterization was performed in 349 of 100,000 patients in the white population, 235 of 100,000 in the black population, and 316 of 100,000 in other races.

The use of cardiac catheterization continues to grow. According to data from Medicare (37), the combined number of inpatient left-heart catheterizations and right- and left-heart catheterizations, ie, those procedures that most often include coronary angiography, increased from 575,000 in 1991 to 793,000 in 1995, an increase of 38% over 4 years. The number of outpatient cardiac catheterizations is more difficult to determine. It is estimated that in 1986, ≈5% of the total volume of catheterizations in Medicare patients were performed in outpatients, whereas in 1993, that figure had risen to 23%.

Although it has been suggested by many that managed care will curtail further growth in the frequency of cardiac catheterization, that has yet to occur. Given a prediction of 40% growth in the population aged >45 years from 1995 to 2010, and the present trend of increased utilization, it is possible that by 2010, ≈3,000,000 cardiac catheterizations will be performed annually in the U.S.

In 1994, ≈10% of cardiac catheterizations were performed in patients with a Diagnosis Related Group (DRG) diagnosis of acute MI (38,39). Although this is only a small percentage of those patients studied by coronary angiography, the infarction subgroup has been well characterized. The frequency of its use is growing in this group of patients: from 1987 to 1990, the proportion of Medicare patients with infarction who had cardiac catheterization increased from 24% to 33% (40). Infarction patients admitted to hospitals with cardiac catheterization laboratories are ≈3 times more likely to undergo angiography than are patients admitted to hospitals without such facilities (41,42). Patients treated for MI by invasive cardiologists have a similar likelihood of undergoing angiography as patients treated by noninvasive cardiologists (68% vs. 59% at Massachusetts General Hospital), but the likelihood of having angioplasty or surgery is higher for patients treated by invasive cardiologists (43).

In the U.S., there are substantial regional differences in the use of coronary angiography (35). In the GUSTO-1 (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) study of patients with acute MI, the proportion undergoing angiography varied substantially between 7 regions evaluated (44). In New England, 52% of patients with acute MI underwent coronary angiography, whereas in the other 7 regions, the frequency of use was much higher at between 66% and 81%. The regional use of angiography was closely related to its availability in all regions, except for New England. Despite these regional variations in utilization, there was no apparent relationship between procedure rate and certain patient outcomes. The incidence of recurrent infarction or death at 30-day and one-year follow-up did not vary from region to region. In another study that evaluated Medicare patients with MI, the frequency of catheterization was 45% in patients in Texas but only 30% in patients in New York (45). In Texas, use was higher for all clinical subgroups analyzed except for those at greatest risk for reinfarction, that is, non–Q-wave infarction or patients with postinfarction angina, for whom the rates were similar to those in New York. Despite the increased use of coronary angiography in Texas, the adjusted mortality at two-year follow-up was significantly lower in New York, and patients in New York had fewer symptoms. Conversely, in an analysis of use of coronary angiography within three months of an acute MI among 6,851 patients hospitalized at 16 Kaiser Permanente hospitals from 1990 to 1992, the rates of angiography (ranging from 30% to 77%) were inversely related to the risk of death from heart disease ($p = 0.03$) and the risk of heart disease events ($p < 0.001$) over one to four years of follow-up (46). This association was strongest among patients for whom published criteria indicated that angiography was necessary.

For postinfarction patients, there is also an international difference in use of angiography. In both the GUSTO (47) and the SAVE (Survival and Ventricular Enlargement) trials (48), angiography was used more frequently after infarction in patients in the United States than in Canada. Despite this difference in utilization, there were no differences in mortality or reinfarction rates between the two countries, although for both studies there was a higher incidence of symptoms in Canadian patients at follow-up. Similar conclusions were formed in a recent study comparing elderly patients with MI in the U.S. and Canada (49).

This variation in use has led many to question the appropriateness of angiography (50,51), particularly for patients with MI. Appropriateness was evaluated for patients treated in the Myocardial Infarction Triage and Intervention Project (MITI), a study of acute MI performed in Seattle and King County, Washington (38). It was found that except for recurrent angina, clinical risk factors that predict higher mortality were associated with a lower rather than a higher use of angiography, which suggests that many patients who needed angiography did not receive it. Although these data do not determine with certainty whether angiographic procedures are overused in patients at low mortality risk or underused in patients at greater mortality risk, they suggest that the current balance between patient survival risk and procedure utilization may not be the most efficient use of this expensive resource (38).

Other studies examining the appropriateness of angiography have yielded widely varied results (Table 4). These studies generally rely on criteria established by an expert panel to determine if angiography was necessary and appropriate. How well the opinion of such expert panels actually agreed with practicing physicians had not been examined until recently, but the level of agreement was found to be quite good (58). Areas of patient management in which variation in the appropriateness of coronary angiography was greater were in older individuals and in those with uncomplicated MI. Estimates for the rate of inappropriate angiography have varied from as high as 58% in a two-hospital study in Israel (53) to as low as 2% in a Swedish report (56). The U.S. studies have included several reports from the Rand Corporation investigators (52,55,59). Using criteria for appropriateness developed through a consensus panel of both specialists and generalists, Rand investigators categorize angiography as appropriate, of "uncertain" value, or inappropriate. By their criteria, angiography in New York State was judged as appropriate in 76% of cases, of uncertain value in 20%, and inappropriate in only 4% (52). Other studies, particularly those that compare U.S. care with that in Canada, have suggested that inappropriate indications may be as high as 15% to 18% in some centers (57). Unfortunately, current studies do not allow a final estimate as to how frequently coronary angiography is performed inappropriately.

Although most analyses have examined how often unnecessary or inappropriate angiography is performed, few have focused on how frequently patients fail to undergo angiography despite firm indications for its use. A recent

Table 4. Appropriateness of Angiography: Range of Findings in Literature

Author	Study Cohort	Methods	Results
Bernstein et al. (52)	1,335 patients 15 hospitals in New York	Rand method	Inappropriate, 4%
Mozes and Shabtai (53)	499 patients 2 hospitals in Israel	Consensus panel	Inappropriate, 58%
Hampton et al. (54)	3 centers in England	Expert panel	Inappropriate, 10%–28%
McGlynn et al. (55)	1,336 patients 15 hospitals in New York; 15 in Canada	Rand method in United States Consensus panel in Canada	Inappropriate, 4%–10%
Bengston et al. (56)	831 patients in Sweden	Expert panel	Inappropriate, 2%
Roos et al. (57)	351 patients in Canada 1,677 patients in United States	Expert panel	In Canada, inappropriate, 9% In United States, inappropriate, 15%–18%

study from southern California examined how frequently patients with a "necessary" indication for angiography, defined as a very positive stress test, were not referred for further evaluation by angiography (60). Among >160 patients with a "necessary" indication, only 47% underwent angiography within three months of the stress test and 61% within 12 months. After adjustment for demographics and clinical presentation, patients cared for by a cardiologist were more likely to undergo necessary angiography than those cared for by nonspecialists (74% vs. 44% by one year). These data, although preliminary, raise concern that widely accepted and effective diagnostic tests and therapies are not being used in substantial numbers of patients. They also confirm findings from other studies that specialists in cardiovascular disease are more likely to provide appropriate or "necessary" procedures than generalists (61,62).

There are no data available regarding how often coronary angiography can appropriately be performed in any one patient. It seems reasonable that a significant clinical change could warrant a repeat angiogram in a patient with known CAD, if the indication for angiography was in agreement with these guidelines. The committee considers it unreasonable to perform a repeat angiogram in a patient with recurrent chest pain who has had a previously normal coronary angiogram within the preceding five years, unless there is an intervening documented MI or significantly worsening findings on noninvasive testing. However, in patients with angiographically significant CAD, who were initially treated medically but in whom coronary revascularization later becomes clinically necessary, it is common practice to allow such a patient to proceed with revascularization without a repeat angiogram if <6 months have elapsed since the prior coronary angiogram, but to repeat angiography if >6 months have passed.

On occasion, angiographic image quality or lesion visualization is inadequate to make a judgment regarding the best route of care for a patient, especially in deciding on a revascularization procedure. In this case, a repeat angiogram may be necessary. However, if repetitive angiography becomes an ongoing problem in any laboratory, the laboratory director should critically review the equipment and staff performance and especially the practice of those physicians who undertake repetitive angiographic procedures. In the absence of clinical indications, repeat angiography is both costly and potentially dangerous.

F. Costs

The total cost of coronary angiography includes laboratory fee, professional fee and costs related to preprocedure and postprocedure observation and laboratory testing (63). Additional costs may accrue if inadequate studies must be repeated or if complications develop (64). Charges generally are different from costs and are usually higher. Charge information is more readily available than cost information (65). There is disagreement regarding the effect that laboratory volume has on costs. Some recommend that a laboratory should perform ≥300 to 400 procedures per year to maximize economic efficiency, primarily to make up for capital outlay and its amortization (66,67), whereas others have found no relation between volume and costs (68,69).

The 1992 mean charge for cardiac catheterization for inpatients younger than 65 years without a diagnosis of acute MI was $10,880, varying by state from a low of $6,400 in Maryland to $17,600 in California (70). Eighty-two percent of the total charge was for hospital care. Of this amount, 62% was related to catheterization laboratory and ancillary charges and 38% for room and board. The physician charge made up 18% of the total, averaging $2,000 and varying from $1,300 in South Carolina to $2,550 in California. Costs related to physician fees are falling. Medicare payment for physician services for a typical procedure, e.g., a left-heart catheterization with a left ventriculogram or angiography of the native coronaries as well as one additional angiographic component, with supervision and interpretation, was $725 in 1994 and $700 in 1996, and further reductions are anticipated (37).

Outpatient catheterization may be lower in cost, but how much lower is unclear. A prospective study of patients who, on the basis of published guidelines, were candidates for outpatient procedures found that charges for outpatient procedures were $580 less than for inpatient procedures, but

actual cost savings were only $218 per patient (71). Previous reports suggested that the nonprofessional component of charges could be reduced by 31% to 55% for an outpatient procedure (72,73).

G. Cost-Effectiveness

There has been relatively little study of the cost-effectiveness of coronary angiography compared with noninvasive techniques for the diagnosis and subsequent management of CAD (74). In part, this lack of evidence exists because coronary angiography frequently leads to a revascularization procedure, and thus it is difficult to separate the cost-benefit aspects of the diagnostic test from those of the procedure that subsequently follows. However, several reports regarding the cost-effectiveness of coronary angiography have recently been published.

Patterson et al. (74) compared the cost-effectiveness of coronary angiography with that of ECG stress testing, single photon emission-computed tomography (SPECT) imaging, and stress positron emission tomography (PET) scanning as a first technique to diagnose CAD. In this Bayesian analysis, effectiveness was defined as the number of patients with diagnosed CAD and utility as the clinical outcome, i.e., the number of quality-adjusted life years (QALY) extended by therapy after the diagnosis of CAD. The authors used published values for costs, accuracy, and complication rates of the various tests. At a clinically derived pretest probability of significant CAD of <70%, noninvasive testing was more cost-effective than coronary angiography as an initial procedure. Above a threshold probability of 70% (for example, middle-aged men with typical angina), proceeding directly to angiography as the first test had the lowest cost per effect or utility.

Other studies have examined the cost-effectiveness of combined diagnostic coronary angiography and angioplasty as a single procedure rather than having patients undergo two procedures. Rozenman and colleagues (75) studied >2,000 patients over a three-year period and found no difference in success or complication rates for patients who had diagnostic angiography and angioplasty performed at the same time, compared with having them done as separate procedures. They found no difference in length of stay after angioplasty between combined and staged treatment strategies and concluded that same-setting angioplasty was likely to be more cost-effective. However, a formal analysis of true costs was not performed. In a similar manner, O'Keefe et al. (76) compared 219 patients undergoing combined procedures with a matched population of 191 patients who had separate procedures. The success and complication rates were similar, and the average total charge for a combined procedure was $11,128 compared with $13,160 in those undergoing separate procedures. The authors also estimated that significant savings would occur with respect to total contrast, fluoroscopic time and total procedure time.

Kuntz et al. (77) recently estimated the cost-effectiveness of routine coronary angiography after acute MI. Decision-tree chance node probabilities were estimated with the use of pooled data from randomized clinical trials and other relevant literature, costs were estimated with the use of the Medicare Part A database, and quality-of-life adjustments were derived from a survey of 1,051 patients with a recent MI. Routine coronary angiography increased quality-adjusted life expectancy in almost all post-MI subgroups compared with patients given initial medical therapy without angiography; however, the cost per QALY gained ranged widely, from $17,000 to >$1 million. When a threshold of <$50,000 was considered cost-effective, which compares favorably with the cost of using various medical strategies after MI, routine angiography was cost-effective for patient subgroups with severe postinfarction angina or a strongly positive exercise tolerance test, and for most subgroups with a prior MI, even with a negative stress test. Clearly, more research on the cost-effectiveness of coronary angiography is needed before the optimal use of this procedure in a wide range of clinical circumstances can be determined.

III. CORONARY ANGIOGRAPHY FOR SPECIFIC CONDITIONS

*A. Known or Suspected CAD**

1. General Considerations. Coronary atherosclerosis is a slowly progressive process that can be clinically inapparent for long periods of time (78–80). Coronary disease often becomes clinically evident because of the occurrence of symptoms, such as angina or those associated with MI. Patients with known CAD are those in whom the disease has been documented by either angiography or MI (i.e., using WHO criteria). "Suspected coronary disease" means that a patient's symptoms or other clinical characteristics suggest a high likelihood for significant CAD and its related adverse outcomes but that evidence of CAD has not yet been documented as defined above.

Patients may develop symptoms at one point in time but may become asymptomatic thereafter as the result of a change in the disease or as the result of therapy. For instance, many patients are asymptomatic after an uncomplicated MI, as are patients with mild angina, who can be rendered asymptomatic by medications. The severity of clinical presentations and the degree of provokable ischemia on noninvasive testing are the principal factors used in determining the appropriateness of coronary angiography. Although the extent of coronary disease defined by coronary angiography does predict outcome, use of coronary angiography as a "screening tool" in unselected populations is neither prudent nor cost-effective (74). The same can be stated regarding the routine use of exercise testing (81),

*As used in this document, the term "coronary artery disease" is broadly inclusive, encompassing atherosclerotic coronary disease with or without clinical manifestations as well as rarer forms of coronary disease that can produce obstruction and/or flow limitation, eg, embolus, spasm, arteritis, congenital abnormality and trauma.

radionuclide imaging (82) and stress echocardiography (83) in unselected patients. With only a few exceptions, coronary angiography is not clearly indicated in asymptomatic patients with either known or suspected CAD, unless noninvasive testing (performed as recommended in the ACC/AHA noninvasive guidelines), reveals findings that suggest a high risk for adverse outcome (81,82). Coronary angiography is also frequently done during evaluation for other cardiac conditions, such as valvular heart disease, congestive heart failure, or assessment of congenital heart disease. In this setting, angiography may be performed in asymptomatic patients. The details of indications for coronary angiography in specific conditions are described below.

2. Stable Angina

a. Definitions

Patients with CAD may become symptomatic in many different ways but most commonly develop angina pectoris. In this document, angina pectoris (or simply angina) means a chest discomfort due to myocardial ischemia, often described as a transient squeezing, pressure-like precordial discomfort. Angina is generally provoked by physical effort (particularly during the postprandial state), with exposure to cold environment or by emotional stress. The discomfort on effort is relieved by rest, its duration being a matter of minutes. The ease of provocation, frequency and duration of episodes may remain relatively unchanged in individuals for extended time periods, leading to the term "stable angina pectoris."

Not all stable chest pain syndromes are truly anginal. Various authors have subdivided stable chest pain syndromes in an attempt to link the quality of symptoms with the prevalence of significant CAD. Diamond and Forrester (84) found significant CAD at angiography in 89% of patients with typical angina but in only 50% with atypical angina and merely 16% of patients with nonanginal chest pain.

In CASS, 8,157 patients with chronic stable chest pain who underwent coronary angiography were characterized by type of symptoms reported. The CASS definitions of anginal type have become standards for much subsequent literature (85). "Definite angina" was defined as substernal discomfort precipitated by exertion and relieved by rest or nitroglycerin in <10 min. Most patients reported typical radiation to the shoulders, jaw or inner aspect of the arm. Patients with probable angina had most of the features of definite angina, but the features were atypical in some respects (e.g., radiation, unpredictable relief with nitroglycerin or duration up to 15 to 20 min). The third group had "nonspecific chest pain" that did not fit either of the above two groups. The prevalence of significant CAD in patients with definite angina, probable angina and nonspecific chest pain was 93%, 66% and 14% in men, and 72%, 36% and 6% in women ($p < 0.001$). The age and sex of the patients as well as the character of chest pain were important determinants of disease prevalence and severity. Coronary disease associated with high risk for adverse outcomes, that is, left main or three-vessel disease, occurred in >50% of middle-aged men and older women with definite angina and most men who had probable angina who were >60 years. In contrast, high-risk coronary disease was uncommon in both men and women with nonspecific chest pain, especially in patients <60 years.

The definition and diagnosis of angina is sometimes made more difficult by the predominance of other symptoms such as exertional dyspnea or fatigue, which may be "anginal equivalents." Women frequently present with symptoms that do not have the features classically described in studies of large populations of middle-aged men. Furthermore, women have a higher frequency of asymptomatic ischemia (86).

Angina is further defined according to a gradient of severity as outlined by the CCS classification (87) (Appendix D). In addition, *asymptomatic patients with CAD* are those with no symptoms to suggest myocardial ischemia in the previous *six weeks* (88). It is recognized that when tested, a subgroup of these patients will have transient abnormalities consistent with myocardial ischemia in the absence of symptoms. This is termed *silent ischemia*, and the abnormalities detected may consist of reversible ECG ST-segment shifts on exercise testing or ambulatory monitoring, perfusion abnormalities on radionuclide scans (i.e., stress ^{201}Tl, sestamibi, and PET) or regional wall motion abnormalities during left ventricular imaging (i.e., stress echocardiography or radionuclide ventriculography). It is appropriate to use the term ischemia in this context and to reserve the term angina to describe the subjective symptom felt by patients during episodes of myocardial ischemia. In general, these ischemic test results relate to the functional severity of CAD and are predictors of risk for future adverse outcome, independent of the perception of, or severity of symptoms. Thus, the absence of current symptoms does not necessarily mean either the absence of ischemia or the absence of an impaired prognosis. Diabetes, older age, female gender, hypertension, polyneuropathy, and cardiac transplantation, when accompanied by significant CAD, are all associated with a high frequency of ischemia or even MI without symptoms (89–92).

Patients with known CAD can be divided into two groups based on whether or not they ever had symptoms. One group includes those who were never symptomatic but in whom CAD was documented for other reasons. For example, abnormalities on a stress test led to an angiogram; the patient was a cardiac surgical candidate (e.g., valve replacement) and therefore angiography was done as a preoperative evaluation; or other clinical findings (e.g., asymptomatic MI or abnormal ECG) led to an angiogram. The other group includes those who were previously symptomatic but are currently asymptomatic (i.e., no symptoms within six weeks). This group would include, for example, those who previously had angina but are now asymptomatic; patients after symptomatic MI with no postinfarction angina; patients after revascularization (either CABG or

PTCA) who now have no angina; and those who were effectively treated (i.e., drugs or activity restriction) who now have no angina. Although this grouping is convenient because it summarizes how these patients present to the clinician, there are no data to suggest that such clinical grouping, based on whether or not patients are currently symptomatic, has prognostic significance.

b. Management Approach for Symptomatic Patients

Patients with stable chest pain syndromes should undergo a thorough clinical evaluation, including classification of chest pain type into definite or probable angina or nonspecific chest pain, and identification of risk factors (age, tobacco use, dyslipidemia, hypertension, family history of premature coronary disease, activity profile, obesity, postmenopausal status and diabetes). The physical examination will usually detect evidence of other types of heart disease that can cause angina, e.g., aortic stenosis, hypertrophic cardiomyopathy or severe pulmonary hypertension. An assessment of contraindications for coronary angiography should be part of this clinical assessment. The CCS classification of angina provides a useful guide for the assessment of severity of definite or probable angina. Severe symptoms (CCS class III or IV) suggest severe CAD and are an indication for cardiac catheterization.

Optimal medical management may include nitrates, long-acting calcium channel blockers, and beta-adrenergic blocking agents, as well as attention to associated conditions such as hypertension, dyslipidemia and diabetes. Therapy is considered adequate if it includes two of the three antianginal agents used at or near maximum recommended doses in addition to antiplatelet therapy. For most patients, medical therapy is considered successful when angina has been eliminated or no longer adversely influences their lifestyle, and they are able to exercise beyond the end of stage II of the Bruce protocol without experiencing angina and ST-segment depression. Patients with definite or probable angina for whom optimal pharmacologic therapy has failed and those with an intolerance to these medications are candidates for coronary angiography. Patients who are treated medically but who demonstrate subsequent deterioration on noninvasive testing that suggests progression of disease are often considered for coronary angiography. Coronary angiography should also be considered for patients whose angina accelerates or intensifies despite adequate medical care, even if their symptoms do not fulfill the criteria for a diagnosis of unstable angina. Stable angina patients who have survived sudden cardiac death or sustained ventricular tachycardia are generally referred for coronary angiography to identify coronary lesions that, if treated appropriately, could relieve the ischemic substrate for lethal arrhythmias (93).

From time to time, CCS class I to II patients, whose occupation or other circumstance constitutes a risk to themselves or others, should undergo coronary angiography even in the absence of high-risk markers for adverse outcome on noninvasive testing. Such "need-to-know" circumstances may exist for airplane pilots, train operators, firefighters, school bus drivers, serious athletes and others.

c. Management Approach for Asymptomatic or Mildly Symptomatic Patients With Known or Suspected CAD

A scheme for noninvasive evaluation of a mildly symptomatic or asymptomatic patient suspected or known to have significant CAD is shown in Figure 1. Exercise-induced ECG changes, abnormalities on radionuclide myocardial perfusion scans, and abnormalities on ventricular wall motion studies (Table 5) are established markers for high risk of adverse outcomes. Although these noninvasive stress test markers are neither 100% sensitive nor 100% specific, when properly used, they do have very acceptable predictive value for adverse outcome. Thus, they aid in the selection of appropriate candidates for coronary angiography when symptom severity alone does not support such a recommendation. A minority of patients undergoing noninvasive testing will have findings that suggest a high risk for adverse outcome, but in most of these high-risk cases, a recommendation for coronary angiography is warranted.

The criteria (Fig. 2) cited for identifying patients at high risk for adverse outcome during exercise ECG testing have evolved from both the original and the revised joint ACC/AHA Task Force reports (81,95) and a special report on exercise standards from the AHA (96). These reports emphasize the difficulties in interpreting ECG changes in selected populations, such as premenopausal women with a low pretest likelihood of coronary disease. Also, it should be noted that most apparently healthy men who have a positive (i.e., 1-mm ST depression) exercise ECG test (without high-risk criteria) but who lack clinical risk factors do not have significant CAD (97).

Radionuclide perfusion imaging techniques generally have higher specificity for significant CAD than ECG-based tests used alone but are much more costly. The radionuclide techniques are most cost-effective in identifying severe multivessel CAD in patients with uninterpretable ECGs and in patients who have an abnormal exercise ECG that does not fulfill high-risk criteria (Table 5). These findings are summarized in the "ACC/AHA Guidelines for Clinical Use of Cardiac Radionuclide Imaging" (82,98). That committee concluded that use of exercise or pharmacologic myocardial perfusion imaging with thallium or rest and exercise radionuclide angiography was usually appropriate and considered useful for assessment of severity of ischemia and risk stratification of patients with known or suspected CAD. They thought that the use of gated sestamibi perfusion imaging was also acceptable for this purpose but that its usefulness was less well established. The most consistent predictor of cardiac death or nonfatal MI was the number of transient perfusion defects provoked by either exercise or pharmacologic stress. Patients with CAD and redistribution defects on stress thallium imaging in >1 coronary artery region or who have a combination of

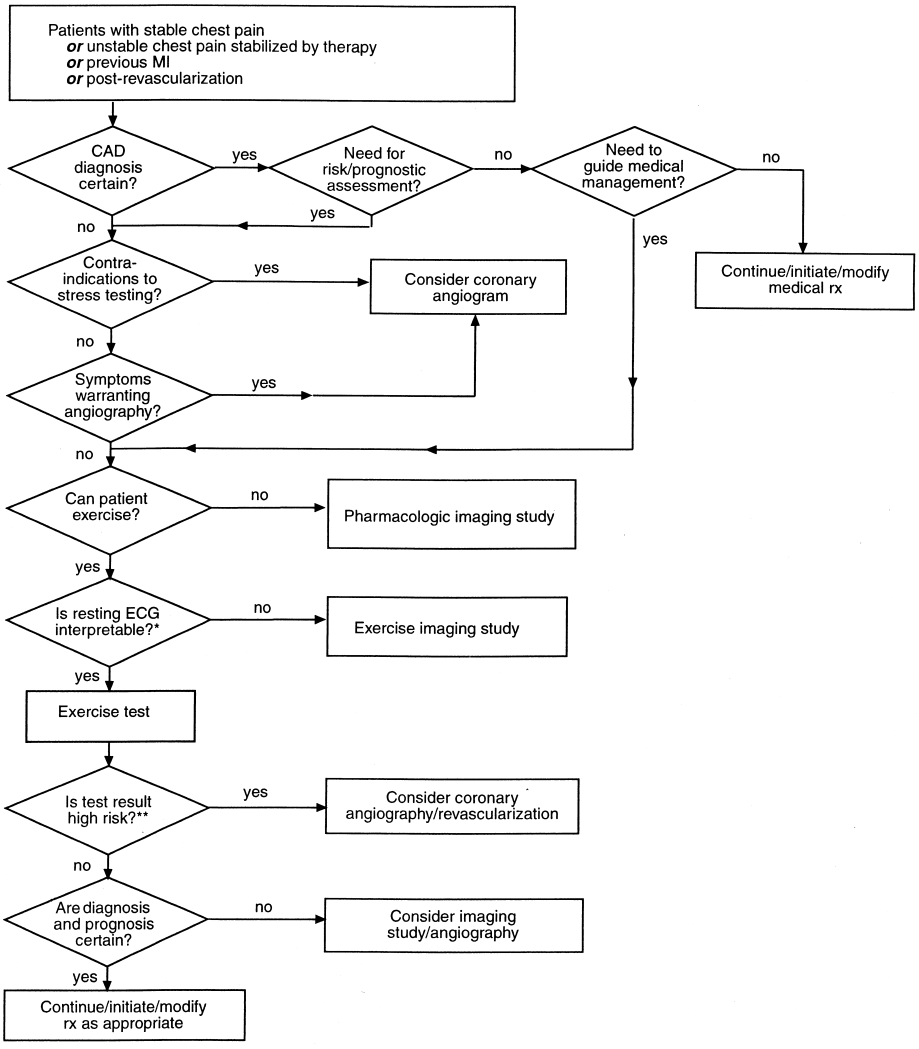

Figure 1. Clinical context for noninvasive and invasive diagnostic testing of patients with suspected ischemic heart disease. *ECG interpretable unless preexcitation, electronically paced rhythm, left bundle-branch block or resting ST-segment depression >1 mm. See text for discussion of digoxin use, left ventricular hypertrophy, and ST depression <1 mm. **For example, high risk if Duke treadmill score predicts average annual mortality >3% (see Fig. 2 for nomogram). Modified from Figure 1 of the "ACC/AHA Guidelines for Exercise Testing" (81).

redistribution abnormalities and increased lung uptake are at increased risk for adverse outcome (98). Normal stress ^{201}Tl scans are highly predictive of a good outcome, even in patients with documented CAD. An analysis of 3,595 such patients, followed up for ≤29 months in 16 separate studies, revealed a 0.9% annual rate of cardiac death or MI (99), nearly as low as that seen in the general population (100).

Assessment of left ventricular function (radionuclide ventriculography or echocardiography) shows that mortality rates progressively increase as left ventricular ejection fraction at rest decreases. When ejection fraction decreases ≥10% with exercise or fails to exceed 0.50 during exercise, particularly in association with new or worsening regional wall motion abnormalities, prognosis is also impaired (98). Similarly, patients at increased risk for adverse outcome can be identified by a reduced ejection fraction with rest echocardiography or by stress echocardiography that shows multiple new or worsening regional wall motion abnormalities during stress (100–109).

Appropriate treatment of patients with ischemia but not severe symptoms was addressed in the Asymptomatic Cardiac Ischemia Pilot (ACIP) study (88,110,111). Clinically stable patients with CAD (a third were asymptomatic, and the majority had multivessel disease and normal ventricular function) and ischemia on both stress testing and ambulatory ECG monitoring were randomized to either initial medical or revascularization treatment strategies. Patients randomized to a medical strategy could cross over to revascularization at any time to relieve severe symptoms. Although there were only a small number of events, the results suggested that patients randomized to initial revascularization had better outcomes (fewer deaths and nonfatal

Table 5. Noninvasive Test Results Predicting High Risk* for Adverse Outcomes in Patients With Known or Suspected Coronary Artery Disease†

Severe resting left ventricular dysfunction (LVEF <35%)
High-risk treadmill score (score ≤−11)†
Severe exercise left ventricular dysfunction (exercise LVEF <35%)
Stress-induced large perfusion defect (particularly if anterior)
Stress-induced multiple moderate perfusion defects
Large, fixed perfusion defect with LV dilatation or increased lung uptake (thallium 201)
Stress-induced moderate perfusion defect with LV dilatation or increased lung uptake (thallium 201)
Echocardiographic wall motion abnormality (involving >2 segments) developing at low dose of dobutamine (≤10 mg/kg per minute) or low heart rate (<120 beats/min)
Stress echocardiographic evidence of extensive ischemia

LVEF indicates left ventricular ejection fraction.
*Annual mortality rate >3%.
†Treadmill score is calculated using Bruce protocol, duration of exercise in minutes − (5 × maximal ST-segment deviation during or after exercise in mm) − (4 × treadmill angina index). The numerical treadmill angina index was 0 for no angina, 1 for nonlimiting angina, and 2 for exercise-limiting angina.
From Mark et al. (94).

MIs as well as hospitalizations) at one and two years than did those randomized to initial medical treatment (110,112). Although these findings require confirmation in a larger trial with mortality as the outcome, they do support overviews of nonrandomized (113,114) and randomized (115) trial data that concluded that asymptomatic or mildly symptomatic patients with severe ischemia on noninvasive testing do better with initial revascularization than with initial medical therapy.

There is varying opinion as to when coronary angiography should be performed in asymptomatic patients in whom noninvasive testing indicates ischemia (i.e., a high probability of CAD), but in whom test criteria do not indicate high risk for adverse outcomes. In part, this is attributable to the observation that the development of ischemia on these tests may not in itself indicate a poor prognosis (99). In this group with ischemia, but no test abnormalities to suggest high risk, the presence of multiple clinical risk factors such as increased age, diabetes, or occupational or lifestyle risks become increasingly important considerations when determining whether coronary angiography should be performed. However, it should be recognized that there are no controlled studies that show an advantage for angiography or revascularization over a conservative medical "wait and see" approach for any of these clinical subsets.

Because transplanted hearts often develop occlusive coronary arteriopathy, and because ischemia in patients with denervated hearts is generally asymptomatic, it has become common practice to perform periodic coronary angiography (and often intravascular coronary ultrasound), usually annually, after transplantation. The prognostic benefit of this practice has not been clearly established. It has also become a common part of the screening process to perform coronary angiography in candidates for liver, lung or kidney transplantation if they are ≥40 years of age, even in the absence of significant clinical risk factors for coronary disease. It would seem that noninvasive testing could be substituted for coronary angiography in many of these patients.

d. Management Approach for Patients Resuscitated From Sudden Cardiac Death

Adult patients successfully resuscitated from cardiac arrest who do not have clinical findings that suggest other causes of the arrest generally have extensive CAD. In the absence of recognized precipitating factors, such as acute MI, these patients are at high risk for recurrent cardiac arrest, and coronary angiography is of value in determining the underlying cause and planning the most appropriate therapeutic approach. Observational data indicate that coronary bypass surgery may be associated with reduced adverse outcome in that subgroup with significant coronary disease (93). It has been reported that immediate coronary angiography in survivors of out-of-hospital cardiac arrest reveals acute coronary occlusion in ≈50% of patients and that successful emergency angioplasty of an acute occlusion is an independent predictor of survival (116). A recent AHA statement further addresses this issue (117).

Recommendations for Coronary Angiography in Patients With Known or Suspected CAD Who Are Currently Asymptomatic or Have Stable Angina

Class I

1. **CCS class III and IV angina on medical treatment.** ***(Level of Evidence: B)***
2. **High-risk criteria on noninvasive testing regardless of anginal severity (Table 5).** ***(Level of Evidence: A)***
3. **Patients who have been successfully resuscitated from sudden cardiac death or have sustained (>30 s) monomorphic ventricular tachycardia or nonsustained (<30 s) polymorphic ventricular tachycardia.** ***(Level of Evidence: B)***

Class IIa

1. **CCS class III or IV angina, which improves to class I or II with medical therapy.** ***(Level of Evidence: C)***
2. **Serial noninvasive testing using identical testing protocols, at the same level of medical therapy, showing progressively worsening abnormalities.** ***(Level of Evidence: C)***
3. **Patients with angina and suspected coronary disease who, due to disability, illness, or physical challenge, cannot be adequately risk stratified by other means.** ***(Level of Evidence: C)***
4. **CCS class I or II angina with intolerance to adequate medical therapy or with failure to respond, or patients who have recurrence of symptoms during adequate medical therapy as defined above.** ***(Level of Evidence: C)***
5. **Individuals whose occupation involves the safety of others (e.g., pilots, bus drivers, etc.) who have**

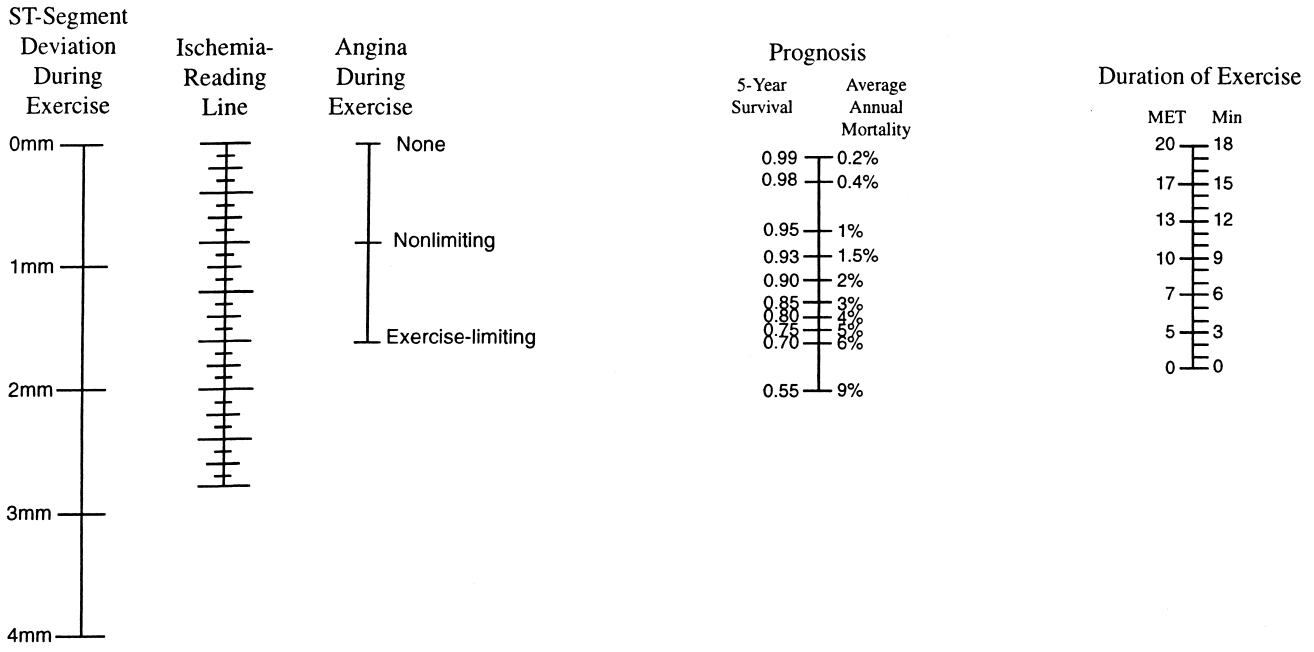

Figure 2. Nomogram of the prognostic relations in the treadmill score. Determination of prognosis proceeds in five steps:

1. The observed amount of exercise-induced ST-segment deviation (the largest elevation or depression after resting changes have been subtracted) is marked on the line for ST-segment deviation during exercise.
2. The observed degree of angina during exercise is marked on the line for angina.
3. The marks for ST-segment deviation and degree of angina are connected with a straight edge. The point where this line intersects the ischemia reading line is noted.
4. The total number of minutes of exercise in treadmill testing according to the Bruce protocol (or the equivalent in multiples of resting oxygen consumption [METs] from an alternative protocol) is marked on the exercise-duration line.
5. The mark for ischemia is connected with that for exercise duration. The point at which this line intersects the line for prognosis indicates the five-year survival rate and average annual mortality for patients with these characteristics.

Patients with <1 mm of exercise-induced ST-segment depression should be counted as having 0 mm. Angina during exercise refers to typical effort angina or an equivalent exercise-induced symptom that represents the patient's presenting complaint. This nomogram applies to patients with known or suspected coronary artery disease, without prior revascularization or recent myocardial infarction, who undergo exercise testing prior to coronary angiography.

Modified from Mark et al. (94).

abnormal but not high-risk stress test results, or multiple clinical features that suggest high risk. ***(Level of Evidence: C)***

Class IIb

1. **CCS class I or II angina with demonstrable ischemia but no high-risk criteria on noninvasive testing.** ***(Level of Evidence: C)***
2. **Asymptomatic man or postmenopausal woman with ≥2 major clinical risk factors and abnormal but not high-risk criteria on noninvasive testing (performed for indications stated in the ACC/AHA noninvasive testing guidelines) without known coronary heart disease.** ***(Level of Evidence: C)***
3. **Asymptomatic patients with prior MI with normal resting left ventricular function and ischemia on noninvasive testing, but without high-risk criteria.** ***(Level of Evidence: C)***
4. **Periodic evaluation after cardiac transplantation.** ***(Level of Evidence: C)***
5. **Candidate for liver, lung or renal transplant ≥40 years old as part of evaluation for transplantation.** ***(Level of Evidence: C)***

Class III

1. **Angina in patients who prefer to avoid revascularization even though it might be appropriate.** ***(Level of Evidence: C)***
2. **Angina in patients who are not candidates for coronary revascularization or in whom revascularization is not likely to improve quality or duration of life.** ***(Level of Evidence: C)***
3. **As a screening test for CAD in asymptomatic patients.** ***(Level of Evidence: C)***

4. **After CABG or angioplasty when there is no evidence of ischemia on noninvasive testing, unless there is informed consent for research purposes.** ***(Level of Evidence: C)***
5. **Coronary calcification on fluoroscopy, electron beam CT, or other screening tests without criteria listed above.** ***(Level of Evidence: C)***

e. Management of Patients With Nonspecific Chest Pain

Chest pain syndromes that are not characteristic of angina have previously been called noncardiac, atypical, or angiographically negative chest pain, as well as chest pain of undetermined origin (37–39). These terms are generally used to describe chest pain syndromes that are not associated with myocardial ischemia and are not of a cardiac cause. However, "atypical angina" generally means that myocardial ischemia is the cause of the symptoms, but the clinical presentation is unusual and should not be confused with nonspecific chest pain. For the purpose of this document and for consistency with previous documents, chest pain or cardiac symptoms not thought to be consistent with definite or probable angina are classified as nonspecific chest pain.

Nonspecific chest pain is very infrequently due to myocardial ischemia secondary to significant CAD, with a prevalence of 14% in men and 6% in women in one study (85). Other causes of myocardial ischemia, such as variant angina due to coronary spasm, or cocaine abuse, or syndrome X due to microvascular dysfunction, can infrequently present as nonspecific chest pain as well. Other cardiac causes include mitral valve prolapse, myocarditis, pericarditis and aortic dissection. Mitral valve prolapse is often associated with nonspecific chest pain. Although the cause is poorly understood, one postulate is that traction of the papillary muscle, induced by abnormal mitral valve motion, causes ischemia (118).

Noncardiac causes of nonspecific chest pain include costochondritis and esophageal disorders. Several disorders of the esophagus cause retrosternal chest pressure that can mimic myocardial ischemic-type chest pain. These include gastroesophageal reflux, irritable esophagus with altered gastroesophageal motility and a hypertensive lower esophageal sphincter (119). Many patients with both ischemic cardiac and esophageal pain can distinguish the symptoms, but some cannot. Exertional symptoms resulting from an esophageal source may also occur (119–121). Gastroesophageal reflux is a common, treatable cause of chest discomfort in patients with CAD who have nonspecific chest pain symptoms and remain symptomatic despite aggressive antianginal therapy (122). In one study, esophageal manometry, pH, and Holter monitoring were performed in patients with refractory nonspecific chest pain on optimal medical therapy for CAD. Of the 88% with chest pain identical to their anginal syndrome, 23% had acid reflux, 4% had cardiac ischemia, and 73% had no demonstrable cause. Up to 30% of patients with nonspecific chest pain will have an esophageal motility disorder (123). In some cases, antianginal therapy may exacerbate esophageal reflux symptoms because many of the drugs used to reduce these symptoms also lower esophageal sphincter tone (124,125).

A generalized disorder of smooth muscle function involving the esophagus, airways, musculoskeletal vasculature, central nervous system, and coronary microvasculature has been proposed (121). Some data suggest that gastroesophageal reflux and esophageal motility abnormalities may elicit myocardial ischemia and chest pain, a phenomenon termed "linked" angina. Acid stimulation caused typical angina (associated with a reduction in coronary blood flow velocity) in about half of syndrome X patients, which suggests that linked angina may indeed occur (119). However, other studies refute this concept (125,126).

If noncardiac causes are excluded or unlikely, or if the patient has significant cardiovascular risk factors that raise the suspicion of coronary disease, a noninvasive evaluation is appropriate. A number of guidelines specifically address this issue in detail (81–83,95–99). If noninvasive testing indicates a high risk for adverse outcome, then referral for coronary angiography should be made. Patients with nonspecific chest pain and evidence of myocardial ischemia but without indicators of high risk may be started on medical therapy with careful follow-up to assess their clinical response (127). Those who are intolerant of medical therapy, who fail to respond adequately to medical therapy, or in whom chest pain limits their lifestyle significantly despite taking $\geq$2 antianginal medications should be considered for coronary angiography. Patients who repeatedly present to the hospital with nonspecific chest pain, but who fail to have high-risk markers for ischemia, may also benefit from coronary angiography. The findings of a normal coronary angiogram in such patients indicate a good long-term prognosis that is reassuring to both the patient and the physician. Studies have indicated that a normal angiogram in this setting significantly reduces symptoms and subsequent hospitalizations (128).

Recommendations for Coronary Angiography in Patients With Nonspecific Chest Pain

Class I

High-risk findings on noninvasive testing. ***(Level of Evidence: B)***

Class IIa

None.

Class IIb

Patients with recurrent hospitalizations for chest pain who have abnormal (but not high-risk) or equivocal findings on noninvasive testing. ***(Level of Evidence: B)***

Class III

All other patients with nonspecific chest pain. ***(Level of Evidence: C)***

3. Unstable Angina

a. Definitions

The acute coronary syndromes include unstable angina, non–Q-wave MI, and acute Q-wave MI. The diagnosis of unstable angina has been complicated by a broad range of presentations that can vary between atypical chest pain and acute MI. An expert panel of clinicians attempted to clarify the definition of unstable angina in the recently published "Clinical Practice Guideline for Unstable Angina" (129,130). Three possible presentations are described:

- Symptoms of angina at rest (usually prolonged >20 min);
- New-onset (<2 months) exertional angina of at least CCS class III in severity;
- Recent (<2 months) acceleration of angina as reflected by an increase in severity of at least one CCS class to at least CCS class III.

Variant angina, non–Q-wave MI and recurrent angina >24 h after MI are considered part of the spectrum of unstable angina. However, in this document, non–Q-wave MI is discussed in the section on acute MI.

Our understanding of stable and unstable coronary syndromes continues to evolve along with our increased understanding of their pathophysiology. Locally produced vasoactive mediators and complex coronary morphologic characteristics may promote a dynamic process of thrombosis and fibrinolysis via platelet activation that can lead to acute coronary syndromes. Serum markers, such as creatine phosphokinase isoforms and cardiac troponin T and I, have led to an increased appreciation of the close relationship between unstable angina and MI.

b. Pathophysiology

Unstable ischemic coronary syndromes are characterized by severe but often transient episodes of myocardial ischemia caused by a critical obstruction to coronary blood flow. These episodes are almost always caused by ≥1 of several pathophysiologic mechanisms that interfere with the balance of myocardial oxygen supply and demand. The spontaneous rupture of lipid-laden, macrophage-rich atherosclerotic plaques may initiate unstable angina, acute MI, or sudden death (131) through platelet aggregation and thrombus formation over the fissured plaque (132). Plaque rupture leads to total or subtotal occlusion, resulting in a silent progression of the occlusive process or an acute coronary syndrome. Coronary angiography cannot predict vulnerable plaques, but once thrombosis has occurred, a filling defect indicating thrombus may be detected by angiography (133). Patients with unstable angina have more complex coronary lesions and more intracoronary thrombus on angiography than patients with stable angina (134,135). The coronary angiographic findings in unstable angina are often indistinguishable from those of non–Q-wave MI (133). Unstable angina with a clinical duration of <2 months is characterized angiographically by a high incidence of complex lesions. In a blinded retrospective angiographic study of 52 patients with unstable angina <2 months in duration compared with 32 patients having "chronic" unstable angina for >6 months, those with chronic unstable angina had a greater number of diseased vessels, fewer eccentric lesions and a better collateral circulation (136).

c. Risk Stratification

Within the group of patients with unstable angina, variable clinical outcomes are seen. The Braunwald classification (137) was developed as a means to grade patients with unstable angina according to severity of expected outcome, on the basis of the clinical manifestations and circumstances of their presentation (137). In this classification, consideration is given to history, associated ECG changes, and concurrent medical therapy in evaluating symptomatology. Risk stratification based on the Braunwald classification system has recently been validated by two groups, confirming its prognostic utility (138,139). The Agency for Health Care Policy and Research (AHCPR) Clinical Practice Guideline for unstable angina is a refinement of the Braunwald classification. Categories of severity are different, but as with the original scheme, the AHCPR guideline uses clinical circumstances, ECG changes, and intensity of therapy to develop an algorithm for the diagnosis and management of patients with suspected unstable angina (140).

d. Prognosis

Overall, the risk of a major adverse cardiac clinical event (death or nonfatal MI) in patients with unstable angina is less than that observed with acute MI but greater than in stable angina. This risk is highest at the time of presentation and declines to baseline within two months (141). One-year follow-up of the 1,473 Thrombolysis in Myocardial Infarction (TIMI) IIIB patients revealed a 4.3% mortality rate and an 8.8% incidence of nonfatal infarction at one year, but a substantial percentage of these cases had a non–Q-wave MI (142). In another study of 1,897 patients admitted to the coronary care unit in whom an infarction did not evolve and some of whom may not have had CAD, the 10-year cardiac mortality rate was 22% (143). Accordingly, identification of the high-risk patient is of paramount importance.

Silent ischemia has also been identified as a marker for unfavorable outcome in patients with unstable angina (144). In addition to the clinical history and ECG findings, certain serum markers have recently been shown to identify a high-risk subgroup (145–147). In these studies, elevations in creatine kinase (CK) isoforms, cardiac troponin T and I, and acute phase reactants appear to identify a subgroup of patients with unstable angina at high risk for adverse outcome (148–150).

e. Management Approach

A management approach to unstable angina is outlined in the AHCPR Clinical Practice Guideline that is based on an

Table 6. Short-Term Risk of Death or Nonfatal Myocardial Infarction in Patients With Unstable Angina

High Risk	Intermediate Risk	Low Risk
At least 1 of the following features must be present:	No high-risk features but must have any of the following:	No high- or intermediate-risk features but may have any of the following features:
Prolonged ongoing (>20 min) chest pain	Prolonged (>20 min) angina at rest, now resolved, with moderate or high likelihood of CAD	Increased frequency, severity, or duration of angina
Pulmonary edema, most likely related to ischemia	Angina at rest (>20 min or relieved with rest or sublingual nitroglycerin)	Angina provoked at lower threshold
Angina at rest with dynamic ST changes ≥1 mm	Nocturnal angina	New-onset angina with 2 wk to 2 mo before presentation
Angina with new or worsening MR murmur	Angina with dynamic T-wave changes	Normal or unchanged ECG
Angina with S_3 or new/worsening rales	New-onset CCSC III or IV angina in the past 2 weeks with moderate or high likelihood of CAD	
Angina with hypotension	Pathological Q waves or resting ST depression ≤1 mm in multiple lead groups (anterior, inferior, lateral)	
	Age >65 y	

MR indicates magnetic resonance; CAD, coronary artery disease; and CCSC, Canadian Cardiovascular Society classification.

Note: Estimation of the short-term risks of death and nonfatal myocardial infarction in unstable angina is a complex, multivariable problem that cannot be fully specified in a table. Therefore, this table is meant to offer general guidance and illustration rather than rigid algorithms. In addition, more recent studies have shown that elevated serum troponin levels are associated with intermediate or high risk.

From Braunwald et al (129).

assessment of both the likelihood of CAD and the short- and long-term prognoses of such patients (129). For those judged in their initial evaluation and treatment phase to be at low risk for adverse outcomes (Table 6), the guidelines recommend outpatient management. Patients thought to be at intermediate or high risk for death or nonfatal MI should be admitted to the hospital for intensive medical management. For patients who do not respond after an hour of aggressive therapy or who have recurrence of symptoms after initial stabilization and are thus considered refractory, emergency or urgent coronary angiography should be performed and intraaortic counterpulsation considered. Emergency catheterization refers to a diagnostic catheterization study that is performed immediately or as soon as possible, i.e., within 6 h. Urgent coronary angiography refers to a study performed within 24 h of hospitalization.

For patients whose condition stabilizes after initial treatment, the AHCPR Unstable Angina Clinical Practice Guideline proposes either an "early invasive" or "early conservative" strategy. With the early invasive strategy, all hospitalized patients (intermediate and high risk) without contraindications, receive elective cardiac catheterization within 48 h. With the early conservative strategy, only patients with high-risk indicators (prior revascularization, congestive heart failure, left ventricular ejection fractions <0.50, malignant ventricular arrhythmia, persistent or recurrent ischemic pain and/or functional study indicating high risk) are referred for cardiac catheterization. In the TIMI IIIB trial, a low six-week mortality rate (2.4%) and occurrence of infarction or reinfarction (6.3%) were achieved with either an early conservative or early invasive strategy. However, the early invasive strategy resulted in a reduced length of stay and reduced number of readmissions as well as less use of antianginal drugs (151). In a further analysis of patients treated with PTCA in the TIMI IIIB study, PTCA within 24 h of admission was an independent predictor of the occurrence of a subsequent cardiovascular event, especially if these patients were being treated emergently (152). This committee believes that an early invasive strategy with early coronary angiography is useful and effective, although probably better done after 24 h of aggressive medical management, including aspirin, standard or low-molecular-weight heparin and a glycoprotein IIb/IIIa inhibitor, if the clinical situation allows.

As summarized earlier, coronary angiography is indicated in unstable angina when subsequent revascularization is likely to alter the natural history or when patients have continued symptoms. When symptoms are intractable, the guidelines recommend emergent or urgent coronary angiography. The incidence of truly refractory angina was evaluated in a group of 125 patients with unstable angina studied over a five-year period in the recent era of five-drug therapy (intravenous heparin, aspirin, nitrates, calcium channel blockers and beta-blockers). All patients had >20 min of angina at rest with reversible ECG changes. Of the 52% who were thought to be medically refractory by the referring practitioners, 83% could be rendered free of chest pain by a more aggressive medical regimen. The incidence of truly medically refractory unstable angina with this five-drug regimen was found to be infrequent at 8.8% (153) and would probably be even less frequent with the addition of low-molecular-weight heparin and/or glycoprotein IIb/IIIa

inhibitors, as used today. Coronary angiography may be deferred for 48 h in these patients who have been thus stabilized.

Outpatient evaluation of low-risk patients (Table 6) should begin promptly and should include exercise stress testing for patients with normal rest ECGs who are not taking digoxin or exercise or pharmacologic stress testing with myocardial perfusion scanning or echocardiography for all others. Evaluation of left ventricular function is also important. In the low-risk patient with known coronary disease, the goal is to determine whether revascularization is indicated. In those not previously known to have CAD, the goal is to establish a diagnosis and further stratify the patients according to risk.

Many patients with recurrent chest discomfort not suggestive of angina have had normal coronary angiograms during the past five years. Even though many of these patients repeatedly seek cardiovascular care, repeat angiography is generally not considered to be indicated unless their clinical presentations convincingly suggest the presence of new CAD.

Patients with variant angina may present with chest pain and acute ECG changes. Cardiac catheterization is often performed in these patients to establish a diagnosis and to exclude fixed obstructive disease, which might require revascularization.

Recommendations for Coronary Angiography in Unstable Coronary Syndromes

Class I

1. **High or intermediate risk for adverse outcome in patients with unstable angina (Table 6) refractory to initial adequate medical therapy, or recurrent symptoms after initial stabilization. Emergent catheterization is recommended.** ***(Level of Evidence: B)***
2. **High risk for adverse outcome in patients with unstable angina (Table 6). Urgent catheterization is recommended.** ***(Level of Evidence: B)***
3. **High- or intermediate-risk unstable angina that stabilizes after initial treatment.** ***(Level of Evidence: A)***
4. **Initially low short-term-risk unstable angina (Table 6) that is subsequently high risk on noninvasive testing (Table 5).** ***(Level of Evidence: B)***
5. **Suspected Prinzmetal variant angina.** ***(Level of Evidence: C)***

Class IIa

None.

Class IIb

Low short-term–risk unstable angina, without high-risk criteria on noninvasive testing. ***(Level of Evidence: C)***

Class III

1. **Recurrent chest discomfort suggestive of unstable angina, but without objective signs of ischemia and with a normal coronary angiogram during the past five years.** ***(Level of Evidence: C)***
2. **Unstable angina in patients who are not candidates for coronary revascularization or in patients for whom coronary revascularization will not improve the quality or duration of life.** ***(Level of Evidence: C)***

4. Recurrence of Symptoms After Revascularization

a. Definitions

Evidence of myocardial ischemia in the patient who has undergone a revascularization procedure (PTCA or CABG) may represent ischemic myocardium that was not revascularized by intention for either technical or clinical reasons, or was deferred for later treatment if the patient remained symptomatic. Alternatively, it may represent recurrent ischemia due to restenosis, graft occlusion or progression of atherosclerosis. Ischemia may present as a recurrence of the preprocedural symptoms. However, not uncommonly, especially after surgical revascularization, recurrent ischemia may present with atypical features. Indeed, there is an increased incidence of silent ischemia in postoperative patients (154,155).

b. Recurrence of Symptoms After Catheter-Based Revascularization

(1) Abrupt Closure After Catheter-Based Revascularization

Acute coronary closure complicates 2% to 11% of percutaneous coronary interventions and, if treated by balloon angioplasty alone, is associated with a high incidence of death (up to 5%), MI (up to 27%), and the need for emergency bypass surgery (up to 10%) (156–159). In most cases, acute closure can be managed by stenting and is successfully reversed in most of such patients, reducing the complication rate to <2%. However, those patients whose arteries are not successfully reopened are at high risk for death, MI, or emergency CABG. Furthermore, follow-up of patients with major clinical ischemic events after abrupt closure suggests that they continue to be at increased risk compared with those who are successfully redilated (159). In contrast, when closure is successfully treated, outcome is favorable. In a study from the Cleveland Clinic (160), 88 of 4,863 consecutive patients undergoing angioplasty who had successful treatment of in-laboratory closure were compared with the 4,775 patients who had a successful uncomplicated procedure. No difference in one-year outcomes between the groups was found. On the basis of these observations, coronary angiography is generally performed emergently on any patient with suspected abrupt closure with the intent for repeat intervention, if possible.

Acute closure after balloon angioplasty primarily occurs within the first 24 h. With intracoronary stent implantation, closure occurs over a more prolonged (3 to 11 days) time course and has been termed "subacute thrombosis." The incidence of subacute thrombosis is substantially higher (10.1%) for bailout stenting compared with stents placed

electively. With current stent-placement methods and antiplatelet therapies, the incidence of subacute closure is <1% (161,162). When it occurs, subacute stent thrombosis presents as an acute coronary syndrome similar to acute closure and acute MI. Emergent catheterization is indicated.

(2) Periprocedural Enzyme Elevation

Elevations in enzyme markers of myocardial necrosis occur in 12% to 22% of patients after percutaneous interventional procedures. In patients with unstable angina and non–Q-wave MI, elevations in these markers portend an unfavorable prognosis. Asymptomatic enzyme elevations after coronary interventions previously had been regarded by many as clinically inconsequential. However, evaluation of the CAVEAT population (n = 1,012) showed a worse clinical outcome for patients with an elevated CK level after the procedure (163). Likewise, in a study of new device angioplasty, elevated enzymes were shown to predict in-hospital complications (164). In contrast, in a study of 565 patients after directional atherectomy, a correlation between CK-MB isoform elevations and adverse long-term sequelae was not confirmed (165). Preliminary evidence suggests that platelet IIb/IIIa glycoprotein receptor blockade may reduce the risk of enzyme elevation in patients treated with angioplasty, directional atherectomy, or stents and in patients undergoing saphenous vein graft percutaneous intervention (164,166,167).

Although a poorer long-term outcome appears to be associated with micronecrosis, clear indications for coronary angiography in this situation are currently lacking. Accordingly, the committee believes that treatment of these patients should be based on the other clinical guidelines discussed in this document.

(3) Restenosis

Recurrence of stenosis after percutaneous transluminal coronary intervention is still the major limitation to long-term clinical success of the procedure. A distinction should be made between clinical and angiographic restenosis. Clinical, i.e., symptomatic, restenosis should be suspected in patients who present with recurrent angina within nine months of a catheter-based revascularization procedure. The incidence of clinical restenosis parallels the number of target lesions revascularized, as documented in many controlled clinical trials with angiographic follow-up. The clinical presentation of restenosis tends to mirror the index presentation; 75% of patients who initially presented with unstable angina will re-present with unstable angina. Other patients will demonstrate a steady progression of anginal symptoms over several weeks. Angiographic restenosis (often defined as the return of stenosis ≥50%) is not always apparent clinically, and its incidence is higher than the rate of clinical restenosis. Although coronary angiography in asymptomatic postangioplasty patients who have a positive stress test may reveal angiographic restenosis, these patients generally have a good outcome, and asymptomatic angiographic restenosis may regress (168). The development of clinical symptoms >9 months after PTCA is more likely due to progression of native coronary disease than restenosis (169,170).

Coronary angiography is generally performed in symptomatic patients with suspected restenosis to reassess anatomy and to repeat revascularization as needed. Consequently, when suspicion of restenosis is high, coronary angiography is generally performed in a center where repeat revascularization can be performed immediately after the angiogram.

In agreement with the noninvasive testing guidelines, the committee discourages routine noninvasive evaluation of asymptomatic patients after angioplasty. It does recommend selective testing of patients considered to be at particularly high risk, such as those with decreased left ventricular function, multivessel CAD, proximal LAD disease, previous cardiac arrest, diabetes mellitus, hazardous occupations and suboptimal PTCA results. When noninvasive testing has been done in asymptomatic patients after angioplasty and reveals markers of high risk for adverse outcome, coronary angiography is indicated. Asymptomatic patients with an abnormal but not high-risk noninvasive test result often can be successfully treated medically, with coronary angiography performed only when symptoms develop or high-risk markers present on noninvasive testing.

c. Recurrence of Symptoms After Coronary Artery Bypass Surgery

Patients with prior bypass surgery who develop postoperative angina represent an important subset of patients who require thoughtful evaluation and therapy. Arterial conduits often provide long-term patency over at least 15 years. Saphenous vein grafts are more vulnerable to graft atherosclerosis and subsequent closure. Approximately 10% of patients will have vein graft closure within the first two months after surgery and another 10% within the first year (171). Vein graft patency is relatively stable from years 3 to 5, but after 10 years, 40% of vein grafts are occluded (172). In a study of 977 patients after bypass surgery, 30% had angina in the first year, 46% at 3 years and 50% at 8 years of follow-up (173). Postoperative angina occurs more frequently in women than men (174). Furthermore, many postoperative patients have asymptomatic myocardial ischemia (155). Postoperative angina is an increasing problem. For example, in the BARI registry (175), the percentage of patients presenting for revascularization who had prior surgical revascularization increased from 20% to 33% over the time period of enrollment. It is generally believed that patients with recurrent ischemia after coronary artery bypass surgery have an increased risk of adverse outcomes; treatment must balance the risk of reoperation with the risk of medical management or percutaneous revascularization. Reoperative risk is dependent on both age and the patient's clinical presentation (176). In a study of 2,030 patients followed up for a mean of 7.8 years after surgery at a single

site, there was a 5.7% mortality rate for patients undergoing elective reoperation, compared with a 10.9% mortality rate in patients having urgent reoperation, and a 16.4% mortality rate in those undergoing emergent reoperation (177). Five- and 10-year survival rates were 76% and 55%, respectively, for patients aged <50 years at reoperation and 63% and 40%, respectively, for those >70 years of age.

Catheter-based techniques are attractive as an alternative to the high risk of reoperation but are not without risk, especially when performed in an older vein graft. In a study of 89 saphenous vein graft lesions treated percutaneously in 75 patients with medically refractory angina, clinical success (angiographic success plus hospital discharge without major complication) was achieved in 70 (178). In this series, there was a 3% incidence of early mortality, 3% had nonfatal MI, and 1% required emergency reoperation. During late follow-up, 23% had a repeat PTCA, 3% needed reoperation, and 25% died. Long-term survival of this cohort was compared with a similar surgically treated group. At 30 days, survival was better in the graft angioplasty patients (97% vs. 92%), but there was no difference at six months, and by five years there was a trend toward better survival in the reoperative group.

Other percutaneous techniques such as transluminal extraction atherectomy, excimer laser, and directional coronary atherectomy do not appear to offer superior effectiveness in dealing with vein graft atherosclerosis compared with standard balloon angioplasty (179–183). The use of coronary artery stents for disease in saphenous vein grafts is becoming almost routine (184,185). One randomized controlled study has evaluated the role of stent placement in saphenous vein graft disease. In the SAVED trial, patients were randomized to stenting or balloon annuloplasty. In-hospital outcomes were similar, but there was a significant reduction in repeat revascularization six months after the procedure in the stent group (186).

Coronary angiography is reasonable in patients who are symptomatic within the first 12 months after bypass surgery, because relatively low-risk revascularization by percutaneous techniques can often be offered. Angiography should be avoided in postbypass patients who, by virtue of age or other comorbidity, are poor candidates for repeat revascularization by either reoperation or angioplasty. Postbypass patients who are suitable candidates for further revascularization and who have noninvasive evidence of high-risk disease are appropriate subjects for coronary angiography. Those who are symptomatic but deemed to be low risk by noninvasive testing, perhaps due to collateralization, can be treated medically before angiography is considered.

Recommendations for Coronary Angiography in Patients With Postrevascularization Ischemia

Class I

1. **Suspected abrupt closure or subacute stent thrombosis after percutaneous revascularization.** ***(Level of Evidence: B)***
2. **Recurrent angina or high-risk criteria on noninvasive evaluation (Table 5) within nine months of percutaneous revascularization.** ***(Level of Evidence: C)***

Class IIa

1. **Recurrent symptomatic ischemia within 12 months of CABG.** ***(Level of Evidence: B)***
2. **Noninvasive evidence of high-risk criteria occurring at any time postoperatively.** ***(Level of Evidence: B)***
3. **Recurrent angina inadequately controlled by medical means after revascularization.** ***(Level of Evidence: C)***

Class IIb

1. **Asymptomatic post-PTCA patient suspected of having restenosis within the first months after angioplasty because of an abnormal noninvasive test but without noninvasive high-risk criteria.** ***(Level of Evidence: B)***
2. **Recurrent angina without high-risk criteria on noninvasive testing occurring >1 year postoperatively.** ***(Level of Evidence: C)***
3. **Asymptomatic postbypass patient in whom a deterioration in serial noninvasive testing has been documented but who is not high risk on noninvasive testing.** ***(Level of Evidence: C)***

Class III

1. **Symptoms in a postbypass patient who is not a candidate for repeat revascularization.** ***(Level of Evidence: C)***
2. **Routine angiography in asymptomatic patients after PTCA or other surgery, unless as part of an approved research protocol.** ***(Level of Evidence: C)***

5. Acute MI

a. Introduction

During the past 15 years, the treatment of Q-wave MI has shifted from a passive approach emphasizing supportive care and management of complications to a more active therapeutic approach. Coronary angiography is rarely performed during or after MI solely for diagnostic purposes. The vast majority of procedures are done to evaluate the patient for a percutaneous or surgical revascularization procedure. Therefore, the appropriateness of performing coronary angiography after MI is, by necessity, linked to the efficacy of these revascularization procedures as measured by an improved outcome for the patient. As discussed in section II, several recent studies have shown considerable variation in the use of coronary angiography after MI within regions of the U.S., between the U.S. and Canada, between health maintenance organizations and fee-for-service hospitals, between primary care physicians and cardiologists, and between invasive and noninvasive cardiologists (43–45,47,48,60,187). These data do not show a consistent

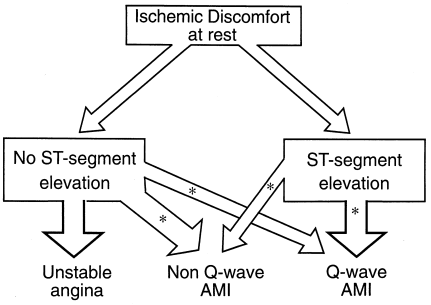

Figure 3. Nomenclature of acute coronary syndromes. Patients with ischemic discomfort may present with or without ST-segment elevation on the ECG. The majority **(large arrow)** of patients with ST-segment elevation ultimately develop a Q-wave acute MI, whereas a minority **(small arrow)** develop a non–Q-wave acute MI. Of the patients who present without ST-segment elevation, the majority (large arrows) are ultimately diagnosed as having either unstable angina or non–Q-wave acute MI on the basis of the presence or absence of a cardiac marker such as CK-MB detected in the serum; a minority of such patients ultimately develop a Q-wave acute MI. The spectrum of clinical conditions ranging from unstable angina to non–Q-wave acute MI and Q-wave acute MI is referred to as the acute coronary syndromes. Reprinted with permission from Antman EM, Braunwald E. Acute myocardial infarction. In: Heart Disease. A Textbook of Cardiovascular Medicine. 5th ed. Philadelphia, PA: WB Saunders, 1996. *Positive serum cardiac marker.

relationship between the increased use of coronary angiography after MI and improvements in outcome.

Guidelines covering PTCA, CABG surgery and the treatment of patients with acute MI have been published by the ACC/AHA Task Force on the Assessment of Diagnostic and Therapeutic Procedures within the past five years and contain recommendations relevant to the use of coronary angiography (188–190).

b. Definitions

According to World Health Organization criteria, the diagnosis of MI is based on the presence of at least two of the following: 1) a clinical history of ischemic-type chest discomfort, 2) changes on ECG tracings obtained serially and 3) a rise and fall in enzyme markers of myocardial cell necrosis (191,192). A convenient way to categorize patients who present with ischemic chest discomfort and suspicion of MI is by the presence or absence of ST-segment elevation, and this distinction will be used in these guidelines. The majority of patients presenting with ischemic chest pain and ST elevation will subsequently have some enzyme marker of myocardial necrosis with or without development of Q waves. Of those who present with ischemic chest pain and no ST-segment elevation, some will evolve serum markers of myocardial necrosis with or without Q waves while others, without an elevation in serum markers, will later be classified as having unstable angina (Fig. 3).

These guidelines were developed following the general pattern used to organize the "ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction" (190). Accordingly, the use of coronary angiography was evaluated in three distinct time periods after infarction. It must be emphasized, however, that these time periods are somewhat arbitrary, because patients who present with MI may not be immediately identified, do not uniformly present at a common starting point in the event and may evolve through the infarction at different rates. It is also clinically useful to stratify patients with suspected MI by the presence or absence of ST-segment elevation on the ECG. Because clinical outcomes, especially after thrombolysis, are similar, we have included in the group with ST elevation patients with typical ischemic chest pain and a new (or presumed new) bundle-branch block obscuring the ECG diagnosis of MI. Patients with ongoing ischemic chest pain but without ST-segment elevation are a distinct group with different indications for coronary angiography compared with those who have ST-segment elevation.

The first time period discussed relates to the use of coronary angiography during the initial recognition and management of the patient in the emergency department. For the patient who presents acutely with ST-segment elevation or bundle-branch block obscuring the diagnosis of MI, coronary angiography is coupled with the intent to perform primary PTCA as an alternative to thrombolytic therapy. Other indications discussed are related to patients who present with similar ECG findings and are not treated by primary PTCA (i.e., who receive thrombolytic or no reperfusion therapy) or who have a strong suggestion of MI, but do not have ST-segment elevation.

The second general time period relates to the use of coronary angiography during the hospital-management phase of the patient with MI. During this phase, the need for coronary angiography is generally driven by the development of some complication of the infarction, such as spontaneous recurrent ischemia, heart failure related to ventricular septal defect, or papillary muscle dysfunction or persistent malignant arrhythmias occurring beyond the first 24 h after infarction.

The final general time period after MI during which coronary angiography may be necessary occurs when the patient is being prepared for hospital discharge and undergoes risk stratification. In practical terms, this is defined not by a specific time but rather by the evaluations performed to determine the risk of future morbid events and the need for additional therapies. The process of risk stratification occurs throughout the clinician's entire encounter with the patient as information is gathered about the extent and consequences of the infarction.

c. Coronary Angiography During the Initial Management of Patients in the Emergency Department

(1) Patients Presenting With Suspected MI and ST-Segment Elevation or Bundle-Branch Block

Of all patients who ultimately are diagnosed with acute MI, those presenting with ST-segment elevation have been

studied most extensively. Patients with ST-segment elevation have a high likelihood of thrombus occluding the infarct-related artery (193,194). Considerable data exist showing that coronary reperfusion can be accomplished either by intravenous thrombolytic therapy or direct mechanical intervention within the infarct-related artery. Because the benefit obtained is directly linked to the time required to reestablish normal (TIMI grade 3) distal blood flow (195–197), rapid triage decisions are mandatory, and delays in instituting reperfusion therapy must be minimized. The "ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction" provide a comprehensive discussion of the indications, contraindications, advantages, and disadvantages of thrombolytic therapy and direct coronary angioplasty (190). Although it is not the purpose of these guidelines to re-examine in detail the merits of these two reperfusion strategies, this is a rapidly evolving area, and some new information exists.

(a) Coronary Angiography Immediately After Thrombolytic Therapy

Once the clinician has made the decision to administer a systemic thrombolytic drug, there are two circumstances in which coronary angiography coupled with the intention to perform PTCA have been evaluated. The first involves the routine use of coronary angiography and PTCA immediately after thrombolytic therapy. Throughout many early trials of intravenous thrombolytic therapy, it was documented that the infarct-related artery failed to open by 90 minutes in 20% to 40% of patients (198–200). Even with current regimens, thrombolytic failures occur in 10% to 25% of patients (197,201). Reocclusion despite successful initial reperfusion occurs in an additional 12% (202), and in the majority of patients, a significant stenosis remains after thrombolysis (198–200). Because of these issues, a few small studies and three randomized, prospective trials evaluated strategies in which coronary angiography followed by PTCA of a residual stenosis was routinely performed in all patients immediately after thrombolytic therapy (198–200,203–207). It was the hypothesis of these trials that identifying and dilating the residual stenosis might improve outcome. The TIMI IIA study (200), the Thrombolysis in Acute Myocardial Infarction (TAMI) study (198), and the European Cooperative Study Group trial (199) were concordant in their conclusions that immediate coronary angiography and PTCA neither preserves myocardium nor reduces the incidence of reinfarction or death compared with a more conservative approach in which angiographic evaluation and intervention is reserved for patients who have spontaneous or inducible ischemia after infarction. Furthermore, those treated with immediate PTCA within hours of thrombolytic therapy had a higher 24-h complication rate and mortality at one year (199,205,207).

Although the routine use of coronary angiography and PTCA immediately after thrombolytic therapy in all patients cannot be advised, a separate circumstance exists when there is serious concern that thrombolysis has failed. In this clinical situation, recanalization of the infarct-related artery by so-called "rescue" or "adjuvant" (190) PTCA has been suggested to establish patency of the affected artery, salvage any remaining viable myocardium, and improve survival. Unfortunately, there is no reliable way to identify patients in whom thrombolytic therapy has failed. Clinical markers of reperfusion, such as relief of chest pain, resolution of ST-segment elevation, and occurrence of reperfusion arrhythmias do not accurately predict the success or failure of thrombolysis (208), and immediate coronary angiography in all patients after thrombolytic therapy is impractical and expensive and would likely cause increased bleeding. Nevertheless, there are some patients whose clinical course leads to a strong suspicion that thrombolysis has failed. These patients often have continuing severe chest pain and a worsening of their clinical or hemodynamic status. In this circumstance, the option of immediate coronary arteriography followed by PTCA has been studied in several nonrandomized (209–211) and randomized (212–214) trials. In the largest randomized trial to date, only patients with their first anterior infarction demonstrated to have an occluded artery within 8 h of presentation were allocated to PTCA or conservative therapy (aspirin, heparin and coronary vasodilators) after coronary angiography (212). Although there was no difference in resting ejection fraction 30 days after MI, exercise ejection fraction was higher ($0.43 \pm 0.15\%$ vs. $0.38 \pm 0.13\%$) and a composite end point of death or severe heart failure was lower in those treated by rescue angioplasty (6% vs. 17%). The outcome after rescue PTCA was also evaluated in the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-1) angiographic substudy (211). Clinical and angiographic outcomes in 198 patients treated with rescue PTCA were compared with those of 266 patients managed conservatively after failed thrombolysis and 1,058 patients with successful thrombolysis, the latter two groups documented by angiography. Although the assignment of thrombolytic therapy was randomized, patients were selected for the rescue PTCA attempt by the investigators and tended to be those patients with clinical predictors of a poor outcome. Rescue PTCA successfully opened 88.4% of the closed arteries, with 68% attaining TIMI grade 3 flow. Although the majority of arteries were opened by rescue PTCA, left ventricular function and 30-day mortality were not different from the group who had a closed infarct-related artery and were managed conservatively. The mortality rate associated with a failed rescue PTCA attempt was 30.4%, but 5 of the 7 patients who died were in cardiogenic shock before the procedure. These data are similar to the experience from the TIMI study in which rescue PTCA was successful in 82% but there was no difference in mortality rate at 21 days (12% for rescue PTCA vs. 7% for medical therapy), and the mortality for a failed rescue PTCA attempt was 33% (210). On the basis of the available data, the committee cannot recommend the widespread use of

coronary angiography followed by rescue PTCA in all patients with suspected failure of thrombolytic therapy but believes it may benefit some selected patients.

(b) Coronary Angiography With Primary Angioplasty for Acute MI

It is the intent of this document to provide guidelines related only to the use of coronary angiography, but coronary angiography is an obligatory part of the primary PTCA procedure, and the strategy of primary PTCA really involves coronary angiography followed by triage to the most appropriate means of reperfusion. This is an area of considerable interest not only for evaluation of the efficacy of primary PTCA, but also of the usefulness of immediate coronary angiography as a triage tool (215). Therefore, the committee believes it is necessary to reinforce the recommendations of the ACC/AHA Acute Myocardial Infarction Committee (190), emphasizing relevant information upon which the recommendations were made and some new data that are now available.

Those who advocate primary PTCA highlight several possible advantages of initial triage angiography to direct a revascularization strategy. First, although PTCA is used for revascularization after initial coronary angiography in ≈90% of those studied, a small subset (≈5%) is identified with severe three-vessel or left main coronary disease, or anatomic features unfavorable for PTCA in whom surgical revascularization may be more appropriate (216). Second, immediate angiography identifies an additional 5% of patients in whom the infarct-related artery has spontaneously opened with a <70% residual narrowing and normal flow beyond the culprit stenosis. In these patients, conservative management may be used, and it is argued that the risks of thrombolytic therapy can be avoided. Third, on occasion, patients are identified for whom thrombolytic therapy would be inappropriate or unnecessary, such as patients in whom the cause of the MI is an aortic dissection or those with suspected MI and bundle-branch block in whom immediate angiography shows the absence of a coronary occlusion. Finally, immediate angiography during the initial evaluation of MI may be valuable for the identification not only of high-risk patients, but also of low-risk patients.

Results from the Primary Angioplasty in Myocardial Infarction-2 (PAMI-2) trial show that a combination of clinical and catheterization variables can stratify patients with MI treated successfully by primary PTCA into high- and low-risk subgroups (217,218). In PAMI-2, low-risk patients were not hospitalized in an intensive care unit, received no further noninvasive testing and were discharged on day 3 after MI. In addition to a shorter length of stay and lower hospital costs compared with traditional care, there was no difference in mortality or nonfatal complications at six months. Mortality in the other half of patients, judged to be at high risk, was ≈10 times greater (3.8%) than in low-risk patients (0.4%), and these high-risk patients had a greater incidence of in-hospital reinfarction and recurrent ischemic events.

Although the initial results of primary PTCA for the treatment of acute MI were encouraging (216,219–222), the treatment advantage for primary PTCA compared with thrombolytic therapy has been smaller in recent trials. In the GUSTO IIb trial, 1,138 patients were randomly assigned to treatment by either primary PTCA or accelerated tissue plasminogen activator (tPA) (223). At 30 days, the primary end point (a composite of death, reinfarction, or disabling stroke) was 13.7% in the tPA group compared with 9.6% in the PTCA group ($p = 0.03$). Mortality was 7% in the thrombolysis group versus 5.7% in the primary PTCA group ($p = 0.037$). The treatment advantage of primary PTCA was less than that observed in previous studies, and by six months, there was no difference in the primary end point between the groups. Moreover, data from the Myocardial Infarction Triage and Intervention (MITI) Project Registry showed no difference in mortality during hospitalization (5.6% vs. 5.5%) or over three years of follow-up among the 1,050 patients treated by primary PTCA compared with the 2,095 receiving thrombolytic therapy (224). It is difficult to predict how these two therapies will compare in the future because newer, more effective thrombolytic drugs are being developed, there is an expanding role for glycoprotein IIb/IIIa inhibitors in the treatment of acute MI, and there are increasing data to suggest that stenting may provide a better outcome than primary PTCA both acutely and after six months. A growing number of observational and randomized trials have evaluated the role of coronary stent placement compared with balloon angioplasty in patients with acute MI (225–231). All but one have shown, with a variety of stent designs, that acute angiographic results are improved and the incidence of in-hospital and 30-day ischemic events is significantly reduced. The rate of target-vessel restenosis is also lower than that seen with balloon angioplasty alone. A large multinational trial is currently under way to evaluate the role of glycoprotein IIb/IIIa antagonists and stenting in acute MI. However, from the available data comparing thrombolysis and angioplasty in patients who are candidates for thrombolytic drugs, some conclusions can be made. None of these reports show that patients treated with primary angioplasty fare worse than those treated with thrombolytic drugs; thus, a conservative interpretation of the current data would be that the two therapies are equivalent. It is important to emphasize that one factor contributing to the excellent outcome of primary angioplasty is the skill and experience of the operator. This committee shares the concerns expressed in the "ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction" (190) regarding the widespread use of primary PTCA for the treatment of acute MI. The investigators performing primary PTCA studies were highly experienced interventional cardiologists, which resulted in their ability to perform PTCA successfully within a short time frame (60 to 90 min) after presentation.

Recent preliminary data suggest that this level of proficiency may not be duplicated in all settings for all acute MI patients (232–234). Moreover, there has been a general assumption that the results of primary PTCA can be extrapolated to all patients with acute MI, but these studies only included patients who were in fact eligible for thrombolytic therapy and who generally were at fairly low risk. Despite the fact that primary PTCA is used frequently in patients excluded from thrombolytic therapy, only a few small retrospective studies have examined this important issue (222,235,236). When used in this setting, primary PTCA has a success rate approximating that seen in patients who are thrombolytic candidates. Furthermore, mortality at six months, one year and three years is satisfactory, and the occurrence of other adverse cardiac events during follow-up is not excessive. A randomized trial examining this issue may never be conducted. Knowing the potential benefits of reperfusion, it would be difficult to justify randomizing patients with contraindications to thrombolytics to only supportive therapy when the option of angioplasty exists. Until there are data to the contrary, the use of primary PTCA in patients with contraindications to thrombolytic therapy seems warranted.

The use of primary PTCA in patients with acute MI who present with or rapidly develop cardiogenic shock has been studied in several observational and nonrandomized series. Immediate coronary angiography followed by PTCA in this setting results in a better survival rate than with traditional care, averaging 55% among studies (237–243). However, the benefit of primary PTCA is strongly related to establishing an open artery. In the study by Lee et al. (238), survival was 77% if the artery was opened successfully compared with 18% if the procedure failed to open the artery. In another study, 30-month actuarial survival was 54% after a successful PTCA but only 29% after an unsuccessful procedure (239). Other factors, such as the increased use of intra-aortic balloon pumps or other left ventricular assist devices, may contribute to the benefit of primary PTCA in this situation (238,242). Immediate coronary angiography followed by emergency coronary bypass surgery has also been used in patients with cardiogenic shock after acute MI. In recent series, operative mortality rates vary from 12% (241) to 42% (244) in such patients, and data from the nonrandomized SHOCK Registry suggests that emergency bypass surgery has a lower mortality rate (19%) than emergency PTCA (60%) (245). A more complete set of guidelines and indications for bypass surgery has recently been published by another ACC/AHA Task Force Committee (189). At the 48th Scientific Sessions of the ACC (1999), Hochman presented the preliminary report of the SHOCK Trial, wherein 152 patients with cardiogenic shock secondary to acute MI were randomized to an emergency revascularization (ERV) strategy, and 150 others to an initial medical stabilization (IMS) strategy, with delayed revascularization as needed clinically. At 30 days, mortality for the two groups was not significantly different, but at six months, mortality was significantly lower in the ERV group (53.7% vs. 65.7%; $p = 0.04$). The prespecified subgroup analysis of patients less than 75 years showed a significant 16% reduction in mortality (41% ERV group vs. 57% IMS group, $p < 0.01$). Of the entire ERV group, approximately 60% had PTCA and 40% had CABG; the respective 30 day mortality rates were 45% and 42%. It is important to note that patients with cardiogenic shock were excluded from many of the major thrombolytic trials. Recent retrospective analyses by the Fibrinolytic Therapy Trialists' Collaborative Group suggest, however, that thrombolytic therapy may provide a greater benefit than initially appreciated in this subgroup of patients (246). Nevertheless, at the present time, most clinicians have adopted an aggressive invasive approach to the management of patients with cardiogenic shock.

In summary, this committee accepts the use of primary PTCA and stenting as an alternative to thrombolysis but is seriously concerned about the widespread use of mechanical interventions in acute MI by operators without adequate training or experience. Furthermore, although precedent exists in the literature (247,248), the extension of primary PTCA to hospitals without immediate surgical backup is premature. Indiscriminately applied, this could result in unacceptable delays in achieving reperfusion in some patients and less than optimal outcomes if performed by operators with inadequate experience. Strict performance criteria are necessary for programs offering primary PTCA so that delays in revascularization do not occur and acceptable outcomes are established and documented. Otherwise, the focus of treatment should be the early use of thrombolytic therapy.

Recommendations for Coronary Angiography During the Initial Management of Acute MI (MI Suspected and ST-Segment Elevation or Bundle-Branch Block Present)

Coronary Angiography Coupled With the Intent to Perform Primary PTCA

Class I

1. **As an alternative to thrombolytic therapy in patients who can undergo angioplasty of the infarct related artery within 12 hours of the onset of symptoms or beyond 12 hours if ischemic 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)***
2. **In patients who are within 36 hours of an acute ST elevation/Q-wave or new LBBB MI who develop cardiogenic shock, are less than 75 years of age and**

*Performance standard: within 90 min. †Individuals who perform >75 PTCA procedures per year. ‡Centers that perform >200 PTCA procedures per year and have cardiac surgical capability.

revascularization can be performed within 18 hours of the onset of shock.

Class IIa

1. **As a reperfusion strategy in patients who are candidates for reperfusion but who have a contraindication to fibrinolytic therapy, if angioplasty can be performed as outlined above in class I.** ***(Level of Evidence: C)***

Class III

1. **In patients who are beyond 12 h from onset of symptoms and who have no evidence of myocardial ischemia.** ***(Level of Evidence: A)***
2. **In patients who are eligible for thrombolytic therapy and are undergoing primary angioplasty by an unskilled operator in a laboratory that does not have surgical capability.** ***(Level of Evidence: B)***

Recommendations for Early Coronary Angiography in the Patient With Suspected MI (ST-Segment Elevation or Bundle-Branch Block Present) Who Has Not Undergone Primary PTCA

Class I

None.

Class IIa

Cardiogenic shock or persistent hemodynamic instability. ***(Level of Evidence: B)***

Class IIb

1. **Evolving large or anterior infarction after thrombolytic treatment when it is believed that reperfusion has not occurred and rescue PTCA is planned.** ***(Level of Evidence: B)***
2. **Marginal hemodynamic status but not actual cardiogenic shock when standard management (eg, optimizing filling pressures) does not result in improvement.** ***(Level of Evidence: C)***

Class III

1. **In patients who have received thrombolytic therapy and have no symptoms of ischemia.** ***(Level of Evidence: A)***
2. **Routine use of angiography and subsequent PTCA within 24 hours of the administration of thrombolytic agents.** ***(Level of Evidence: A)***

(2) Patients Presenting With Suspected MI but Without ST-Segment Elevation

Approximately 50% of patients with MI do not present with ST-segment elevation, but rather have nondiagnostic ECG changes (249,250). It is believed that most non–Q-wave MIs are caused by disruption of an atherosclerotic plaque with transient occlusion of the coronary artery (133,251–253). This may occur with or without transient ST-segment elevation (254). Although total coronary occlusion is frequently found in patients with Q-wave MI, it is much less common in those with non–Q-wave MI (193,194,251,255). Angiography within 24 h of symptom onset in non–Q-wave MI documents coronary occlusion in only 26% to 39% of patients. Paradoxically, when performed between three and seven days after the event, the incidence of occlusion increases to 42%. Many early studies suggested that patients with non–Q-wave MI had a relatively low in-hospital mortality (256), but it is now known that recurrent ischemia or MI and death occur at a worrisome frequency in this population (256–260).

Although most thrombolytic trials focus on patients with ST elevation (261–263), some data exist within these trials relevant to patients without ST-segment elevation. In the first GISSI trial, there was no benefit of thrombolytic therapy with streptokinase in patients without ST-segment elevation, and, in fact, mortality rates were slightly higher (261). Similar observations were made in the ISIS-II trial (Second International Study of Infarct Survival) (262) and in two randomized trials of tPA in patients with unstable angina or MI without diagnostic ST changes (151,264). In these latter studies, tPA had no benefit compared with aspirin and heparin alone. In the TIMI IIIB trial, which included patients with both non–Q-wave MI and unstable angina, the results of treatment with PTCA were not improved by routine pretreatment with intravenous tPA (152). Because thrombolytic therapy appears to have no benefit in non–Q-wave MI, some clinicians have advocated a very aggressive approach to management, including immediate coronary angiography in all patients without ST-segment elevation, but with a high probability of MI. Typically, these are patients with risk factors for CAD who have prolonged and/or recurrent (stuttering) ischemic pain, some ECG abnormalities and the echocardiographic demonstration of a wall motion abnormality. Treatment decisions are then based on the results of coronary angiography, with some patients referred for percutaneous or surgical revascularization and those with normal angiography discharged as soon as possible for outpatient evaluation to determine the cause of their symptoms. Although PTCA for non–Q-wave MI can be performed safely with a high success rate and can improve function in the infarct zone (151,265,266), the efficacy and cost-effectiveness of this very aggressive approach has not been tested. Moreover, some data suggest that a period of heparin anticoagulation before intervention in patients with unstable coronary syndromes results in a lower rate of procedure-related complications (267,268). Rather than immediate coronary angiography in non–Q-wave MI, more moderate management strategies have been evaluated in studies like TIMI IIIb (151) and the Veterans Affairs Non–Q-Wave Infarction Strategies in Hospital (VANQWISH) trial (269). These are discussed later in these guidelines; thus, the recommendations below refer only to coronary angiography in the early management of patients with suspected MI.

Recommendations for Early Coronary Angiography in Acute MI (MI Suspected but No ST-Segment Elevation)

Class I

1. **Persistent or recurrent (stuttering) episodes of symptomatic ischemia, spontaneous or induced, with or without associated ECG changes.** ***(Level of Evidence: A)***
2. **The presence of shock, severe pulmonary congestion, or continuing hypotension.** ***(Level of Evidence: B)***

Class II

None.

Class III

None.

d. Hospital-Management Phase of Acute MI

The hospital-management phase of acute MI can encompass several clinical situations. Some patients with acute MI present too late in their course to be candidates for reperfusion therapy, and in others, the occurrence of infarction may not be appreciated at the time of presentation. These groups skip the acute-treatment phase of MI and enter the hospital-management phase directly. During the hospital-management phase, the actions of the clinician are driven by the consequences of the infarction, such as congestive heart failure, hemodynamic instability, recurrent ischemia or arrhythmias. Although it is still convenient to divide patients into those with Q-wave and non–Q-wave infarctions, some indications for coronary angiography are common to all patients with MI regardless of how they have been treated initially and whether or not Q waves ultimately develop.

(1) Concepts Common to All Patients With MI

The development of spontaneous myocardial ischemia or ischemia with minimal activity during the hospital-management phase is a significant event. Both short and long-term mortality are higher among patients with recurrent ischemia (270–276). For any given degree of left ventricular dysfunction and any burden of CAD, survival is related to the frequency, severity and magnitude of myocardial ischemia (277). Survival is diminished in patients with frequent recurrent episodes of myocardial ischemia at rest or at very low workloads compared with those who have the same degree of left ventricular dysfunction and coronary disease but who exhibit no ischemia at high workloads. Because revascularization procedures relieve myocardial ischemia, coronary angiography is indicated in patients who are potential candidates for revascularization under the assumption that mortality will be decreased. Data supporting the use of coronary angiography and then revascularization in patients who develop spontaneous or inducible ischemia comes from the DANish trial in Acute Myocardial Infarction (DANAMI) (278). In the DANAMI trial, 1,008 patients with acute MI treated with thrombolytic therapy who had subsequent ischemia were randomized to coronary angiography and revascularization versus medical management. At a median follow-up of 2.4 years, mortality was 3.6% in the invasive arm versus 4.4% in the conservative arm (p = NS). However, patients in the invasive arm had a lower incidence of subsequent MI (5.6% vs. 10.5%; $p = 0.004$) and a lower incidence of admissions for unstable angina (17.9% vs. 29.5%; $p < 0.00001$) compared with the conservative arm.

There are several mechanical complications of acute MI that require prompt and aggressive evaluation, including coronary arteriography. These complications potentially can occur with any infarction but are much more likely to occur in patients with Q-wave MI. Mitral regurgitation due to papillary muscle rupture or dysfunction develops in ≈5% of patients within the first week after infarction (279). In those with complete rupture, medical treatment alone has a 75% mortality rate within the first 24 h (280). The size of the infarction in patients who die after developing mitral regurgitation is often small, which suggests that early surgical intervention can be beneficial, although surgical mortality is high (27% to 55%) (279,281,282). Acute ventricular septal defect is less common, occurring in 0.5% of patients within two to three days from the onset of the infarction (283). However, there is some indication that it may occur more frequently and earlier after thrombolytic therapy (284). There is debate over the proper management of this severe complication of infarction. Some recommend emergency coronary angiography followed by surgical repair for all but the moribund (285,286). Others recommend this aggressive approach only for those patients with pulmonary edema or cardiogenic shock (≈90% of patients with this defect) and a delayed approach for the minority whose hemodynamic status is stable or easily controlled with drugs (287). Despite cardiogenic shock, 45% of patients will survive closure of a ventricular septal defect acutely, and 70% will survive if surgery can be delayed until later in their course (287). Rupture of the left ventricular free wall is often fatal, but a subacute form exists that is associated with leakage of a small amount of blood into the pericardial space without overwhelming tamponade, sometimes subsequently forming a left ventricular pseudoaneurysm (288–290). Coronary angiography is indicated before surgical repair of this condition as well as for the rare patient who requires early resection of a left ventricular aneurysm because of refractory congestive heart failure, uncontrollable arrhythmias or systemic embolization despite anticoagulation.

Patients who develop significant congestive heart failure or who have evidence of left ventricular dysfunction during the hospital-management phase are an important subgroup. Numerous studies have demonstrated that prognosis after acute MI is largely dependent on residual left ventricular function, as determined by global ejection fraction (291). The probability of surviving one to four years after MI has a curvilinear relationship to ejection fraction soon after the event. In the prethrombolytic era, one-year mortality was $<5\%$ for those with an ejection fraction >0.40 but declined sharply at ejection fraction levels <0.40 and approached

50% in patients with an ejection fraction ≤0.20 (292). In more recent trials, one-year mortality is lower than that stated above but still increases inversely with decreasing ejection fraction (293,294). Evidence from randomized trials comparing bypass surgery with medical therapy shows improved survival with surgery in patients with depressed left ventricular function who have three-vessel disease or two-vessel disease with involvement of the LAD coronary artery (295–297). Although these studies were performed in patients with chronic stable angina, the results are frequently extrapolated to patients with recent MI. Randomized trials specifically addressing revascularization versus medical therapy early after infarction in the patient with depressed left ventricular function and multivessel disease have not been done. However, the importance of left ventricular function and coronary anatomy is underscored in a database study of 1,214 medically treated patients with CAD (298). The incidence of new cardiac events, both fatal and nonfatal, increased with the number of stenotic vessels and decreasing left ventricular function. In patients with multivessel disease, the likelihood that the next event would be fatal was markedly increased in the subset of patients with depressed left ventricular function. For example, only 23% of patients with normal left ventricular function suffered a new event during the five-year follow-up period, whereas 64% of patients with impaired left ventricular function had a new event. In those with good left ventricular function, 44% of the new events were fatal compared with 86% in patients with impaired left ventricular function. Therefore, although not specifically evaluated or proven in a large randomized study, it seems reasonable to evaluate patients with depressed left ventricular function after a recent MI by coronary angiography.

At the extreme of patients with left ventricular dysfunction are those who develop cardiogenic shock after MI. Data from the Worcester Heart Study (299) accumulated over a 13-year period show that ≈7.5% of patients with acute MI present with or develop cardiogenic shock after MI and, without any interventions, have a mortality rate between 74% and 82%. Even among those who survive their initial hospitalization, mortality remains high. The use of coronary angiography as a precursor to revascularization in patients with shock was discussed previously in the section on the early treatment of acute MI.

(2) Patients With Q-Wave Infarction Treated With Thrombolytics

Several large prospective and randomized studies have examined the routine use of coronary angiography followed by PTCA at various times after thrombolytic therapy. The use of both coronary angiography and PTCA immediately (within 2 h) after thrombolytic therapy was examined in the TIMI IIA trial, the TAMI trial, and the European Cooperative Study Group (198–200) and was discussed previously. Routine immediate coronary angiography followed by PTCA was not found to be beneficial in any of these studies. Subsequent investigations examined routine use of coronary angiography and PTCA in all patients at later time intervals. PTCA later after MI was thought to possibly be safer because there would be more time for a stable hemostatic environment to develop at the site of the lesion and less chance of bleeding complications at catheter-insertion sites. This strategy was examined in two large prospective trials. In the TIMI IIB trial (300), patients who received tPA were randomized to receive coronary angiography and PTCA within 18 to 48 h of thrombolysis or conservative management. After six weeks, there was no difference in mortality, nonfatal recurrent MI, or left ventricular ejection fraction between the groups. Follow-up reports from this study show no difference in survival, anginal class or the frequency of bypass surgery between the two groups after one and three years (127,301). In the Should We Intervene Following Thrombolysis (SWIFT) Study (302), 800 patients treated with anistreplase were randomly assigned to coronary angiography and PTCA within two to seven days or conservative management with invasive treatment only for spontaneous or provokable ischemia. There was no difference in left ventricular function, incidence of recurrent MI, in-hospital survival or one-year survival between the two treatment groups. Thus, the automatic use of coronary angiography and PTCA in all patients with MI within days after thrombolytic therapy is not justified. Other smaller trials have examined the routine use of coronary angiography and PTCA at even longer intervals after thrombolysis. Maturation of the clot and remodeling of the infarct-related stenosis continues after the event and thus could possibly lower the risks and increase the benefits of a later intervention. Coronary angiography with PTCA of suitable lesions, including occluded arteries, was performed >72 h after tPA and compared with conservative management and revascularization only for recurrent ischemia in a randomized study of 201 patients (303). After 10 months, there was no difference in left ventricular function, recurrent infarction or death between the groups. In another study, 87 asymptomatic patients were randomized to coronary angiography and PTCA versus conservative management 4 to 14 days after thrombolytic therapy (304). Patients with postinfarction angina or exercise-induced ischemia were excluded. There was no difference in mortality between the two groups, but those treated with PTCA did have less angina after one year of follow-up. However, neither of these trials was of sufficient power to detect small differences among the groups.

(3) Patients Treated With Primary Angioplasty

Similar to patients receiving thrombolytic drugs, patients treated by primary angioplasty can experience recurrent ischemia and reinfarction, although the incidence is lower (9% to 15%) compared with patients receiving thrombolytic therapy (28% to 38%) (216,220,305). This may be due to reocclusion of the infarct-related artery or ischemia from another artery. Repeat coronary angiography may be neces-

sary in these circumstances as a precursor to a second revascularization procedure.

(4) The "Open Artery Hypothesis"

The benefits of early reperfusion therapy, whether by thrombolytic drugs or PTCA, have been attributed to salvage of severely ischemic myocardium, thereby limiting infarct size and preserving left ventricular function. However, there is increasing evidence that achieving patency in the infarct-related artery even later may have a favorable influence on outcome by mechanisms other than myocardial salvage (306–308). Late restoration of patency appears to reduce infarct expansion (309), reduce the severity of ventricular remodeling (310,311) and attenuate the risk for the development of ventricular arrhythmias (312,313). These effects could all contribute to improvements in survival without the acute salvage of myocardium (314–316). The usefulness of opening persistently occluded infarct-related arteries 7 to 48 h after symptom onset was assessed in the randomized TAMI-6 study (317). Six months after infarction, coronary angiography showed a high incidence of infarct-artery patency in those who did not have PTCA as well as a high incidence of reocclusion in those who did, so that infarct-related artery patency was similar among the two groups. There were no differences in left ventricular ejection fraction, or the incidence of recurrent MI, hospitalizations or mortality between the two groups at follow-up. Although the argument to open occluded infarct-related arteries is persuasive, at least for large arteries subtending large areas of myocardium, there are few data from randomized trials to support its widespread use. However, large studies are being planned to evaluate this treatment strategy.

(5) Patients With Non–Q-Wave Infarction

Before the impact of thrombolytic and other therapies on survival in Q-wave MI, short-term mortality from non–Q-wave MI (10%) was about half that of Q-wave MI (19.9%) (256). However, long-term mortality in patients with non–Q-wave infarction was equal to or slightly greater than that of Q-wave MI, and the incidence of reinfarction was ≈3-fold higher (15.7% vs. 5.7%). Recurrent angina also occurs more frequently after non–Q-wave MI than Q-wave MI, affecting between 35% and 50% of patients (256). In this setting, if angina is associated with ST-segment changes, patients are at extremely high risk (274). On the basis of these outcome data, many clinicians have adopted an aggressive approach to the management of patients with non–Q-wave MI, including coronary angiography in all patients. Advocates of this approach argue that it allows a definitive anatomic diagnosis, improved assessment of prognosis and the formation of a therapeutic plan early during hospitalization (318,319). Alternatively, a more conservative approach is to perform coronary angiography and revascularization only in those patients with spontaneous or inducible ischemia during provocative testing.

The TIMI IIIB study is the largest randomized, controlled trial of early intervention (angiography and PTCA within 18 to 48 h of presentation) versus conservative strategy (invasive testing and PTCA only for recurrent ischemia) in patients with either unstable angina or MI and nondiagnostic ECG changes (151). All patients were treated with beta-blockers, calcium channel blockers, nitrates, heparin and aspirin. Patients were randomized in a 2×2 factorial design to thrombolytic therapy with tPA or placebo and an early invasive strategy or conservative management. The study showed that thrombolytic therapy was not beneficial and possibly even detrimental. The incidence of fatal and nonfatal MI after randomization was higher (7.4% vs. 4.9%) in the tPA group, and there were more intracranial hemorrhages. There was no significant difference in the composite end point of death, MI, or failed symptom-limited exercise-tolerance test at six weeks between those in the invasive group (16.2%) and those in the conservative group (18.1%). However, those in the invasive group did have a slightly shorter (0.7 days) length of stay, a lower need for second hospitalizations (7.8% versus 14.1%), and a reduced use of antianginal medications. No economic analyses were performed as part of TIMI IIIB, and therefore it is not known whether the cost of routine coronary angiography and intervention was offset by the reduced need for further hospitalization and antianginal medications. In TIMI IIIB, however, 64% of the patients in the conservative arm had coronary angiography within 42 days of their infarction; there were no subgroup analyses of only patients with non–Q-wave MI.

Other data exist, including a small retrospective study limited to patients with anterior non–Q-wave MI. Early angiography with revascularization by PTCA or surgery resulted in a significant decrease in recurrent MI (7.2% vs. 29%) and improved survival after three years of follow-up compared with patients treated conventionally (320). Although many clinicians have adopted an aggressive approach with coronary angiography and revascularization in patients with non–Q-wave MI, a more conservative approach is supported by data from the VANQWISH trial (269). In that trial, 920 patients (97% male) with non–Q-wave MI were randomized to an early invasive strategy with coronary angiography and revascularization, if appropriate, versus a conservative strategy with noninvasive testing and invasive management only for spontaneous or inducible ischemia. Although the cumulative rate of death or recurrent MI did not differ between the two study groups during the duration of follow-up (12 to 44 months), the rates of death and nonfatal MI were higher at hospital discharge after 30 days and during the first year in the invasive group. These data argue against the aggressive approach of early angiography for all patients with non–Q-wave MI and suggest that a conservative strategy with medical therapy, noninvasive testing, and only ischemia-driven invasive therapy is both safe and effective.

Recommendations for Coronary Angiography During the Hospital-Management Phase (Patients With Q-Wave and Non–Q-Wave Infarction)

Class I

1. **Spontaneous myocardial ischemia or myocardial ischemia provoked by minimal exertion, during recovery from infarction.** ***(Level of Evidence: C)***
2. **Before definitive therapy of a mechanical complication of infarction such as acute mitral regurgitation, ventricular septal defect, pseudoaneurysm or left ventricular aneurysm.** ***(Level of Evidence: C)***
3. **Persistent hemodynamic instability.** ***(Level of Evidence: B)***

Class IIa

1. **When MI is suspected to have occurred by a mechanism other than thrombotic occlusion at an atherosclerotic plaque (e.g., coronary embolism, arteritis, trauma, certain metabolic or hematologic diseases or coronary spasm).** ***(Level of Evidence: C)***
2. **Survivors of acute MI with left ventricular EF ≤0.40, congestive heart failure, prior revascularization or malignant ventricular arrhythmias.** ***(Level of Evidence: C)***
3. **Clinical heart failure during the acute episode, but subsequent demonstration of preserved left ventricular function (left ventricular EF >0.40).** ***(Level of Evidence: C)***

Class IIb

1. **Coronary angiography to find a persistently occluded infarct-related artery in an attempt to revascularize that artery (open artery hypothesis).** ***(Level of Evidence: C)***
2. **Coronary angiography performed without other risk stratification to identify the presence of left main or three-vessel disease.** ***(Level of Evidence: C)***
3. **All patients after a non–Q-wave MI.** ***(Level of Evidence: C)***
4. **Recurrent ventricular tachycardia and/or ventricular fibrillation, despite antiarrhythmic therapy, without evidence of ongoing myocardial ischemia.** ***(Level of Evidence: C)***

Class III

Patients who are not candidates for or who refuse coronary revascularization. ***(Level of Evidence: C)***

e. Risk Stratification Phase in Preparation for Discharge From the Hospital After MI

The purpose of risk stratification is to assemble information that will help predict prognosis and the need for further therapies to improve prognosis (321). This process occurs throughout the entire encounter with the patient and is not strictly limited to the days before discharge. For example, rales, tachycardia, hypotension or congestion on the chest radiograph early in a patient's course are all important predictors of increased risk and likely indicate depressed left ventricular performance (322). Many prior studies have shown that left ventricular ejection fraction is highly predictive of survival (323,324). In the prethrombolytic era, mortality one year after infarction was 2% to 5% when left ventricular ejection fraction was >0.40, 10% to 15% when it was between 0.20 and 0.39, and up to 50% when it was <0.20. One-year mortality is significantly lower now than it was in the past but is still related to left ventricular performance (293,294). The cause of the improvement in outcome is multifactorial and includes the use of thrombolytic agents, beta-blockers and angiotensin converting enzyme inhibitors and perhaps includes more aggressive invasive investigation and interventional treatment. Numerous factors have been related to prognosis after acute MI; these are summarized in Table 7 (321–326). Of the deaths that occur within the first year after infarction, 50% happen within the first three weeks and 75% within the first three months (327). Therefore, patients at increased risk must be identified relatively early if they are to be considered for coronary angiography and possible revascularization.

Cardiac catheterization and coronary arteriography can identify major determinants of mortality after MI, such as left ventricular ejection fraction and the presence of multivessel CAD (325,328–332). Because of the skewed incidence of cardiac events and mortality early within the first year after infarction, some have proposed that coronary angiography be performed in all survivors even though it involves a small risk and is expensive (318). However, there are ample other data that suggest that evaluation by noninvasive methods such as standard exercise testing (Table 8), two-dimensional echocardiography, radionuclide ventricu-

Table 7. Factors Associated With Risk After Acute Myocardial Infarction

Age >70 yr
Congestive heart failure or LVEF <0.40
Extent of CAD
Large infarct size, anterior infarction, or non–Q-wave myocardial infarction
New bundle branch block of any type, Mobitz 2, or transient third-degree heart block
Recurrent angina, reinfarction, or infarct extension
Frequent VPBs, ventricular tachycardia, or ventricular fibrillation occurring after acute phase or inducible monomorphic ventricular tachycardia during electrophysiological testing
Supraventricular arrhythmias except sinus bradycardia
Abnormal signal-averaged electrocardiogram
Provokable ischemia during exercise testing or inability to exercise
Diabetes, hypertension
Female sex

LVEF indicates left ventricular ejection fraction; CAD, coronary artery disease; and VPB, ventricular premature beat.

Modified with permission from Hessen SE, Brest AN. Risk profiling the patient after acute myocardial infarction. In: Pepine CJ, ed. Acute Myocardial Infarction. Philadelphia, Pa: FA Davis; 1989:284.

Table 8. Exercise Test Predictors of Adverse Outcome in Postinfarction Patients (81)

Ischemic ST-segment depression ≥1 mm, particularly if accompanied by symptoms, or at a low level of exercise, or in the presence of controlled heart failure
Functional capacity <5 METs
Inadequate blood pressure response (peak systolic blood pressure <110 mm Hg or <30 mm Hg increase from resting level)

METs indicates metabolic equivalents.

lography, thallium scintigraphy or these imaging techniques coupled with dynamic or pharmacologic stress can identify most high-risk patients who may benefit from revascularization (321,322,328,329,333–339). Moreover, coronary angiography demonstrates the anatomy and morphology of a stenosis at a discrete point in time. Progression of CAD is quite variable, but it is a major factor affecting prognosis (340,341). Although some angiographic predictors of future infarction have been identified (342,343), other studies have shown that 66% to 78% of infarctions are related to an artery with a ≤50% stenosis on a previous angiogram (344,345). Such lesions would not likely be the target of revascularization attempts.

Various strategies for the use of coronary angiography after MI have been discussed in the literature (291,318,321, 337,346), but careful research in this area has been sparse. Ross et al. (347) developed a scheme in patients younger than 75 years of age that would avoid early coronary angiography in those at low risk (≤3%) for one-year mortality and recommends angiography in those at increased risk (average one-year mortality 16%). Indications for coronary angiography in this scheme included the following: severe resting ischemia at any time beyond the first 24 h after infarction (one-year mortality 18%); hospital survivors with a history of previous MI and clinical or radiographic signs of left ventricular failure in the hospital (one-year mortality 25%); an ischemic exercise response or poor workload achieved (one-year mortality 11%); and a resting left ventricular ejection fraction between 0.20 and 0.44 alone when exercise testing is not performed (one-year mortality 12%). With this approach, ≈55% of patients who survive to the fifth day after infarction would undergo coronary angiography. By comparison, data from the National Registry of Myocardial Infarction during 1990 through 1993 and the GUSTO trial show that ≈72% of patients treated by American participants undergo coronary angiography during their initial hospitalization after MI (47,259). This rate is considerably higher than the rate of 55% proposed by Ross et al. and the rate of 33% for coronary angiography used in the selective approach of the TIMI II trial (300). Although the frequent use of invasive evaluations and therapy in the United States is subject to debate, a recent subgroup analysis from the GUSTO trial shows that patients treated in the United States had a better quality of life, less angina and lower mortality during the first year after infarction than did their Canadian counterparts, of whom only 25% underwent coronary angiography (47). However, this approach has not been verified in other studies and is costly (44,45,346).

The most recent scheme for evaluation and risk stratification of patients early after MI was presented in the 1996 "ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction" (190). This approach is recommended by the committee and is outlined in Figure 4.

Recommendations for Coronary Angiography During the Risk-Stratification Phase (Patients With All Types of MI)

Class I

Ischemia at low levels of exercise with ECG changes (≥1-mm ST-segment depression or other predictors of adverse outcome) (Table 8) and/or imaging abnormalities. ***(Level of Evidence: B)***

Class IIa

1. **Clinically significant CHF during the hospital course.** ***(Level of Evidence: C)***
2. **Inability to perform an exercise test with left ventricular EF ≤0.45.** ***(Level of Evidence: C)***

Class IIb

1. **Ischemia occurring at high levels of exercise.** ***(Level of Evidence: C)***
2. **Non–Q-wave MI in a patient who is an appropriate candidate for a revascularization procedure.** ***(Level of Evidence: C)***
3. **Need to return to an unusually active form of employment.** ***(Level of Evidence: C)***
4. **Remote history of MI without evidence of congestive heart failure during the current event and without evidence of inducible ischemia.** ***(Level of Evidence: C)***
5. **Recurrent ventricular tachycardia, fibrillation, or both, despite antiarrhythmic therapy, without ongoing myocardial ischemia.** ***(Level of Evidence: C)***

Class III

Patients who are not candidates for or who refuse coronary revascularization. ***(Level of Evidence: C)***

6. Perioperative Coronary Angiography for Patients Undergoing Noncardiac Surgery

Each year, more than 25 million patients undergo noncardiac surgery. Of these patients, it is estimated that nearly 3 million have CAD, >4 million are older than 65 years of age, and ≈50,000 will suffer a perioperative MI (348). As many as half of the annual 40,000 deaths associated with noncardiac surgery are secondary to coronary disease (348), and nearly one million patients undergoing noncardiac surgery will have a serious cardiac complication. The annual cost of this perioperative morbidity exceeds $10 billion

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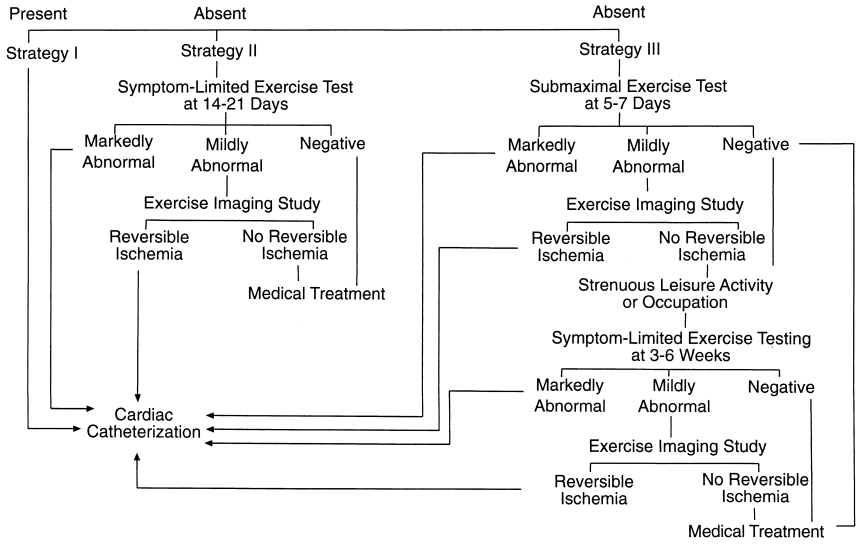

Figure 4. Clinical indications of high risk at predischarge. Strategies for risk stratification soon after myocardial infarction. If patients are at high risk for ischemic events, on the basis of clinical criteria, they should undergo invasive evaluation to determine if they are candidates for coronary revascularization procedures (strategy I). For patients initially deemed to be at low risk at time of discharge after MI, two strategies for performing exercise testing can be used. One is a symptom-limited test at 14 to 21 days (strategy II). If the patient is taking digoxin or if baseline ECG precludes accurate interpretation of ST-segment changes (e.g., baseline left bundle-branch block or left ventricular hypertrophy), then an initial exercise imaging study can be performed. Results of exercise testing should be stratified to determine the need for additional invasive or exercise perfusion studies. A third strategy is to perform a submaximal exercise test five to seven days after MI or just before hospital discharge. The exercise test results could be stratified using the guidelines in strategy I. If exercise test studies are negative, a second symptom-limited exercise test could be repeated at three to six weeks for patients undergoing vigorous activity during leisure or at work. From Figure 10 of the ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction (190).

(348). Most of these adverse outcomes are directly related to myocardial ischemia or infarction.

The perioperative evaluation of patients undergoing noncardiac surgery has recently been detailed in an ACC/AHA task force report (349). This document outlines a comprehensive approach to perioperative risk assessment that stresses the patient's prior clinical indicators of coronary heart disease, functional status, type of noncardiac surgery and the role of selected preoperative stress testing in patients believed to be at intermediate or high risk for major perioperative coronary events.

A number of studies have suggested that detection of ischemia-related abnormalities before noncardiac surgery identifies a subgroup of patients at high risk for perioperative coronary events. In the past, this led some to argue for routine coronary angiography for all patients undergoing peripheral vascular surgery (350,351). Others, however, suggested that such patients should be subjected to multifactorial clinical risk assessment (352) before consideration of coronary angiography. Between these two extremes lies the practice of combining clinical and noninvasive test information to stratify these patients (349,353,354). In addition, the anticipated cardiovascular stress of the particular type of surgery is an important determinant of the most appropriate perioperative strategy.

By and large, the indications for coronary angiography for patients being considered for noncardiac surgery should be virtually identical to those already outlined in this document. However, the presentation for noncardiac surgery, its potential urgency, the level of cardiovascular stress that is anticipated, and the general condition of the patient all play critical roles in determining the most logical sequence of events for any given patient. The following indications for coronary angiography in perioperative evaluation before and after noncardiac surgery reflect these different attributes of any given patient. In addition, the types of clinical markers that portend particularly high risk and those noncardiac procedures that are associated with greater cardiovascular stresses are listed beneath the table of indications for easy reference.

Recommendations for Coronary Angiography in Perioperative Evaluation Before (or After) Noncardiac Surgery

Class I: Patients with suspected or known CAD

1. **Evidence for high risk of adverse outcome based on noninvasive test results (Table 5).** ***(Level of Evidence: C)***
2. **Angina unresponsive to adequate medical therapy.** ***(Level of Evidence: C)***
3. **Unstable angina, particularly when facing intermediate-* or high-risk* noncardiac surgery.** ***(Level of Evidence: C)***

4. **Equivocal noninvasive test result in high-clinical-risk† patient undergoing high-risk* surgery.** ***(Level of Evidence: C)***

Class IIa

1. **Multiple-intermediate-clinical risk markers† and planned vascular surgery.** ***(Level of Evidence: B)***
2. **Ischemia on noninvasive testing but without high-risk criteria (Table 5).** ***(Level of Evidence: B)***
3. **Equivocal noninvasive test result in intermediate-clinical-risk† patient undergoing high-risk* noncardiac surgery.** ***(Level of Evidence: C)***
4. **Urgent noncardiac surgery while convalescing from acute MI.** ***(Level of Evidence: C)***

Class IIb

1. **Perioperative MI.** ***(Level of Evidence: B)***
2. **Medically stabilized class III or IV angina and planned low-risk or minor* surgery.** ***(Level of Evidence: C)***

Class III

1. **Low-risk* noncardiac surgery, with known CAD and no high-risk results on noninvasive testing.** ***(Level of Evidence: B)***
2. **Asymptomatic after coronary revascularization with excellent exercise capacity (≥7 METs).** ***(Level of Evidence: C)***
3. **Mild stable angina with good left ventricular function and no high-risk noninvasive test results.** ***(Level of Evidence: B)***
4. **Noncandidate for coronary revascularization owing to concomitant medical illness, severe left ventricular dysfunction (e.g., left ventricular EF <0.20), or refusal to consider revascularization.** ***(Level of Evidence: C)***
5. **Candidate for liver, lung or renal transplant ≥40 years old as part of evaluation for transplantation, unless noninvasive testing reveals high risk for adverse outcome.** ***(Level of Evidence: C)***

B. Valvular Heart Disease

In all forms of valvular heart disease, the presence of significant coronary disease worsens prognosis (355–358). For instance, Iung and colleagues (356) found a nine-year actuarial survival rate of 79% after aortic valve replacement in patients without coronary disease versus a 66% survival rate in patients who underwent both aortic valve replacement and coronary bypass grafting ($p < 0.01$). Most studies suggest that in patients with both CAD and aortic valve disease, coronary bypass reduces the early and late mortality of aortic valve replacement compared with patients who only undergo aortic valve replacement, although statistical significance was often not achieved (359–362). Because it is widely accepted that reoperation has an increased risk, most practitioners are compelled to assess coronary anatomy before surgery and to bypass significant obstructions during surgery with the hope of avoiding late reoperation. The presence of valvular heart disease makes the noninvasive assessment of ischemia less predictive than in the general population, because valve disease often limits exercise capacity and increases hemodynamic instability and for some lesions may be accompanied by left ventricular hypertrophy, which can lead to false-positive testing. Although there are no large clinical trials to prove its value, angiography seems to have an important role in the preoperative evaluation of patients with valvular heart disease.

Patients with aortic stenosis pose the most difficult problem in the decision of whether or not to perform preoperative angiography. Approximately 35% of patients with aortic stenosis have coronary disease (363–365). This high incidence exists because both diseases occur with advancing age and because they share other risk factors in common. In these patients, the complaint of angina pectoris is a poor guide to the presence or absence of coronary disease. Coronary disease is present in ≈25% of all patients with aortic stenosis who do not complain of chest pain (365,366). Conversely, of the 40% of patients with aortic stenosis who do complain of angina, the presence of coronary disease varies from 40% to 80% (363–366). Until recently, coronary angiography was considered to be the only method available to establish the presence or absence of coronary disease because exercise scintigraphy or exercise echocardiography, the other potential modalities for detecting coronary disease, were considered hazardous in patients with aortic stenosis. However, as a substitute for exercise, pharmacologic interventions to alter coronary blood flow have now been used safely in conjunction with thallium or sestamibi imaging to search for coronary disease in patients with aortic stenosis. Depending on the definition of a thallium defect, both sensitivity and specificity for this procedure in detecting coronary disease in the face of aortic stenosis are as high as 80% (367–370).

Currently, all patients with aortic stenosis who complain of chest discomfort should undergo coronary angiography before surgery. This is the only reliable way to define the presence or absence of CAD and to determine whether simple aortic valve replacement or valve replacement plus coronary bypass is necessary. In patients without angina, it seems prudent to perform coronary angiography for those who are at increased risk for the presence of CAD because of their age or other risk factors.

*Cardiac risk according to type of noncardiac surgery. High risk: emergent major operations, aortic and major vascular, peripheral vascular, anticipated prolonged surgical procedure associated with large fluid shifts and blood loss; intermediate risk: carotid endarterectomy, major head and neck, intraperitoneal and intrathoracic, orthopedic, prostate; and low risk: endoscopic procedures, superficial procedures, cataract, breast. †Cardiac risk according to clinical predictors of perioperative death, MI or congestive heart failure. High clinical risk: unstable angina, recent MI and evidence of important residual ischemic risk, decompensated congestive heart failure, high degree of atrioventricular block, symptomatic ventricular arrhythmias with known structural heart disease, severe symptomatic valvular heart disease, patient with multiple intermediate risk markers such as prior MI, congestive heart failure, and diabetes; intermediate clinical risk: CCS class I or II angina, prior MI by history or ECG, compensated or prior congestive heart failure, diabetes mellitus.

In patients with significant aortic regurgitation, coronary disease is found in ≈25% of affected subjects. Angina is less common in aortic regurgitation than in aortic stenosis, occurring in ≈25% of cases (365,371). As with aortic stenosis, there is a discordance between the presence or absence of coronary disease and angina. In patients without angina, the presence of coronary disease ranges from 7% to 15%. It seems prudent to perform coronary angiography for patients with aortic insufficiency without angina as well as for those with aortic stenosis if they are at increased risk because of age or other coronary risk factors.

Coronary angiography should be performed in most patients before mitral valve surgery for mitral regurgitation because it is the only valve lesion that commonly has coronary disease as its cause. Young patients in whom other origins of mitral regurgitation can clearly be discerned echocardiographically may not need coronary angiography before valve surgery.

Although most patients with mitral stenosis are women, the disease usually presents in people during midlife or later in the U.S. Because many patients with mitral stenosis have unrecognized coronary disease, coronary angiography is usually advised before surgery or balloon mitral valvotomy. Evidence suggests that coronary angiography might detect the presence of left atrial thrombus. The finding of neovascularity between the coronary arteries and the left atrium during injection of the left coronary artery has a sensitivity of 75% and a specificity of 90% for diagnosing left atrial thrombus (372,373). However, there are insufficient data to recommend coronary angiography solely for the purpose of discovering a left atrial thrombus, nor has this method been compared with transesophageal echocardiography, which is frequently used for this purpose.

The role of coronary angiography in the preoperative evaluation of the patient undergoing valve surgery continues to evolve. All patients with chest pain or noninvasive evidence of coronary disease should undergo this procedure. Although it seems that a negative thallium study may obviate the need for angiography, the number of studies examining this question is limited. Thus, it seems prudent to perform coronary angiography for those patients who are at increased risk for the presence of coronary disease because of their age or other risk factors.

Infective endocarditis, whether acute or subacute, may produce valvular insufficiency that requires valve replacement. In acute aortic insufficiency, the presence of heart failure may constitute a surgical emergency that requires immediate valve replacement. In such patients, the risk of delaying surgery to perform coronary angiography must be weighed against its benefit. Often, these patients are relatively young and have no risks for coronary disease. In such patients, coronary angiography is not indicated. However, in some patients, endocarditis may result in ≥1 coronary embolus, resulting in a clinical picture of acute MI together with endocarditis. If valve replacement is being undertaken for this type of patient, it is desirable to evaluate the coronary anatomy to determine whether ≥1 proximal obstructive lesion is present that may warrant concomitant bypass grafting. Although cardiac catheterization is generally safe in patients with endocarditis (374), care should be taken to avoid contacting the aortic valve during coronary angiography to decrease the risk of vegetation dislodgement.

Recommendations for Use of Coronary Angiography in Patients With Valvular Heart Disease

Class I

1. **Before valve surgery or balloon valvotomy in an adult with chest discomfort, ischemia by noninvasive imaging, or both.** ***(Level of Evidence: B)***
2. **Before valve surgery in an adult free of chest pain but with multiple risk factors for coronary disease.** ***(Level of Evidence: C)***
3. **Infective endocarditis with evidence of coronary embolization.** ***(Level of Evidence: C)***

Class IIa

None.

Class IIb

During left-heart catheterization performed for hemodynamic evaluation before aortic or mitral valve surgery in patients without preexisting evidence of coronary disease, multiple CAD risk factors or advanced age. ***(Level of Evidence: C)***

Class III

1. **Before cardiac surgery for infective endocarditis when there are no risk factors for coronary disease and no evidence of coronary embolization.** ***(Level of Evidence: C)***
2. **In asymptomatic patients when cardiac surgery is not being considered.** ***(Level of Evidence: C)***
3. **Before cardiac surgery when preoperative hemodynamic assessment by catheterization is unnecessary, and there is neither preexisting evidence for coronary disease, nor risk factors for CAD.** ***(Level of Evidence: C)***

C. Congenital Heart Disease

Although there are no large trials to support its use, coronary angiography is performed in congenital heart disease for two broad categorical indications. The first indication is to assess the hemodynamic impact of congenital coronary lesions (375). The second is to assess the presence of coronary anomalies, which by themselves may be innocent but whose presence, if unrecognized, may lead to coronary injury during the correction of other congenital heart lesions. Congenital anomalies with hemodynamic significance include congenital coronary artery stenosis or atresia, coronary artery fistula (376), anomalous left coronary artery arising from the pulmonary artery (377), and

anomalous left coronary artery arising from the right coronary artery or right sinus of Valsalva and passing between the aorta and right ventricular outflow tract (378). Patients with congenital coronary stenoses may present with angina or unexplained sudden death in childhood, whereas patients whose left coronary passes between the pulmonary artery and aorta often have the same symptoms later in life. Patients with a coronary arteriovenous fistula often present with a continuous murmur or may have unexplained angina or congestive heart failure. Anomalous origin of the left coronary artery from the pulmonary artery should be suspected when there is unexplained MI or heart failure in early childhood. Other coronary anomalies of position or origin may cause no physiologic abnormality by themselves. Some, such as origin of the circumflex artery from the right sinus of Valsalva, are not associated with other congenital anomalies and present only as incidental findings and are significant only because they complicate the performance and interpretation of coronary angiograms.

Some coronary anomalies are important because their anomalous position may lead to their injury at the time of surgical correction of an associated structural abnormality. In this category, the most frequently occurring example is anomalous origin of the LAD coronary artery from the right coronary artery passing across the anterior right ventricle in patients with tetralogy of Fallot (379). Important coronary anomalies are also common in transposition of the great arteries (380).

Finally, although most congenital heart disease is discovered early in life before patients are at risk for atherosclerotic coronary disease, in some cases surgical correction is performed at older ages, when the risk of coronary disease increases. Although there are almost no data addressing this issue, it seems prudent to perform coronary arteriography in patients being considered for repair of congenital heart disease if angina, ischemia by noninvasive testing or multiple coronary risk factors are present.

Recommendations for Use of Coronary Angiography in Patients With Congenital Heart Disease

Class I

1. **Before surgical correction of congenital heart disease when chest discomfort or noninvasive evidence is suggestive of associated CAD.** ***(Level of Evidence: C)***
2. **Before surgical correction of suspected congenital coronary anomalies such as congenital coronary artery stenosis, coronary arteriovenous fistula and anomalous origin of left coronary artery.** ***(Level of Evidence: C)***
3. **Forms of congenital heart disease frequently associated with coronary artery anomalies that may complicate surgical management.** ***(Level of Evidence: C)***
4. **Unexplained cardiac arrest in a young patient.** ***(Level of Evidence: B)***

Class IIa

Before corrective open heart surgery for congenital heart disease in an adult whose risk profile increases the likelihood of coexisting coronary disease. ***(Level of Evidence: C)***

Class IIb

During left-heart catheterization for hemodynamic assessment of congenital heart disease in an adult in whom the risk of coronary disease is not high. ***(Level of Evidence: C)***

Class III

In the routine evaluation of congenital heart disease in asymptomatic patients for whom heart surgery is not planned. ***(Level of Evidence: C)***

D. Congestive Heart Failure

1. Systolic Dysfunction

Although it was once believed that myocardial ischemia was either short-lived and resulted in little or no muscle dysfunction or resulted in infarction with permanent damage, it is now clear that a middle state may exist in which chronic ischemic nonfunctioning myocardium is present, to which function may return after myocardial revascularization (381,382). This intermediate state has been termed "myocardial hibernation." Although most cases of myocardial dysfunction resulting from CAD are probably irreversible when due to infarction and subsequent deleterious ventricular remodeling (ischemic cardiomyopathy) (383), some patients with hibernating myocardium have been shown to experience a doubling of resting ejection fraction with resolution of congestive heart failure after coronary revascularization (384,385). However, in most cases of hibernation, a more modest improvement in ejection fraction of ≈5% occurs after revascularization (386). In view of this phenomenon, the possibility of reversible myocardial systolic dysfunction should always be considered, especially before consideration for a cardiac transplantation. Usually, segmental wall motion abnormalities in ischemic cardiomyopathy coupled with perfusion defects during myocardial scintigraphy allow the diagnosis of ischemia as a probable cause of myocardial dysfunction before angiography. Likewise, the presence of a thin-walled dilated cardiomyopathy with homogeneously poor wall motion and normal myocardial scintigraphy strongly suggests that nonischemic cardiomyopathy is present (387). However, the two conditions may overlap such that some patients with idiopathic dilated cardiomyopathy may have regional wall motion abnormalities, whereas some patients with ischemic cardiomyopathy may have global left ventricular dysfunction. Currently, thallium scintigraphy is the most widely used test of viability

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(387). Thallium, a potassium analog, requires an intact (viable) sarcolemma for myocardial uptake. Sestamibi scintigraphy, which detects intact mitochondria as its measure of viability, and PET scanning, which relies on intact glucose metabolism as a marker of viability, are alternatives to thallium imaging. By way of example, the circumstance in which echocardiography demonstrates an akinetic anterior wall while scintigraphy demonstrates anterior thallium uptake suggests anterior wall viability with hibernating myocardium in that region. In such cases, coronary angiography should be performed to identify a potential revascularization target in the LAD artery.

It is worth noting that most centers do perform coronary angiography in the workup for cardiac transplantation.

2. Diastolic Dysfunction

Isolated diastolic dysfunction is the cause of heart failure in 10% to 30% of affected patients. This disorder is common in older patients with hypertension and often is suspected because of echocardiographically detected concentric left ventricular hypertrophy, normal systolic function and abnormal transmitral flow velocity patterns (388). However, in some patients with normal systolic function, the abrupt onset of pulmonary edema raises the suspicion that transient ischemia was the cause of decompensation, because elderly patients with hypertension have, by definition, at least two risk factors for coronary disease. In these patients, who are often too ill to undergo stress testing, coronary angiography may be necessary to establish or rule out the diagnosis of ischemically related diastolic dysfunction and heart failure.

Recommendations for Use of Coronary Angiography in Patients With Congestive Heart Failure

Class I

1. **Congestive heart failure due to systolic dysfunction with angina or with regional wall motion abnormalities and/or scintigraphic evidence of reversible myocardial ischemia when revascularization is being considered.** ***(Level of Evidence: B)***
2. **Before cardiac transplantation.** ***(Level of Evidence: C)***
3. **Congestive heart failure secondary to postinfarction ventricular aneurysm or other mechanical complications of MI.** ***(Level of Evidence: C)***

Class IIa

1. **Systolic dysfunction with unexplained cause despite noninvasive testing.** ***(Level of Evidence: C)***
2. **Normal systolic function, but episodic heart failure raises suspicion of ischemically mediated left ventricular dysfunction.** ***(Level of Evidence: C)***

Class III

Congestive heart failure with previous coronary angiograms showing normal coronary arteries, with no new evidence to suggest ischemic heart disease. ***(Level of Evidence: C)***

E. Other Conditions

1. Aortic Dissection

The need for coronary angiography before surgical treatment for aortic dissection remains controversial because there are no large trials to support its use. In young patients with dissection due to Marfan syndrome or in dissection in peripartum females, coronary angiography is unnecessary unless there is suspicion that the dissection has affected one or both coronary ostia. In older patients, in whom dissection is usually related to hypertension, coronary angiography is often necessary, especially if patients are suspected of having coronary disease because of a history of angina or objective evidence of myocardial ischemia. In patients who have no history of coronary disease, the indications for coronary angiography are much less certain. Because of the high incidence of coronary disease in older patients with dissection, some studies have advocated routine coronary angiography (389), whereas others have found increased mortality when angiography is performed (390).

2. Arteritis

Some patients with inflammatory processes affecting the aorta, such as Takayasu arteritis, may have coronary artery involvement requiring coronary artery revascularization. In such patients, coronary angiography is required before the surgical procedure. Kawasaki disease can result in coronary artery aneurysm and coronary artery stenosis producing myocardial ischemia or silent occlusion and may require coronary angiographic assessment (391,392).

3. Hypertrophic Cardiomyopathy

Significant CAD due to atherosclerosis is found in ≈25% of patients aged >45 years with hypertrophic cardiomyopathy (393). Because symptoms due to CAD and hypertrophic cardiomyopathy are similar, patients with ischemic symptoms not well controlled with medical therapy may require coronary angiography to resolve the cause of chest pain. Coronary angiography also is indicated in patients with chest discomfort and hypertrophic cardiomyopathy in whom a surgical procedure is planned to correct outflow tract obstruction.

4. Chest Trauma

Patients who have an acute MI shortly after blunt or penetrating chest trauma may have atherosclerotic CAD, but coronary artery obstruction or damage has been reported in the absence of coronary atherosclerosis (394). Furthermore, myocardial contusion may simulate acute MI. Infrequently, coronary angiography is indicated in the management of such patients.

5. Miscellaneous Conditions

Preoperative coronary angiography may be indicated in patients undergoing cardiac operations such as pericardiectomy or removal of chronic pulmonary emboli if they have ≥1 risk factor for coronary disease, especially advanced age. Because of the concern about transplanting a donor heart affected by coronary disease, many advocate coronary angiography before transplantation, at least for those donors with a significant likelihood of CAD.

Recommendations for Use of Coronary Angiography in Other Conditions

Class I

1. **Diseases affecting the aorta when knowledge of the presence or extent of coronary artery involvement is necessary for management (e.g., aortic dissection or aneurysm with known coronary disease).** ***(Level of Evidence: B)***
2. **Hypertrophic cardiomyopathy with angina despite medical therapy when knowledge of coronary anatomy might affect therapy.** ***(Level of Evidence: C)***
3. **Hypertrophic cardiomyopathy with angina when heart surgery is planned.** ***(Level of Evidence: B)***

Class IIa

1. **High risk for coronary disease when other cardiac surgical procedures are planned (e.g., pericardiectomy or removal of chronic pulmonary emboli).** ***(Level of Evidence: C)***
2. **Prospective immediate cardiac transplant donors whose risk profile increases the likelihood of coronary disease.** ***(Level of Evidence: B)***
3. **Asymptomatic patients with Kawasaki disease who have coronary artery aneurysms on echocardiography.** ***(Level of Evidence: B)***
4. **Before surgery for aortic aneurysm/dissection in patients without known coronary disease.**
5. **Recent blunt chest trauma and suspicion of acute MI, without evidence of preexisting CAD.** ***(Level of Evidence: C)***

APPENDIX A

Anatomic angiographic definitions. Proper communication of the results of coronary arteriography requires some standardization of nomenclature regarding measurement and description of the coronary arterial tree. Clinical investigators of the CASS, TIMI, and BARI trials have presented standardized systems. These guidelines endorse the system developed by the BARI investigators and published by Alderman and Stadius in *Coronary Artery Disease* (395). This system provides for nomenclature of the most frequently encountered coronary arterial segments as shown in Figure 5 and as described in Table 9.

Coronary artery dominance refers to the origin of blood flow to the inferolateral wall of the left ventricle. Right dominance denotes right coronary origin of flow (segments 1 through 9), left dominance to left coronary artery origin of flow (segments 18 and 19 and 23 through 27), and mixed dominance to an intermediate pattern.

Coronary artery lesions can be described by their location, severity and classification. Location description uses the scheme shown in Figure 5, with the proximal shoulder of the lesion defining the location. Stenosis severity may be estimated visually, but is more accurately estimated by

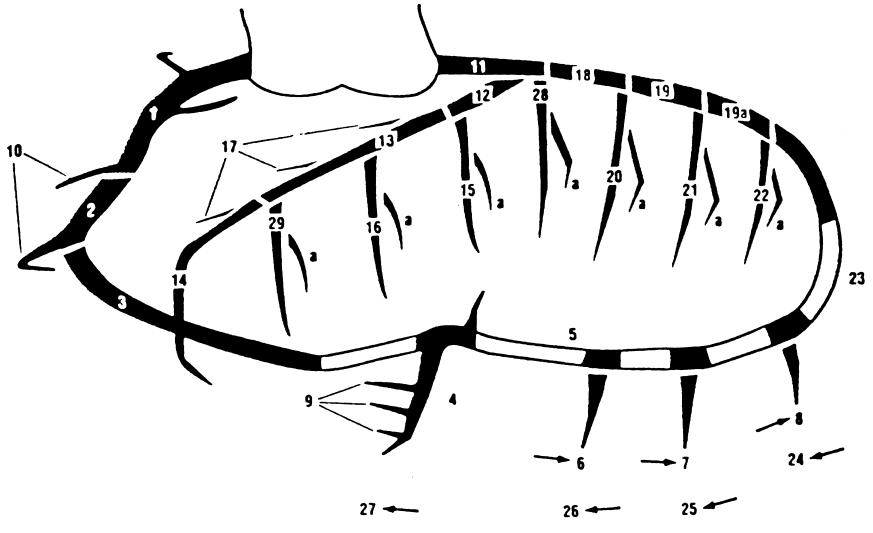

Figure 5. The coronary artery map used by the BARI investigators. The map is derived from that used in CASS with the addition of branch segments for the diagonal, marginal and ramus vessels. Reprinted with permission from Alderman et al. (395). See Table 9 for corresponding map location.

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Table 9. Bypass Angioplasty Revascularization Investigation (BARI) Coronary Artery Segments and Corresponding Map Location

Segment	Map Location
1	Proximal right coronary artery conduit segment
2	Mid-right coronary artery conduit segment
3	Distal right coronary artery conduit segment
4	Right posterior descending artery segment
5	Right posterior atrioventricular segment
6	First right posterolateral segment
7	Second right posterolateral segment
8	Third right posterolateral segment
9	Posterior descending septal perforators segment
10	Acute marginal segment(s)
11	Left main coronary artery segment
12	Proximal LAD artery segment
13	Mid-LAD artery segment
14	Distal LAD artery segment
15	First diagonal branch segment
15a	Lateral first diagonal branch segment
16	Second diagonal branch segment
16a	Lateral second diagonal branch segment
17	LAD septal perforator segments
18	Proximal circumflex artery segment
19	Mid-circumflex artery segment
19a	Distal circumflex artery segment
20	First obtuse marginal branch segment
20a	Lateral first obtuse marginal branch segment
21	Second obtuse marginal branch segment
21a	Lateral second obtuse marginal branch segment
22	Third obtuse marginal branch segment
22a	Lateral third obtuse marginal branch segment
23	Circumflex artery AV groove continuation segment
24	First left posterolateral branch segment
25	Second left posterolateral branch segment
26	Third posterolateral descending artery segment
27	Left posterolateral descending artery segment
28	Ramus intermedius segment
28a	Lateral ramus intermedius segment
29	Third diagonal branch segment
29a	Lateral third diagonal branch segment

AV indicates atrioventricular; and LAD, left anterior descending.

electric or digital means, with percent stenosis defined as the ratio of reference luminal diameter divided by the reference diameter vessel measurement.

Severe stenoses (>85%) defy quantitative methods and should be so stated. Vessel occlusion (100% stenosis) is defined as termination of the original luminal channel and TIMI flow 0 through it.

In addition to the above characteristics of coronary lesions, a scaled qualitative measurement of flow through the stenosis has been proposed by Sheehan for the TIMI investigators. Table 10 describes TIMI flow grades for native coronary vessels, collateral vessels, and coronary bypass graft conduits (396).

Table 10. Distal Flow of Native Vessel, Collaterals, and Grafts

Contrast Flow	TIMI Grade	Native Vessel Flow	Collateral Flow	Graft Flow
Prompt anterograde flow and rapid clearing	3	3	Excellent	3
Slowed distal filling but full opacification of distal vessel	2	2	Good	2
Small amount of flow but incomplete opacification of distal vessel	1	1	Poor	1
No contrast flow	0	0	No visible flow	0

TIMI indicates Thrombolysis in Myocardial Infarction.

APPENDIX B

Special Considerations Regarding Coronary Angiography

1. Accuracy

Cineangiographic images of coronary arteries have been the principal clinical tool for determining the severity of coronary luminal stenosis. Modern angiographic equipment has a resolution of four to five line pairs per millimeter with a six-inch field of view, the usual image magnification for coronary angiography (397). Validation studies that use known phantoms show a high correlation between actual size and that measured by quantitative coronary angiography (QCA) ($r = 0.95$) (398–401). The resolution of these phantom studies indicates the precision of coronary angiography to be 0.02 to 0.04 mm. Factors that limit resolution in the clinical setting include grainy films from "quantum mottling" and motion artifact that, in a clinical setting, limit resolution to 0.2 mm, far less than that realized from static images of known phantoms. Other factors, such as angulation, overlap of vessels and image tube resolution can also influence accuracy in the clinical setting. Nevertheless, the accuracy of coronary angiography does allow for anatomic detail that is not obtainable by current noninvasive or other invasive technology. Only intravascular ultrasound, which is discussed in Appendix C, has an image resolution greater than that of coronary angiography. However, intravascular ultrasound cannot visualize the entire coronary tree nor define the anatomic course of the coronary vessels. It is also limited by shadowing from heavy calcification and by its inability to image very small vessels or very severe stenosis.

2. Reproducibility

In clinical practice, the degree of coronary artery obstruction is commonly expressed as the percent diameter stenosis. This is done by comparing the diameter of the site of greatest narrowing (minimal lumen diameter) to an adjacent

segment assumed to be free of disease. In clinical practice, the most common method used to estimate the percent diameter narrowing is subjective visual assessment. Because vasomotor tone can alter the reference diameter, nitroglycerin is frequently administered before angiography to improve the reproducibility of the measurement. Several studies have shown that measurement of the degree and extent of luminal narrowing correlates with symptoms as well as with assessments of coronary flow reserve (CFR) and abnormalities on treadmill exercise testing, perfusion imaging with ^{201}Tl or sestamibi, stress echocardiography and fast computerized tomography (402–406). In addition, the percent diameter reduction and the number of stenoses of ≥50% to 70% correlate with long-term outcome (407–414). When other clinical variables predictive of mortality, such as age or left ventricular function, are considered, the number and extent of luminal coronary diameter narrowings on coronary angiography remain important independent predictors of outcome (8,409,413,415).

Despite the relationship between visual assessments of coronary disease and outcome, it is well recognized that visual assessments have significant interobserver and intraobserver variability ranging from 7.5% to 50% (416–424). Originally described in the late 1970s, QCA with a computer-based system can reduce the wide variability in readings of the angiogram (399–401,425–433). Although both videodensitometric and edge-detection techniques have been used, the latter is more commonly used. Validation studies in which static images were used have shown that reproducibility is greatly improved. However, results vary among different QCA systems, ranging from 0.07 mm to 0.31 mm (398). An additional advantage of this type of assessment is the ability to measure the degree of luminal narrowing in absolute terms as the minimal lumen diameter (432,434–436). This measurement is not influenced by the adjacent segment, which may also be significantly diseased and can lead to inaccuracies in determination of the percent stenosis (437). Studies have shown that the minimal lumen diameter is a reliable measurement that can be used to follow the progression or regression of disease by angiography (434–436). It has also been used extensively to define the presence of restenosis and is the standard for restenosis trials that have used coronary angiography as the primary end point (434,435). In addition, it correlates well with noninvasive assessments of myocardial ischemia. In one recent study, QCA-determined percent stenosis of >50% had a positive predictive value of 79% and a negative predictive value of 80% for a positive dobutamine echo, whereas a minimal lumen diameter of <1.0 mm had a positive predictive value of 81% and a negative predictive value of 90% (438). Similar relationships have been found with other noninvasive tests of myocardial ischemia.

Although QCA systems are becoming more readily available, they have not yet been used routinely in clinical practice (428,439,440). Recent studies have shown that handheld or digital calipers are a suitable alternative for QCA, and many laboratories have adopted this quantitative methodology to reduce interobserver and intraobserver variability. The variability of digital calipers (5.9% to 9%) is lower than that of visual assessments (7.5% to 50%); however, computer-generated QCA measurements have the lowest interobserver and intraobserver variabilities (3.5% to 7.3%) (441–443). QCA measurements also are superior to visual readings when the angiographic measurements are repeated weeks to months later, resulting in the lowest medium and long-term variability (5% to 14%) (399,400). Use of QCA, although more reproducible, is limited by the use of one or two selected cine frames for analysis (433,444). Coronary lesions are frequently eccentric, and overlapping and nontangential views can result in poor definition. Projections that position the vessel over other structures, such as the spine, can also lead to significant difficulty in quantitative assessment (444–447). The frame selection is also important, because any single frame can misrepresent the true extent of a coronary narrowing (433,444). The value of cineangiography is that motion can improve the assessment of the stenosis and allow for the visual integration of many frames. Several recent studies suggest that despite a greater interobserver variability, visual assessments with caliper measurements are more predictive of long-term outcome than QCA after angioplasty (448,449).

The maintenance of high-quality angiographic readings that have low interobserver and intraobserver variabilities requires a formal quality-assurance/quality-control program (450). Some of the responsibilities of the cardiac catheterization laboratory director are to ensure that the cineangiographic quality of the laboratory is high, that optimal views of the coronary vessels are obtained in each case, and that angiographic interpretation by the participating physicians is as uniform and as reproducible as possible. Standardization of methodology, periodic cine review and the use of some form of lesion quantification, such as handheld calipers, are strongly recommended.

3. Digital Imaging of Coronary Angiography

Recent advances in computer storage technology have made feasible digital acquisition, processing and archival storage of angiographic images obtained during cardiac catheterization. Widespread conversion from cineangiographic film to digital archiving and storage is anticipated during the next decade. Analog storage technologies such as super VHS videotape and analog optical disks have inadequate resolution to faithfully record coronary angiography. Digital storage methods are generally adequate but until recently have lacked standardization, which precluded easy exchange of digital angiograms between centers with different equipment. The development of the Digital Imaging and Communication standard (DICOM) for cardiac angiography ensures compatibility between equipment from participating vendors.

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In the interventional era, the advantages of digital angiography are important. The image quality provided by digital angiography is better than any common videotape format. Improvements in computer speed and processing capability enable rapid replay of coronary injection sequences, as well as evaluation of the results of each intervention and identification of complications such as intraluminal thrombus and dissection. In many laboratories, the availability of high-quality images during catheterization permits diagnostic and therapeutic catheterization to consist of a single procedure, a capability with significant implications for the cost of interventional procedures. Industry sources now estimate that >75% of existing laboratories are equipped with digital imaging capability.

In some cases, the conversion to filmless catheterization has resulted in inadequate archiving. For example, storage of digital angiographic studies on analog super VHS videocassette tape results in significant image degradation, offering at best only ≈50% the resolution of the original digital image. Angiograms stored on analog videocassette tape are often inadequate for clinical decision making. Another format, analog optical disks, has been commonly used to replace cine film. Image quality is better than videotape, and equivalency to film has been reported. Other proposed systems use data compression to enable storage of complete studies on limited-capacity media. However, high levels of data compression may produce measurable image degradation with an uncertain clinical impact.

a. The DICOM Standard

The ACC Cardiac Catheterization Committee is coordinating efforts to develop and promote a standard for archival storage and exchange of digital cardiac angiography. The committee has joined in this common cause with an industry organization, the National Electrical Manufacturers Association (NEMA), and representatives of the American College of Radiology (ACR). The ACR and NEMA have recently released an interim standard known as Digital Imaging Communication in Medicine (DICOM version 3.0).

The initial efforts of the standards committee have focused on adoption of a file format and physical medium for interchange of digital angiographic studies. To transfer images between medical centers, the sender would generate a DICOM-compatible file for review by the receiver. Recently, this working group has chosen a recordable form of the common CD-ROM, termed CD-R, as the official exchange medium. Nearly all equipment vendors have announced support for this format.

Recommendations

Class I

None.

Class IIa

Replacement of cine film by a digital storage modality that meets the DICOM standards to ensure exchangability of angiographic studies. ***(Level of Evidence: C)***

Class III

Replacement of cineangiographic film by videotape or other existing analog storage media that do not meet DICOM standards. ***(Level of Evidence: C)***

4. Limitations

Although coronary angiography is considered the reference standard for anatomic assessment of coronary obstructions, there are limitations to the technique. When luminal narrowings are present on coronary angiography (in the absence of spasm), pathological analyses almost always demonstrate severe atherosclerotic obstruction. Even minor angiographic abnormalities are associated with a poorer long-term outcome than are completely normal–appearing angiograms. Coronary angiography has a high predictive value for the presence of CAD when abnormalities are present. However, the converse is not true. A normal coronary angiogram does not exclude atherosclerosis, and in fact, most pathological studies suggest that angiography grossly underestimates the extent and severity of atherosclerosis (451–455). Several factors contribute to this discrepancy.

First, angiography depicts coronary anatomy from a planar two-dimensional silhouette of the contrast-filled vessel lumen. However, coronary lesions are often geometrically complex, with an eccentric luminal shape such that one angle of view may misrepresent the extent of narrowing (452). Two orthogonal angiograms should demonstrate more correctly the severity of most lesions, but adequate orthogonal views are frequently unobtainable because the stenosis may be obscured by overlapping side branches, disease at bifurcation sites, radiographic foreshortening or tortuosity. This can be especially difficult in the left main coronary artery, where identifying a significant stenosis is of utmost clinical importance (420).

Second, an adaptive phenomenon, coronary "remodeling," contributes to the inability of coronary angiography to identify mild atherosclerosis (456). Remodeling was initially observed on histology as the outward displacement of the external vessel wall in vascular segments with significant atherosclerosis. In the early phases of atherosclerosis, this vessel enlargement "compensates" for luminal encroachment, thereby concealing the atheroma from the angiogram. When the atherosclerotic plaque becomes severe, luminal encroachment becomes evident. Although such mild lesions do not restrict blood flow, clinical studies have demonstrated that these minimal or even unseen angiographic lesions represent an important predisposing cause of acute coronary syndromes, including MI (344).

Third, assessment of luminal diameter narrowing is complicated by the frequent absence of a normal reference segment

(437). Angiography visualizes only the lumen of the vessel and cannot determine if the wall of the reference segment has atherosclerosis (451–455). In the presence of diffuse reference-segment disease, percent stenosis will predictably underestimate the true amount of diameter narrowing.

Finally, in the setting of percutaneous intervention, the assumptions underlying simple projection imaging of the lumen are further impaired. Necropsy studies and intravascular ultrasound demonstrate that most mechanical coronary interventions exaggerate the extent of luminal eccentricity by fracturing or dissecting the atheroma within the lesion (457–461). The angiographic appearance of the postintervention vessel often consists of an enlarged, although frequently "hazy" lumen (458). In this setting, the lumen size on angiography may overestimate the vessel cross-sectional area and misrepresent the actual gain in lumen size.

Experimental and clinical studies have shown that when percent stenosis is >50%, the ability to increase blood flow in response to metabolic demands is impaired (462). This augmentation of coronary blood flow to demand is termed the coronary flow reserve. Determination of CFR requires measurement of blood flow at rest and after induction of reactive hyperemia, usually by administration of a coronary vasodilator. Several methods for measurement of CFR in patients have been developed, including intracoronary Doppler flow probes, digital angiography and quantitative PET (463–466). Although each of these approaches correlates with the angiographic severity of coronary lesions and their physiological effects, significant discrepancies exist among the techniques. Animal and human studies show that a normal CFR should exceed ≈5:1 (hyperemic to basal flow ratio). Flow reserve remains normal until stenosis severity approaches a 75% luminal area reduction or 50% diameter narrowing. For stenoses between 75% and 95% diameter narrowing, CFR falls progressively to reach values approaching unity. Because important stenoses occur in vessels 2 to 5 mm in diameter, the difference in minimal lumen diameter by angiography between a moderate and severe stenosis may comprise only a few tenths of a millimeter. Accordingly, the dissociation between angiographic and physiologic estimates is not surprising given the resolution limitations of angiography, the confounding effects of projection angles, the irregularity of luminal shape and the effect of diffuse disease (467). Several other factors weaken the correlation between angiographic measures of lesion severity and CFR, including ventricular hypertrophy, the metabolic state of the myocardium, and microvascular impairment (468–470). Thus, the epicardial stenosis seen by angiography is only one factor responsible for a reduction in flow reserve in patients with clinical symptoms. Accordingly, a stenosis incapable of producing angina in one patient can result in severe functional limitation in another.

Coronary collaterals can provide significant additional blood flow to territories served by stenotic vessels (471). In general, collaterals are not evident unless resting ischemia is present, such as that which occurs with a stenosis >90%. In many patients, collateral flow merely restores normal resting blood flow but does not provide adequate flow when metabolic demand increases. The presence of collaterals, however, is associated with preservation of myocardial function after MI, reduced myocardial ischemia on noninvasive stress testing, and reduced ischemia during angioplasty (472,473). Paradoxically, a greater ischemic response on noninvasive functional testing with adenosine than with exercise has been reported in the presence of collaterals, presumably due to an increase in the coronary steal phenomenon (474). Collateral blood flow can only be semiquantified by angiography (475), and precise assessment of perfusion by angiography is poor. This inability to adequately measure collateral flow is one of the factors that prevent accurate assessment of the functional significance of coronary stenoses by angiography alone (470).

These limitations have resulted in the development of new adjunctive imaging methods and physiologic measurements to help improve the assessment of CAD, as discussed later (476). Although these new adjunctive techniques have not replaced coronary angiography, they have provided additional valuable information that has allowed further determination of the severity and extent and physiologic significance of luminal obstructions. Coronary angiography, despite its limitations, remains the principal clinical tool in assessment of CAD and will likely remain so in the near future.

5. Contrast Agents

For an understanding of the pharmacologic properties and adverse effects of contrast agents, the reader is referred to the 1993 review of the subject by the ACC Cardiovascular Imaging Committee (477) and the 1996 review by Hirshfeld (478).

a. Selection of a Contrast Agent for Coronary Angiography

Except for a less potent anticoagulant effect, nonionic agents are better tolerated and have fewer side effects than ionic agents (477). Several randomized trials have compared their use during cardiac angiography. Barrett et al. (479) compared a nonionic low-osmolar contrast agent with an ionic high-osmolar contrast agent. Although adverse events were reduced, severe reactions were confined to patients with underlying severe cardiac disease. These authors supported the use of nonionic low-osmolar agents in these high-risk patients. Steinberg et al. (480) compared high- versus low-osmolar agents in 505 patients and found a significant difference in moderate but not severe reactions. They concluded that routine use of low-osmolar agents in all patients was not justified. In a single-center, randomized, blinded study of 2,166 patients undergoing coronary angiography, diatrizoic acid (Hypaque 76) was compared with iohexol (Omnipaque) (25). The overall incidence of severe contrast-related adverse reactions was lower with iohexol versus diatrizoic acid (2.6% vs. 4.6%; $p = 0.02$). The study

also demonstrated the important fact that in very high-risk patients, a two-fold lower incidence of adverse reactions occurred with nonionic agents. In patients not at high risk, however, no significant benefit was demonstrated.

The reduction in adverse events seen with the use of nonionic contrast media in diagnostic angiography may not be the same for patients undergoing interventional procedures because of their less potent anticoagulant effect compared with that of ionic agents. In a randomized trial of 211 patients with acute MI or unstable angina undergoing angioplasty, patients receiving ionic contrast media had fewer acute complications, fewer symptoms of angina and less need for subsequent bypass surgery during follow-up. Whether these differences would still be evident with the widespread use of new antiplatelet therapy, including platelet glycoprotein IIb/IIIa receptor inhibitors, remains to be demonstrated.

The primary reason not to routinely use nonionic agents is cost, because the price difference between nonionic and ionic agents in the U.S. is 12- to 25-fold. It has been estimated that uniform use of nonionic contrast agents would cost $1.1 billion in the U.S. alone (481). As reported above, patients at high risk for adverse outcomes benefit the most from the use of nonionic contrast agents. The difference in the incidence of any major contrast reaction is proportional to the New York Heart Association clinical function class, rising from 0.5% for class I patients to 3.6% for class IV patients (482). Given these observations, it has been suggested that nonionic agents should be reserved for patients who are at high risk for adverse reactions and that ionic agents should be used for all other patients (478). Factors that have been associated with high risk of adverse reactions to contrast media include prior adverse reaction to contrast agents, age >65 years, New York Heart Association functional class IV (or hemodynamic evidence of congestive heart failure), impaired renal function (creatinine >2.0 mg/dL), acute coronary syndromes (unstable angina or acute MI) and severe valvular disease (aortic valve area <0.7 cm^2 or mitral valve area <1.25 cm^2) (478). It is recommended that the individual practitioner appropriately assess the cost and benefit relationship when selecting contrast agents in any individual patient and that a strategy of reserving nonionic agents for patients who are at high risk of adverse reactions is prudent and cost-effective.

6. Pharmacologic Assessment of Coronary Spasm

a. Coronary Artery Spasm

Epicardial coronary arteries exhibit vasoactivity similar to that of many systemic arteries of a similar caliber. The presence of atherosclerotic plaque is associated with endothelial dysfunction, which can increase or decrease segmental responses to endogenous and exogenous vasoactive substances. Thus, patients with coronary atherosclerosis may have spontaneous increases in coronary vasomotor tone, resulting in myocardial ischemia. These regional coronary vasospastic events can cause ischemia associated with a variety of ST and T-wave changes. Tobacco and cocaine abuse are important risk factors for the provocation of vasospasm. Provocative testing with either methylergonovine or acetylcholine often demonstrates the presence of coronary spasm. Although vasomotion can result in as much as a 20% change in lumen diameter, coronary spasm is considered to be present when a reduction in lumen caliber of >50% occurs during a provocative test and reversal is achieved with intracoronary nitroglycerin.

Prinzmetal variant angina is a clinical syndrome occurring in a small percentage of patients without angiographic evidence of significant stenosis or normal angiograms in whom ischemia is caused by severe spasm of an epicardial coronary artery. Variant angina, as described by Prinzmetal in 1959 (483), is an unusual syndrome characterized by ischemic myocardial pain that usually occurs at rest, with accompanying ECG ST-segment elevation. Basal coronary artery vasoreactivity and tone are increased in variant angina. Studies using ^{123}I metaiodobenzylguanidine (^{123}I MIBG) SPECT demonstrate regional myocardial sympathetic dysinnervation in patients with variant angina (484). Tobacco and cocaine may cause episodes of variant angina, the latter because it blocks presynaptic uptake of norepinephrine and dopamine, thereby facilitating alpha-adrenergically mediated vasospasm. Cardiac arrhythmias, including ventricular tachycardia and fibrillation, heart block, acute infarction and sudden death, may occur in association with variant angina. Studies using ^{123}I BMIPP, a branched fatty acid, have demonstrated myocardial injury in association with some episodes of variant angina (485).

b. Provocative Testing for Spasm

Of the tests available to demonstrate coronary spasm, provocation by ergonovine maleate, methylergonovine maleate, acetylcholine or hyperventilation are the most useful. Ergonovine maleate for injection is no longer available, and the availability of methylergonovine is limited. The intravenous administration of incremental doses of methylergonovine starting at 0.05 mg to a maximum of 0.40 mg is both sensitive and specific, and there is an inverse relationship between the dose required to provoke spasm in the laboratory and the frequency of spontaneous episodes experienced by the patient. To ensure a valid test, nitrates and calcium antagonists must be withdrawn for ≥48 h before testing. Women are more sensitive than men to methylergonovine (486).

The intracoronary route of administration of methylergonovine for provocation of spasm is safe, sensitive and specific. This route is preferable in hypertensive patients and affords the opportunity to evaluate the left and right coronary circulations separately. Small dosing increments of 5 to 10 μg are used, with a total dose not to exceed 50 μg (487).

Absolute contraindications to methylergonovine include pregnancy, severe hypertension, severe left ventricular dys-

function, moderate to severe aortic stenosis and high-grade left main coronary stenosis. Relative contraindications include uncontrolled or unstable angina, uncontrolled ventricular arrhythmia, recent MI and advanced coronary disease.

Alternatively, intracoronary acetylcholine can be used as a provocative test for spasm, and its effectiveness is comparable to methylergonovine. Acetylcholine is infused over 1 min into a coronary artery in incremental doses of 10, 25, 50 and 100 μg. Doses should be separated by 5-min intervals. The same procedural safeguards must be used with acetylcholine and methylergonovine (486).

In patients with ≥1 episode of variant angina per day, the hyperventilation provocative test is nearly as effective as methylergonovine in causing vasospasm (488). In patients with less frequent attacks, hyperventilation is less sensitive. The test requires a patient to hyperventilate vigorously at 30 respirations per minute for 5 min. With this degree of hyperventilation, arterial pH will increase to ≈7.60 and pCO_2 will decrease to ≈20 mm Hg. Variant angina, if provoked, will occur during hyperventilation and will subside more rapidly than after methylergonovine infusion. The cold presser test can also provoke coronary spasm but is less reliable than pharmacologic techniques.

In patients with ST-segment elevation during episodes of chest pain and a normal coronary angiogram, provocative tests are usually not necessary, because ample clinical evidence is present to confirm the diagnosis of coronary spasm.

Recommendations for Pharmacologic Assessment of Coronary Disease 48 H After Withdrawal of Coronary Vasodilators

Class I

None.

Class IIa

Recurrent episodes of apparent ischemic cardiac pain at rest in a patient found to have a normal or mildly abnormal coronary angiogram and in whom there have been no clinical observations substantiating the diagnosis of variant angina, i.e., ST-segment elevation during pain. ***(Level of Evidence: C)***

Class IIb

1. **Recurrent episodes of ischemic cardiac pain at rest with associated transient ST-segment elevation in a patient subsequently found to have a normal or mildly abnormal coronary angiogram in whom medical therapy has been unsuccessful in controlling symptoms of ischemia.** ***(Level of Evidence: C)***
2. **After recovery from sudden cardiac death in a patient subsequently found to have a normal or mildly abnormal coronary angiogram and no other detectable significant cardiac disease.** ***(Level of Evidence: C)***

Class III

1. **Any absolute contraindication to pharmacologic challenge, including possible pregnancy, severe hypertension, severe left ventricular dysfunction, moderate to severe aortic stenosis or high-grade left main coronary stenosis.** ***(Level of Evidence: C)***
2. **Patients with any relative contraindication to pharmacologic testing, including uncontrolled or unstable angina, uncontrolled ventricular arrhythmia, recent MI or severe three-vessel coronary disease.** ***(Level of Evidence: C)***

APPENDIX C

Alternative Imaging Modalities

1. Coronary Intravascular Ultrasound

The recent development of intravascular ultrasound represents an emerging alternative to angiography for direct visualization of coronary anatomy during diagnostic and interventional catheterization (118,489–491). Unlike angiography, which depicts a silhouette of the coronary lumen, intravascular ultrasound portrays the vessel from a tomographic, cross-sectional perspective. This orientation enables direct measurements of lumen dimensions, including minimum and maximum diameter and cross-sectional area. Measurements obtained by ultrasound are considered more accurate than angiographic dimensions. In addition to luminal measurements, the ability of coronary ultrasound to image the soft tissues within the arterial wall enables characterization of atheroma size, plaque distribution and lesion composition during diagnostic or therapeutic catheterization. Accordingly, ultrasound can detect the presence or absence of structural abnormalities of the vessel wall after mechanical interventions, including dissections, tissue flaps, and irregular surface features.

Intravascular Ultrasound Devices

Intracoronary ultrasound equipment consists of two major components, a catheter incorporating a miniaturized transducer and a console containing the necessary electronics to reconstruct an ultrasound image. Modern catheters typically range in size from 2.9F to 3.5F, a corresponding diameter of 0.96 to 1.17 mm. Two dissimilar technical approaches to transducer design have emerged: mechanically rotated imaging devices and a 64-element electronic array device. Most systems use a monorail design to facilitate rapid catheter exchanges.

Artifacts and Limitations

Mechanical transducers may exhibit cyclical oscillations in rotational speed, with nonuniform rotational distortion (NURD), which arises from mechanical drag on the catheter driveshaft producing visible distortion. The NURD is most evident when the driveshaft is bent into a small radius of curvature by a tortuous vessel and is recognized as

circumferential "stretching" of a portion of the image with compression of the contralateral vessel wall. An additional artifact, transducer ring-down, appears in virtually all medical ultrasound devices. This artifact arises from acoustic oscillations in the piezoelectric transducer material, resulting in high-amplitude signals that obscure near-field imaging. All intravascular imaging systems are vulnerable to geometric distortion produced by oblique imaging. Thus, when the ultrasound beam interrogates a plane not orthogonal to the vessel walls, an artery with a circular lumen appears elliptical in shape. Repeat ultrasound studies can be unreliable owing to imprecision in placement of the imaging transducer in exactly the same location on reimaging.

Safety of Coronary Ultrasound

Although intravascular ultrasound requires intracoronary instrumentation, initial studies conducted during diagnostic catheterization demonstrated few serious untoward effects. Transient coronary spasm occurs in ≈5% of patients but usually responds rapidly to administration of intracoronary nitroglycerin (492). The imaging transducer can transiently occlude the coronary when advanced into a tight stenosis or a small distal vessel, but patients generally do not experience chest pain if the catheter is promptly withdrawn. In interventional practice, operators have safely used coronary ultrasound after most types of procedures, including balloon angioplasty, atherectomy, rotablation and stent deployment. Despite the relative safety of coronary ultrasound, any intracoronary instrumentation carries the potential risk of intimal injury or acute vessel dissection. Although many centers use intravascular ultrasound during diagnostic catheterization, most laboratories limit credentialing for intravascular imaging procedures to personnel with interventional training. In the unlikely event of intimal disruption, this safety measure ensures that the necessary personnel and equipment are immediately available to initiate appropriate interventional corrective action.

Quantitative Luminal Measurements

Diagnostic and interventional practitioners routinely use luminal measurements to evaluate the severity of stenoses, determine the size of the "normal" reference segment and assess gain in lumen size achieved by revascularization. Comparisons of vessel dimensions by angiography and intravascular ultrasound generally reveal a limited correlation, particularly for vessels with an eccentric luminal shape (490,492–494), presumably owing to the inability of angiography to accurately portray the complex, irregular cross-sectional profiles of atherosclerotic vessels.

Angiographically Unrecognized Disease

Intravascular ultrasound commonly detects atherosclerotic abnormalities at angiographically normal coronary sites (493–495). The long-term implications of these findings remain uncertain. However, Little and others (344) have demonstrated that plaques with minimal to moderate angiographic narrowing are the most likely to rupture and cause acute MI. Accordingly, the presence of angiographically occult coronary disease may have important prognostic significance. Studies are currently under way to determine the predictive value of intravascular ultrasound in determining the prognosis in patients with coronary disease.

Lesions of Uncertain Severity

Despite thorough radiographic examination with multiple projections, angiographers commonly encounter lesions that elude accurate characterization. Lesions of uncertain severity often include ostial lesions and moderate stenoses (angiographic severity ranging from 40% to 70%) in patients whose symptomatic status is difficult to evaluate. For these ambiguous lesions, ultrasound provides tomographic measurements, enabling quantification of the stenosis independent of the radiographic projection (476,492–494). Bifurcation lesions are particularly difficult to assess by angiography because overlapping side branches often obscure the lesion.

Cardiac Allograft Disease

Identification of atherosclerotic lesions in cardiac allograft recipients represents a particularly challenging task (495,496). These patients may have diffuse vessel involvement that for reasons already enumerated conceals the atherosclerosis from angiography. Many large transplant centers now routinely perform intravascular ultrasound as an annual catheterization in all cardiac transplant recipients. Recent studies have revealed two pathways to transplant-associated atherosclerosis, with some patients receiving atherosclerotic plaques from the donor heart, whereas others develop immune-mediated vasculopathy (496).

Intravascular Ultrasound and Restenosis

The relatively poor correlation between angiographic and ultrasonic dimensions after angioplasty raises the issue of whether poor long-term results represent recurrence of disease or an inadequate initial procedure. Several multicenter clinical trials have shown that certain findings on ultrasound, such as minimal lumen diameter and plaque buildup, can predict restenosis after intervention (497,498). Ultrasound has also been shown to determine if "vascular remodeling" has occurred in de novo lesions or after PTCA (499).

Wall Morphology After Angioplasty

Pre- and post-PTCA imaging reveals that plaque fissuring occurs in 40% to 80% of patients, stretching of the vessel wall occurs in at least 20% of patients, and apparent "compression" of the atheromatous material occurs in at least 10% (500,501). More recent studies using automatic pullback devices (which withdraw the ultrasound catheter at a constant rate) have shown that "compression" may represent redistribution of plaque along the long axis of the

vessel. The prognostic significance of different mechanisms of luminal enlargement is under investigation.

Guidance of Directional Atherectomy

Intravascular ultrasound has been used to guide directional coronary atherectomy. By determining the location and composition of the target atheroma, ultrasound potentially improves preprocedural planning and may aid intraprocedural decision making by assisting in device orientation and extent of cuts (459,502).

Guidance of Rotational Atherectomy

Rotational ablation uses a high-speed, diamond-coated burr to debulk atheromata within coronary stenoses. This approach has been proved effective for removing superficial calcium from stenotic vessels. There is a poor correlation between ultrasound and fluoroscopy in assessment of the presence and amount of calcification (503,504). Accordingly, the demonstration of a heavily calcified vessel by ultrasound permits the operator to use rotational ablation in settings in which it may be particularly efficacious (505). Ultrasound is often used to size the vessel and determine the largest burr that can be safely used. Observational ultrasound studies to date have confirmed that ablation of plaque constitutes the primary mechanism of rotational atherectomy, particularly the more fibrotic or calcified components of the lesion.

Coronary Stent Deployment

Intravascular ultrasound has significantly influenced understanding of the mechanism underlying stent deployment and is now widely used in guiding clinical procedures. A large, nonrandomized ultrasound study of angiographically guided stent deployment revealed an average residual stenosis of 51% when ultrasound was used to compare minimum stent diameter with reference-segment diameter (506). Additional balloon inflations resulted in a final ultrasound that showed an average residual stenosis of 34% with a negative final angiographic percent stenosis (−7.0%). Ultrasound was used to guide deployment; this study reported a subacute thrombosis rate of only 0.3% with antiplatelet agents alone.

Optimal goals for ultrasound-guided stent deployment are yet to be determined. Most authorities recommend that operators attempt to achieve a minimum percentage of reference-vessel diameter within the stent, usually ≥70%. In addition, most protocols require nearly complete apposition, with separation of any strut from the vessel wall not >0.3 mm.

In stenting as a bailout for coronary dissection, intravascular ultrasound can prove helpful in determining the longitudinal extent of dissection before placement of a stent for vessel salvage.

Future Directions of Intravascular Ultrasound

During the next several years, technological advances in intravascular imaging are anticipated, including further reductions in the size of imaging catheters to guidewire dimensions (<0.025 in. [0.06 cm]). Higher-frequency transducers (e.g., 35 MHz) are now available and should improve resolution further. Combination devices are also undergoing refinement, permitting online guidance during revascularization procedures. An angioplasty balloon with an ultrasound transducer has been approved by the Food and Drug Administration, and a transducer combined with an atherectomy device is under development (507). As a consequence of refinements in equipment and knowledge derived from clinical investigations, it is anticipated that intravascular ultrasound will play an increased role in the diagnosis and therapy of coronary disease in the near future.

Recommendations for Coronary Intravascular Ultrasound

Class I

None.

Class IIa

1. **Evaluation of lesion severity at a location difficult to image by angiography in a patient with a positive functional study and a suspected flow-limiting stenosis.** ***(Level of Evidence: C)***
2. **Assessment of a suboptimal angiographic result after coronary intervention.** ***(Level of Evidence: C)***
3. **Diagnosis and management of coronary disease after cardiac transplantation.** ***(Level of Evidence: C)***
4. **Assessment of the adequacy of deployment of the Palmaz-Schatz coronary stent, including the extent of stent apposition and determination of the minimum luminal diameter within the stent.** ***(Level of Evidence: B)***

Class IIb

1. **Determination of plaque location and circumferential distribution for guidance of directional coronary atherectomy.** ***(Level of Evidence: C)***
2. **Further evaluation of patients with characteristic anginal symptoms and a positive functional study with no focal stenoses or mild CAD on angiography.** ***(Level of Evidence: C)***
3. **Determination of the mechanism of stent restenosis (inadequate expansion versus neointimal proliferation) and to enable selection of appropriate therapy (plaque ablation versus repeat balloon expansion).** ***(Level of Evidence: C)***
4. **Preinterventional assessment of lesional characteristics 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.**
2. **Intracoronary Doppler Ultrasound**

2. Intracoronary Doppler Ultrasound

Intracoronary Doppler Velocimetry

The development of small intracoronary devices incorporating a Doppler flow transducer has made feasible the physiological assessment of coronary blood flow in vivo during diagnostic or therapeutic catheterization. Doppler flow probes are commonly used to evaluate ambiguous lesions and to determine the success of coronary interventions at restoring normal flow reserve.

Principles of Doppler Flow Measurement

Blood flow velocity is calculated by the Doppler equation. Analysis of the Doppler coronary blood flow signal typically relies on one of two common techniques. The zero-crossings method is simple and accurate in areas of laminar flow but is imprecise in nonlaminar flow such as that which occurs distal to stenosis and in the measurement of peak velocities (508). The second method of signal processing uses spectral analysis with the fast Fourier transformation (FFT). In vitro, animal and human models have consistently shown that FFT analysis is more accurate and correlates more closely with implanted electromagnetic flowmeter measurements in animals (509,510), and thus, the FFT has become the method of choice for intracoronary use.

Intracoronary Doppler Equipment and Techniques

The most commonly used device employs a miniaturized Doppler-equipped guidewire with a 12-MHz piezoelectric transducer integrated into the tip. The major advantages of this system include the small profile (0.018-in. [0.045 cm] or 0.014-in. [0.035 cm] diameter), favorable handling characteristics, and a negligible effect on luminal cross-sectional area, allowing the operator to advance the device into distal coronary segments and beyond stenoses. In addition, the guidewire device accommodates typical over-the-wire or monorail balloon angioplasty systems, thus enabling diagnostic and therapeutic procedures without exchange of the wire.

On this device, the transducer uses a pulsed waveform Doppler that samples 5.2 mm beyond the guidewire tip at an angle of 14° on either side of the centerline of flow using FFT signal processing and an adjustable pulse-repetition frequency ranging from 16 to 94 kHz. This system has been validated in in vitro and in vivo models by comparison with electromagnetic quantitative voltmetry (511). These studies have shown that blood flow velocity measurements by the Doppler guidewire exhibit a close correlation to measured flow (r^2 = 0.85 to 0.99).

Safety

This device has proved safe in a large number of procedures, and the risks of its use are similar to those of other intracoronary instrumentation (512).

Limitations of Doppler Flow

The Doppler guidewire device, like all similar catheters, is highly dependent on positioning within the coronary, and care and experience are necessary to obtain reliable measurements. Various artifacts related to wall motion and signals from adjacent venous structures can often be eliminated by repositioning the device to a more central location or by adjusting the J curve of the tip.

The measured velocity (V) is highly dependent on the angle of incidence (F). Alignment of the transducer to the direction of blood flow (F = 0°) is a requisite for accurate velocity measurement. The greater the angle, the smaller its cosine and the less accurate is the measurement of flow (508). The tight spatial coupling of transducer position to the sampled volume, which limits sampling of the blood volume, may not accurately reflect the velocity of the whole bloodstream at the interrogated location (513). This problem is particularly important in zones of turbulent flow (such as areas distal to severe stenoses) or lumen segments with odd geometric configuration, where different strata of the bloodstream may move at different velocities.

The blood flow velocity measured in coronary arteries is used as a surrogate for the actual volumetric flow. The two parameters are related by the formula:

$$Q = k \times A \times V$$

where Q is the volume of flow in mL/s, V is the velocity in cm/s, A is the cross-sectional area of the blood vessel in cm^2, and k is the constant that adjusts for mean velocity. In a conduit with a relatively constant cross-sectional area, the velocity is directly related to the volumetric flow. Conversely, under conditions of constant blood flow, velocity is inversely related to vessel cross-sectional area. However, it must be remembered that velocity may not represent a good surrogate for flow if the cross-sectional area changes or the Doppler probe moves slightly and lies in an adjacent coronary segment with a different cross-sectional area.

Coronary Flow: Normal and Abnormal

Flow patterns differ substantially among different coronary segments. The proximity of most of the left coronary artery to the transmitted pressure from the left ventricle has a major effect on flow characteristics, whereas the right coronary artery is subject to much smaller variations. Under normal conditions, flow in the left coronary artery and its branches occurs primarily in diastole, whereas the right coronary artery exhibits a more homogenous distribution of flow throughout the cardiac cycle. Pulsatile flow is presumed secondary to the "reservoir" that is compressed during the systolic phase of the cardiac cycle, which subsequently is refilled during the following diastole (514).

The pulsatile pattern of flow represents one method for Doppler assessment of a coronary stenosis, because a hemodynamically important narrowing significantly depresses the diastolic component (515,516). Under these circumstances, most of the flow occurs in systole, although average peak velocity may remain relatively preserved. The redistribution of flow is a marker for the hemodynamic significance of the lesion, although this approach is limited to vessels with a systolic-to-diastolic flow distribution characteristic of the

left coronary. Preliminary data suggests that the relative contribution of collateral flow to the perfusion of an ischemic territory may be assessed by Doppler flow measurements (517). The venous flow pattern in the heart has mostly a systolic component, while saphenous vein grafts and arterial conduits behave according to the pattern of flow in the native artery to which they are grafted.

In the human coronary artery, average peak velocity varies between 9 and 70 cm/s. In an individual patient, this value is similar among the three coronary vessels (516). The value of peak flow in the assessment of coronary flow is limited, because a number of confounding variables (such as cardiac output, vessel cross-sectional area and abnormal myocardium) affect the average peak velocity. Despite branching, experimental data demonstrate that the coronary arterial tree maintains relatively constant flow velocities (518). This phenomenon can be used to characterize hemodynamically significant lesions as a reduction in the velocity (and volume) of flow in the distal portion of the stenotic artery. This translates into an abnormally high ratio of proximal to distal average peak velocities (516,519).

Assessment of Intermediate Coronary Lesions

In clinical practice, intermediate lesions, typically with a 30% to 70% diameter reduction, are difficult to assess by angiography alone. The intracoronary Doppler guidewire has been used to evaluate such lesions by providing physiological measurements of stenosis severity. Measurement of proximal and distal diastolic-to-systolic velocity ratios (DSVRs) can be obtained and a proximal-to-distal (P/D) ratio of average peak velocities calculated (463,520).

In evaluating a stenosis, the final assessed parameter is CFR. Doppler assessment of CFR requires measurement of the ratio of hyperemic to basal flow after the pharmacological stimulation (usually by adenosine) of maximal blood flow (521). The absence of an appropriate increase in velocity during hyperemia constitutes abnormal flow reserve. However, other factors, for example, left ventricular hypertrophy or myocardial scar, are associated with abnormal CFR (521,522). Despite these limitations, the CFR parameter often provides valuable information.

In clinical practice, a DSVR <1.8 for the left coronary artery, a P/D ratio >1.7, and a CFR <2.0 are indicators of hemodynamically significant lesions. The validity of these observations has been shown in studies comparing Doppler with SPECT ^{201}Tl imaging, which report an overall predictive accuracy of 94% (523,524). Donohue et al. (525) compared angiographic findings with translesional pressure gradients and Doppler wire measurements. There was a highly statistically significant difference in the distal average peak velocity, DSVR, and CFR values in patients with lesional gradients >20 mm Hg compared with those with lesser gradients.

Intracoronary Doppler measurements can also identify patients who do not need revascularization. Mozes et al. (53) used Doppler-derived measurements to defer intervention in 42 patients with intermediate lesions who subsequently showed an excellent event-free survival at 10 ± 6 months of follow-up. Similar results were reported by Lesser et al. (526). Although additional work is required before this technique can be more widely adopted, these data support the hypothesis that patients can be stratified in the catheterization laboratory with the information derived from intracoronary Doppler measurements.

Flow Alterations After Angioplasty

Doppler flow measurements are sometimes used to assess the results of percutaneous revascularization. Angiographically successful coronary revascularization is usually associated with restoration of normal Doppler flow characteristics, including normalization of the P/D ratio and a return of diastolic predominance. In some patients, the CFR normalizes immediately after angioplasty, but flow reserve must be interpreted cautiously, because angioplasty may increase absolute flow velocity secondary to transient, postischemic (postballoon) hyperemia (519,527).

The continuity equation can be used to estimate the residual lumen narrowing:

$$APV_L \times A_L = APV_D \times A_D$$

where APV is average peak velocity, A_L is area within the lesion, and A_D is area distal to the lesion.

The calculated diameter reflects the actual channel through which blood flows rather than the anatomic dimensions. Nevertheless, this value can be useful in evaluating the functional stenosis after intervention, particularly in segments poorly visualized angiographically (such as bends and superimposed vessels) (528,529). Onodera et al. (530) reported that postintervention Doppler flow characteristics correlate with the relative risk of restenosis. These investigators observed a higher proximal and distal average peak velocity in arteries that subsequently developed restenosis, independent of angiographic stenosis severity immediately after intervention.

Recommendations for Intracoronary Doppler Ultrasound

Class I

None.

Class IIa

Assessment of the physiological effects of intermediate coronary stenoses (30% to 70% luminal narrowing) in patients with anginal symptoms. Doppler velocimetry may also be useful as an alternative to performing a noninvasive functional study to determine whether an intervention is warranted for intermediate lesions (or when the functional study is ambiguous). ***(Level of Evidence: C)***

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)***

2. **After cardiac transplantation, diagnosis of impaired CFR in patients with anginal symptoms but no apparent angiographic culprit lesion.** ***(Level of Evidence: C)***
3. **Assessment of the severity of coronary flow abnormalities in patients with anginal symptoms and a positive noninvasive functional study but no apparent angiographic lesion.** ***(Level of Evidence: C)***

Class III

Routine assessment of the severity of angiographic disease in patients with a positive noninvasive functional study. ***(Level of Evidence: C)***

3. Coronary Angioscopy

Coronary angioscopy uses visible light conducted through fiberoptic filaments to provide direct visual assessment of the surface characteristics and intraluminal morphology in vivo. The images appear in color on a television monitor, which enables examination of the hue of the target lesion and associated plaques. Although difficult to use, angioscopy allows the differentiation of platelet-rich from fibrin-rich thrombus, and it may provide evidence of atheroma rupture, intraplaque hemorrhage, and coronary dissection. Accordingly, this diagnostic imaging modality yields information on the pathogenesis of acute coronary syndromes (531–536).

Angioscopy Equipment and Technique

All angioscopes require a blood-free field for clear visualization of the arterial wall. This is obtained by inflating a proximal balloon to temporarily occlude blood flow, followed by continuous saline irrigation, which requires a second catheter lumen. Two additional lumens are required for the optical fibers, one for visualization and another to serve as a light source. Videotape recording allows for more detailed offline analysis. A commonly used device is a 120-cm-long 4.5 monorail catheter with an imaging bundle containing 3,000 fibers that permits a viewing arc of ≈55° and a depth-of-field of 0.5 mm. A video camera displays the images in real time on a color monitor, while videotape recording allows for more detailed offline analysis.

Angioscopy of Unstable Coronary Syndromes

Small-scale studies of fiberoptic angioscopy demonstrate differences in the intraluminal appearance of stable versus unstable coronary lesions (537). An intraoperative study of 32 patients showed distinctive intimal abnormalities in all 10 patients with unstable angina: four patients had "complex plaque" and seven had overt intraluminal thrombus. Neither complex plaques nor thrombi were observed by angioscopy in any patient with stable coronary disease. These findings were later confirmed by percutaneous angioscopy (538). In 16 patients with unstable angina, 50% had thrombus and 14% had overt dissection. Neither thrombus nor dissection was seen in any of the four patients with stable angina.

In addition to identifying the presence of thrombus, angioscopy can differentiate platelet-rich from fibrin-rich thrombi. Mizuno et al. (539) performed angioscopy in 15 patients with unstable angina and 16 patients with acute MI. Angioscopy identified intraluminal thrombus in 29 of 31 patients. However, the typical thrombus in patients with unstable angina was grayish-white in color, suggesting the predominance of platelets, whereas in patients with acute MI, angioscopy identified a preponderance of red thrombi, suggesting an erythrocyte and fibrin-rich clot. Angioscopy can distinguish other surface features of coronary atheromata. Stable plaques are recognized by their elevated contour, smooth configuration, and yellowish-white color. In a study of 199 patients, those with predominantly yellow plaques were found to have higher LDL cholesterol and apolipoprotein B levels (540).

Angioscopy During Interventions

Assessment of lesions before or after coronary intervention represents the most commonly reported application of coronary angioscopy (533,534,536,538,541,542). Angioscopy after balloon angioplasty demonstrates that dissections and thrombus are present in almost all cases. However, no prospective data exist that demonstrate a different outcome for patients on the basis of angioscopic findings. The preprocedural identification of thrombus may also prove useful in selecting candidates for coronary stenting and for the use of any of the new antiplatelet agents. Although the value of angioscopy in identifying thrombus is well established, no data exist to suggest that angioscopy can reduce stent-related complications.

Limitations of Coronary Angioscopy

Despite recent technical advances, angioscopy is still limited to the proximal and mid portions of relatively straight, large epicardial coronary arteries. Furthermore, the rapid development of ischemia during balloon inflation limits the time of examination. For successful imaging, lesions need to be located ≥20 mm distal to the balloon site, which makes it impossible to visualize ostial or very proximal lesions. Angioscopy shows only the surface characteristics of plaques and cannot discern the underlying atheroma morphology. Accordingly, it remains unproved whether visualization of surface anatomy alone warrants the time, expense and risk of angioscopy. In addition, occlusion of coronary flow may produce important imaging artifacts. A recently published study of the European Working Group on Coronary Angioscopy (543) demonstrated that the identification of red thrombus and dissection has relatively close interobserver agreement. However, other angioscopic diagnoses have wide interobserver variability.

Recommendations for Coronary Angioscopy

Class I

None.

Class II

None.

Class III

Coronary angioscopy should be considered a research tool for which there are no established clinical indications.

4. Fractional Flow Reserve

The measurement of pressure gradients across coronary stenoses was the earliest method used to assess the adequacy of coronary angioplasty. However, because of the size of the catheter and changes in technology, angiographic and now ultrasonic assessments are more commonly used. Recently, small catheters and guidewires have been developed to more accurately measure pressure gradients across stenoses before and after interventional procedures. Pijls and colleagues demonstrated that just as with CFR measurements by Doppler ultrasound, fractional flow reserve is useful in assessing the severity of a coronary stenosis (544–549). The ratio of the mean pressure distal to a coronary stenosis to that proximal to the stenosis, usually measured through the guiding catheter after maximal vasodilation induced by adenosine or papaverine, can assess the severity of the stenosis. When this ratio falls below 75%, there is an 88% sensitivity and an 84% specificity for an abnormal exercise test. Similar correlations have been made with PET and CFR measured by Doppler ultrasound. The technique is easier to use than Doppler ultrasound. Although it is still in development and validation, it appears likely to be a useful tool in the future to assess coronary stenoses.

APPENDIX D

Canadian Cardiovascular Society Classification of Angina Pectoris

Class	Description of Stage
Class I	Ordinary physical activity does not cause angina, such as walking or climbing stairs. Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.
Class II	Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs quickly, walking uphill, walking or climbing stairs after meals, in the cold, in wind, under emotional stress, or only during the first few hours after awakening. Walking >2 blocks on the level and climbing >1 flight of ordinary stairs at a normal pace under normal conditions.
Class III	Marked limitations of ordinary physical activity. Angina occurs on walking 1–2 blocks on the level and climbing 1 flight of stairs in normal condition and at a normal pace.
Class IV	Inability to carry on any physical activity without discomfort: anginal symptoms may be present at rest.

From Campeau (87).

APPENDIX E

Elements of a Coronary Angiographic Report

This appendix lists certain items that may be useful if included in the coronary angiographic report. Practice will vary from laboratory to laboratory. Although this list is not inclusive, it should provide for adequate transmission of useful clinical information as well as for other purposes of medical record keeping.

Commercial coronary angiography laboratory systems provide for a semiautomated report to be generated promptly after the procedure. These also may include a graphic presentation of the coronary arterial anatomy. This is often a useful summary presentation of the examination.

I. Patient demographic information to include
   - Age
   - Gender
   - Height
   - Weight
   - Body surface area
   - Medical record number
   - Referring physician
   - Laboratory number

II. Operators and laboratory assistants

III. Indications for angiography

IV. Technical procedures to include
   - Informed consent
   - Anesthetic technique
   - Vascular approach and location
   - Catheter selection
   - Anatomic site of cannulations achieved
   - Injection technique
   - Contrast agent used
   - Volume of contrast agent used
   - Views recorded
   - Filming or recording modalities used
   - Baseline hemodynamics and alterations, if any
   - Radiographic views recorded
   - Preprocedure or intraprocedure medications administered

V. Hemodynamic data
   - Pressures
   - Cardiac outputs, if measured

VI. Angiographic interpretation
   - General considerations
     - Adequacy of examination
     - General anatomic presentation
   - Coronary artery arterial analysis by segment
     - The map depicted in Appendix A allows for examination of 29 named segments. Each can be judged for size, location and extent of arterial lesions.

Segments uninvolved by significant lesions should also be mentioned. The presence of features such as clot, aneurysm, collaterals and spasm should also be noted.

Analysis of vascular conduits (coronary bypass grafts, left internal thoracic grafts) should be assessed to include patency of the origin, body and anastomotic site, flow pattern and other abnormalities.

Analysis of left ventriculogram to include
- Adequacy of examination
- Rhythm
- Diastolic appearance
- Systolic appearance
- Global function
- Focal abnormality

Mitral and aortic valve function

Unusual features
- Clots
- Masses
- Aneurysms

VII. Diagnosis

VIII. Comments (if necessary)

IX. Recommendations (may or may not be included)

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