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# ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery)

*Developed in Collaboration With the American Association for Thoracic Surgery and the Society of Thoracic Surgeons*


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# 1. PREAMBLE and INTRODUCTION

## *1.1. 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 or 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 favorably affect 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, whose 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 when data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, as well as frequency of follow-up and cost-effectiveness. When available, information from studies on cost will be considered; however, review of data on efficacy and clinical outcomes will be the primary basis for preparing recommendations in these guidelines.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur. The relationships with industry information for the writing committee members is posted on the ACC (www.acc.org) and AHA (www.americanheart.org) World Wide Web sites with the full-length version of the update (Appendix 1), along with names and relationships with industry of the peer reviewers (Appendix 2).

These practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all of the circumstances presented by that patient.

The ACC/AHA 2004 Guideline Update for CABG was approved for publication by the ACCF Board of Trustees in March 2004 and the AHA Science and Advisory Coordinating Committee in June 2004. The summary article, describing the major areas of change reflected in the update, is published in the August 31, 2004 issue of *Circulation* and the September 1, 2004 issue of the *Journal of the American College of Cardiology.* The full-text guideline is posted on the ACC (www.acc.org) and the AHA (www.americanheart.org) World Wide Web sites. These guidelines will be reviewed 1 year after publication and yearly thereafter and considered current unless the Task Force on Practice Guidelines revises or withdraws them from circulation.

*Elliott M. Antman, MD, FACC, FAHA*
*Chair, ACC/AHA Task Force on Practice Guidelines*

## *1.2. Introduction*

The ACC/AHA Task Force on Practice Guidelines was formed to make recommendations regarding the appropriate use of diagnostic tests and therapies for patients with known or suspected cardiovascular disease. Coronary artery bypass graft (CABG) surgery is among the most common operations performed in the world and accounts for more resources expended in cardiovascular medicine than any other single procedure. Since the initial guidelines for CABG surgery were updated and published in 1991 (1), there has been additional evolution in the surgical approach to coronary disease while at the same time there have been significant advances in preventive, medical, and percutaneous catheter approaches to therapy.

The current Writing Committee was charged with updating the guidelines published in 1999 (1a). The Committee reviewed pertinent publications, including abstracts, through a computerized search of the English literature since 1999 and performed a manual search of final articles. Special attention was devoted to identification of randomized trials published since the original document. A complete listing of all publications covering coronary bypass surgery in the past 4 years is beyond the scope of this document. However, evidence tables were updated to reflect major advances over this time period. Inaccuracies or inconsistencies present in the original publication were identified and corrected when possible. Recommendations provided in this document are based primarily on published data. Because randomized trials are unavailable in many facets of coronary artery disease (CAD) treatment, observational studies and, in some areas, expert opinion form the basis for recommendations that are offered. In each section of the Indications (Section 9), the relative levels of evidence favoring the Class I, II, and III indications were noted.

All of the recommendations in this guideline update have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document, would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines. Also, the level of evidence, either an A, B, or C, for each recommendation is now provided.

Classification of Recommendations and Level of Evidence are expressed in the ACC/AHA format as follows and described in more detail in Table 1.

### Classification of Recommendations

**Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.**

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

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

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

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

### Level of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.

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

Level of Evidence C: Only consensus opinion of experts, case studies, or standard-of-care.

The Committee consists of acknowledged experts in cardiac surgery, interventional cardiology, general cardiology, and family practice. The Committee included representatives from the American Academy of Family Physicians (AAFP) and the Society of Thoracic Surgeons (STS). Both academic and private practice sectors were represented. The document was reviewed by 3 outside observers nominated by the ACC, 3 outside reviewers nominated by the AHA, and outside reviewers nominated by STS and the Society of Cardiovascular Anesthesiologists. This document was approved by the American College of Cardiology Foundation's Board of Trustees and the American Heart Association's Science Advisory and Coordinating Committee, as well as endorsed by the American Association for Thoracic Surgery and the Society of Thoracic Surgeons.

These guidelines overlap several previously published ACC/AHA guidelines, including those for the management of acute myocardial infarction (MI), for the management of stable angina, for percutaneous coronary intervention (PCI), and for exercise testing. For each of these guidelines, an analysis of overlap or contradiction has been explored by the Committee with attempts to create consensus in each instance. Finally, it is acknowledged that no guideline can take into account all of the various parameters that must be part of the individual decision to recommend CABG for a single patient. However, this entire report is intended to provide a framework that healthcare providers can use in combination with other types of knowledge and patient preferences to make rational decisions about treatment.

## 2. GENERAL CONSIDERATIONS AND BACKGROUND

Surgical revascularization for atherosclerotic heart disease is one of the great success stories in medicine. Relief of angina after revascularization, improvement in exercise tolerance, and the realization of survival benefit have attended the operation since the early stages of development. The evolution of coronary surgery is a story of focused thought, dedication, courage, collaboration, and serendipity.

Alexis Carrel (1872 to 1944) understood the association between angina pectoris and coronary stenosis (2). Before World War I, he had developed a canine model of aortocoronary anastomosis using carotid arteries as a conduit. For his seminal work in the development of cardiovascular surgical techniques, he was awarded the Nobel Prize. Carrel's contributions lay fallow, as he had predicted, until a time when advances in technology would allow safe application to humans.

Carrel and the aviator Charles Lindbergh collaborated in the 1930s in developing a primitive heart-lung machine intended to allow direct cardiac operation. Lindbergh was driven to this project by the desire to save a family member dying of valvular heart disease. The project did not produce a clinically useful device, but it did make incremental progress toward the ultimate goal (3). Over a professional lifetime of intense dedication, John Gibbon developed a clinically useful cardiopulmonary bypass (CPB) technology and applied it successfully to a patient in 1953 (4).

With direct coronary operation awaiting advancing techniques, surgical efforts to relieve angina pectoris in the mid-20th century included suppression of metabolic stimulation through thyroidectomy and augmentation of noncoronary flow to the myocardium through creation of pericardial or omental adhesions. Attempts to create an artificial collateral by implantation of the internal mammary artery (IMA) into the myocardium, the Vineberg procedure, met with limited success (5).

Coronary surgery moved into the modern era in the 1950s. It is not entirely clear to whom credit should be given for the first coronary bypass. The first direct surgical approach to the coronary circulation in a patient was likely performed by William Mustard in 1953 in Toronto, who used a carotid-to-coronary bypass. The patient did not survive the operation.

The first clinical use of the IMA to graft a coronary vessel appears to have been in response to an intraoperative misadventure. William Longmire applied the technique of coronary endarterectomy in a series of patients in 1958. A right coronary artery disintegrated during one of these operations, and an IMA was placed as a direct graft to restore flow. In retrospect, the surgeon thought it to be a good operation (2).

**Table 1.** Applying Classification of Recommendations and Level of Evidence

"Size of Treatment Effect"

"Estimate of Certainty (Precision) of Treatment Effect"

| | Class I<br><br>*Benefit >>> Risk*<br><br>Procedure/Treatment SHOULD be performed/administered | Class IIa<br><br>*Benefit >> Risk*<br>*Additional studies with focused objectives needed*<br><br>IT IS REASONABLE to perform procedure/administer treatment | Class IIb<br><br>*Benefit ≥ Risk*<br>*Additional studies with broad objectives needed; Additional registry data would be helpful*<br><br>Procedure/Treatment MAY BE CONSIDERED | Class III<br><br>*Risk ≥ Benefit*<br>*No additional studies needed*<br><br>Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL |
|---|---|---|---|---|
| Level A<br><br>*Multiple (3-5) population risk strata evaluated**<br><br>*General consistency of direction and magnitude of effect* | • Recommendation that procedure or treatment is useful/effective<br>• Sufficient evidence from multiple randomized trials or meta-analyses | • Recommendation in favor of treatment or procedure being useful/effective<br>• Some conflicting evidence from multiple randomized trials or meta-analyses | • Recommendation's usefulness/efficacy less well established<br>• Greater conflicting evidence from multiple randomized trials or meta-analyses | • Recommendation that procedure or treatment not useful/effective and may be harmful<br>• Sufficient evidence from multiple randomized trials or meta-analyses |
| Level B<br><br>*Limited (2-3) population risk strata evaluated** | • Recommendation that procedure or treatment is useful/effective<br>• Limited evidence from single randomized trial or non-randomized studies | • Recommendation in favor of treatment or procedure being useful/ effective<br>• Some conflicting evidence from single randomized trial or non-randomized studies | • Recommendation's usefulness/efficacy less well established<br>• Greater conflicting evidence from single randomized trial or non-randomized studies | • Recommendation that procedure or treatment not useful/effective and may be harmful<br>• Limited evidence from single randomized trial or non-randomized studies |
| Level C<br><br>*Very limited (1-2) population risk strata evaluated** | • Recommendation that procedure or treatment is useful/effective<br>• Only expert opinion, case studies, or standard-of-care | • Recommendation in favor of treatment or procedure being useful/ effective<br>• Only diverging expert opinion, case studies, or standard-of-care | • Recommendation's usefulness/efficacy less well established<br>• Only diverging expert opinion, case studies, or standard-of-care | • Recommendation that procedure or treatment not useful/effective and may be harmful<br>• Only expert opinion, case studies, or standard-of-care |
| **Suggested phrases for writing recommendations †** | should<br>is recommended<br>is indicated<br>is useful/effective/beneficial | is reasonable<br>can be useful/effective/ beneficial<br>is probably recommended or indicated | may/might be considered<br>may/might be reasonable<br>usefulness/effectiveness is unknown /unclear/uncertain or not well established | is not recommended<br>is not indicated<br>should not<br>is not useful/effective/beneficial<br>may be harmful |

*Data available from clinical trials or registries about the usefulness/efficacy in different sub-populations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use.

†In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All recommendations in the CABG guideline update have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers' comprehension of the guidelines and will allow queries at the individual recommendation level.

Michael DeBakey and Edward Garrett had a similar experience with a left anterior descending (LAD) coronary endarterectomy in 1964 (6). This situation was salvaged by an aortocoronary saphenous vein graft (SVG). The patient did well and had a patent aortocoronary SVG when restudied 8 years later. This experience was subsequently recorded and recognized as the first successful clinical aortocoronary SVG. An aortocoronary SVG operation by David Sabiston at Duke in 1962, involving an anastomotic end-to-end technique done without the use of CPB, was the first planned saphenous vein operation but was complicated by an early fatal outcome (7,8).

Mason Sones showed the feasibility of selective coronary arteriography and amassed a large library of cineangiograms that were studied in depth by Rene Favaloro (9). Sones and Favaloro formed an innovative team that demonstrated the efficacy and safety of SVG interposition and aortocoronary SVGs for single-vessel, left main, and multivessel coronary disease. An explosive growth in the application of these techniques ensued, such that within a decade, coronary bypass operation became the most frequent surgical procedure in the United States.

Recognition of the value of the IMA (also known as the internal thoracic artery) as a conduit came slowly. V.I. Kolessov, working in the 1960s at the Pavlov Institute in Leningrad, described a series of patients in whom the IMA was used for coronary revascularization without the aid of routine arteriography or CPB (10,11). Frank Spencer developed extensive experimental experience with the IMA to the coronary circulation in canine models. After preliminary animal and cadaveric work with microscopic methods, George Green brought this technique to successful clinical application. Floyd Loop and colleagues at the Cleveland Clinic incorporated the IMA into the coronary operation in a large series of patients and subsequently published the landmark article demonstrating the powerful survival benefit afforded by use of the IMA for LAD coronary distribution revascularization (12).

The 1970s, the first full decade of CABG, helped to define its appropriate role relative to medical therapy. Coronary bypass was found to consistently relieve angina and improve the quality of life in symptomatic patients. Three large, prospectively randomized, multicenter trials, The Coronary Artery Surgery Study (CASS), The Veteran's Administration Coronary Artery Bypass Trial, and the European Coronary Artery Bypass Trial, were conducted. These trials and several smaller studies helped to define subsets of patients likely to benefit from coronary bypass surgery in terms of prolongation of life and specifically identified patients with more advanced disease as those most appropriate for application of the operation for survival benefit. In addition to patients with triple-vessel disease and left main disease, patients with ischemic left ventricular (LV) dysfunction were found to benefit from the operation relative to medical therapy. These results led to the application of coronary bypass to progressively sicker patients in the 1980s.

Improvements in operative techniques and new technologies have allowed increasingly difficult patients to be approached with success. Improvements in cardiac anesthesia have paralleled improvements in operative techniques. Operation on complex patients became routine as sophisticated perioperative monitoring techniques, such as Swan-Ganz pulmonary artery catheters and intraoperative transesophageal echocardiography (TEE), were applied to specific problem situations. Anesthetic techniques, CPB technology, and most important, methods of myocardial protection were refined and successfully applied to specific problem situations. Close collaboration between the surgeon, the anesthesiologist, the perfusionist, and the intensive care team has been critically important to these advances. These refinements, discussed in Section 6, have led to an expected 30-day mortality of less than 1% in patients receiving elective coronary bypass who are less than 65 years of age and who have no severe LV dysfunction or congestive heart failure (CHF). Even in otherwise uncomplicated patients aged less than 65 years and with an ejection fraction (EF) of 0.25 to 0.35, first-time coronary bypass has an operative mortality risk of less than 5%.

In addition to improvements in short-term outcomes, evolving technology has contributed to improved long-term results. The widespread use of the IMA, the use of other arterial conduits, long-term antiplatelet therapy, and lipid management are discussed in later sections of these guidelines. Progress has also been significant in the moderation of perioperative morbidity. Central nervous system (CNS) injury, the systemic insults of CPB, infection, and bleeding are addressed in subsequent discussions. Finally, the application of CABG without CPB and through limited incisions has presented the prospect of further reductions in perioperative morbidity.

# 3. OUTCOMES

## *3.1. Hospital Outcomes*

### 3.1.1. Introduction

As the clinician and the patient consider the decision for CABG, an understanding of probable immediate outcomes (events that occur during the immediate hospitalization or within 30 days of operation) is of paramount importance. In particular, it is important to be able to predict the hospital mortality of the procedure and the risk of the major complications of coronary bypass, including cerebrovascular accidents, major wound infection, and renal dysfunction.

### 3.1.2. Predicting Hospital Mortality

**Class IIa**

**It is reasonable that statistical risk models be used to obtain objective estimates of CABG operative mortality. *(Level of Evidence: C)***

The risk of death with CABG has been the focus of numerous studies in the last 2 decades. Although early reports were

useful in correlating patient factors with outcomes such as in-hospital mortality (13), they were inadequate in their ability to risk stratify (14,15). Subsequently, a number of large single-center and multicenter cardiac surgical databases were established (13,16,17). From these databases, risk stratification models were created to better understand the variation in institutional and surgeon performance and to provide a more accurate risk prediction of mortality for patients facing CABG. Although all data sets identified patient and disease characteristics that consistently predicted mortality, the inclusion or exclusion of certain variables, variations in definitions of the same variables, and institutional and regional differences in practice styles have made it difficult to compare results across data sets. A review of 7 large data sets, representing more than 172 000 patients who underwent surgery between 1986 and 1994, was carried out to find the predictive power of certain preoperative variables (18). Seven core variables (i.e., urgency of operation, age, prior heart surgery, sex, LVEF, percent stenosis of the left main coronary artery, and number of major coronary arteries with more than 70% stenosis) were found to be predictive of mortality after CABG in all 7 data sets. Variables relating to the urgency of operation, age, and prior coronary bypass surgery were found to have the greatest predictive power, while variables describing coronary anatomy had the least predictive power. Besides these 7 core variables, 13 "level 1" variables were identified that, when added to the core variables, had a modest influence on the predictive capability of the model. These level 1 variables included the following: height; weight; PCI during index admission; recent (less than 1 week) MI; history of angina, ventricular arrhythmia, CHF, or mitral regurgitation (MR); comorbidities including diabetes, cerebrovascular disease, peripheral vascular disease (PVD), and renal dysfunction; and creatinine level. While the level 1 variables carry predictive power, their addition beyond these 7 core variables has been found to have a minimal impact on predictability (18).

While Jones and others have attempted to develop a common risk stratification language, general application of risk stratification models across populations must be done with caution. Although it may be possible to generalize the relative contribution of individual patient variables, rules must be calibrated to regional mortality rates and should be updated periodically to maximize accuracy (19,20). Table 2 compares the relative risk of the 7 core variables identified by Jones et al (18) as being most predictive of mortality as reported by 6 data sets.

Age has consistently predicted mortality after CABG (16,21), with advancing age associated with higher mortality. Assuming that age less than 65 years carries a relative risk of 1, Tu et al (22) found that the relative risk increased to 2.07 for patients between 65 and 74 years old and to 3.84 for those older than 75 years. Despite this increased short-term risk of mortality after CABG treatment, long-term results remain encouraging. When patients less than 50 years of age are compared with those 70 years and older and are matched by age to a population that did not undergo CABG, the older patients experience a longer hospitalization and higher hospital mortality, although their long-term survival more closely matches the general population compared with their younger counterparts. While elderly patients face an increased likelihood of morbidity after CABG and a particularly high incidence of stroke compared with the general population (23,24), age itself should not exclude a patient from being offered treatment with CABG, assuming that there is no prohibitive comorbidity. A careful quality of life and longevity assessment should be made in the oldest age groups.

Sex also predicts early mortality after CABG, with females facing an increased risk. Reported relative risks have ranged from 1.5 to 2.0. Smaller body size (25), smaller diameter of coronary arteries (26), increased age, and comorbidity status (27) have all been suggested as explanations for this increased risk. Another study based on the STS national database shows that female gender is an independent risk factor of operative mortality in low- and moderate-risk subsets but not in high-risk populations (28). Despite the increased risk, long-term results appear similar to those of males (29).

Having had previous open heart surgery adds considerable risk for patients having subsequent coronary artery surgery. The relative risk of early mortality appears to be around 3.0 compared with first-time CABG patients (16). An additional factor that further increases risk in this subset appears to be whether reoperation is carried out within 1 year of the primary operation (30). Despite the significant increased risk, long-term results after reoperative CABG are encouraging (31).

Coronary artery surgery in the presence of or immediately after an acute MI is controversial. Despite optimistic reports of low mortality if the operation is carried out within 6 hours of the onset of chest pain (32), many authors have found this approach to carry excessive mortality (33-35). Fibrinolytic therapy and/or PCI appears to be the preferable first-line therapy in the presence of an evolving MI. CABG surgery is reserved for patients with evidence of ongoing ischemia despite these interventions, or it may be performed coincident with repair directed at mechanical complications of infarction (i.e., ventricular septal defect or papillary muscle rupture). It also may benefit patients with shock complicating a recent acute MI, as demonstrated in the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial (35a).

The presence of comorbidities is also related to survival after CABG. Though not identified by Jones et al (18) as a core variable, treated diabetes (36), the presence of PVD (37), renal insufficiency (38), and COPD have all been shown to have a negative impact on outcome after CABG.

An intraoperative variable that seems to have both a short-term and a long-term impact on survival is the use of the IMA as a bypass conduit. Loop, Lytle, and others have reported that use of the IMA is an independent predictor of survival 10 to 20 years after CABG (39,40). Hospital mor-

**Table 2.** Relative Mortality Risk: Core CABG Variables for 6 Data Sets

| | NNE(13) | VA(718) | STS(16) | NYS(23) | CC(12) | AGH(383) |
|---|---|---|---|---|---|---|
| No. of patients | 3055 | 12 712 | 332 064 | 57 187 | 4918 | 1567 |
| Year of publication | '92 | '92 | '97 | '94 | '97 | '96 |
| Years included | '87-'89 | '87-'90 | '90-'94 | '89-'92 | '93-'95 | '91-'92 |
| Type | Vol reg | Man nat | Vol nat | Man state | SI | SI |
| Database variables | | | | | | |
| Age/y | 1.04 | 1.04 | 1.1 | 1.0 | 1.05 | NA |
| Sex, F | 1.2 | NA | 1.5 | 1.5 | 1.63 | 1.48 |
| Prior heart surgery | 3.6 | 3.2 | 3.0 | 3.7 | 1.72 | 1.39 |
| | | | 3.5 (Mult reops) | | | |
| LMD (70%) | NA | NA | 1.3 | 1.43 (>90%) | NA | NA |
| No. of diseased vessels | | | | | | |
| 1 | 1 | NA | 1.0 | NA | NA | NA |
| 2 | 1.3 | NA | 1.0 | NA | NA | NA |
| 3 | 1.6 | NA | 1.2 | NA | NA | NA |
| Urgency of operation* | | | | | | |
| Elective | 1 | 1.0 | 1.0 | 1.0 | 1 | 1 |
| Urgent | 2.1 | 2.4 | 1.2 | 1.42 (USA) | NA | 3.5 |
| Emergent | 4.4 | 3.8 | 2.0 | 4.0 | 5.07 | 7.14 |
| Salvage | NA | NA | 6.7 | NA | NA | 29.9 |
| Ejection fraction | | | | | | |
| 0.6 | | NA | ... | 1.0 (>40%) | NA | ... |
| 0.50-0.59 | | NA | ... | ... | NA | ... |
| 0.40-0.49 | | NA | ... | ... | NA | ... |
| 0.30-0.39 | | NA | ... | 1.6 | NA | 2.89 (<30%) |
| 0.20-0.29 | | NA | ... | 2.2 | NA | ... |
| <0.20 | | NA | ... | 4.1 | NA | ... |

NNE indicates Northern New England Cardiovascular Disease Study Groups; VA, Veterans Affairs cardiac surgical database; STS, Society for Thoracic Surgery national cardiac surgical database; NYS, New York State cardiac surgery reporting systems; CC = Cleveland Clinic; AGH = Allegheny General Hospital; LMD, left main disease; Vol, voluntary; reg, regional; Man, mandatory; nat, national; state, single state; SI, single institution; NA, not available; and mult reops, multiple reoperations.

The relative risk coefficient for age indicates the additional mortality risk per year of age greater than 50 years.

*Urgent indicates patients are required to stay in the hospital but may be scheduled and operated on within a normal scheduling routine; Emergent, ongoing refractory cardiac compromise, unresponsive to other forms of therapy except for cardiac surgery; and Salvage, ongoing cardiopulmonary resuscitation en route to the operating room.

tality after CABG has also been reported to be lower when the IMA is used (41,42).

In summary, early mortality after CABG is associated particularly with advancing age, poor LV function, and the urgency of operation. Additional coronary anatomic and comorbid conditions further influence risk. If overall risk for an institution or region is known, then a general estimate for the individual patient can be rendered preoperatively by using mathematical models, as illustrated in Table 3 and Figure 1. This application may find utility as patients and their physicians weigh the potential benefits versus risks of proceeding with bypass surgery.

### 3.1.3. Morbidity Associated With CABG: Adverse Cerebral Outcomes

**Class I**

**Significant atherosclerosis of the ascending aorta mandates a surgical approach that will minimize the possibility of arteriosclerotic emboli.** ***(Level of Evidence: C)***

Neurological abnormalities after CABG are a dreaded complication. The reported incidence ranges from 0.4% to nearly 80%, depending on how the deficit is defined (43-45). Neurological derangement after CABG has been attributed to hypoxia, emboli, hemorrhage, and metabolic abnormalities (46,47). Despite the many advances made in cardiac surgery, postoperative stroke remains a problem.

Postoperative neurological deficits have been divided into 2 types: type 1 deficits are those associated with major, focal neurological deficits, stupor, and coma; type 2 deficits are characterized by deterioration in intellectual function or memory. Roach et al (48) reported on a multi-institutional prospective study aimed at determining the true incidence of both stroke (type 1 deficits) and encephalopathy (type 2 deficits) after CABG. In this study, 2108 patients operated

**Table 3. Preoperative Estimation of Risk of Mortality, Cerebrovascular Accident and Mediastinitis**

For use **only** in isolated CABG surgery

**Directions:** Locate outcome of interest, e.g., mortality. Use the score in that column for each relevant preop variable; then sum these scores to get the total score. Take the total score and look up the approximate preoperative risk in the table below.

| Patient or Disease Characteristic | Mortality score | CVA score | Mediastinitis score |
|---|---|---|---|
| Age 60-69 | 1.5 | 1.5 | 1 |
| Age 70-79 | 2.5 | 2.5 | 1.5 |
| Age ≥80 | 6.5 | 3 | 2 |
| Female sex | 2 | 1.5 | |
| Obesity (BMI 31-36) | | | 2 |
| Severe obesity (BMI ≥ 37) | | | 4.5 |
| Diabetes | 1 | 1.5 | 1.5 |
| COPD | 2 | | 2 |
| PVD | 1.5 | 1.5 | |
| Dialysis | 4 | 2 | 3 |
| Creatinine ≥ 2 | 2 | 2 | |
| MI ≤7 days | 1.5 | | |
| Prior CABG | 2.5 | | |
| EF < 40% | 2 | 1.5 | 1.5 |
| 3-Vessel disease | 1.5 | | |
| LM 50-89% | 1.5 | | |
| LM ≥ 90% | 2 | | |
| WBC >12K | 2.5 | | |
| Urgent surg. | 2 | 1.5 | 2 |
| Emergency surg. | 5 | 3.5 | 2 |
| **Total Score** | | | |

**Preoperative Risk**

| Total Score | Mortality % | CVA % | Mediastinitis % |
|---|---|---|---|
| 0 | 0.2 | 0.4 | 0.3 |
| 1 | 0.2 | | 0.3 |
| 2 | 0.3 | 0.6 | 0.4 |
| 3 | 0.3 | 0.9 | 0.5 |
| 4 | 0.5 | 1.3 | 0.7 |
| 5 | 0.7 | 1.4 | 0.9 |
| 6 | 1.0 | 2.0 | 1.3 |
| 7 | 1.3 | 2.7 | 1.7 |
| 8 | 1.8 | 3.4 | 2.5 |
| 9 | 2.3 | 4.2 | 3.2 |
| 10 | 3.0 | 5.9 | 4.2 |
| 11 | 4.0 | 7.6 | 5.6 |
| 12 | 5.3 | ≥10.0 | ≥7.3 |
| 13 | 6.9 | | |
| 14 | 8.8 | | |
| 15 | 11.5 | | |
| 16 | 14.1 | | |
| 17 | 18.7 | | |
| 18 | ≥23.0 | | |

**Calculation of Mortality Risk:** An 80-year-old female, with an EF less than 40% who is having elective CABG surgery, has had no prior CABG surgery and has no other risk factors. Her total score = 6.5 (age greater than or equal to 80) + 2 (EF less than 40%) = 10.5. Since her total score equals 10.5, round up to 11; her predicted risk of mortality = 4.0%.

**Definitions:**

**Obesity:** Find the approximate height and weight in the table below to classify the person as obese or severely obese. **Obesity:** BMI 31-36. **Severe obesity:** BMI greater than or equal to 37.

Example: A patient is 5'7" and weighing 200 lbs. is classified obese. If the patient weighed 233 lbs. or more, he/she would be classified severely obese.

| Height (feet and inches) | Weight (lbs.) Obesity BMI 31-36 | Weight (lbs.) Severe Obesity BMI≥37 | Height (feet and inches) | Weight (lbs.) Obesity BMI 31-36 | Weight (lbs.) Severe Obesity BMI ≥37 |
|---|---|---|---|---|---|
| **5'0"** | 158-186 | ≥187 | **5'8"** | 203-239 | ≥240 |
| **5'1"** | 164-192 | ≥193 | **5'9"** | 209-246 | ≥247 |
| **5'2"** | 169-199 | ≥200 | **5'10"** | 215-254 | ≥255 |
| **5'3"** | 175-205 | ≥206 | **5'11** | 222-261 | ≥262 |
| **5'4"** | 180-212 | ≥213 | **6'0"** | 228-268 | ≥269 |
| **5'5"** | 186-219 | ≥220 | **6'1"** | 235-276 | ≥277 |
| **5'6"** | 191-225 | ≥226 | **6'2"** | 241-283 | ≥284 |
| **5'7"** | 198-232 | ≥233 | **6'3"** | 248-291 | ≥292 |

**Diabetes:** Currently treated with oral medications or insulin.

**COPD (chronic obstructive pulmonary disease):** treated with bronchodilators or steroids.

**PVD (peripheral vascular disease):** Cerebrovascular disease, including prior CVA, prior TIA, prior carotid surgery, carotid stenosis by history or radiographic studies, or carotid bruit. Lower-extremity disease including claudication, amputation, prior lower-extremity bypass, absent pedal pulses or lower-extremity ulcers.

**Dialysis:** Peritoneal or hemodialysis-dependent renal failure.

**MI less than 7 days:** The development of a) new Q wave on EKG or b) new ST-T changes with a significant rise (defined locally) in CPK with positive (defined locally) isoenzymes.

**EF less than 40% (left ventricular ejection fraction):** The patient's current EF is less than 40%.

**WBC greater than 12K (white blood cells greater than 12 000):** Use the patient's last preoperative measurement of WBC taken before the procedure.

**Urgent:** Medical factors require patient to stay in hospital to have operation before discharge. The risk of immediate morbidity and death is believed to be low.

**Emergency:** Patient's cardiac disease dictates that surgery should be performed within hours to avoid unnecessary morbidity or death.

**Data set and definitions for dependent variables:**

The regression models that generated the scores for these prediction rules were based on 14 971 patients receiving isolated CABG surgery between 1999 and 2002. The dependent variables and observed event rates are as follows: inhospital mortality (2.5%); cerebrovascular accident, defined as a new focal neurologic event persisting at least 24 hours (1.6%); and mediastinitis during the index admission defined by positive deep culture and/or gram stain and/or radiographic findings indicating infection and requiring reoperation (1.0%).

Northern New England Cardiovascular Disease Study Group 4/03.
BMI indicates body mass index; CVA, cerebrovascular accident; LM, left main; TIA, transient ischemic attack; EKG, electrocardiogram.

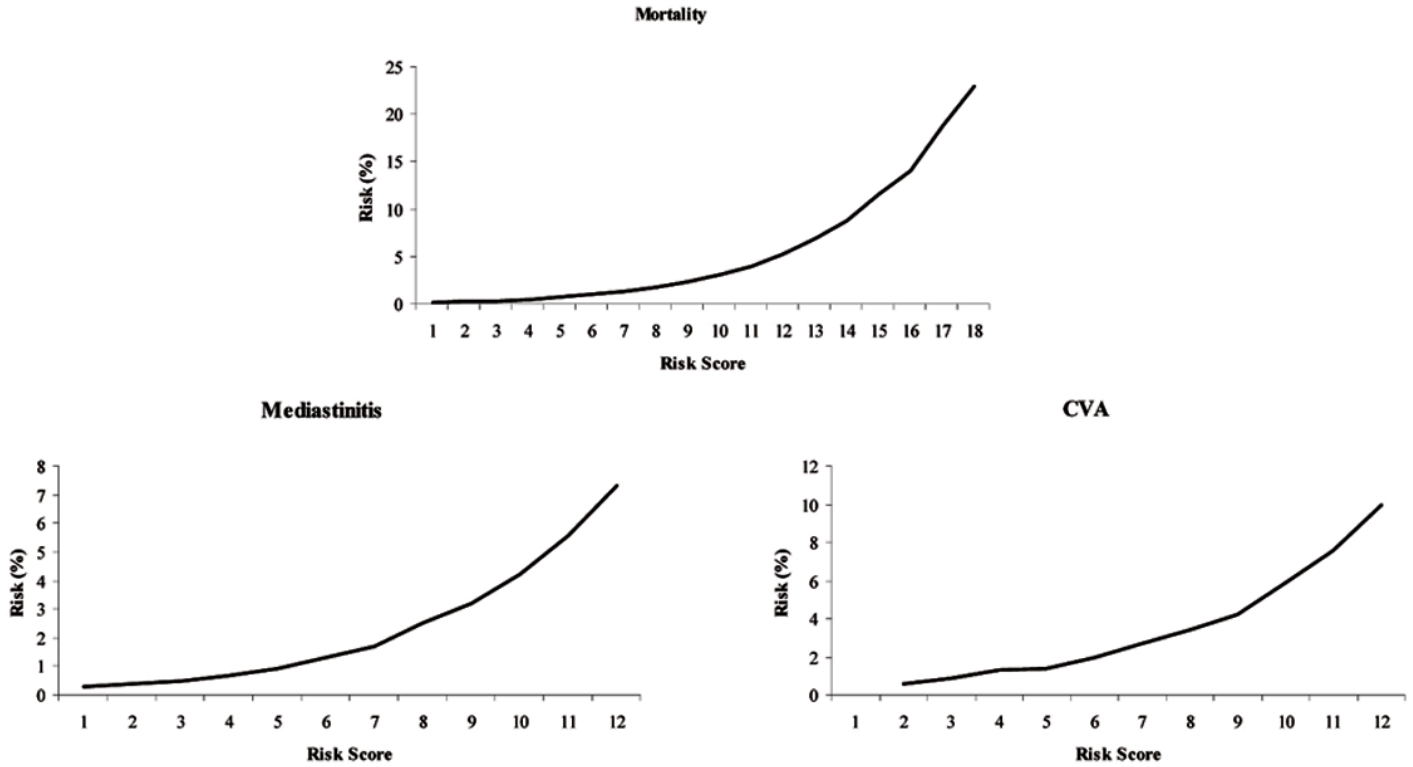


**Figure 1.** Event curves. For calculation of risk score, see Table 3.

on at 24 institutions were observed for signs of neurological dysfunction after CABG. Adverse cerebral outcomes occurred in 129 patients (6.1%) and were evenly distributed between type 1 (3.1%) and type 2 (3.0%) deficits. The influence of these complications included a 21% mortality for those with type 1 deficits and a 10% mortality for those with type 2 deficits. In addition, patients with neurological complications had, on average, a 2-fold increase in hospital length of stay and a 6-fold likelihood of discharge to a nursing home.

Independent risk factors were identified for both type 1 and type 2 deficits (48). Predictors of both types of cerebral complications included advanced age, especially age greater than or equal to 70 years, and a history or the presence of significant hypertension. Both of these variables have previously been reported to be associated with adverse cerebral outcomes after CABG (49,50).

Predictors of type 1 deficits included the presence of proximal aortic atherosclerosis as defined by the surgeon at the time of surgery (odds ratio [OR] 4.52), a history of prior neurological disease (OR 3.19), use of the intra-aortic balloon pump (IABP; OR 2.60), diabetes (OR 2.59), a history of hypertension (OR 2.31), a history of unstable angina (OR 1.83), and increasing age (OR 1.75 per decade). Perioperative hypotension and the use of ventricular venting were also weakly associated with this type of outcome.

Proximal aortic atherosclerosis has been reported to be the strongest predictor of stroke after CABG, supporting the theory that liberation of atheromatous material during manipulation of the aorta is the main cause of this complication (49). Although palpation of the aorta has traditionally been used by surgeons to identify patients with atheromatous disease of the ascending aorta and to find “soft spots” for cannulation or cross-clamping, the use of ultrasound has been suggested as a more accurate means of assessing the aorta (51). Duda et al (51) have suggested that once aortic atherosclerosis is identified, alternative strategies to prevent mobilization of aortic atheroma should be considered, including techniques such as groin or subclavian placement of the aortic cannulas, fibrillatory arrest without aortic cross-clamping, use of a single cross-clamp technique, modifying the placement of proximal anastomoses, or all-arterial revascularization in cases of severe aortic involvement. Other authors recommended ascending aortic replacement under circulatory arrest as the best means of minimizing this complication (52,53).

A history of previous neurological abnormality or the presence of diabetes is also a predictor of type 1 CNS complications. These are likely markers for patients with marginal cerebral blood flow, alterations in CNS vasomotor autoregulatory mechanisms, or diffuse atherosclerosis. The need for an IABP is likely correlated with a higher risk of atheromatous emboli and is often required in patients with systemic hypoperfusion, each of which may cause stroke after CABG. The fact that use of an LV vent—or other devices that have potential for introducing air into the arterial circulation—has been associated with stroke suggests air emboli as the cause and argues for meticulous technique when placing these devices to prevent this complication.

Factors predictive of type 2 neurological deficits include a history of alcohol consumption, dysrhythmia (including atrial fibrillation), hypertension, prior CABG, PVD, or CHF. Because aortic atherosclerosis is not a strong predictor of type 2 complications, encephalopathic changes may be related not only to microemboli but also to the brain's microcirculation. Type 2 complications are more likely to occur after periods of hypotension or inadequate perfusion.

Off-pump coronary artery bypass (OPCAB) avoids both aortic cannulation and cardiopulmonary bypass. Accordingly, one would expect postoperative neurological deficits to be reduced in patients undergoing OPCAB. Three randomized controlled trials (54-56) have not firmly established a significant change in neurological outcomes between OPCAB patients and conventional CABG patients. Each trial demonstrates problems inherent with small patient cohorts, differing definitions, and patient selection. At this point, there is insufficient evidence of a difference in neurological outcomes for patients undergoing OPCAB compared with those undergoing conventional CABG (57).

Individual patient counseling regarding postoperative stroke risk represents an important opportunity to assist patients as they weigh the risks and benefits of elective CABG. Although postoperative stroke rates may vary between hospitals or regions, if local rates are known, then these may be used to assist the patient in appreciating the general risk of this dreaded complication. Strategies to reduce the risk of postoperative neurological complications are discussed in depth in Section 4.1.1.

### 3.1.4. Morbidity Associated With CABG: Mediastinitis

Deep sternal wound infection has been reported to occur in 1% to 4% of patients after CABG and carries a mortality rate of nearly 25% (58,59). Studies have consistently associated obesity and reoperation with this complication, while other risk factors such as use of both IMAs, duration and complexity of operation, and the presence of diabetes have been reported inconsistently. Most studies examining deep sternal wound infection have been single-center, retrospective reviews, and variation in wound surveillance techniques and the definition of deep sternal wound infection limit comparisons.

Obesity is a strong correlate of mediastinitis after CABG (60). In one report of 6459 patients undergoing CABG at a single institution, Milano et al (61) found obesity to be the strongest independent predictor of mediastinitis (OR 1.3). In a prospective multi-institutional study, the Parisian Mediastinitis Study Group also found obesity to carry the greatest association with the development of postoperative mediastinitis (OR 2.44) (62). The mechanism by which obesity leads to this complication is poorly understood but is likely multifactorial. Perioperative antibiotics may be poorly distributed in adipose tissue, skin folds present a special challenge in maintaining sterility, and large regions of adipose tissue serve as an ideal substrate for bacteria and represent a clinical challenge for diagnosis when early infection occurs.

Another patient characteristic that has been associated with postoperative mediastinitis is the presence of diabetes (55,57), especially in patients requiring regular insulin (58). In addition to the microvascular changes seen in diabetic patients, elevated blood glucose levels may impair wound healing. The use of a strict protocol aimed at maintaining blood glucose levels less than or equal to 200 mg/dL by the continuous, intravenous infusion of insulin has been shown to significantly reduce the incidence of deep sternal wound infection in patients with diabetes (58a,314).

Prior cardiac surgery is another factor associated with the development of mediastinitis (61-63). Reoperation requires additional dissection, necessitates longer operative and/or perfusion times, produces more bleeding, and results in a higher likelihood of needing transfusion, variables that have all been linked to this complication.

Operator-dependent variables may also contribute to the development of deep sternal wound infection. These include the use of both IMAs for bypass conduits and excessive use of electrocautery for hemostasis (61,320). No studies have found the use of a single IMA to be predictive of mediastinitis. Two reports identified the use of both IMAs to be an independent predictor (62,62a), while several others have shown no correlation with the development of mediastinitis (58,61). Because the use of both IMAs may predispose to devascularization of the sternum, it seems likely that this technique promotes infection, especially when combined with other risk factors such as diabetes and/or obesity.

In summary, deep sternal wound infection after CABG is an expensive and potentially lethal complication that appears to have a multifactorial etiology. Strategies to reduce the incidence of this complication include meticulous aseptic technique, keeping perfusion times to a minimum, avoidance of unnecessary electrocautery, appropriate use of perioperative antibiotics, and strict control of blood glucose levels during and after operation. Each of these is discussed in greater depth in Section 4.1.4.

### 3.1.5. Morbidity Associated With CABG: Renal Dysfunction

The first major multicenter study of renal dysfunction after CABG surgery was published in 1998 (64). This study of 2222 patients who underwent myocardial revascularization with CPB defined postoperative renal dysfunction (PRD) as a postoperative serum creatinine level of greater than or equal to 2.0 mg/dL or an increase in the serum creatinine level of greater than or equal to 0.7 mg/dL from preoperative to maximum postoperative values. PRD occurred in 171 (7.7%) of the patients studied; 30 of these (18%, or 1.4% of all study patients) required dialysis. The mortality rates were 0.9% among patients who did not develop PRD, 19% in patients with PRD who did not require dialysis, and 63% among those who required dialysis.

Several preoperative risk factors for PRD were identified, including advanced age, a history of moderate to severe CHF, prior CABG, type 1 diabetes mellitus, and preexisting renal disease (preoperative creatinine levels greater than 1.4 mg/dL). The risk of PRD in patients less than 70 years of age nearly tripled with 1 preoperative risk factor and increased further with 2 risk factors. A detailed analysis of the impact of these preoperative risk factors for PRD for 3 age groups is presented in Table 4 (64). These findings allow identification of high-risk patients for PRD and a general estimation of the risk for PRD for an individual patient. The reported risk for patients with moderate renal dysfunction is consistent with previous reports from smaller, single-center studies (65-67).

Although data from large, multicenter studies are not available, it is reasonable to conclude that patients with more advanced, chronic, preoperative renal failure (but without end-stage renal disease [ESRD]) would have an even higher incidence of PRD requiring dialysis. Because their kidneys have a greater reduction in functioning nephrons than those in patients with lesser degrees of renal failure in the study cited above, they would be more vulnerable to the maldistribution of renal blood flow, an increase in renal vascular resistance, and the decreases in total renal blood flow and glomerular filtration rate that occur during CABG surgery (68-70). This conclusion has been supported by a study of 31 patients who underwent CABG with a baseline serum creatinine level greater than or equal to 1.6 mg/dL in the 6 months before surgery and who did not require preoperative dialysis (71). The mean age of the patients was 71 years, and nearly 80% were males. The hospital mortality was 19%, and 26% of surviving patients required chronic dialysis. Among 19 patients with a creatinine level greater than or equal to 2.6 mg/dL, 42% of survivors required chronic hemodialysis, whereas none of the surviving patients with a creatinine level less than or equal to 2.6 mg/dL required chronic dialysis. This study suggests that patients greater than 70 years old with a creatinine level greater than or equal to 2.6 mg/dL are at extreme risk for dialysis dependency after CABG, and alternative options for coronary management should be strongly considered.

The importance of perioperative renal function is emphasized by a report that correlated acute renal failure sufficient to require dialysis and operative mortality after cardiac surgery (72). The 42 773 patients who underwent CABG or valvular heart surgery at 43 Department of Veterans Affairs medical centers between 1987 and 1994 were evaluated to determine the association between acute renal failure sufficient to require dialysis and operative mortality. This degree of acute renal failure occurred in 460 (1.1%) patients. Overall, operative mortality was 63.7% in these patients, compared with 4.3% in patients without this complication.

**Table 4.** Risk of Postoperative Renal Dysfunction (PRD) After Coronary Artery Bypass Graft Surgery

| No. of Risk | Combinations of Preoperative Risk Factors for PRD | | | | Risk of PRD in Various Clinical Strata Depending on Risk Factors and Age | | |
|---|---|---|---|---|---|---|---|
| Factors | CHF | Reop | DM | Creat greater than 1.4 | Greater than 70 years | 70 to 79 years | Greater than or equal to 80 years |
| 0 | - | - | - | - | 1.9% (n=909) | 7.0% (n=330) | 11.8% (n=68) |
| 1 | - | - | - | + | 5.0% (n=80) | 18.4% (n=76) | 12.5% (n=16) |
| | - | - | + | - | 5.9% (n=68) | 4.8% (n=81) | * |
| | - | + | - | - | 6.2% (n=130) | 14.3% (n=56) | 25.0% (n=4) |
| | + | - | - | - | 7.6% (n=144) | 12.3% (n=73) | 29.4% (n=17) |
| 2 | - | - | + | + | 22.2% (n=9) | 0% ( n=7) | * |
| | - | + | - | + | 20.0% (n=25) | 30.8% (n=13) | * |
| | - | + | + | - | 37.6% (n=8) | 33.3% (n=3) | * |
| | + | - | - | + | 47.4% (n=19) | 7.7% (n=26) | 44.4% (n=9) |
| | + | - | + | - | 25.9% (n=27) | 18.2% (n=11) | * |
| | + | + | - | - | 31.6% (n=19) | 7.1% (n=14) | * |
| 3 | - | + | + | + | 100% (n=1) | 100% (n=1) | * |
| | + | - | + | + | 8.3% (n=12) | 25% (n=4) | * |
| | + | + | - | + | * | 33.3% (n=9) | * |
| | + | + | + | - | 33.3% (n=3) | * | * |
| 4 | + | + | + | + | 50.0% (n=2) | * | * |

CHF indicates prior congestive heart failure; Reop, redo coronary bypass operation; DM, type 1 diabetes mellitus; Creat greater than 1.4, preoperative serum creatinine level greater than 1.4 mg/dL; n, observed number of patients within each clinical stratum; -, risk factor absent; and +, risk factor present.
*Insufficient patient numbers, number is less than five.
Reprinted with permission from Mangano et al. Ann Intern Med 1998;128:194-203 (64).

**Table 5.** Multivariate Analysis Predictors of Late Overall Mortality and Late Cardiac Mortality

| Predictor | Risk Ratio | 95% CI | *P* |
|---|---|---|---|
| Late overall mortality | | | |
| Diabetes | 2.94 | 1.81-4.77 | <0.001 |
| Advancing age | 1.1 | 1.06-1.13 | <0.001 |
| Reduced EF | 1.03 | 1.01-1.04 | <0.007 |
| No IMA | 1.22 | 0.75-1.99 | 0.423 |
| Late cardiac mortality | | | |
| Diabetes | 1.73 | 2.40-9.32 | <0.001 |
| Advancing age | 1.08 | 1.04-1.13 | <0.001 |
| Reduced EF | 1.05 | 1.02-1.08 | <0.001 |
| No IMA | 1.78 | 0.83-3.79 | 0.138 |

CI indicates confidence interval; EF, ejection fraction; IMA, internal mammary artery.

Acute renal failure requiring dialysis was independently associated with early mortality after cardiac surgery, even after adjustment for comorbidity and postoperative complications.

### 3.1.6. Posthospital Outcomes

The extensive application of CABG has been a consequence of its effectiveness in the relief of angina and prolongation of survival in certain subsets. The 1999 Guidelines provided data that allow a general understanding of expectation after CABG (1). In a heterogeneous group of patients, survival at 5 years was 92% and at 10 years was 81%. Freedom from angina was 83% at 5 years and 63% at 10 years. The previous guidelines provided equations for predicting patient-specific outcomes, including freedom from unfavorable events, in a comparison of coronary bypass surgery versus medical treatment. These detailed predictive instruments remain appropriate for use and are not presented here. While a discussion of the comparative benefits of CABG versus medical therapy appears in Section 3.2, a brief description of the factors that influence the long-term results of the operation is appropriate here.

The predictors of long-term survival after CABG have been analyzed in a number of studies. In an analysis of 23 960 patients from 1977 to 1994 from Emory University, advanced age, EF, presence of diabetes, number of diseased vessels, and sex were significant multivariate predictors of survival, while angina class, hypertension, history of MI, renal dysfunction, and CHF were other important factors identified by univariate analysis (Table 5) (73). Other studies have identified predictors for the recurrence of angina and for postoperative MI (Table 6). Importantly, untoward events after coronary bypass tend to increase in frequency between 5 and 10 years after the operation, apparently coincident with the gradual occlusion of vein grafts. Approximately 50% of vein grafts are closed by 10 years after operation.

The delayed return of angina and the fact that approximately half of the survivors of CABG eventually die of cardiac-related causes identifies the “Achilles heel” of the procedure: late vein-graft atherosclerosis and occlusion. The most important surgical gain has been verification of excellent late patency with IMA grafts (74). From this encouraging result with the use of a single arterial graft has sprung the arterial arborization of today, with reports of multiple and “complete” arterial grafting (75-78). This is discussed further in Sections 4.2. and 6.2.

## 3.2. Comparison of Medical Therapies Versus Surgical Revascularization

Since the 1991 Guidelines, relatively little clinical trial information comparing medical with surgical treatment of CAD has been published. However, longer follow-up of patients enrolled in the earlier, major randomized trials has solidified the appropriate indications for surgical treatment.

The traditional stratification of patients has been based on the extent of CAD (i.e., number of vessels with anatomically significant disease and whether or not the major epicardial

**Table 6.** Multivariate Analysis Predictors of Anginal Recurrence, Late MI, and Any Cardiac Event

| Predictor | Risk Ratio | 95% CI | *P* |
|---|---|---|---|
| Anginal recurrence | | | |
| Female sex | 1.81 | 1.22-2.69 | 0.003 |
| Obesity | 1.69 | 1.21-2.19 | 0.002 |
| Preoperative hypertension | 1.54 | 1.87-2.19 | 0.015 |
| No IMA | 2.47 | 1.49-4.10 | <0.001 |
| Late MI | | | |
| Diabetes | 3.39 | 1.81-6.34 | 0.001 |
| Single IMA | 2.31 | 1.15-4.67 | 0.019 |
| Any cardiac Event | | | |
| No IMA | 2.88 | 1.48-5.15 | <0.001 |

MI indicates myocardial infarction; CI, confidence interval; and IMA, internal mammary artery.

**Table 7.** Limitations of Randomized Trials in View of Current Practice

| Patient Selection | Surgical Factors | Medical/Nonsurgical Therapy |
|---|---|---|
| Patients less than or equal to 65 years of age | Only 1 trial used arterial grafts (CASS) (in only 14% of patients) | Lipid-lowering therapy not used or standard |
| Only 1 trial included women (CASS) | Newer modalities of cardioprotection not used | Aspirin not widely used |
| Predominantly low-risk, stable patients | Minimally invasive, off-bypass techniques not used | Beta-blockers used in only half of patients |
| | Aspirin not routinely given early postoperatively | ACE inhibitor not used<br>Coronary angioplasty not widespread |

CASS indicates Coronary Artery Surgery Study; ACE, angiotensin-converting enzyme.

obstruction is proximal) in association with the extent of LV dysfunction (determined by a simple measure of global LVEF). The major end point of the studies has been survival. The major randomized trials studied patients between 1972 and 1984, at which time the predominant medical therapy was the use of beta-blockers and nitrates.

There are several important limitations of the randomized trials in view of current practice (Table 7). In the ensuing years, calcium channel blockers have been added, particularly for symptomatic patients. The use of aspirin has become more widespread in all patients with CAD. The role of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors and other lipid-lowering agents has now been recognized as important in reducing recurrent ischemic events. Angiotensin converting enzyme inhibitors are now used routinely, particularly in patients with symptomatic heart failure after acute myocardial infarction or those with LV systolic dysfunction. It is hoped that these agents will be used equally in patients treated with medications alone and in patients after CABG surgery, whose revascularization therapy is complemented by appropriate medical treatment to reduce ischemic complications. The contribution of advances in surgical revascularization techniques cannot be fully assessed. The potential value of arterial conduits for revascularization, particularly the IMA, cannot be evaluated from these early randomized studies, yet their use is now routine in CABG surgery. There are also no prospective, randomized studies comparing the more recent off-bypass or minimally invasive surgical approaches to medical therapy. Finally, the randomized trials oversimplify the designation of 1-, 2-, and 3-vessel disease. Several reports show that prognosis is also critically related to the location of lesions within vessels, not simply the number of vessels involved (9,18).

### 3.2.1. Overview

There were 3 major randomized trials (79-81) and several smaller ones (82-84). These studies addressed similar clinical questions and, as shown in Figure 2 and Figure 3, had similar outcomes. Much of the primary patient information for the 2649 patients enrolled in these randomized trials has been combined in a collaborative meta-analysis, which has facilitated comparison of outcomes at 5 and 10 years of follow-up (Table 8) (85). Extension of survival is a useful

**Table 8.** Total Mortality at 5 and 10 Years

| Trial | No. of Patients Randomized | | 5-Year Mortality | | | 10-Year Mortality | | |
|---|---|---|---|---|---|---|---|---|
| | CABG | Medical Treatment | CABG | Medical Treatment | Odds Ratio (95% CI) | CABG | Medical Treatment | Odds Ratio (95% CI) |
| VA (79) | 332 | 354 | 58 | 79 | 0.74 (0.50–1.08) | 118 | 141 | 0.83 (0.61–1.14) |
| European (81) | 394 | 373 | 30 | 63 | 0.40 (0.26–0.64) | 91 | 109 | 0.72 (0.52–0.99) |
| CASS (80) | 390 | 390 | 20 | 32 | 0.60 (0.34–1.08) | 72 | 83 | 0.84 (0.59–1.19) |
| Texas | 56 | 60 | 10 | 13 | 0.79 (0.31–1.97) | 23 | 25 | 0.97 (0.46–2.04) |
| Oregon | 51 | 49 | 4 | 8 | 0.44 (0.12–1.56) | 14 | 14 | 0.94 (0.39–2.26) |
| New Zealand | 51 | 49 | 5 | 7 | 0.65 (0.19–2.20) | 15 | 16 | 0.94 (0.38–2.31) |
| New Zealand | 50 | 50 | 8 | 8 | 1.00 (0.34–2.91) | 17 | 16 | 1.15 (0.50–2.65) |
| Total | 1324 | 1325 | 135 | 210 | 0.61 (0.48–0.77) | 350 | 404 | 0.83 (0.70–0.98) |
| | | | (10.2%) | (15.8 %) | P less than 0.0001 | (26.4 %) | (30.5 %) | P equals 0.03 |

CABG indicates coronary artery bypass graft; CI, confidence interval; VA, Veterans Administration; CASS, Coronary Artery Surgery Study.
*P* values for heterogeneity across studies were 0.49, 0.84, and 0.95 at 5, 7, and 10 years, respectively. Reprinted with permission from Elsevier Science, Inc. (Yusuf et al. The Lancet 1994;344:563-70) (85).

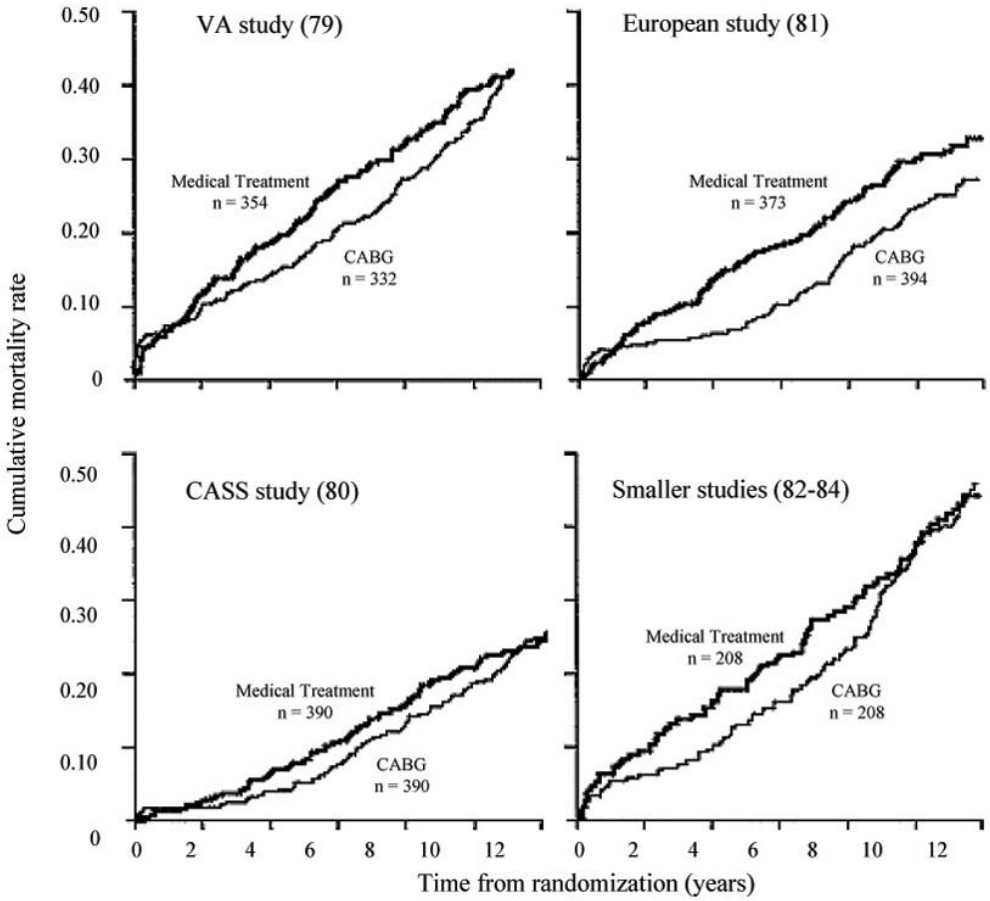


**Figure 2.** Survival curves of the 3 large studies and several small studies combined. VA indicates Veterans Administration; CABG, coronary artery bypass graft surgery; CASS, Coronary Artery Subject Study. Reprinted with permission from Elsevier Science, Inc. (Yusuf et al. The Lancet. 1994;344:563-70) (85).

measure to compare different treatment strategies and can be adjusted for patient characteristics (Figure 4). Across all patients, the improvement in survival with CABG compared with medical treatment is 4.3 months at 10-year follow-up (*P* equals 0.003). In patients with left main disease, the survival benefit is 19.3 months. Subset analyses for other subgroups show statistical benefit for those with 3-vessel disease, and in those with 1- or 2-vessel disease including LAD CAD. Relative risk reductions were similar with abnormal or normal LV function. However, a similar relative risk reduction is associated with a greater absolute survival benefit in the high-risk population with depressed LV function. The survival benefit of CABG surgery for individuals with 1- and 2-vessel disease without LAD involvement is small, particularly in the setting of normal LV function. A higher clinical risk score, more severe angina, and a positive exercise test are associated with a greater prolongation of survival after CABG surgery than with medical therapy at 5 and 10 years (Table 8) (85). Two clinical scoring systems have been used. The Veterans Administration trial used the clinical variables of angina class, history of hypertension, and MI as well as the degree of ST-segment depression at rest. The Coronary Artery Bypass Graft Surgery Trialists' Collaboration (85) developed a stepwise logistic regression analysis-based risk score that included clinical and angiographic variables as well as EF (Tables 8-10) (85). Patients can be stratified according to these clinical criteria and by using these scoring systems. There was little survival benefit in those with a low risk (1% annual mortality) but increasingly significant survival extension in those at moderate (annual mortality of 2.5%) or high (annual mortality of 5%) risk.

The randomized trials provide robust results for the populations studied. However, there are important limitations in generalizing the results of these studies to most patients with coronary disease because of the way patients were selected for the randomized studies. Specifically, the mean age of randomized patients was 50.8 years, there were very few patients greater than 65 years, 96.8% were male, and only 19.7% had an LVEF less than 0.50 (85). The challenge of choosing a therapeutic option in patients with CAD is that the clinical course is highly variable, and the "average" patient does not fit perfectly into 1 of the groups studied. The large registries (86-88) and other studies (89-91) provide useful confirmatory information in support of the clinical trials and, if interpreted with appropriate caution, can help in the subsets not well studied in the randomized trials. The following discussion combines information from randomized and nonrandomized trials in which the directional trends are consistent with the randomized information.

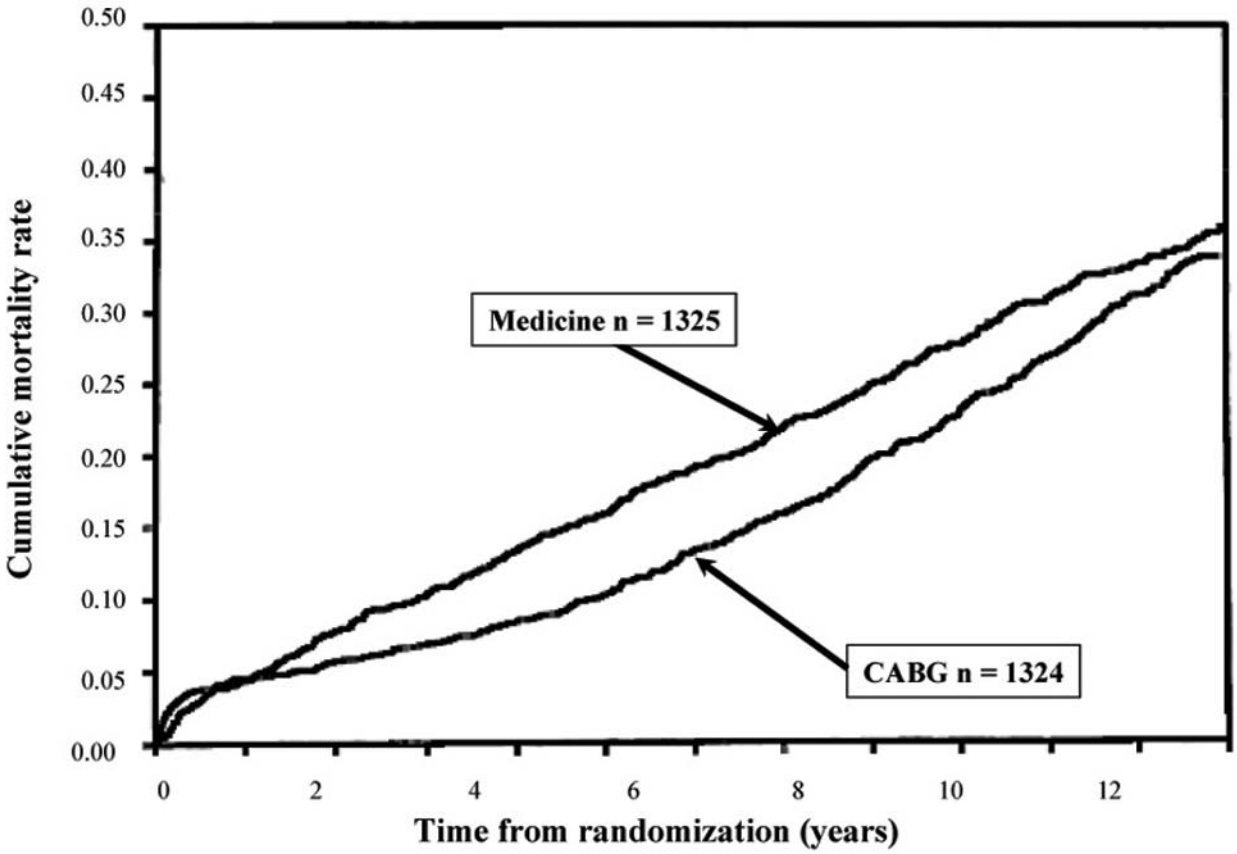


**Figure 3.** Cumulative total mortality from all studies. CABG indicates coronary artery bypass graft. Modified with permission from Elsevier Science, Inc. (Yusuf et al. The Lancet. 1994;344:563-70) (85).

### 3.2.2. Location and Severity of Stenoses

#### *3.2.2.1. Left Main Disease*

The benefit of surgery over medical treatment for patients with significant left main stenosis is little argued. All of the trials define significant left main stenosis as being greater than 50% diameter stenosis as judged by contrast angiography. The median survival for surgically treated patients is 13.3 years versus 6.6 years in medically treated patients (92,93).

Left main equivalent disease, defined as severe (greater than or equal to 70%) diameter stenosis of the proximal LAD and proximal left circumflex disease, appears to behave similarly to true left main disease. Median survival for surgical patients is 13.1 years versus 6.2 years for medically assigned patients (92). However, there are few randomized or randomizable patients with this anatomy. By 15 years, there is less survival benefit for patients assigned to surgery. It is estimated that if all medical patients survived 15 years, 65% would eventually have surgery (85). At 15 years, cumulative survival in the CASS registry for patients with left main equivalent disease was 44% for surgical patients and 31% for the medical group (92,94,95).

#### *3.2.2.2. Three-Vessel Disease*

Significant CAD is defined variably in the major studies. CASS originally reported results with significant stenosis defined as greater than or equal to 70%. The Veterans Administration and European studies used 50% as the cutoff for significant stenosis, and when the studies were combined for the meta-analysis (85), the 50% criterion defined significant disease for all vessels. For the purposes of this guideline, unless otherwise specified, the term significant will indicate greater than 50% reduction in visual stenosis.

The outcome of patients with 3-vessel CAD assigned to surgical or medical treatment is similar at the 10-year follow-up to that reported earlier in randomized trials. The more severe the symptoms, the more proximal the LAD CAD, and the worse the LV function, the greater is the benefit from surgery (81,85,96-100). In patients with 3-vessel disease, the relative risk reduction for surgery at 5 years is 42% and at 10 years is 24%, with an increase in survival of 5.7 months at 10-year follow-up (85). The definitions of single-, double-, and triple-vessel disease in these guidelines are those from the Bypass Angioplasty Revascularization Investigation (BARI) (101,102).

#### *3.2.2.3. Proximal LAD Disease*

Proximal LAD CAD (greater than 50% stenosis) is an important contributor to outcome. In patients with proximal LAD disease, the relative risk reduction of CABG is 42% at 5 years and 22% at 10 years. In LAD disease without proximal involvement, the relative risk reduction is 34% at 5 years and 10% at 10 years. In the presence of depressed LV func-

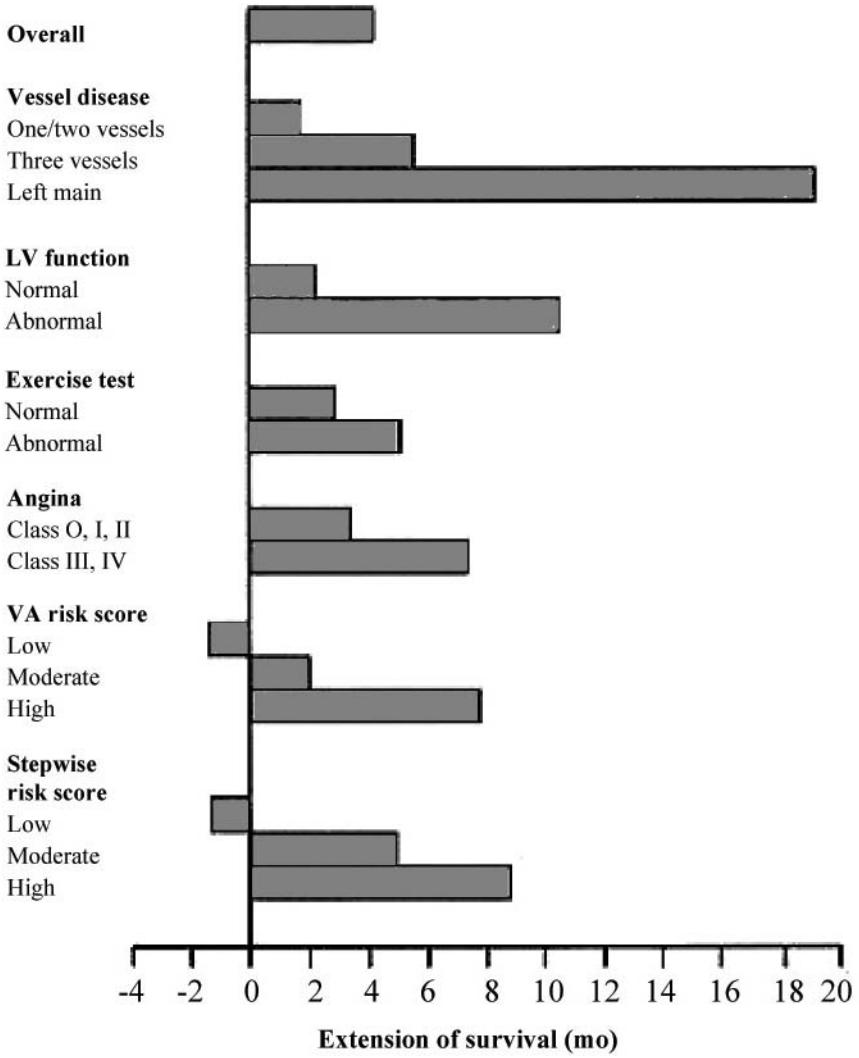


**Figure 4.** Extension of survival after 10 years of follow-up in various subgroups of patients, from a meta-analysis of 7 randomized studies. LV indicates left ventricular; VA, Veterans Administration. Reprinted with permission from Elsevier Science, Inc. (Yusuf et al. The Lancet. 1994;344:563-70) (85).

tion, the absolute benefit of surgery is greater because of the risk of this population (81,103).

### *3.2.2.4. LV Function*

LV systolic function remains an important predictor of which patients are likely to benefit from surgery (97-99,104). In patients with a normal EF, surgical revascularization generally provides little survival benefit. In patients with mild to moderately depressed function, the poorer the LV function, the greater is the potential benefit of surgery (97-99,105,106). The relative benefit is similar, but there is greater absolute benefit because of the high-risk profile of these patients. It is important to note that the randomized trials did not include patients with an LVEF less than 0.35. Thus, many of the patients operated on today were not well represented in the randomized trials.

A major growth in our understanding of the potential reversibility of chronic systolic dysfunction among patients with CAD has occurred in the past few years. Systolic dysfunction that is a result of chronic hypoperfusion ("hibernating") and not a result of infarction can now be identified noninvasively by positron emission tomographic scanning, radioisotope imaging, or dobutamine echocardiography. Patients with large areas of myocardial viability may benefit from revascularization. Small, observational studies of patients with hibernating myocardium who are undergoing coronary revascularization have shown functional and perhaps survival benefit, especially when LV function is particularly poor. This is discussed further in Section 5.9.

There are few data regarding optimal choices for women. The higher early surgical mortality needs to be weighed against the lessons derived from the predominantly male subjects (107), and this as well as other subsets will be discussed in Section 5.

It is important to note that the randomized trials did not include patients with an LVEF less than 0.35. Thus, many of the patients operated on today were not well represented in the randomized trials. Results are anticipated from the Surgical Treatment for Ischemic Heart Failure (STICH) study that is a randomized, multicenter trial of medical ther-

**Table 9.** Subgroup Results at 5 Years

| Subgroup | Overal Numbers | | Mortality Rates % | | Ratio (95% CI) | *P* for CABG Surgery vs Medical Therapy |
|---|---|---|---|---|---|---|
| | Deaths | Patients | Surgical | Medical | | |
| No. of diseased vessels | | | | | | |
| 1 | 21 | 271 | 5.4 | 9.9 | 0.54 (0.22–1.33) | 0.18* |
| 2 | 92 | 859 | 9.7 | 11.7 | 0.84 (0.54–1.32) | 0.45* |
| 3 | 189 | 1341 | 10.7 | 17.6 | 0.58 (0.42–0.80) | <0.001* |
| Left main artery | 39 | 150 | 15.8 | 36.5 | 0.32 (0.15–0.70) | 0.004* |
| No LAD disease | | | | | | |
| 1 or 2 Vessels | 50 | 606 | 8.3 | 8.3 | 1.05 (0.58–1.90) | 0.88 |
| 3 Vessels | 46 | 410 | 7.7 | 14.5 | 0.47 (0.25–0.89) | 0.02 |
| Left main artery | 16 | 51 | 18.5 | 45.8 | 0.27 (0.08–0.90) | 0.03† |
| Overall | 112 | 1067 | 8.6 | 12.3 | 0.66 (0.44–1.00) | 0.05 |
| LAD disease present | | | | | | |
| 1 or 2 Vessels | 63 | 524 | 9.2 | 14.6 | 0.58 (0.34–1.01) | 0.05 |
| 3 Vessels | 143 | 929 | 12 | 19.1 | 0.61 (0.42–0.88) | 0.009 |
| Left main artery | 22 | 96 | 12.8 | 32.7 | 0.30 (0.11–0.84) | 0.02‡ |
| Overall | 228 | 1549 | 11.2 | 18.3 | 0.58 (0.43–0.77) | 0.001 |
| LV function | | | | | | |
| Normal | 228 | 2095 | 8.5 | 13.3 | 0.61 (0.46–0.81) | <0.001 |
| Abnormal | 115 | 549 | 16.5 | 25.2 | 0.59 (0.39–0.91) | 0.02§ |
| Exercise test status | | | | | | |
| Missing | 102 | 664 | 13.1 | 17.4 | 0.69 (0.45–1.07) | 0.1 |
| Normal | 60 | 585 | 9 | 11.6 | 0.78 (0.45–1.35) | 0.38 |
| Abnormal | 183 | 1400 | 9.4 | 16.8 | 0.52 (0.37–0.72) | <0.001 |
| Severity of angina | | | | | | |
| Class I, II | 178 | 1716 | 8.3 | 12.5 | 0.63 (0.46–0.87) | 0.005 |
| Class III, IV | 167 | 924 | 13.8 | 22.4 | 0.57 (0.40–0.81) | 0.001 |

CI indicates confidence interval; CABG, coronary artery bypass graft; LAD, left anterior descending coronary artery; and LV, left ventricular.
*Includes only (79,80).
†Excludes (81).
‡Excludes (81-84).
§Excludes (80).
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apy versus CABG for patients with heart failure, LVEF less than 0.35, and coronary artery disease amenable for CABG.

### *3.2.2.5. Symptoms/Quality of Life*

More attention has been paid to improvement in symptoms and quality-of-life measurements. The findings from randomized trials for these outcomes parallel those of the survival data. Apart from its effect on survival, CABG is potentially indicated for 2 symptom-based indications: to alleviate symptoms of angina pectoris over and above medical therapy and to reduce the incidence of nonfatal outcomes such as MI, CHF, and hospitalization. CABG is considered to improve or to relieve angina pectoris in a much broader group of patients than the subgroups in which it has been found to improve survival. Registry studies have suggested a favorable impact on late MI among highest-risk subsets, such as patients with 3-vessel disease and severe angina pectoris. However, in the pooled data from the randomized trials (85), no overall beneficial impact of CABG on subsequent MI could be demonstrated. This may reflect an early increase in MI perioperatively in patients undergoing CABG surgery balanced by fewer MIs in the long term.

At 5 years, patients treated surgically used less antianginal medicines, with 63% of patients completely symptom-free compared with 38% of medically assigned patients (96). At 10 years, however, these differences were no longer significant. Patients treated surgically and medically used similar amounts of long-acting nitrates and beta-blockers, with 47% of surgical patients asymptomatic compared with 42% of medical patients. Recreational status, employment, frequency of CHF, use of other medicines, and hospitalization frequency were also similar between the groups (108-115).

At 10 years, the frequency of angina and other quality-of-life measurements were similar between surgically and medically treated groups. Those who have multivessel disease and who receive complete revascularization are less symptomatic, and symptom benefit is most apparent in patients with severe angina and LV dysfunction (EF less than 0.35) (108,110-116). Perhaps because of the symptomatic relief associated with surgical revascularization, the “crossover” from medical treatment to surgery may be of greater signif-

**Table 10.** Subgroup Analysis of 5-Year Mortality by Risk Stratum

| | Deaths, n | Patients, n | Medical Treatment Mortality Rate, % | Odds Ratio (95% CI) | *P* for CABG vs Medical Treatment |
|---|---|---|---|---|---|
| Risk strata derived by risk score* | | | | | |
| Lowest tertile | 23 | 406 | 5.5 | 1.18 (0.51–2.71) | 0.70 |
| Middle tertile | 90 | 930 | 11.5 | 0.63 (0.39–1.01) | 0.05 |
| Highest tertile | 153 | 849 | 23 | 0.50 (0.35–0.72) | 0.001 |
| Risk strata by stepwise risk score† | | | | | |
| Lowest tertile | 52 | 783 | 6.3 | 1.17 (0.66–2.07) | 0.60 |
| Middle tertile | 85 | 784 | 13.9 | 0.55 (0.34–0.88) | 0.01 |
| Highest tertile | 157 | 783 | 25.2 | 0.54 (0.37–0.77) | 0.001 |

CI indicates confidence interval; CABG, coronary artery bypass graft.

*Veterans Administration-type risk score = (0.70 × presence of Class III/IV angina) + (0.37 × history of hypertension) + (0.83 × ST-segment depression at rest) + (0.39 × history of myocardial infarction).

†Stepwise risk score = (0.015 × age) + (0.56 × presence of Class III/IV angina) + (0.35 × history of myocardial infarction) + (0.62 × abnormal ejection fraction) + (0.53 × proximal lesion greater than 50% in the left anterior descending coronary artery) + (0.29 × right coronary artery lesion greater than 50%) + (0.43 × history of diabetes) + (0.37 × history of hypertension).

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icance in improving quality of life. Medically assigned patients who had persistent angina despite medical therapy were able to undergo surgical revascularization and thus obtain relief of symptoms.

### *3.2.2.6. Loss of Benefit of Surgery*

The meta-analysis based on individual patient data from all of the available randomized trials indicates a gradually increasing reduction in mortality over the first 5 to 7 years when coronary surgery is compared with medical therapy. After this period, at about the 10- to 12-year follow-up, there is a tendency of the survival curves to converge. This diminished continued benefit has been shown in the individual studies as well and is likely due to a combination of factors. First, it is inevitable in studies with long-term follow-up that survival curves of various treatment groups will eventually merge. This result has to do with the reduced life expectancy of patients with coronary disease, regardless of treatment.

Second, there is an increased event rate in late follow-up of surgically assigned patients because of the progression of native and graft disease, with a disproportionate increase in late surgical mortality. Finally, crossover to surgery of medically assigned patients is important. Thus, high-risk, medically assigned patients may gain the "benefit" of surgery even when assigned to medical therapy. The crossover rate at 10 years is between 37% and 50%, and this may contribute to the better survival and improved quality of life in such "medically assigned" patients.

### *3.2.2.7. Summary*

CABG improves long-term survival in a broad spectrum of patients at moderate to high risk with medical therapy. Although a relative risk reduction of around 40% can be expected overall in comparison with medical therapy, absolute benefits are proportional to the expected risk with medical therapy. As such, absolute benefit is greatest among those at highest risk with medical therapy (5-year mortality greater than 20%). Clinical and angiographic markers of risk, including severity of CAD, LV dysfunction, and myocardial ischemia, can identify patients in various risk strata.

## *3.3. Comparison With Percutaneous Techniques*

Although PTCA was initially used only for the treatment of single-vessel CAD, advances in technique, equipment, and experience have resulted in its expanded use for patients with multivessel disease. In general, PTCA is less invasive and requires a shorter hospitalization and recovery time than does bypass surgery. However, the disadvantages of PTCA as initial therapy for coronary disease include restenosis of treated lesions and, compared with CABG, a lesser ability to revascularize all lesions in patients with multivessel disease. Clinical trials comparing PTCA and CABG have further defined the relative advantages and disadvantages of these treatments.

### 3.3.1. Overview of Randomized Trials

Nine randomized, clinical trials comparing PTCA and CABG have been published (Table 11). Before discussing the results of these trials, it is important to consider what we can expect to learn from them. A comparative trial must be large enough to have sufficient statistical power to detect a difference in survival, the usual primary end point. If no difference is observed between CABG and PTCA, it can be concluded that the treatments are equivalent only if trials are large enough to reliably detect or exclude relative differences in mortality of around 20% and include a large number of patients in whom CABG has been shown to improve prognosis. Because 600 deaths would be needed in the "control" group to exclude a relative risk difference of 20% with 90% power, trials with 4000 moderate- to high-risk patients per treatment arm would be needed. However, if a 30% risk difference is considered the smallest clinically important difference, trials of about 2000 patients in each group are required. Unfortunately, all of these trials excluded patients in whom survival had already been shown to be better with CABG when compared with medical therapy. Second, follow-up must be long enough (generally 4 to 5 years) to detect a survival advantage with either approach. Third, to reliably compare the 2 treatments, there must be a high rate of compliance with the original treatment allocation; if a substantial proportion of patients "cross over" (30% to 40% by 5 years), the ability to detect differences in survival decreases markedly. Finally, the patients enrolled in the trial must be similar to those not enrolled to allow generalization of the findings. All of the randomized trials fall short of 1 or more of these criteria. However, the largest of the 9 randomized trials, BARI, comes closest to fulfilling these criteria and will be discussed in detail (117).

In this trial, 1829 patients with multivessel disease were randomized at 18 centers to PTCA or CABG. The primary end point was all-cause mortality at 5 years, and predefined subgroup analyses were performed for the severity of angina, the number of diseased vessels, LV function, and lesion complexity. In addition, a separate analysis of diabetic patients was added partway through the trial. Baseline characteristics of the BARI study population included a mean age of 61 years, mean LVEF of 0.57, a 41% prevalence of 3-vessel disease, and 26% women; there were no significant differences between treatment groups. Revascularization was accomplished by PTCA in a mean of 2.4 lesions per patient, with a success rate of 88% for at least 1 lesion, and by CABG with a mean of 2.8 grafts per patient (82% with an IMA). Stents were not routinely employed (117). The average postprocedure length of stay was shorter with PTCA (3 versus 7 days). The rate of in-hospital Q-wave MI was higher for CABG than for PTCA (4.6% versus 2.1%, $P$ less than 0.05), and 6.3% of PTCA patients required urgent CABG. At a mean follow-up of 5.4 years, there was no statistically significant difference in long-term survival or freedom from MI, but patients initially randomized to PTCA had more hospitalizations and required more repeat revascularization procedures (Table 11). Thirty-one percent of patients initially assigned to PTCA underwent CABG during the trial (117). Compared with the other randomized comparisons, overall mortality in BARI was higher owing to the inclusion of older patients, more women, and more patients with multivessel disease and other comorbidities. This difference underscores the importance of comparing the methodology of these trials before discussing their conclusions.

The most important limitation of all of the randomized trials relates to the ability to generalize the conclusions. The findings are not applicable to all patients with multivessel coronary disease for 2 reasons. First, only around 5% of screened patients with multivessel disease were enrolled in the trials (118,119). In the BARI trial, more than 25 000 patients with multivessel coronary disease by diagnostic angiography were screened for eligibility. About 50% of these patients were ineligible because of left main disease, insufficient symptoms, or other reasons. One third of the remaining patients (4110) had multivessel disease suitable for both PTCA and CABG, and only half of these (7% of those screened) were enrolled in the randomized trial (120). Second, examination of the Emory Angioplasty versus Surgery Trial (EAST) registry suggests that physician judgment may be an important determinant of outcome that is eliminated by a randomized design. In this registry of 450 eligible patients who refused randomization, survival was slightly better than in the 392 randomized patients despite similar baseline features (121). This may reflect physician judgment, as CABG was utilized more often in patients with 3-vessel disease and PTCA more often in patients with 2-vessel disease (121).

The age range (mean age varied from 56 to 61 years) and sex distribution (around 20% female) were similar in most trials, although the Medicine, Angioplasty, or Surgery Study (MASS) trial had 42% women (122). All of the randomized trials excluded patients with low EFs and those for whom CABG was known to provide a survival advantage. Six trials included only patients with multivessel disease and 2, only single-vessel disease (MASS, Lausanne); the Randomized Intervention Treatment of Angina (RITA) trial included both (Table 11). Several trials were conducted in single centers, whereas RITA, the German Angioplasty Bypass-surgery Investigation (GABI), the Coronary Angioplasty versus Bypass Revascularization Investigation (CABRI), and BARI were multicenter. The CABRI and EAST trials permitted incomplete revascularization, whereas the others had a goal of complete revascularization. CABRI and RITA included vessels with total occlusion, accounting for the lower success rate of PTCA; the success rate for these vessels in RITA was only 48%. Asymptomatic patients were excluded from GABI, and the extent of coronary disease also varied widely. Three-vessel disease was present in only 12% and 18% of RITA and GABI subjects, respectively, and present in greater than 40% of BARI and Estudio Randomizado Argentino de Angioplastia vs Cirugia (ERACI) patients. The incidence of diabetes mellitus varied

**Table 11.** CABG vs PCI: Randomized Controlled Trials

| | Trial (Ref) | Age, y (% Female) | CAD | N | Acute Outcome% Death: CABG PCI | Acute Outcome% QW-MI:CABG PCI | Acute Outcome% Hosp CABG | Late Outcome, % Death | Late Outcome, % QW-MI | Late Outcome, % Angina | Late Outcome, % RR% Total/PCI/CABG | Primary End Point | Primary End Point, % | F/U, y |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PTCA Trials | BARI | 61 (26%) | MV | 1829 | 1.3 | 4.6 | N/A | 15.6¶ | 19.6 | N/A | 8/7/1 | D | 15.6¶ | 8§ |
| | (117) | | | | 1.1 | 2.1 | 6.3 | 19.1¶ | 21.3 | N/A | 54/34/31 | | 19.1¶ | |
| | EAST | 61 (26%) | MV | 392 | 1 | 10.3 | N/A | 17 | 19.6 | 12 | 13/13/1 | D+MI+T | 27.3 | 8‖ |
| | (119) | | | | 1 | 3.0† | 10.1 | 21 | 16.6 | 20† | 54/41/22 | | 28.8 | |
| | GABI | N/A (20%) | MV | 359 | 2.5 | 8 | N/A | 6.5 | 9.4 | 26 | 6/5/1 | A | 26 | 1 |
| | (776) | | | | 1.1 | 2.3† | 8.5 | 2.6 | 4.5 | 29 | 44/27/21 | | 29 | |
| | Toulouse | 67 (23%) | MV | 152 | 1.3 | 6.6 | N/A | 10.5 | 1.3 | 5.3 | 9/9/0 | A | 5.2 | 5 |
| | (778) | | | | 1.3 | 3.9 | 3.9 | 13.2 | 5.3 | 21.1† | 29/15/15 | | 21.1† | |
| | RITA | 57 (19%) | SV+ | 1011 | 1.2 | 2.4 | N/A | 3.6 | 5.2 | 21.5 | 4/3/1 | D+MI | 8.6 | 2.5‡ |
| | (126) | | MV* | | 0.8 | 3.5 | 4.5 | 3.1 | 6.7 | 31.3† | 31/18/19 | | 9.8 | |
| | ERACI | 58 (13%) | MV | 127 | 4.6 | 6.2 | N/A | 4.7 | 7.8 | 3.2 | 6/3/3 | D+MI+A+RR | 23 | 3 |
| | (132) | | | | 1.5 | 6.3 | 1.5 | 9.5 | 7.8 | 4.8 | 37/14/22 | | 53† | |
| | MASS | 56 (42%) | SV | 142 | 1.4 | 1.4 | N/A | N/A | N/A | 2 | 0/0/0 | D+MI+RR | 3 | 3 |
| | (122) | | (LAD) | | 1.4 | 0 | 11 | N/A | N/A | 18 | 22/29/14 | | 24† | |
| | Lausanne | 56 (20%) | SV | 134 | 0 | 0 | N/A | 1.5 | 1.5 | 5 | 3/3/0 | D+MI+RR | 7.6 | 2‡ |
| | (134) | | (LAD) | | 0 | 0 | 2.9 | 0 | 2.9 | 6 | 25/12/13 | | 36.8† | |
| | CABRI | 60 (22%) | MV | 1054 | 1.3 | N/A | N/A | 2.7 | 3.5 | 10.1 | 9/6/1 | D | 2.7 | 1 |
| | (143) | | | | 1.3 | N/A | N/A | 3.9 | 4.9 | 13.9† | 36/21/18 | | 3.9 | |
| STENT Trials | SoS | 61 (21%) | MV | 988 | N/A | N/A | N/A | 2 | 8 | 21 | 6/4/1 | RR | 6 | 1 |
| | (139) | | | | | | | 5† | 5 | 34† | 21†/13/9 | | 21† | |
| | ERACI II | 62 (21%) | MV | 450 | N/A | N/A | N/A | 8 | 6 | 8 | 5/0/0 | D+MI+CVA+RR | 19 | 1.6 |
| | (780) | | | | | | | 3† | 3[b] | 15† | 17†/0/5 | | 23 | |
| | ARTS | 61 (24%) | MV | 1205 | N/A | N/A | N/A | 3 | 5 | 10 | 4/3/1 | D+MI+CVA+RR | 12 | 1 |
| | (137) | | | | | | | 3 | 6 | 21† | 21†/16/7 | | 26† | |
| | AWESOME | 67 (N/A) | MV | 454 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | D | 21 | 3 |
| | (140) | | | | | | | | | | | | 20 | |
| | SIMA | 59 (21%) | SV | 121 | N/A | N/A | N/A | 4 | 4 | 5 | 0/0/0 | D+MI+RR | 7 | 2.4 |
| | (141) | | | | | | | 2 | 5 | 9 | 24†/13/6 | | 31† | |
| | LEIPZIG | 62 (25%) | SV | 220 | N/A | N/A | N/A | 2 | 5 | 21 | 8/8/0 | D+MI+RR | 15 | 0.5 |
| | (781) | | | | | | | 0 | 3 | 38† | 29/25/4 | | 31† | |

CABG indicates coronary artery bypass graft; PCI, percutaneous coronary intervention; CAD, coronary artery disease; QW, Q wave; MI, myocardial infarction; Hosp CABG, required CABG after PCI and before hospital discharge; RR, repeated revascularization; F/U, follow-up; BARI, Bypass Angioplasty Revascularization Investigation; EAST, Emory Angioplasty Surgery Trial; GABI, German Angioplasty Bypass-surgery Investigation; RITA, Randomized Intervention Treatment of Angina; ERACI, Estudio Randomizado Argentino de Angioplastia vs Cirugia; MASS, Medicine, Angioplasty, or Surgery Study; CABRI, Coronary Angioplasty versus Bypass Revascularization Investigation; SoS, the Stent or Surgery Trial; ERACI II, Coronary Angioplasty with Stenting vs Coronary Artery Bypass in patients with MV disease; ARTS, Arterial Revascularization Therapies Study; AWESOME, Angina with Extremely Serious Operative Mortality Evaluation; SIMA, Stenting vs Internal Mammary Artery; LEIPZIG, Stenting vs Minimally Invasive Bypass Surgery; MV, multivessel; D, death; T, thallium defect; A, angina; SV, single vessel; and LAD, left anterior descending coronary artery.

*Included total occlusion.

†*P* is less than 0.05 comparing CABG and PCI cohorts.

‡Planned 5-year follow-up (interim results).

§Primary end point and mortality at 8 years, other end points at 5 years.

‖Primary end point and mortality at 8 years, other end points at 3 years. Statistically significant.

from 10% to 12% (Toulouse, Goy, ERACI, GABI, and CABRI) to greater than 20% (EAST and BARI).

Finally, the trials used different primary end points and follow-up periods. Neither CABG nor PTCA has been shown to reduce the risk of subsequent nonfatal MI, and therefore inclusion of such an end point would dilute relative differences and decrease the likelihood of detecting differences. End points included survival (BARI), freedom from angina (GABI and Toulouse), freedom from death and MI (RITA), and other combinations including symptoms, stress thallium defects, and repeated revascularization (Table 11). Most required Q waves and a clinical event to define an MI, but EAST included "silent" MIs as well. Follow-up ranged from 1 to 5 years, and only MASS required angiography in all patients (122). Overall, all of the trials except BARI were underpowered and lacked sufficient follow-up.

### 3.3.2. Results of Randomized Trials

#### *3.3.2.1. Acute Outcome*

Despite the differences in design and follow-up, the results of randomized trials comparing PTCA and CABG have been similar. Procedural complications including death (1% to 2%) and Q-wave MI (up to 10%) were low for both procedures but tended to be higher with CABG (Table 11). A statistically significant increase in MI rate was present only in GABI and EAST and in 2 meta-analyses including many of the trials (118,123). For patients initially randomized to PTCA, CABG was needed during the initial hospitalization for 6% (range 1.5% to 10%) and was performed in close to 20% by 1 year (123).

The cost and length of stay were lower for PTCA than for CABG. In BARI, the cost of PTCA was 50% of that for CABG, but over time this was nearly equal (124,125). The lengths of stay in RITA were 4 and 12 days for PTCA and CABG, respectively (126). Patients having PTCA returned to work sooner and were able to exercise more at 1 month (127). The extent of revascularization achieved with CABG was higher than with PTCA (117,119). In the EAST trial, the percentage of revascularizable segments successfully treated was 99% for CABG versus 75% for PTCA (119). When the comparison was limited to severe and physiologically important lesions, the extent of early revascularization was similar, although this analysis includes the patients who crossed over from PTCA to CABG (119,128).

#### *3.3.2.2. Long-Term Outcome*

There was no significant difference in survival in 8 of the 9 randomized trials that compared PTCA and CABG at follow-up periods ranging from 1 to 8 years (Table 11). BARI was the largest trial with the longest follow-up. The combined end point of cardiac mortality and MI was similar at 5 years with both treatments (129). An update of the BARI trial results with a mean follow-up of 7.8 years has now demonstrated a survival advantage in the overall study (84.4% with CABG versus 80.9% with PTCA, *P* equals 0.043), due to a marked survival benefit in the study subjects with diabetes who were treated surgically (76.4% versus 55.7% with PTCA, *P* equals 0.0011) (130). Longer follow-up analyses of EAST and ERACI have not demonstrated any differences in mortality (131,132).

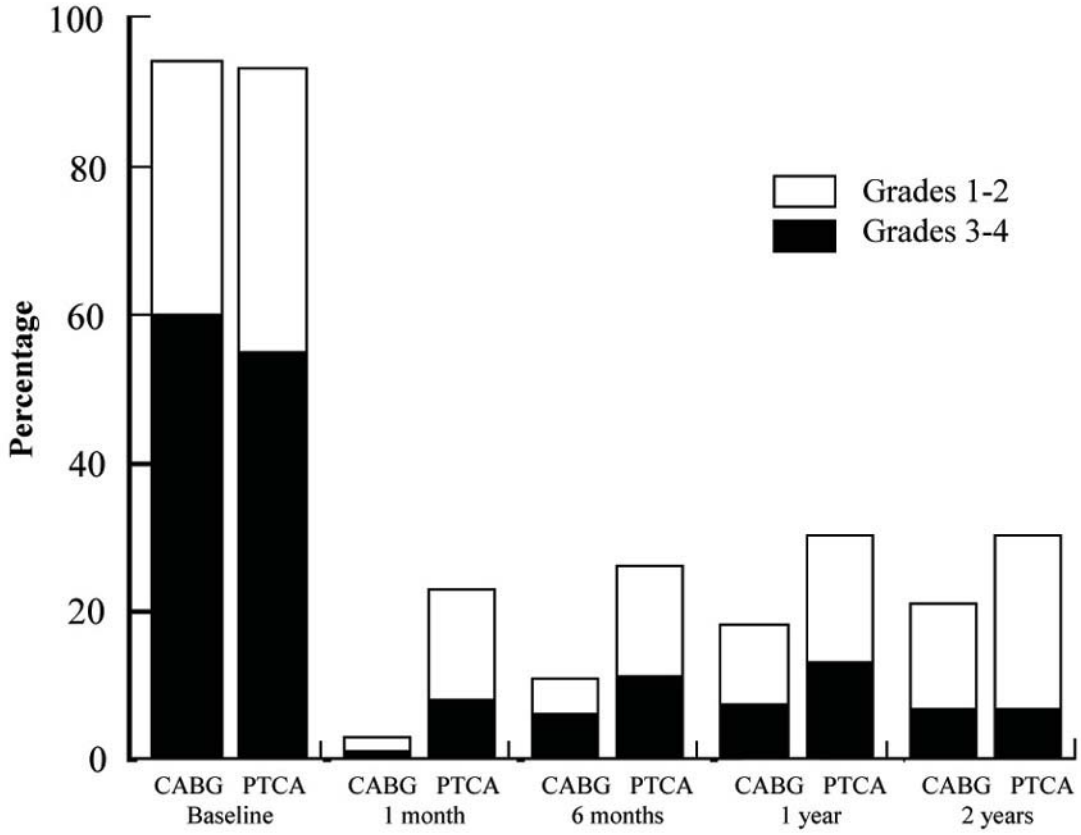
None of the trials or meta-analyses were able to demonstrate a difference in Q-wave MI or the combined end point of death and MI (Table 11) (118,123). Most trials found that CABG resulted in greater freedom from angina, and the difference from PTCA was statistically significant in EAST, Toulouse, RITA (Figure 5), and CABRI. Exercise time at 2.5 years was assessed in RITA and favored patients initially treated by PTCA (191 versus 171 minutes) (126). Large thallium defects (assessed in EAST) were slightly more common in PTCA patients at 3 years (119). The relative risk for angina with PTCA tended to be higher early but decreased with longer follow-up (123) (Figure 5).

The most striking difference between the treatments was in the need for subsequent procedures. The rate was 4- to 10-fold higher for PTCA in every trial (Table 11). Three trials (Lausanne, MASS, and ERACI) that included repeated revascularization as part of the primary, composite end point demonstrated a statistically significant reduction in events with CABG (122,133,134). Eight percent of CABG patients required additional revascularization within 5 years in BARI, compared with 54% of PTCA patients (117). Additional procedures were needed earlier in PTCA patients and included PTCA only (23.2%), CABG only (20.5%), or both (10.8%) (117).

Several studies have compared quality of life and cost with various revascularization strategies (124,127,135,136). In RITA, physical activity and employment were similar for both procedures after 3 years (127). A BARI substudy including 52% of enrollees found that functional status assessed by the Duke Activity Index improved more with CABG early on but was equivalent by 5 years (124). Emotional health and employment were also similar in this study and others (124,127,135). The early cost benefit of PTCA decreased during follow-up owing to the more frequent need for repeated procedures and hospitalization such that, over the long term, PTCA approached the cost of CABG (123,124,135,136). There appeared to be a greater cost benefit to PTCA in patients with 2-vessel disease (124). In BARI, it was estimated that the slight survival advantage of CABG would cost $26 117/year of added life (124).

#### Comparison with stents

Since the previous update of these guidelines, several trials comparing stents with CABG in patients with multivessel disease have been initiated. The Arterial Revascularization Therapies Study Group (ARTS) trial enrolled 1205 patients with multivessel coronary disease in whom a cardiac surgeon and interventional cardiologist agreed that they could achieve a similar extent of revascularization. In this randomized comparison, there was no difference at 1 year in the combined rate of death, MI, and stroke between the 2 revas-




Prevalence of angina (Canadian Cardiovascular Society Classification) over time.

Patient numbers were:

| | *Time (mo)* | | | | |
|---|---|---|---|---|---|
| *Group* | *0* | *1* | *6* | *12* | *24* |
| CABG | 498 | 482 | 480 | 401 | 237 |
| PTCA | 509 | 491 | 491 | 433 | 310 |

**Figure 5**. Freedom from angina in the Randomized Intervention Treatment of Angina (RITA) trial. Reprinted with permission from Elsevier Science, Inc. (The Lancet. 1993;341:573-80) (126).

cularization strategies (137). However, repeat revascularization rates were higher with stenting (16.8% versus 3.5% with surgery), with a net cost savings of $2973 per patient favoring the stent approach. In diabetic patients (n equals 198), the difference in repeat revascularization rates was even more disparate (22.3% with stents versus 3.1% with CABG), although overall event-free survival was similar (138) (Table 11).

Similar results were reported by the Stent or Surgery (SoS) trial investigators. The trial randomized 988 patients with multivessel disease (57% 2-vessel; 42% 3-vessel) to revascularization with PCI (78% received stents) or CABG (81% with pedicled left IMA graft). The primary end point of repeat revascularization occurred in 21% of PCI patients versus 6% of CABG patients at a median follow-up of 2 years (hazard ratio equals 3.85, *P* less than 0.0001). Freedom from angina was also better with surgery (79% versus 66%). Mortality was higher in the PCI group, but this was influenced by a particularly low surgical mortality and a high rate of noncardiovascular deaths in the PCI group (139).

In the Angina with Extremely Serious Operative Mortality Evaluation (AWESOME) study, 454 patients at 16 VA hospitals with high-risk features for adverse outcome with surgery were randomized to either CABG or PCI. High-risk characteristics included prior open-heart surgery, age greater than 70 years, ejection fraction less than 0.35, MI within 7 days, and IABP. Stents were used in 54% of PCI patients. Survival was similar (79% with CABG and 80% with PCI) at 36 months (140). Finally, in the Stenting versus Internal Mammary Artery (SIMA) trial, 121 patients with isolated proximal LAD coronary artery disease were randomly treated with stenting or CABG (using the IMA). At 2.4 years of follow-up, there were no differences in the rates of death, MI, functional class, medications, or change in quality of life. Repeat revascularization was required more often (31%

versus 7%) in the stent group (141). Overall, 6 trials have now been published comparing CABG with PCI using stents in single or multivessel disease. Compared to the earlier trials with balloon angioplasty, stent usage and left IMA revascularization rates have increased. The results in terms of death, MI, and stroke are similar in the more recent trials; however, the disparity in the need for repeat revascularization, which favors surgery, has narrowed (Table 11).

### *3.3.2.3. Special Subsets*

The BARI trial prespecified 4 subsets for analysis. The primary end point of survival did not differ in these subgroups based on severity of angina, extent of disease, LV function, and lesion complexity (117). However, 3-year cardiac mortality was higher with PTCA in several high-risk groups (in unstable angina and non–ST-elevation MI (NSTEMI), PTCA 8.8% versus CABG 4.9%; in CHF, PTCA 27.7% versus 16.4% with CABG) (129). The ERACI trial included a high proportion (83%) of patients with unstable angina, and there was no difference in survival at 1 year (133).

Data from fibrinolytic trials suggesting an adverse effect of diabetes mellitus on PTCA outcome prompted the addition of treated diabetes mellitus as a subgroup for analysis partway through the BARI trial (117,142). This subgroup of 353 patients (19% of total) was more likely to be women or members of minorities and belong to a lower socioeconomic class. They also had more severe heart disease and comorbidities, but their in-hospital complications were similar to those in patients without diabetes and were also higher for CABG than for PTCA (143).

All-cause mortality and cardiac mortality were both higher in patients with diabetes treated with PTCA (34.7% versus 19.1% and 20.6% versus 5.8%, respectively) (Figure 6) (142). This benefit of CABG was confined to patients receiving IMA grafts, which may reflect a selection bias or the low numbers of patients not receiving IMA grafts. A similar result with regard to patients with diabetes was found in a post hoc analysis of 122 patients with diabetes in CABRI (143), but no difference was found for patients with diabetes in EAST (119).

A separate meta-analysis of the randomized trials for single-vessel disease has also been performed (123). As expected, the overall risk for events was less than in patients with multivessel disease. Although the risk of death and MI was lower with CABG, this finding should be interpreted with caution, since no such difference was found for multivessel disease. The need for late CABG was lower in patients with single-vessel disease, and there was less difference in angina frequency (123).

### *3.3.2.4. Results From Nonrandomized Trials and Registries*

Much of the debate relating to the finding for a survival advantage of CABG in treated patients with diabetes is based on the results of nonrandomized trials and registries. Treated patients with diabetes in the BARI registry who

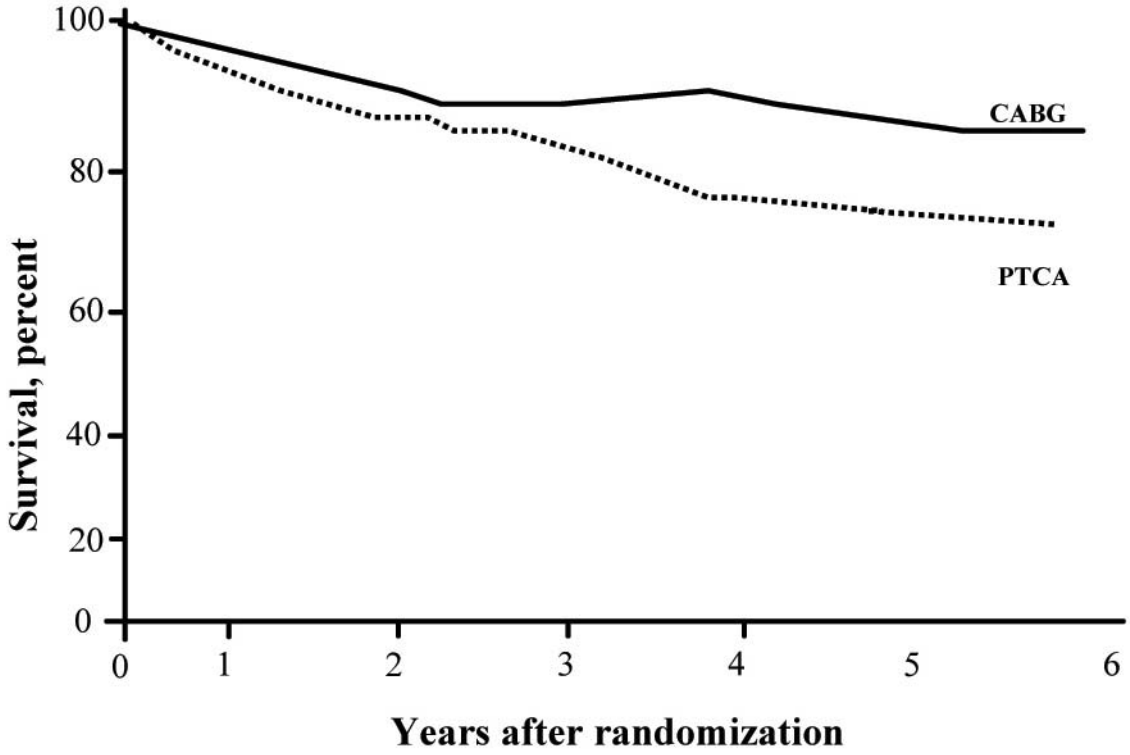



**Figure 6**. Improved survival with coronary artery bypass graft surgery (CABG) versus percutaneous transluminal coronary angioplasty (PTCA) in patients with diabetes mellitus. Results from the Bypass Angioplasty Revascularization Investigation (BARI) showing that patients with multivessel coronary disease who were being treated for diabetes at baseline had a significantly better survival after coronary revascularization with CABG (solid curve) than with PTCA (dashed curve) ($P = 0.003$). Modified with permission from Circulation. 1997;96:1761-9 (142).

refused randomization and selected their form of revascularization did not fare worse with PTCA (144). In a retrospective cohort study comparing PTCA and CABG for patients with diabetes with multivessel disease and similar age, sex, EF, and severity of angina, there was also no difference in survival after 6 years (145). However, in one comparison of CABG and PTCA in a nonrandomized, observational database, patients with diabetes requiring insulin had a lower long-term survival after treatment with multivessel PTCA (146). Limitations of this conclusion include the unknown adequacy of glucose control and the absence of a survival advantage for CABG when patients in the randomized trials are pooled and in other, nonrandomized registries (147).

The majority of patients in the randomized trials had angina. A small trial that demonstrated improved outcomes with revascularization compared with medical therapy in patients with asymptomatic ischemia also examined the relative benefits of the type of revascularization (148). In this nonrandomized trial, CABG provided superior relief of exercise-induced as well as ambulatory ischemia compared with PTCA (149).

A more compelling report was published by Hannan et al (150), which described a 3-year survival analysis of the 30 000 patients enrolled in the New York State PTCA registry compared with that of 30 000 patients in the CABG registry from 1993 to 1995. As opposed to the randomized trials, this large experience showed a survival benefit for patients receiving CABG when proximal LAD stenosis was greater than 70%, regardless of whether 1-, 2-, or 3-vessel disease was present (Figure 7) (Table 12) (150). Patients with 3-vessel disease not involving the proximal LAD also fared better with CABG than with PTCA. Patients with 1-vessel disease without severe proximal LAD stenosis had better survival with PTCA. Several potential limitations of this experience deserve comment. Unmeasured differences in patient severity not accounted for in the risk-adjustment method could have affected the conclusions. Similarly, physicians' choice of treatment may have been based on unmeasured patient factors. Finally, coronary stents were utilized in just 11.8% of the PCI patients.

#### *3.3.2.5. Conclusions*

For patients included in the randomized trials, CABG provided better relief of angina with a lower need for subsequent procedures. Initial complications are higher with CABG, as are the cost and length of hospitalization. Patients may return to work sooner after PCI but are subsequently hospitalized more often, thus generating similar overall long-term costs. Randomized trials do not show any difference in late death or rate of MI, except in patients with treated diabetes mellitus, for whom CABG may be superior. Conversely, data from large registries, particularly those of New York State, suggest that patients with severe, proximal LAD stenosis and/or 3-vessel disease may achieve improved survival with CABG. Patients with 1-vessel disease not involving severe proximal LAD disease may do better with PCI.

Several important caveats and limitations to these conclusions must be discussed. Since completion of the trials, the influence of new technology, particularly on PCI, has been considerable. Intracoronary stents are now used in 70% or more of PCIs and have reduced the need for both urgent CABG and subsequent procedures by as much as 50% (151). Continuing advances in PCI and stent designs, the use of brachytherapy (local radiation), and drug-eluting stents have further reduced the need for repeat procedures. Medical management of atherosclerosis, both before and after revascularization, has continued to evolve, with greater use of beta-blockers and inhibitors of the renin-angiotensin-aldosterone system after MI and the introduction of statins and other lipid-lowering agents. The ability to select patients for revascularization procedures by using a methodology that can separate scarred from viable myocardial segments will undoubtedly alter the outcomes from these procedures. Other changes in patient management that may influence these conclusions include the use of platelet glycoprotein IIb/IIIa inhibitors and/or direct thrombin inhibitors during percutaneous interventions, the more frequent use of IMA grafts, and the emergence of less-invasive surgical approaches.

It is likely that during the progress of their disease, many patients will benefit from a combined application of percutaneous and surgical techniques, taking advantage of the low morbidity of percutaneous methods and the established long-term benefit of surgical revascularization with arterial conduits.

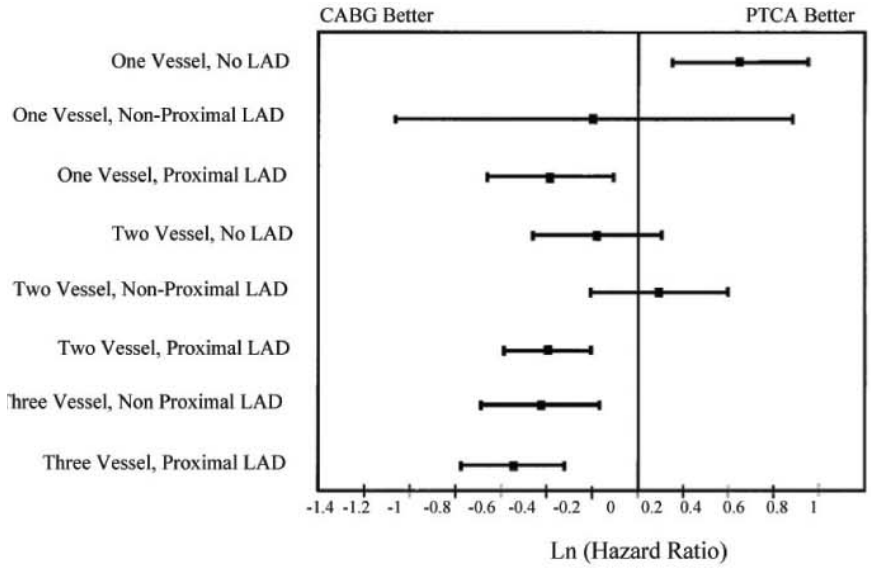
# 4. MANAGEMENT STRATEGIES

## *4.1. Reduction of Perioperative Mortality and Morbidity*

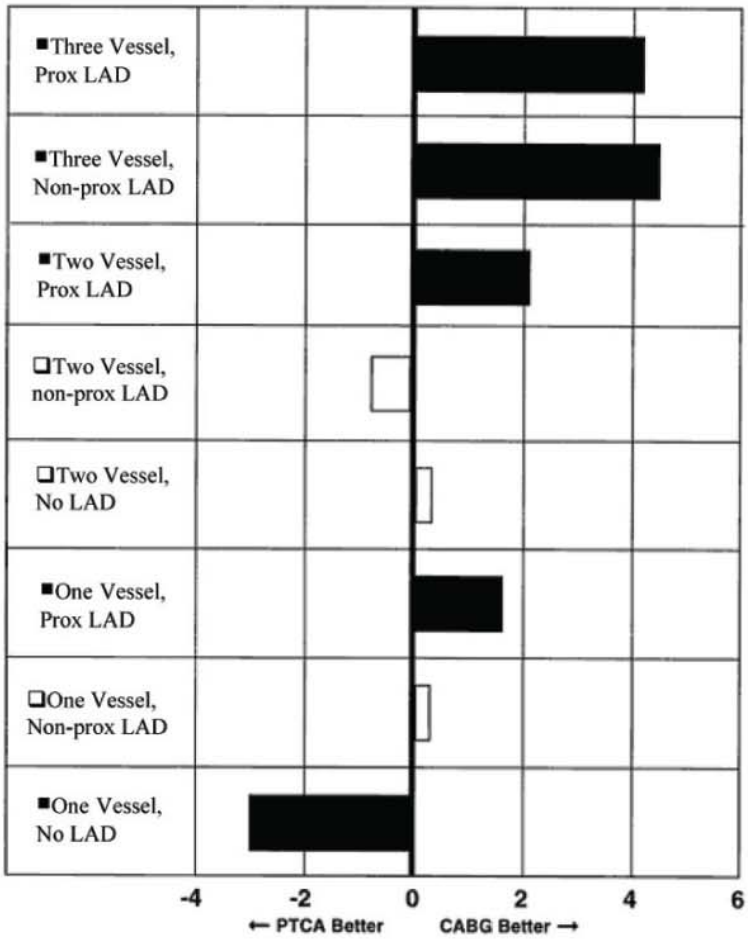
One of every $10 spent on surgical treatment of coronary disease is related to a complication, a sum of 1 billion dollars annually in the United States (152). Careful evaluation of patient characteristics should lead to proper risk stratification and the identification of areas for risk neutralization. Some risk factors that at first appear immutable may in fact be markers or surrogates for conditions that can be modified. The incremental incorporation of new advances can lead to coronary bypass results that are superior to those of the past. The following discussion formalizes this mind-set of risk neutralization to maximize the margin of safety for coronary bypass.

### 4.1.1. Reducing the Risk of Brain Dysfunction After CABG

One of the most devastating complications of coronary bypass surgery is perioperative stroke. In addition to patient morbidity and mortality, there are indirect costs through lost productivity; the direct economic cost of a stroke ranges from $90 000 to $228 000 over a patient's life span (153-155). Postoperative stroke is the second most common cause of operative mortality (after low cardiac output state) (156). The




**Panel A**




**Panel B**

**Figure 7. Panel A:** 95% Confidence interval for ln (adjusted hazard ratio) of PTCA patient death: CABG patient death within a 3-year period (excluding patients with myocardial infarction less than 24 hours before the procedure). For the sample size within each anatomic cohort, see Table 11. **Panel B:** Differences in adjusted percent survival at 3 years: percent CABG survival minus percent PTCA survival. Solid bars show statistically significant differences. Prox indicates proximal; LAD, left anterior descending coronary artery; PTCA, percutaneous coronary angioplasty; CABG, coronary artery bypass graft. Reprinted with permission from Elsevier Science, Inc. (Hannan et al. J Am Coll Cardiol. 1999;33:63-72) (150).

**Table 12.** Three-Year Survival by Treatment in Each Anatomic Subgroup

| Coronary Anatomy Group | | Patients, n | Survival Observed, % | Survival Adjusted, % | *P* |
|---|---|---|---|---|---|
| 1-Vessel, no LAD | CABG | 507 | 89.2 | 92.4 | 0.003 |
| | PTCA | 11,233 | 95.4 | 95.3 | |
| 1-Vessel, nonproximal LAD | CABG | 153 | 95.8 | 96.0 | 0.857 |
| | PTCA | 4130 | 95.7 | 95.7 | |
| 1-Vessel, proximal LAD | CABG | 1917 | 95.8 | 96.6 | 0.010 |
| | PTCA | 5868 | 95.5 | 95.2 | |
| 2-Vessel, no LAD | CABG | 1120 | 91.0 | 93.0 | 0.664 |
| | PTCA | 2729 | 93.4 | 92.6 | |
| 2-Vessel, nonproximal LAD | CABG | 850 | 91.3 | 92.3 | 0.438 |
| | PTCA | 2300 | 93.3 | 93.1 | |
| 2-Vessel, proximal LAD | CABG | 7242 | 93.5 | 93.8 | <0.001 |
| | PTCA | 2376 | 92.8 | 91.7 | |
| 3-Vessel, nonproximal LAD | CABG | 1984 | 90.1 | 90.3 | 0.002 |
| | PTCA | 660 | 86.7 | 86.0 | |
| 3-Vessel, proximal LAD | CABG | 15,873 | 90.1 | 90.3 | <0.001 |
| | PTCA | 634 | 88.2 | 86.1 | |

LAD indicates left anterior descending coronary artery; CABG, coronary artery bypass graft; and PTCA, percutaneous transluminal coronary angioplasty.
Comparative observed and adjusted 3-year survival of patients treated with PTCA or CABG in various anatomic subgroups.
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incidence of stroke after coronary operation is related to increased age (53,157-159) (Figure 8A), which parallels the accelerated involvement of the aorta and great vessels with atherosclerotic plaque (156) (Figure 8B). Age per se is less important than atherosclerosis, which plays a role in at least two thirds of adverse events after coronary bypass.

As discussed in Sections 4.1.1.1 and 4.1.1.2, post-CABG neurological events can be classified into type 1 injuries, which are predominantly focal stroke, transient ischemic attack, and fatal cerebral injuries, and type 2 events, which reflect a more global/diffuse injury, with disorientation or immediate (and usually reversible) intellectual decline.

### *4.1.1.1. Type 1 Neurological Injury*

Type 1 injury occurs in 3.1% of patients, is responsible for a 21% post–coronary bypass mortality rate, 11 days in the intensive care unit, 25 days in hospital, at least an additional $10 266 in hospital boarding charges, and a cost of 5 to 10 times the in-hospital charge for rehabilitative and outpatient support (51,148).

4.1.1.1.1. Aortic Atherosclerosis and Macroembolic Stroke. The surgeon's identification of an atherosclerotic ascending aorta is the single most significant marker for an adverse cerebral outcome after coronary bypass operations (OR 4.5, *P* less than 0.05) (48), reflecting the role of aortic atheroembolism as the cause of ischemic stroke (161-165). Since the early days of the operation, atheroemboli and calcific debris have been detected in the cerebral circulation in patients dying after coronary bypass surgery (166). Since the average age of patients having coronary bypass is increasing, perioperative atheroembolism from aortic arch plaque is also increasing and is likely responsible for 1 in 3 strokes after coronary bypass (167). This risk is particularly increased in patients beyond 75 to 80 years old (49) (Figures 8B and 8C). Most perioperative cerebral atheroembolization likely arises intraoperatively from manipulation of the ascending or transverse aorta during cannulation, clamping, or placement of proximal anastomoses or from the shear effect of the flow from the aortic cannula (168,169,170). Preoperative, noninvasive testing for detection of the high-risk patient has limited sensitivity.

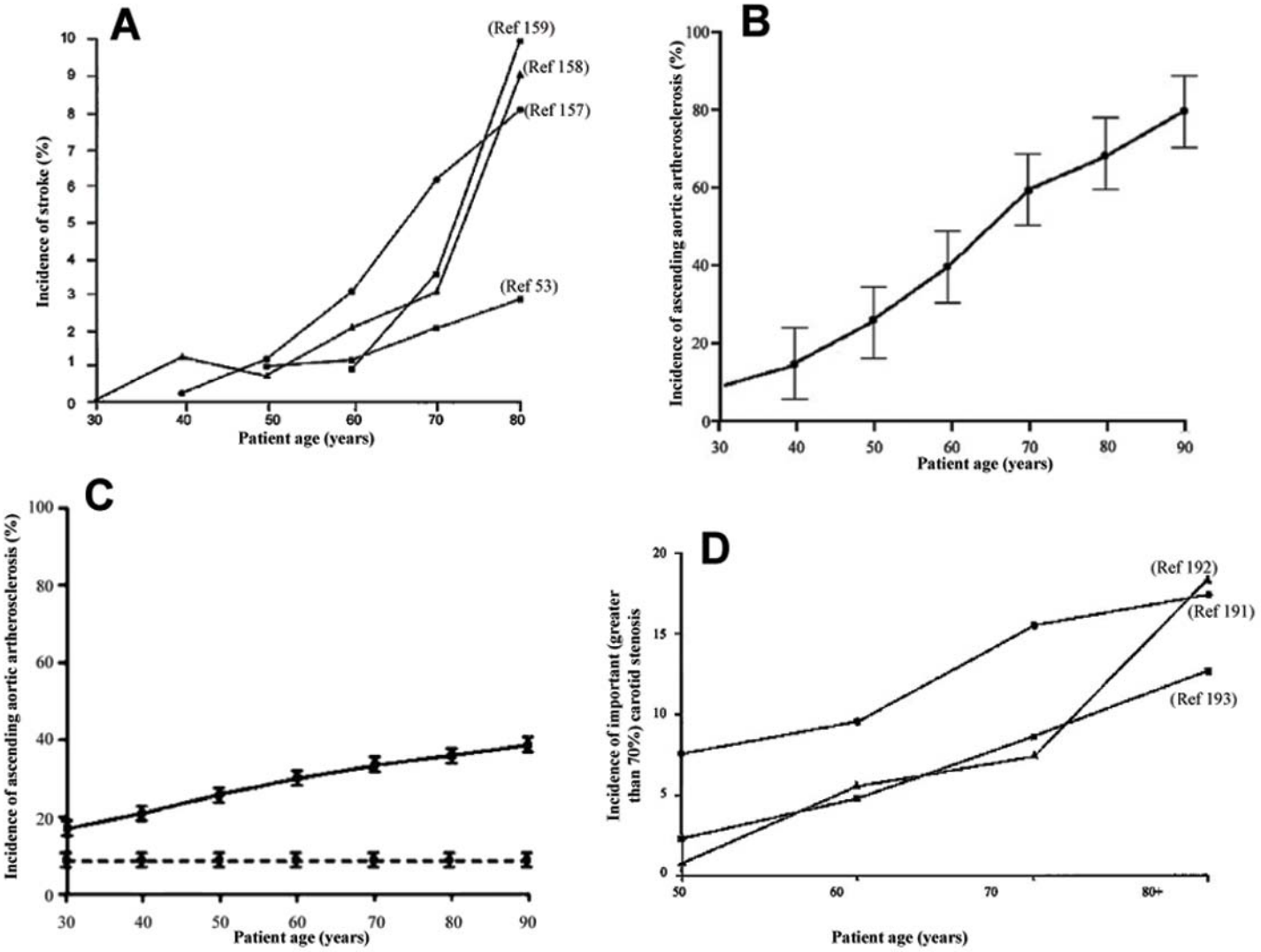


**Figure 8. A:** Incidence of permanent, focal, central nervous system injury after coronary bypass is strongly correlated with increasing age. **B:** Ascending aortic atherosclerosis is a powerful marker of increased risk for perioperative stroke in the coronary bypass population and increases directly with age. **C:** Strong correlation between perioperative atheroembolism and the degree of atherosclerotic involvement of the ascending aorta. The solid line represents severe atherosclerotic involvement the interrupted line, lesser involvement. **D:** Extracranial cerebrovascular disease is a significant contributor to stroke after coronary bypass and is strongly correlated with age, suggesting a population for aggressive preoperative screening. Panels B and C are reprinted with permission from Elsevier Science, Inc. (Blauth et al. J Thorac Cardiovasc Surg.1992;103:1104-11) (169).

Computed tomography identifies most severely involved aortas but underestimates mild to moderate involvement compared with echocardiography (163,171). TEE is useful for examination of the aorta, and although evaluation of the ascending aorta was somewhat limited by the intervening trachea (159) with earlier monoplane techniques, multiplane TEE technology allows good visualization of the aorta. However, the intraoperative assessment of ascending aortic atheroma by epiaortic imaging (in which the imaging probe is placed directly on the aorta) is superior to both TEE and direct palpation (160).

TEE identification of mobile arch atheroma in patients undergoing CABG was associated with a 33% stroke rate versus 2.7% in patients with nonmobile plaque (*P* equals 0.01) (172). Intraoperative palpation is notorious for its underestimation of the high-risk aorta (160). Palpation detected only one third of atherosclerotic lesions identified by epivascular echocardiography (171). The aortic pattern with the highest risk is the protruding or mobile aortic arch plaque, and this eludes intraoperative palpation in 80% of cases (173). Intraoperative epivascular ultrasound represents an important advance and is now used in many centers for intraoperative diagnosis and stroke risk reduction (171,174). The technique is highly sensitive and specific for identification of the high-risk aorta.

An aggressive approach to managing patients with severely atherosclerotic ascending aortas identified by intraoperative epiaortic ultrasound imaging appears to reduce the risk of postoperative stroke (53,175). Twelve hundred of 1334 consecutive open heart surgery patients (88% with coronary

disease) underwent screening with intraoperative epivascular ultrasound. These findings led to a change in intraoperative technique in 19.3% of patients. In patients with 3 mm or less of aortic wall thickening, standard techniques were used. When the aorta demonstrated a greater than 3-mm thickening, the cannulation, clamp, or proximal sites were changed, or a no-clamp fibrillatory arrest strategy (176) was used. For high-risk patients with multiple or circumferentially involved areas or those with extensive mid-ascending aortic involvement, the ascending aorta was replaced under hypothermic circulatory arrest. The 27 high-risk patients had no strokes and a mortality rate of just 3%. Among patients with a moderately to severely involved aorta treated with the less-radical approaches, the incidence of stroke was 6.3%. When epivascular ultrasound showed no or mild atherosclerotic disease, the stroke incidence was low, 1.1% (53,176).

In a smaller study of epivascular echo-directed management, 195 consecutive coronary patients undergoing CABG were compared with a control group of the previous consecutive 165 patients for whom only the surgeon's palpation was used to evaluate the aorta. Ten percent of the epivascular group had the intraoperative technique modified versus 3% of the control group. The most common change in operative approach was use of a no-clamp, cold fibrillatory arrest technique. Three percent of the control group had strokes compared with none of the epivascular echo-managed group (*P* less than 0.02) (51).

With a no-clamp technique, the surgeon may completely revascularize the heart with standard in situ IMA and aortically based SVGs, typically constructing a single, proximal anastomosis during a brief period of total circulatory arrest on a safe area of the aorta. Alternatively, the surgeon may use an all-in situ arterial revascularization approach, or SVGs may be grafted onto the in situ IMA by using an end vein to side artery anastomosis (167,177).

Preoperative risk assessment may identify a small population of patients with such extensive aortic atherosclerosis and poor outlook that the benefit from coronary bypass would appear to be very small. This population is difficult to define, but a starting point may include patients with aortic plaques 4 mm or more or with certain morphologies that are associated with only a 20% chance at 4 years of freedom from peripheral embolism, MI, recurrent stroke, or death (165). This risk, along with an extremely high perioperative risk, would argue for nonoperative treatment. However, if the cardiac risk of medical therapy is high (5-year mortality greater than 20%), alternative forms of revascularization should be considered. These include off-pump bypass surgery; minimally invasive direct CABG (MID-CAB) without CPB, with or without concomitant PCI; and exclusive percutaneous revascularization. These techniques may provide the benefit of revascularization in such high-risk patients while minimizing the perioperative risk of stroke. There are few randomized trials that examine the specific impact of CPB on stroke incidence, but 1 randomized study showed a comparable stroke rate in patients without CPB (off-pump) versus those on-pump (56). These patients were not stratified according to high-risk aortic disease, so the relative value of off-pump surgery in such patients remains unknown.

#### 4.1.1.1.2. Atrial Fibrillation and Postoperative Stroke.

**Class IIa**

**In post-CABG atrial fibrillation that is recurrent or persists more than 24 hours, warfarin anticoagulation for 4 weeks is probably indicated. *(Level of Evidence: C)***

*Chronic* atrial fibrillation is a hazard for perioperative stroke as a result of cardiac thromboembolism. Intraoperative surgical manipulation or spontaneous resumption of sinus rhythm early in the postoperative period may be associated with embolism of a left atrial clot. One potential approach to reduce atrial fibrillation-associated embolism is the performance of preoperative TEE. Absence of a left atrial clot would suggest that the operation may proceed with acceptable risk. If a left atrial clot is identified, 3 to 4 weeks of anticoagulation, restudy, and then subsequent operation is a rational approach if the clinical situation allows this. Unfortunately, few clinical trial data are available to assist physicians in the best management for this situation.

*New-onset postoperative* atrial fibrillation occurs in 30% of patients undergoing CABG (178-180), with the peak incidence on the second to third postoperative day (181). It is associated with a 2- to 3-fold increase in postoperative risk for stroke (182,183). Patients at risk for postoperative atrial fibrillation have been identified and include those with COPD, proximal right CAD, prolonged cross-clamp time, atrial ischemia, advanced age, and withdrawal of beta-blockers. Identifying at-risk patients and directing treatment to these patients (see Section 4.1.5) appears to be effective in reducing the incidence of post-CABG atrial fibrillation and thus the morbid complication of postoperative strokes associated with this arrhythmia. Minimally invasive and off-pump beating-heart procedures may also reduce the incidence of postoperative atrial fibrillation (184,185).

The role of anticoagulation in patients who develop post-CABG atrial fibrillation is unclear. In general, an aggressive anticoagulation and cardioversion philosophy may reduce the neurological complications associated with this arrhythmia. However, the risks of pericardial bleeding and tamponade have to be weighed with early use of full anticoagulation. Early (within 24 hours of onset of atrial fibrillation) attempts at cardioversion can probably be safely performed without anticoagulation. However, if the arrhythmia persists beyond this time, it may be advisable to use intravenous heparin while cardioversion is attempted. In certain patients, TEE can be used to exclude left atrial appendage thrombus and help to direct cardioversion. In such patients, it is generally recommended that anticoagulation be used after the cardioversion (186). If the atrial fibrillation persists, antico-

agulation with warfarin on an outpatient basis is probably indicated when the benefit of anticoagulation in selected patients (186a-c) exceeds the risk of bleeding in the postoperative interval in the judgment of the surgical team. Further attempts at cardioversion are determined by the individual patient profile (187).

#### 4.1.1.1.3. Recent Anterior MI, LV Mural Thrombus, and Stroke Risk.

**Class IIa**

**Long-term (3 to 6 months) anticoagulation is probably indicated for the patient with recent anteroapical infarct and persistent wall-motion abnormality after CABG. *(Level of Evidence: C)***

**Class IIb**

**In patients having a recent anterior MI, preoperative screening with echocardiography may be considered to detect LV thrombus, because the technical approach and timing of surgery may be altered. *(Level of Evidence: C)***

The patient with a recent anterior MI and residual wall-motion abnormality is at increased risk for development of an LV mural thrombus and its potential for embolization. Keren et al (188) identified LV thrombus in 38 of 124 anterior-infarct patients (31%) and in none of 74 patients with inferior infarcts (*P* less than 0.001). Early fibrinolytic therapy was not uniformly protective against LV thrombus, and 30% occurred after discharge. Such patients are at risk for systemic embolization of the LV clot, and the risk is highest in the first few weeks after the acute infarct. Preoperative screening with echocardiography may demonstrate the clot and alter the technical approach and perhaps the timing of surgery. Also, long-term (3 to 6 months) anticoagulation is probably recommended for the patient with persistent anterior wall-motion abnormalities after coronary bypass. LV thrombus may recur in patients receiving short-term (2 months or less) anticoagulation. Apical akinesis at 10 days after infarction was a strong predictor for subsequent thrombus formation, which conferred an increased risk for subsequent stroke (189).

4.1.1.1.4. Recent Antecedent Cerebrovascular Accident. A recent, preoperative cerebrovascular accident presents another situation in which delaying the operation may reduce the perioperative neurological risk. Evidence of a hemorrhagic component to the cerebrovascular accident, based on the results of a computed tomography scan, identifies those patients at particular risk for extension of the neurological damage due to heparinization and CPB (189). It is generally believed that a delay of 4 weeks or more is prudent if coronary anatomy and symptoms permit.

4.1.1.1.5. CPB Time and Neurological Risk. Increased time on CPB is closely correlated with adverse neurological outcome, emphasizing the need for an organized, expeditious operation. On average, patients without postoperative neurological events have shorter pump times than those who develop postoperative stroke and/or type 2 deficits (190).

#### 4.1.1.1.6. Carotid Disease and Neurological Risk Reduction.

**Class IIa**

1. **Carotid endarterectomy is probably recommended before CABG or concomitant to CABG in patients with a symptomatic carotid stenosis or in asymptomatic patients with unilateral or bilateral internal carotid stenosis of 80% or more. *(Level of Evidence: C)***
2. **Carotid screening is probably indicated in the following subsets: age greater than 65 years, left main coronary stenosis, peripheral vascular disease, history of smoking, history of transient ischemic attack or stroke, or carotid bruit on examination. *(Level of Evidence: C)***

Extracranial carotid disease is significantly associated with a type 1 adverse neurological outcome (*P* equals 0.001) (48). Hemodynamically significant carotid stenoses are associated with as many as 30% of early postoperative coronary bypass strokes (158). Strokes caused by carotid disease are particularly devastating, since they often occur on the second to ninth postoperative day in the midst of an apparently smooth recovery (159). The trend for coronary surgery to be performed in an increasingly elderly population underscores the importance of the issue (Figure 8D) (169,191-193). The prevalence of significant carotid disease in the current cardiac surgery population reflects the diffuse nature of the atherosclerotic process: 17% to 22% of patients have 50% carotid stenosis, and 6% to 12% have 80% carotid stenosis (191,194). Perioperative stroke risk is 2% when carotid stenoses are less than 50%, 10% when stenoses are 50% to 80%, and 11% to 18.8% in patients with stenoses greater than 80% (53,195). Although the patient with untreated, bilateral, high-grade stenoses or an occluded carotid artery and contralateral high-grade stenosis is rare, such patients have a 20% chance of stroke (196,197).

Conversely, the leading cause of short- and long-term risk for patients having surgical treatment of carotid disease is the associated coronary disease (198-201). CABG is the most effective treatment for many of these patients. Provided that the surgical team has acceptable results with endarterectomy, prophylactic carotid endarterectomy is superior to conservative therapy for prevention of stroke in symptomatic or asymptomatic patients with high-grade carotid stenoses (202-204).

With proper teamwork, carotid endarterectomy for high-grade stenosis preceding or coincident with a coronary operation can be associated with a low risk for short- and long-term adverse neurological sequelae (114,196,198,205) (Figure 9). Carotid endarterectomy done before or concomi-

tant with coronary bypass carries a low mortality (3.5%), reduces early postoperative stroke risk to less than 4%, and confers a 10-year rate of freedom from stroke of 88% to 96% (196,205,206). Special interest in this problem among caregivers and careful collaboration between the carotid and coronary surgical teams are keys to success. Stroke and mortality rates after carotid endarterectomy also are inversely related to institutional volume (207,208).

The absence of symptoms referable to carotid disease is not reassuring because a carotid stenosis of 75% in an *asymptomatic* patient is an independent predictor of stroke risk immediately after CABG (OR of 9.87, *P* less than 0.005) (158,159). The presence or absence of a cervical bruit is poorly predictive of a high-grade stenosis even in the setting of known symptomatic carotid disease (sensitivity 63%, specificity 61%) (209).

A prospective examination of preoperative carotid duplex scans in 1087 open-heart surgical patients aged 65 or older defined the markers associated with important (80%) carotid stenosis: female sex, PVD, previous transient ischemic attack or stroke, smoking history, or left main disease (*P* less than 0.05) (191). If all patients with at least 1 of these risk factors were screened, 95% of those with an 80% stenosis would be detected and 91% of those with a 50% stenosis would be detected. Unfortunately, this would lead to screening in 85% of patients aged 65 years or older. This example illustrates the correlation of carotid stenosis with age and suggests that the lower limit of age at which carotid screening will be cost-effective is not yet known. For safety and simplicity, many centers screen all of those aged 65 or older. The strong association between left main disease and carotid stenosis argues that left main patients should be screened at any age. Similarly, those with a previous transient ischemic attack or stroke should receive carotid screening independent of age. Preoperative CNS symptoms suggestive of vertebrobasilar artery insufficiency should lead to evaluation by magnetic resonance angiography to allow informed consideration of management options.

When surgical treatment of concurrent carotid and coronary disease is planned, the procedures may be done in either a combined (same operative setting, carotid to precede coronary revascularization) or *staged* fashion. The *staged* approach is most commonly used, particularly in patients with noncritical coronary anatomy. Postoperative care is rendered in a telemetry setting, with aggressive monitoring and treatment to prevent postoperative myocardial ischemia. CABG follows in 1 to 5 days with the use of standard techniques. The superiority of the combined versus staged approach has not been established by prospective trials. Thus, current tactics are best left to local team policies and preferences based on careful examination of team outcomes. An individualized, patient-specific, *selective* approach with the decision based on symptoms and the relative severity of extracranial cerebrovascular disease and coronary disease appears prudent and is used in many institutions. The results of these approaches in a collation (198) of 7 published

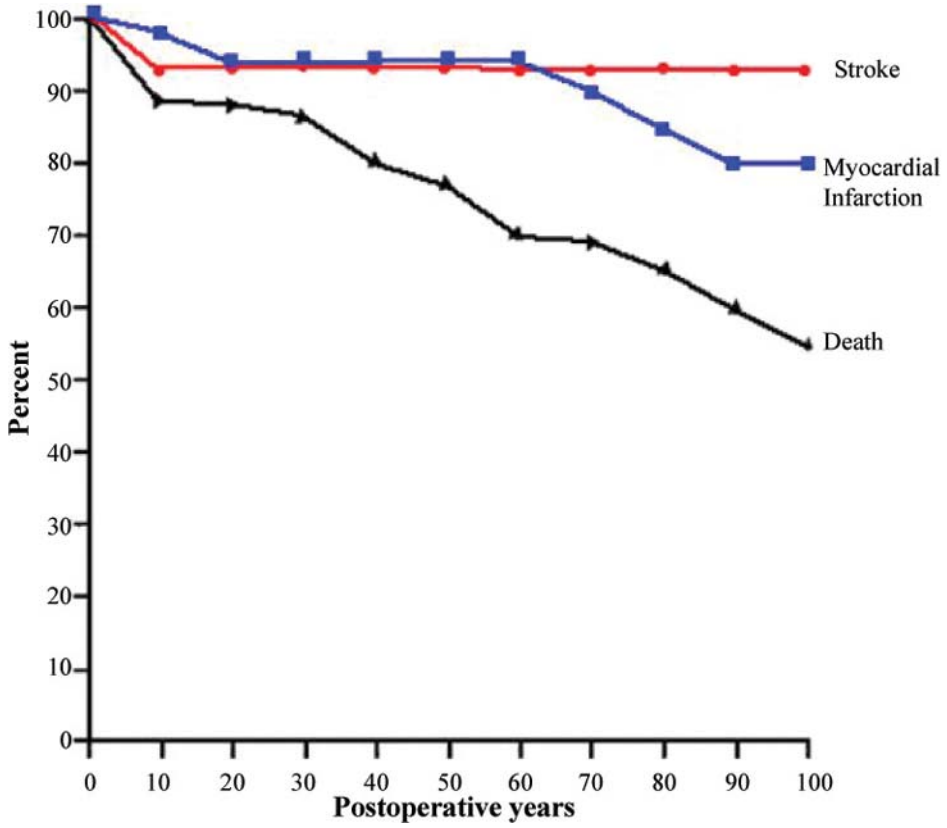


**Figure 9.** Contemporaneous surgical treatment of carotid and coronary disease is associated with an excellent long-term outcome. The gap shows freedom from stroke, myocardial infraction, and death over time. Reprinted with permission from Akins et al. Ann Thorac Surg. 1995;60:311-7) (205).

series, each with 100 patients, published from the mid-1980s to the mid-1990s had an overall mortality rate of 4%, with permanent neurological deficit in 3.4% of patients.

Some observational series have suggested that *combined* carotid/coronary operations carry a higher risk for in-hospital stroke and mortality compared with patients in the same institution having a *staged* procedure (210). These studies may be confounded by selection bias toward recommending *combined* operations in patients with more advanced carotid and coronary disease. Contrariwise, a recent, single-center series in which a *combined operation for all patients* with concurrent carotid and coronary disease was used suggested this approach to be safe and to have low overall resource requirements (205). However, another multicenter study suggested a considerably higher risk (191a). Thus, some uncertainty remains, underscoring the need for prospective appropriately-controlled, randomized study of this method (191b,191c).

Stroke risk appears to be increased when the so-called *reverse-staged* procedure is used. In this strategy, the coronary bypass precedes the carotid endarterectomy by 1 day during the same hospitalization. A prospective, randomized trial that evaluated this approach demonstrated an increased risk of stroke (14% versus 2.8%, *P* less than 0.05) when carotid operation followed rather than preceded (2.8%, *P* less than 0.05) CABG, whereas mortality rates were similar (211). It is generally accepted that cerebral revascularization should precede coronary revascularization when significant carotid disease is known, except in the uncommon situation of the true emergency CABG patient, in whom carotid endarterectomy should then closely follow the heart operation.

Most workers in the field have focused on in-hospital neurological outcomes for treatment of combined carotid and coronary disease. Multicenter trials have shown an advantage of surgical over medical management for significant carotid stenosis in either symptomatic or asymptomatic patients (202,212-214). These data argue for an aggressive surgical approach in this population and demand a longer-range vision. The long-term outlook for combined treatment of carotid and coronary disease is shown in Figure 9. The above-suggested strategy for carotid disease management in the setting of CABG is in concordance with the *Guidelines for Carotid Endarterectomy: A Multidisciplinary Consensus Statement From the Ad Hoc Committee, American Heart Association [Special Report]* (215). The success of this long-term strategy is predicated on assembling a team that can achieve excellent near-term carotid and coronary surgical results (207,208,215-217).

## Summary

Epivascular echocardiographic detection of ascending or transverse aortic atherosclerosis and modification of operative technique hold great promise for significant stroke risk reduction. In the current era, important concurrent carotid and coronary disease should be suspected, sought by screening, and, when found, managed surgically (Table 13). This strategy neutralizes the short-term risk of treatment of either disease alone and enhances long-term quality and length of life for the patient with generalized atherosclerosis.

### *4.1.1.2. Type 2 Neurological Injury*

Type 2 neurological complications have been identified in a percentage of patients after CABG and are associated with increases in postoperative time in the ICU, length of stay, hospital costs, and the need for postdischarge transfer to rehabilitation or extended-care facilities (48,218). Newman identified abnormal neurocognitive function in 53% of CPB-CABG patients at the time of hospital discharge. Six months after surgery, abnormalities could be identified in 24% of patients, which suggests some reversibility of the injury in

**Table 13.** Proven Management Strategies to Reduce Perioperative and Late Morbidity and Mortality

| Timing | Class Indication | Intervention | Comments |
|---|---|---|---|
| **Preoperative** | | | |
| Carotid screening | I | Carotid duplex ultrasound in defined population | Carotid endarterectomy if stenosis greater than or equal to 80% |
| **Perioperative** | | | |
| Antimicrobials | I | Prophylactic antimicrobials | See Table 14 |
| Antiarrhythmics | I | Beta-blockers to prevent postoperative atrial fibrillation | Propafenone or amiodarone are alternatives if contraindication to beta-blocker (see Table 15) |
| **Postoperative** | | | |
| Antiplatelet agents | I | Aspirin to prevent early vein-graft attrition | Ticlopidine or clopidogrel are alternatives if contraindications to aspirin |
| Lipid-lowering therapy | I | Cholesterol-lowering agent plus low-fat diet if low-density lipoprotein cholesterol greater than 100 mg/dL | 3-Hydroxy-3-methyglutaryl/coenzyme A reductase inhibitors preferred if elevated low-density lipoprotein is major aberration |
| Smoking cessation | I | Smoking cessation education, and offer counseling and pharmacotherapies | |

some patients. However, they were able to measure cognitive decline in 42% of patients at 5 years. The strongest predictor of late decline was the presence of an abnormality early after CABG (218).

Abnormal neurocognitive function is frequently present preoperatively in the CABG population (219). There is a further decline in neurocognitive function after any major operation in this population, but this decline is likely worse and more persistent after operations employing CPB (220).

4.1.1.2.1. REDUCING THE RISK OF MICROEMBOLIZATION. Microembolization is a major contributor to postoperative cerebral dysfunction after CABG (221,222). Transcranial Doppler examination of the middle cerebral artery of patients on extracorporeal circulation suggests that most emboli occur during surgical manipulation (clamping, cannulation) of the ascending aorta (221,223,224). Many of these emboli appear to be gaseous, either derived from the oxygenator or entrained directly from the ambient atmosphere. Postmortem examination of the brains of patients dying soon after CPB has shown diffuse, small, capillary-arteriolar dilatations (225). These vacuolated vascular abnormalities have also been seen after catheter manipulation of the ascending aorta, suggesting an atheroembolic etiology. Fat droplets in shed mediastinal blood, which can be returned to the pump circuit via cardiotomy suction, may contribute (226). Small gaseous emboli could also be responsible for the findings. Neuroanatomists have postulated that these could impair circulation and lead to the neurocognitive decline seen after CPB.

The number of microemboli delivered during CPB is correlated with the postoperative neurocognitive decline seen immediately and 8 weeks after CPB (221). The use of a 40-micron arterial-line filter in the heart-lung machine circuit appears to be protective. Type 2 neurological outcomes may be further reduced by routine use of the membrane oxygenator rather than the less-expensive bubble oxygenator, which is still used selectively in the United States (190,227,228). The return of shed mediastinal blood to the CPB circuit via the cardiotomy suction system may increase the microembolic load to the brain. Some centers avoid cardiotomy suction and simply discard shed blood. Alternatively, shed blood may be scavenged and red blood cells returned after washing and centrifugation via cell-saving devices (226).

Some have believed that off-pump bypass surgery may reduce the incidence of type 2 neurological injury because ascending aortic cannulation and cross-clamping are avoided (229). Reports have demonstrated mixed results (54,56). In patients with significant ascending aortic atheromatous disease, it would seem prudent to consider an off-pump and "no touch" aortic technique. Inflow to graft conduits can be achieved via in situ left or right IMAs, the right gastroepiploic artery, or innominate and subclavian arteries.

4.1.1.2.2. CEREBRAL HYPOPERFUSION AND NEUROLOGICAL OUTCOME. Intraoperative electroencephalographic monitoring can detect electrical patterns suggestive of cerebral hypoperfusion and allow real-time intraoperative correction. Decreases from 29% to 44% to 4% to 5% in postoperative neurocognitive and neuropsychological dysfunction (type 2) have been demonstrated by intraoperative electroencephalographic monitoring (230,231). However, the level of training necessary for interpretation of the electroencephalogram and the poor suitability of current technology for the operating room currently preclude its general clinical use for detection of hypoperfusion. Also, the electrical changes associated with microembolization and macroembolization are at the limits of resolution. The limitations cited reinforce the importance of strategies to prevent embolization.

Cerebral blood flow during CPB is kept relatively constant over a wide range of systemic arterial pressures with the alpha-stat extracorporeal circulation acid-base management technique. The incidence of persistent, postoperative neurocognitive deficits at 2 months with the use of this technique is significantly less compared with the alternative (pH-stat) technique (27% of patients versus 44%, *P* equals 0.047) (232).

4.1.1.2.3. POTENTIATORS OF ADVERSE NEUROLOGICAL OUTCOME. If neuroprotective mechanisms fail, there are strategies to minimize damage to the marginally perfused cerebral tissue, which has the potential for recovery. Cerebral hyperthermia potentiates the damage of an acute neurological injury. In the evolution of warm-heart surgery, some centers used techniques that had the potential for intraoperative cerebral hyperthermia. Techniques that have the patient "drift" on CPB toward ambient temperatures (34°C to 35°C or lower) rather than immediate warming (to maintain strict normothermia) allow an improved margin of neurological safety (233-236). During rewarming, arterial return blood temperature should be below 38°C. Hyperglycemia may also amplify the impairment caused by an acute neurological event, emphasizing the importance of meticulous perioperative glucose monitoring and control (236).

Cerebral edema that may be present in patients immediately after extracorporeal circulation (237) may also potentiate CNS damage. Efforts to reduce the potential for brain swelling include maintenance of an unobstructed pathway for venous drainage to the CPB reservoir while on the pump. Anti-inflammatory strategies for CPB may reduce interstitial edema and are discussed subsequently, but pulsatile perfusion does not appear to be protective (238-240).

### 4.1.2. Reducing the Risk of Perioperative Myocardial Dysfunction

Most modern myocardial protection techniques allow the patient undergoing CABG to leave the operating room without a significant perioperative decrement in myocardial performance. Ideally, the surgeon is familiar with the broad

range of myocardial protection principles that allow the adaptation of technique to accommodate varying patient presentations (241,242). There is no substitute for a well-orchestrated, technically sound, expeditious operation to minimize risk.

### *4.1.2.1. Myocardial Protection for the Patient With Satisfactory Preoperative Cardiac Function*

The wide latitude of techniques associated with excellent results for the majority of patients undergoing CABG is testimony to the fact that there is no "ideal" or universally applicable myocardial protection technique (243). The greater the myocardial functional reserve in the patient population studied, the more difficult it is to demonstrate differences in myoprotective techniques. A variety of studies, including prospective trials, confirm the safety of many variations of cardioplegic arrest, which is the most widely used method for intraoperative myocardial protection. A single-center trial of cold crystalloid versus warm blood cardioplegia in 1001 patients undergoing elective CABG demonstrated a low perioperative MI rate (1.4% warm versus 0.8% cold, *P* not significant [NS]), IABP use (warm 1.4% versus cold, 2.0%, NS), and mortality (1.0% warm versus 1.6% cold, NS) with either technique (241). Advances in the understanding of myocardial and endothelial metabolism, temperature management, chemical/electrolyte composition, sanguineous or asanguineous delivery media, substrate enhancement, control of conditions of reperfusion, and delivery route have all led to important incremental advances in patient outcome (244-247). Certain techniques, however, offer a wider margin of safety for special patient subsets.

### *4.1.2.2. Myocardial Protection for Acutely Depressed Cardiac Function*

**Class I**

**Blood cardioplegia should be considered in patients undergoing cardiopulmonary bypass accompanying urgent/emergency CABG for acute MI or unstable angina. *(Level of Evidence: B)***

In contrast to the patient with normal myocardial function, it is easier to demonstrate benefit from specialized protocols (248,249) in the patient with an acutely injured ventricle. One multicenter study of emergency CABG for patients with acute coronary occlusion (some with cardiogenic shock) demonstrated that controlled, surgical reperfusion with prompt, vented CPB and substrate-enhanced sanguineous cardioplegic technique led to a 96.1% survival, which approaches that seen in low-risk, elective CABG series (250). Preoperative regional wall-motion abnormalities improved after bypass in 87% of these patients despite an average of greater than 6 hours from infarct to revascularization.

Another observational study compared consecutive patients receiving cold crystalloid cardioplegia with a warm blood technique that did not include substrate enhancement in emergency CABG after failed angioplasty. There was a significant *reduction in MI* with the sanguineous technique (65% infarcts with crystalloid versus 26% for blood, *P* less than 0.007) (251). Multivariate analysis confirmed normothermic blood cardioplegia as an independent predictor of freedom from infarct in this study (*P* less than 0.005). Prospective, randomized trials have shown a *survival benefit* for patients treated with blood cardioplegia compared with crystalloid cardioplegia in the setting of urgent revascularization for unstable angina. In one trial, the operative mortality (0% versus 5%), incidence of MI (4% versus 13.5%), and low-output syndrome (10% versus 19%) were favorably reduced in patients receiving blood cardioplegia versus crystalloid (252). Multivariate analysis confirmed that crystalloid cardioplegia (*P* equals 0.008) was a significant, independent predictor of postoperative morbidity compared with warm-blood cardioplegia (253).

### *4.1.2.3. Protection for Chronically Dysfunctional Myocardium*

**Class IIa**

**Blood cardioplegia is probably indicated in patients undergoing cardiopulmonary bypass accompanying CABG in the presence of a chronically dysfunctional left ventricle. *(Level of Evidence: B)***

Severe LV dysfunction is an important risk factor for patients undergoing CABG (254). Efforts to document reduction of risk in this cohort are confounded by incomplete data on the prevalence of reversible ischemic systolic dysfunction (hibernating myocardium) and the contribution of improved function from revascularization of myocardium as opposed to myocardial protection strategies (255). There is an emerging consensus, however, that for the chronically impaired ventricle, there is an added margin of safety provided by blood cardioplegic techniques (255-257). Its theoretical advantages include superior buffering capacity, rheological considerations at the capillary level, and free-radical control when compared with crystalloid cardioplegia.

### *4.1.2.4. Cardiac Biomarker Elevation and Outcome*

**Class IIb**

**Assessment of cardiac biomarkers in the first 24 hours after CABG may be considered, and patients with the highest elevations of creatine kinase–MB (greater than 5 times upper limits of normal) are at increased risk of subsequent events. *(Level of Evidence: B)***

The importance of elevation of cardiac biomarkers in the first 24 hours after CABG has been controversial because some degree of elevation of creatine kinase–MB (CK-MB) is very common. New Q-wave MI after CABG occurs in 2% to 4% of patients and is associated with adverse outcome (258-260). However, up to 90% of individuals have some

elevation of CK-MB (261). It has now been demonstrated that marked elevation of CK-MB (5-10 times upper limits of normal) is associated with an adverse prognosis. Increased risk of death and repeat MI in the first 30 days after CABG correlates with progressive increases in CK-MB elevation, with the worst outcome in those with levels greater than 5 times normal (262). Six-month (263) and 1-year (262) mortality also correlate with postoperative CK-MB elevation. Poorer outcomes, including heart failure and death, at an average of 3 to 5 years also appear to correlate with early cardiac biomarker elevation (261,264).

The prognostic value of troponins after CABG is not as well established, but available studies have suggested that troponin T is more discriminatory than CK-MB in predicting early complications (265). For patients with elevated biomarkers after CABG, it is particularly important that attention be given to optimal medical therapy, including the use of beta-blockers, angiotensin converting enzyme (ACE) inhibitors, antiplatelet agents, and statins in eligible individuals.

### *4.1.2.5. Adjuncts to Myocardial Protection*

**Class IIa**

**The use of prophylactic intra-aortic balloon pump as an adjunct to myocardial protection is probably indicated in patients with evidence of ongoing myocardial ischemia and/or patients with a subnormal cardiac index. *(Level of Evidence: B)***

The use of prophylactic IABP as an adjunct to myocardial protection may decrease mortality and overall resource utilization in certain high-risk patients. A retrospective evaluation of 163 consecutive patients with an LVEF less than or equal to 0.25 demonstrated a 4-fold reduction in 30-day mortality in patients treated with IABP. Thirty-day mortality was 2.7% in patients who received a prophylactic IABP placed preoperatively versus 11.9% for patients not receiving a balloon (*P* less than 0.005). IABP use was also associated with a shorter hospital stay and lower hospital charges (266). A randomized trial confirmed the benefit of preoperative IABP support in high-risk patients (35a). Placement of the IABP immediately before the operation afforded similar protection to that accompanying placement the day before CABG (267,268). In patients with severe PVD, a higher threshold for balloon use is required given the high complication rate in this patient group.

Appreciation of the role of the activated leukocyte in the genesis and exacerbation of myocardial reperfusion injury has led to strategies to remove leukocytes from the coronary blood flow. Clinical studies of leukocyte depletion have shown significant benefit to myocardial performance in the hypertrophied LV and in those with acute or chronic ischemia (269-273). However, leukocyte depletion as an adjunct to myocardial protection/reperfusion strategies has yet to achieve widespread recognition and use among surgeons; therefore, no consensus statement is appropriate at this point.

The long-term survival benefit afforded by use of the IMA is well recognized (12,274). Less appreciated is the reduction in immediate, operative mortality associated with the use of the mammary artery as opposed to saphenous vein revascularization. Its use may thus be considered an adjunct to myocardial protection. Its use should be encouraged in the elderly (275,276), the urgent/acutely ischemic patient (277), and other subgroups that previously were thought not to receive its immediate and long-term benefit. The large CABG database available to the STS (42) was analyzed for the influence of use of the IMA on operative mortality. Use of the IMA was associated with reduced operative mortality in all subgroups analyzed with regard to age (*P* less than 0.005), sex (*P* less than 0.005), priority of operation (*P* less than 0.005), normal (*P* less than 0.01) or reduced (*P* less than 0.005) LV function, presence of diabetes (*P* less than 0.005), obese patients (*P* less than 0.005), history of previous infarct (*P* less than 0.005), previous PTCA (*P* less than 0.001), and any pattern of coronary anatomy (*P* less than 0.005). Multivariate analysis also confirmed use of the IMA as an independent predictor of operative survival (*P* less than 0.0025). When risk factors were combined, the only groups found to have similar operative mortality between use/nonuse of the IMA were elective and nonelective *reoperative* patients greater than 70 years of age. Arterial conduits are discussed in more detail in Section 6.2.

### *4.1.2.6. Reoperative Patients*

For patients undergoing repeat CABG surgery who previously have had a left IMA-to-LAD graft, a concern has been the accidental transection of the graft during sternotomy. However, one report from a high-volume center showed that experienced surgeons rarely encountered this complication (less than 3%) (278). The risk of death or serious myocardial dysfunction related to atheroembolism from patent, diseased SVGs is low in the current era and is attributable to recognition of the problem and careful operative techniques by experienced surgeons who encounter an increasing percentage of reoperative candidates in their practices (278). A risk-reducing strategy in this situation is the use of retrograde delivery of cardioplegia. This procedure allows early exclusion of atherosclerotic SVGs from the coronary circulation, as they are no longer needed to deliver cardioplegia.

### *4.1.2.7. Inferior Infarct With Right Ventricular Involvement*

**Class IIa**

**After infarction that leads to clinically significant right ventricular dysfunction, it is reasonable to delay surgery for 4 weeks to allow recovery. *(Level of Evidence: C)***

Right ventricular (RV) failure secondary to an ischemic RV (either infarction or stunning) presents a particularly

hazardous situation (279). The prototypical patient has an occluded right coronary artery proximal to the major RV branches and presents with an inferior MI with or without recognized RV failure (280,281a,282-284). Angiography may demonstrate that the coronary anatomy is best treated surgically, but the opportunity for maximal benefit of an emergency operation (initial 4 to 6 hours) has often passed. There is substantial risk in operating after this small window of opportunity but before the recovery of RV function, which usually occurs at 4 weeks after injury (285). During this postinfarct month, the RV is at great risk for severe postoperative dysfunction, which often requires extraordinary levels of perioperative pharmacological and mechanical support and has a very high mortality. The nonsurgical postinfarction patient can most often be supported with pacing, volume loading, and judicious inotropic administration (286). In the surgical setting, the RV takes on different characteristics. There is loss of the pericardial constraint immediately on exposing the heart, which results in acute dilatation of the dysfunctional RV. The RV often fails to recover in this setting, even when state-of-the-art myocardial protection schemes and revascularization are employed (287). The parallel effects of RV dilatation and dysfunction on LV diastolic and systolic function are magnified and may be associated with the need for high levels of support, inability to close the chest owing to cardiac dilation, need for ventricular assist devices, prolonged convalescence, transplantation, or death (286a). In the acute setting, the potential risk of further RV injury must be weighed against the potential benefit of additional myocardial salvage. If early PCI of the right coronary artery is indicated, it should be performed (35a).

The best defense is an index of suspicion and recognition of the RV dysfunction by physical examination (281,288) electrocardiography (right precordial leads), echocardiography, or radionuclide-gated blood pool study (285,288-290). A successful early PCI may allow recovery of an infarcted RV in as few as 3 days (285).

### 4.1.3. Attenuation of the Systemic Sequelae of CPB

Extracorporeal circulation elicits a diffuse inflammatory response that is attended by a transient, multisystem organ dysfunction that may prolong convalescence (291,292). Numerous strategies have been shown to blunt this counterproductive immune response (291). Preoperative corticosteroid administration is inexpensive and appears to be efficacious. Corticosteroid administration has favorable effects on the systemic inflammatory response associated with extracorporeal circulation. Glucocorticoid, when given before CPB, reduces complement activation and the levels of proinflammatory cytokines (293-297). Compared with placebo, patients receiving glucocorticoid are less febrile postoperatively, have higher cardiac indexes, require less inotropic and volume support, and spend less time in the ICU (298-302).

Although there is no demonstration of an increased risk for infection in studies to date, it may be prudent to avoid the use of steroids in diabetic patients because the studies were not powered to detect modest increases in infection risk (301). The proper timing and duration of administration in this application are incompletely resolved; there is evidence that steroid delivery more in advance of an insult is more efficacious (303). Preoperative corticosteroid administration is inexpensive and appears to reduce the systemic inflammatory response associated with CPB with little downside risk. Current understanding supports liberal prophylactic use in patients undergoing extracorporeal circulation (293).

Aprotinin, a serine protease inhibitor known for its hemostatic characteristics, also attenuates complement activation and cytokine release during extracorporeal circulation. There appears to be an emerging role for its prophylactic use as an anti-inflammatory agent in patients undergoing CPB. There was a significant reduction in length of stay and hospital charges when aprotinin therapy was applied to a high-risk cardiac surgical population (291). By virtue of its effects on coagulation, aprotinin appears to reduce the need for transfusion after repeat CPB. However, there are insufficient data at present to make a strong recommendation for the routine use of this relatively expensive drug (293,297,304).

Perioperative leukocyte depletion through hematologic filtration may benefit patients by improving pulmonary function. One study suggested that low-risk patients benefit from a strategy of leukocyte depletion during CPB in conjunction with leukoreduction of homologous blood products (305-308). Although the literature does support the routine use of arterial-line filters to minimize microembolization in extracorporeal circulation, there is no current consensus on the value of selective leukocyte filtration for the CPB circuit. Although blood-surface interface modifications for the CPB circuit have also been shown to decrease markers of inflammation, translation into clinical benefit in terms of reduced morbidity, mortality, or resource utilization has been equivocal. The concern over thrombotic complications tempered enthusiasm among cardiac surgeons (291,309-313). Surface modification such as heparin-bonded circuitry for extracorporeal circulation holds promise for reduction of the systemic inflammatory response to CPB, but at present the evidence is sufficiently conflicting that firm recommendations are not at hand.

### 4.1.4. Reducing the Risk of Perioperative Infection

**Class I**

1. **Preoperative antibiotic administration should be used in all patients to reduce the risk of postoperative infection. *(Level of Evidence: A)***
2. **In the absence of complicating circumstances, a deep sternal wound infection should be treated with aggressive surgical debridement and early revascularized muscle flap coverage. *(Level of Evidence: B)***

**Class IIa**

**The risk for deep sternal wound infection is reduced by aggressive control of perioperative hyperglycemia by using a continuous, intravenous insulin infusion (314).** ***(Level of Evidence: B)***

Multiple opportunities exist to reduce infection risk in patients undergoing CABG. Interval reporting to individual surgeons of their respective wound infection rates leads to risk reduction through discipline in adherence to sterile operative techniques. Skin and nasopharyngeal Gram-positive organisms are the leading cause of the most threatening complication: deep sternal wound infection or mediastinitis. Skin preparation with topical antiseptics (315,316), clipping rather than shaving the skin (318,319), avoidance of hair removal (62), reduction of operating room traffic, laminar-flow ventilation, shorter operations, minimal electrocautery (320), avoidance of bone wax (321), use of double-gloving barrier techniques for the operating team (322-326), and routine use of an easily constructed pleuropericardial flap (327) have all been shown to be of value in reducing postoperative infection (314).

Several newer strategies that are easily integrated into practice deserve consideration. Diabetes mellitus afflicts 1 of 5 patients undergoing CABG and is an independent risk factor for wound infection (328). The risk for deep sternal wound infection is reduced by aggressive control of perioperative hyperglycemia (glucose levels greater than 150 to 180 mg/dL) by using a continuous intravenous regular insulin infusion (0.9% deep sternal wound infection) versus intermittent subcutaneous insulin treatment (1.9%, *P* equals 0.04) (314).

Homologous blood transfusions after CABG are correlated in a dose-related fashion to increased risk for viral and bacterial infections, increased length of stay, antimicrobial use, and mortality through transfusion-related immunomodulation (329,330). A retrospective study of 238 patients undergoing CABG demonstrated this immunosuppressive effect of transfusion. Wound and remote infections occurred in 4% of patients who received less than or equal to 2 U of red blood cells, in 7% of those transfused with 3 to 5 U, and in 22% of those having received greater than or equal to 6 U (329). Leukodepletion strategies have been shown to blunt the immunosuppressive effect of blood transfusion in surgical patients (330). The dose-related effect of blood transfusion on increased infection risk has been known for general surgical and orthopedic operations and is thought to be caused by the accompanying leukocytes in the red blood cell transfusion (331). A single-center prospective trial of 3 transfusion protocols in 914 patients undergoing cardiac surgery showed a significant reduction for patients receiving leukocyte-depleted blood (17.9%) as opposed to nonfiltered blood (23.5%, *P* equals 0.04) for all infections (respiratory, urinary tract, bacteremia, and wound) (330). Most striking was the reduction in 60-day mortality in transfused patients having received filtered blood: transfused/nonfiltered patient mortality was 7.8%; transfused/filtered at the time of donation, 3.6%; and transfused/filtered at the time of transfusion, 3.3% (*P* equals 0.019) (330). The reduction in the postoperative rate of noncardiac causes of death (i.e., multisystem failure) in leukocyte-depleted/transfused patients compared with patients receiving nonfiltered blood was highly significant (*P* equals 0.001) (330). Leukodepletion can be accomplished by regional blood banks at the time of donation or at the bedside at time of transfusion by using a relatively inexpensive in-line transfusion filter.

Preoperative antibiotic administration reduces the risk of postoperative infection 5-fold (332). Prophylactic antimicrobial efficacy is dependent on adequate drug tissue levels before microbial exposure (333,334). Multi-institutional studies suggest that many centers, including those with training programs in cardiothoracic surgery, are not consistent in delivering or teaching effective use of perioperative antibiotics.

The cephalosporin class of antimicrobials is currently the agent of choice for prophylaxis of infection for coronary operations. There is a trend toward superior efficacy with cefuroxime compared with the other cephalosporins, but this difference does not reach statistical significance (Table 14) (334-338). Institution- or surgeon-specific selection is appropriate within this class (335). Data suggest that a 1-day course of intravenous antimicrobials is as efficacious as the traditional 48-hour (or longer) regimen (339-342). There is little evidence that prolonging (greater than 2 days) the antimicrobial prophylaxis even in high-risk patients provides any benefit (343). A 1-day course of antimicrobial prophylaxis is safe and effective (344). There are insufficient data to suggest that aminoglycosides add substantial benefit to the antimicrobial prophylactic regimen (335). Usual cephalosporin pharmacokinetics mandates administration within 30 minutes of incision and redosing if the operation exceeds 3 hours (335,345).

Antimicrobial selection is a moot point if the agent is not delivered during the optimal 30- to 60-minute window just before incision. The beneficial effect is negated if the drug is given after incision. This is a major issue. A multi-institutional study, including those with cardiothoracic training programs, confirmed the suboptimal use of prophylactic antimicrobials. In 1994, only 23% of the institutions studied had a system that assured proper administration of prophylactic antimicrobials in the generous 2-hour period just before incision for patients undergoing CABG. One year later, compliance was even worse at 20% (346). A practical, fail-safe guideline to assure proper timing is the administration of the cephalosporin by the anesthesiologist after induction but before skin incision. Then the surgeon confirms administration before the scalpel is in hand (334,347). Surgeons should be familiar with the pharmacokinetics of their preferred cephalosporin to modify initial and subsequent dosing based on patient size and duration of operation. This knowledge can favorably influence plasma, sternal, and soft-tissue bacteriocidal activity for the individual patient.

If preventive strategies fail, prompt recognition of deep sternal wound infection or mediastinitis is critical.

**Table 14.** Prophylactic Antimicrobials for Coronary Artery Bypass Graft Surgery

| Antibiotic | Equivalent Efficacy IV Dosing Regimen Dose and Interval | Cost per Dose | Comments |
|---|---|---|---|
| Cefuroxime | 1.5 g preoperatively<br>1.5 g after CPB<br>1.5 g Q12×48 | $6.33/1.5 g | First-line agents; low toxicity; pharmacokinetics vary; shorter prophylaxis duration less than 24 h may be equally efficacious for cefuroxime |
| Cefamandole, cefazolin | 1 g preoperatively<br>1 g at sternotomy<br>1 g after CPB<br>1 g Q6×48 (Initial dose to be given 30-60 minutes before skin incision) | $6.27/g<br>$0.90/g | |
| Vancomycin | 1 g Q12/h/until lines/tubes out<br>At least 2 doses<br>(During 30-60-minute infusion timed to end before skin incision) | $5.77/g | Reserved for penicillin-allergic; justified in periods of methicillin-resistant *Staphylococcus* species outbreaks; vancomycin-resistant *Enterococcus* problem is on horizon; more likely to require vasopressor agent perioperatively |

CPB indicates cardiopulmonary bypass. Data derived from References 334 and 336-338.

Morbidity and mortality for deep sternal wound infection or mediastinitis have decreased over the past 20 years for several reasons. Aggressive surgical debridement and early vascularized muscle flap coverage are key to reducing the cost, length of stay, and mortality (348,349). A prospective trial has lessened debate on proper management of the deeply infected sternotomy incision. Treatment by wound exploration, sternal rewiring, and drainage failed in 88.2% of patients compared with high success in patients treated initially with muscle flap closure (350).

## 4.1.5. Prevention of Postoperative Arrhythmias

**Class I**

**Preoperative or early postoperative administration of beta-blockers in patients without contraindications should be used as the standard therapy to reduce the incidence and/or clinical sequelae of atrial fibrillation after CABG. *(Level of Evidence: B)***

**Class IIa**

1. **Preoperative administration of amiodarone reduces the incidence of postcardiotomy atrial fibrillation and is an appropriate prophylactic therapy for patients at high risk for postoperative atrial fibrillation who have contraindications to therapy with beta-blockers. *(Level of Evidence: B)***
2. **Digoxin and nondihydropyridine calcium-channel blockers are useful for control of ventricular rate but at present have no indication for prophylaxis. *(Level of Evidence: B)***

**Class IIb**

**Low-dose sotalol can be considered to reduce the incidence of atrial fibrillation after CABG in patients who are not candidates for traditional beta-blockers. *(Level of Evidence: B)***

Postoperative atrial fibrillation increases the length of stay after CABG up to 5 days (351), increases the charges by as much as $10 055 (351), and is associated with a 2- to 3-fold increase in postoperative stroke (182,183).

The causal and temporal relationship among atrial fibrillation after CABG, the incidence of new left atrial thrombus, and the potential for embolism and stroke remains ill-defined. However, if atrial fibrillation after CABG persists into a second day, warfarin anticoagulation with a goal of an international normalized ratio (INR) of 2.0 to 3.0 should be considered (352).

Withdrawal of beta-blockers in the perioperative period doubles the incidence of postoperative atrial fibrillation after CABG. One series showed that 40 of 105 patients who had withdrawal of beta-blockers developed postoperative atrial fibrillation compared with 18 of 105 patients who had early postoperative reinstitution of beta-blocker ($P$ equals 0.02). Virtually every study of beta-blockers administered for the purpose of reducing postoperative atrial fibrillation has shown benefit. Most trials have examined the initiation of prophylaxis in the postoperative period. There appears to be an even greater benefit if beta-blockers are begun before operation. For example, in 1 controlled trial, atenolol started 3 days before operation led to a reduction of atrial fibrillation from 37% in the control group to 3% in the atenolol group ($P$ equals 0.001) (Table 15) (353,354).

Low-dose sotalol can also be considered effective for reduction of atrial fibrillation after CABG. In a prospective, double-blind, randomized, placebo-controlled study, the placebo group had an incidence of supraventricular arrhyth-

**Table 15.** Pharmacological Strategies for Prevention of Atrial Fibrillation After Coronary Artery Bypass Graft Surgery

| Treatment | Timing | Dose/Route | AF Incidence, % | Comments | Evidence (Reference) |
|---|---|---|---|---|---|
| **Frontline strategies** | | | | | |
| Resumption of patient's preoperative beta blocker | Postoperative resumption | Same as preoperative | Beta-blocker stopped 38.1% Continued 17.1%; *P*= 0.02 | Resumption of beta-blocker reduced AF by 45% | randomized trial (782) |
| | | | Beta-blocker stopped 28%; Continued 6%; *P*= 0.01 | Nearly 5-fold decrease in incidence; if no longer needed after revascularization, may taper as outpatient | randomized trial (783) |
| • Beta blockers (propranolol prototypical) | Postoperative initiation (10±7 h postoperatively) | 5 mg Orally 4 times per day | Control 23%; Propranolol 9.8%; *P*=0.02 | Reduced AF by 43%; inexpensive, low dose | randomized trial (784) |
| • Almost all beta blockers evaluated | Postoperatively | Varies | Significantly reduced versus placebo | Odds ratio 0.17; confidence interval 0.03–0.98 in favor of beta blocker over controls in meta-analysis | randomized trial (785,786) metanalysis (355) |
| Atenolol | Preoperatively (begun 72 h before operation) | 50 mg Orally twice a day | Control 37%; Atenolol 3%; *P*=0.001 | Excellent option if preoperative phase practical | metanalysis (355) |
| Sotalol | Preoperatively through postoperatively | 160 mg AM of operation, then 160 mg BID PO | Control 29% Sotalol 10% | Class III properties; sotalol not tolerated in 10% of patients | randomized trial (787) |
| Magnesium sulfate | Postoperatively | Continuous IV infusion for a total of 178 mEq over first 4 postoperative days | Control 28%; Mg supplement 14%; *P* =0.02 | Goal is normal serum magnesium: =1 mmol/L, < 2 mEq/L, which is usually low after cardiopulmonary bypass | prospective trial (788) |
| **Alternative/niche strategies** | | | | | |
| Amiodarone | Preoperatively through postoperatively | 600 mg Orally daily for 7 days preoperatively; then 200 mg PO daily postoperatively; stop at discharge; total = 4.8 g | Control 53%; Amiodarone 25%; *P*=0.003 | Mixed group of coronary and valve patients, explaining very high AF incidence | prospective trial (356) |
| Amiodarone | Postoperatively | 300 mg Intravenous bolus; then 1.2 g over 24 h for 2 days; then 900 mg every 24 h for 2 days, for a total of 4.5 g | Control 21%; Amiodarone 5%; *P*=0.05 | Coronary bypass patients only in this study | prospective trial (789) |
| Propafenone | Postoperatively | 300 mg Orally twice a day for 7 days | Propafenone 12%; Atenolol 11%; *P*=NS | Propafenone offers a less negative inotropic option for poor left ventricular function population | prospective trial (354) |
| Triiodothyronine (T3) | Intraoperative | 0.8 mcg/kg IV after cross-clamp then IV infusion 0.113 mcg/kg/hr × 6hr | Control 46%; T3 24%; *P* = 0.009 | All patients in this study had depressed LV function | randomized trial (790) |

*Continued on Next Page*

**Table 15.** *Continued*

| Treatment | Timing | Dose/Route | AF Incidence, % | Comments | Evidence (Reference) |
|---|---|---|---|---|---|
| **Strategies not clearly efficacious for prophylaxis** | | | | | |
| digoxin | Preoperative | oral | Control 17.6%; Digoxin 14.2%; *P*= NS | Doesn't significantly reduce AF but does control ventricular rate for AF | prospective trials (791,792) |
| | | | | digoxin = 139/min control = 161/min *P* = 0.02 | metanalysis (355) |
| Calcium channel blockers • verapamil | Postoperative | oral | Control 18.2%; Verapamil 18.2%; *P*= NS | Does not significantly reduce AF but does control ventricular rate if AF established; verapamil = 131/min; control = 155/min; *P* = 0.002 | prospective trials (793-795) metanalysis (355) |

mias of 43% compared with 26% for sotalol (*P* equals 0.0012, or a 43% reduction) (355).

Amiodarone administered beginning 1 week before surgery reduces the incidence of postcardiotomy atrial fibrillation (53% with placebo to 25% with amiodarone, *P* equals 0.003), reduces hospital costs ($26 000 to $18 000, *P* equals 0.03), and shortens the length of stay (8 to 6.5 days, *P* equals 0.04) (356). This represents another option for patients undergoing elective CABG who have contraindications to beta-blocker therapy.

The Atrial Fibrillation Suppression Trial (AFIST) was a prospective study of patients aged 60 years or older (average age 73 years) undergoing open-heart surgery who were randomized to oral amiodarone therapy or placebo given in addition to beta-blockers (357). Patients received up to a total of 3 grams of oral amiodarone in divided doses 1 to 4 days before to surgery and continued 400 mg by mouth twice a day for 4 days after surgery. The patients who were given amiodarone had a lower frequency of any atrial fibrillation (22.5% versus 38.0%; *P* equals 0.01), symptomatic atrial fibrillation (4.2% versus 18.0%, *P* equals 0.001), cerebrovascular accidents (1.7% versus 7.0% *P* equals 0.04), and postoperative ventricular tachycardia (1.7% versus 7.0%) (357).

Digoxin and nondihydropyridine calcium channel blockers (verapamil has been the most extensively studied) are useful for control of ventricular rate but have no consistent benefit for prophylaxis of supraventricular arrhythmias after CABG (Table 15) (355). Currently, preoperative or early postoperative administration of beta-blockers is considered standard therapy to prevent atrial fibrillation after CABG except in patients with active bronchospasm or marked resting bradycardia.

### 4.1.6. Strategies to Reduce Perioperative Bleeding and Transfusion

Despite the increasing safety of homologous blood transfusion, patients and their families are often far more concerned about transfusion risk than MI, stroke, or death after CABG. Well-publicized cases of transmission of viral illness with transfusion after cardiac operation in the early 1980s have sensitized the North American population. A study of donors who passed current blood donor screens but subsequently seroconverted suggests a current risk for donation of blood during an infectious period of 1/493 000 for human immunodeficiency virus, 1/641 000 for human T-cell lymphotrophic virus, 1/103 000 for hepatitis C virus, and 1/63 000 for hepatitis B virus (358).

Cardiac surgical patients account for 10% of blood transfusions in the United States (359). Twenty percent of patients having cardiac operations use 80% of the blood products attributed to cardiac surgical use. Several of the short-term, deleterious effects of transfusion were discussed in the section on reducing infection (360). Predisposing risk factors for transfusion after CABG include advancing age, lower preoperative red blood cell volume, preoperative aspirin therapy, priority of operation, duration of CPB, recent fibrinolytic therapy, reoperative CABG, and differences in heparin management (361-367). Institutional protocols with thresholds for transfusion lead to an overall reduction in the number of units transfused and the percentage of patients receiving any blood (368).

Aspirin, a very common preoperative medication in patients undergoing CABG, decreases platelet aggregation and increases postoperative blood loss. The magnitude of this effect has been confirmed in prospective, controlled tri-

als (369). Preoperative aspirin is associated with increased risk for transfusion, prolonged wound closure time, and an increase in early reoperation for bleeding (370). The value of aspirin in the treatment of acute coronary syndromes will often outweigh the increased risk for perioperative bleeding should coronary bypass be indicated early in the course of the acute event. In certain patients in an appropriate clinical setting, including chronic stable angina, low-risk plaque morphology, and others, cessation of aspirin and other platelet inhibitors 7 to 10 days before elective cardiac operation appears prudent to decrease the risk of postoperative bleeding and transfusion. For clopidogrel, the recommendation is to discontinue the agent 5 or more days before surgery when the clinical situation will permit it (see Section 5.11).

Aprotinin, a serine protease inhibitor with antifibrinolytic activity, significantly decreases postoperative blood loss and transfusion requirements (both units and number of patients) in high-risk, patients undergoing primary CABG, those on aspirin, and in particular the population undergoing reoperative bypass (371,372). Aprotinin does not appear to decrease early graft patency after coronary bypass despite its benefit in reducing postoperative bleeding and need for blood transfusion (373,374). Mechanical strategies to reduce the need for homologous blood have been only marginally successful.

Both epsilon-aminocaproic acid and an analogue, tranexamic acid, have antifibrinolytic activity. Both have been demonstrated to decrease mediastinal drainage after cardiac operation (375-378). Demonstration of a reduction in transfusion requirements has been inconsistent, however (376). Although these agents are relatively inexpensive, the data are insufficient to recommend their routine use. In contradistinction to aprotinin, the safety regarding the thrombotic potential including graft patency issues is unresolved (374,379). The concept of risk stratification for transfusion requirements has been validated (380) and offers a more rational approach to risk reduction strategies seeking to minimize blood requirements (380).

Efforts to synthesize multiple blood-conservation methods have proven successful in reducing transfusion (381). The most fully evolved protocol using multiple mechanical and pharmacological means achieved a remarkable series of 100 consecutive, selected patients undergoing CABG without transfusion (382). Intrinsic to this strategy was the concept of varying risk for transfusion and an individualized, algorithm-driven approach for the patient undergoing elective CABG. Models for prediction of the need for transfusion postoperatively allow shepherding of resources and application of risk-neutralizing strategies to those more likely to benefit (383). Comparison was made with a consecutive series of concurrent patients with the same transfusion criteria. The multi-modality conservation patients had no transfusion compared with 38% of the concurrent control group who received an average of 2.2 plus or minus 6.7 U of blood. Mediastinal drainage for the conservation group was half that of the control group (370 plus or minus 180 versus 660 plus or minus 270 mL, *P* equals 0.001) (382). Costs were similar between groups. The liberal use of aprotinin (69% of patients), exclusion of anemia patients, and minimal hemodilution appear to be the keys to these results.

Prehospitalization autologous blood donation can be effective. If a patient has no exclusionary criteria (hemoglobin less than 12, heart failure, unstable angina, left main disease, or symptoms on the proposed day of donation) and can achieve 1 to 3 U of donated blood over 30 days before operation, the risk of homologous transfusion is significantly lowered (12.6% versus 46% in a non-preadmission donor control group, *P* equals 0.001). An alternative or additional method of pre-CPB blood "donation" is the removal of blood from the patient in the operating room immediately before CPB. This blood is then set aside, not exposed to the CPB circuitry, and then reinfused into the patient after the patient is disconnected from CPB. This donation immediately before CPB yielded a significantly higher platelet and hemoglobin count in 1 study (*P* less than 0.01) compared with similar postoperative levels in patients who did not undergo harvesting of blood immediately before CPB. In this study, this technique translated into a 6-fold decrease in the percentage of patients requiring transfusion (10% transfusion rate in pre-CPB donors versus a 65% transfusion rate in non–pre-CPB donors, *P* less than 0.01) (384).

A multicenter, prospective study of recombinant human erythropoietin given over a 5-day course failed to demonstrate a significant reduction in transfusion requirement, although a significant rise in preoperative hemoglobin (*P* less than 0.05) was noted (385).

A randomized, placebo-controlled trial demonstrated no advantage of iron supplementation for restoration of red blood cell mass after coronary bypass, but the patients receiving iron did have significantly more gastrointestinal complaints (379,384).

Autotransfusion has had a generally favorable effect on decreasing allogeneic blood use, but concerns about stimulation of fibrinolysis with reinfusion of shed mediastinal blood prevent unequivocal recommendations on its use, particularly in routine low-risk patients (386).

### 4.1.7. General Management Considerations

Acuteness of operation is an important determinant of operative morbidity and mortality. The need for an emergent or even urgent operation can often be forestalled by appropriate pharmacological therapy, placement of an IABP, or even percutaneous revascularization of "culprit" stenoses. In each instance, the benefit of temporizing therapy must be weighed against the risk of waiting and the risk of the therapy used to achieve delay. A discussion of this strategy as applied to the acute coronary syndrome is presented in Section 5.11. Smoking cessation and improvement of chronic bronchitis before elective coronary operation lessen the risk for perioperative pulmonary complications (305). Preoperative pulmonary edema is a particularly hazardous situation, as extracorporeal circulation will worsen the lung water and predispose the patient to prolonged, postoperative mechanical ventilatory support. Ideally, the operation is

deferred until resolution of the edema is accomplished. Obesity is an independent risk factor for perioperative respiratory failure, sternal and leg wound complications, perioperative MI, and arrhythmias (387). If the patient's coronary anatomy and clinical course permit, a concerted effort at weight reduction is appropriate and operation is deferred.

## *4.2. Maximizing Postoperative Benefit*

### 4.2.1. Antiplatelet Therapy for SVG Patency

**Class I**

**Aspirin is the drug of choice for prophylaxis against early saphenous vein graft closure. It is the standard of care (Table 13) and should be continued indefinitely given its benefit in preventing subsequent clinical events.** ***(Level of Evidence: A)***

Aspirin significantly reduces vein graft closure through the first postoperative year. A demonstrable effect on arterial graft patency has not been demonstrated. Aspirin administration before operation offers no improvement in subsequent vein graft patency compared with early postoperative initiation (370). Fail-safe mechanisms should exist to ensure prompt postoperative initiation of aspirin therapy. Prospective controlled trials have demonstrated a graft patency benefit when aspirin was started 1, 7, or 24 hours after operation (388-390). The benefit of postoperative aspirin on SVG patency is lost when started greater than 48 hours after surgery (391). Dosing regimens ranging from 100 to 325 mg daily appear to be efficacious. As the graft recipient coronary artery luminal diameter increases, SVG patency rates improve and the advantage of aspirin over placebo is reduced (392). Aspirin, given early after CABG (within 48 hours) has been shown to significantly reduce subsequent mortality, MI, stroke, renal failure, and bowel infarction (393).

Ticlopidine is efficacious (394) but offers no advantage over aspirin except as an alternative in the truly aspirin-allergic patient. Life-threatening neutropenia is a rare but recognized side effect. When ticlopidine is used, white blood cell count should be periodically monitored in the early months after initiating treatment. Clopidogrel offers the potential for fewer side effects compared with ticlopidine as an alternative to aspirin for platelet inhibition. The incidence of severe leukopenia is rare and similar to that of aspirin in a controlled trial (395). Indobufen is a reversible inhibitor of platelet cyclooxygenase, in contradistinction to aspirin, so platelets recover function within 24 hours of cessation of the drug. It appears to be as effective as aspirin for saphenous graft patency over the first postoperative year but with fewer gastrointestinal side effects (396).

Dipyridamole adds nothing to the aspirin effect for saphenous graft patency (370). Warfarin has shown no consistent benefit in maintaining saphenous graft patency (397) and may be associated with an increased risk for bleeding compared with antiplatelet therapy for this application (398). Whether the combination of aspirin and clopidogrel is superior to aspirin alone is not yet resolved.

In summary, aspirin is the drug of choice for prophylaxis against early saphenous graft thrombotic closure. Perioperative use and/or administration of aspirin within 48 hours of operation should be the standard of care (Table 13) and should be continued indefinitely, given its benefit in the secondary prevention of subsequent clinical events.

### 4.2.2. Pharmacological Management of Hyperlipidemia

**Class I**

**All patients undergoing CABG should receive statin therapy unless otherwise contraindicated.** ***(Level of Evidence: A)***

There is little question that patients with known atherosclerotic disease, including patients undergoing CABG for coronary atherosclerosis, should receive lipid-lowering therapy. If there is no contraindication, statin (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor) therapy is recommended as initial therapy to lower the low-density lipoprotein cholesterol (LDL-C). How low should the LDL-C be lowered? The Adult Treatment Panel III of the National Cholesterol Education Program (NCEP) continues to recommend that the LDL-C goal should be less than 100 mg/dL (399). This recommendation as applied to the CABG patient is supported by the Post Coronary Artery Bypass Graft Trial Investigators. Angiographic progression of atherosclerotic vein-graft disease was significantly retarded by lovastatin (with the occasional addition of cholestyramine to achieve the individualized lipid-lowering goal). Patients having aggressive cholesterol lowering (achieved LDL-C less than 100 mg/dL) had disease progression in 29% of saphenous grafts over an average 4-year follow-up compared with 39% in the moderate treatment group (achieved LDL-C less than 140 mg/dL) ($P$ less than 0.001) (397). The aggressively treated group had a lower repeated revascularization rate over the course of the study compared with the moderate treatment cohort: 6.5% versus 9.2% (29% lower, $P$ equals 0.03).

The Heart Protection Study, which prospectively studied 20 536 patients in a double-blind trial of simvastatin 40 mg daily versus placebo, showed significant benefit of statin therapy even in individuals with LDL-C less than 100 mg/dL (400). Thus, either the LDL-C goal of 100 mg/dL is too high (studies are under way to compare the effect of an LDL-C–lowering goal of 100 mg/dL versus 70 mg/dL) or the pleomorphic benefits of statin therapy are present regardless of the LDL-C level. Based upon the results of the PROVE-IT trial, the NCEP has recently recommended an LDL-C goal of less than 70 mg/dL in patients deemed to be at very high risk (399a). Because patients are more likely to continue on statin therapy begun in the hospital (401), it is recommended that statin therapy be continued or started during hospitalization for CABG surgery.

If the patient is on statin therapy and the LDL-C goal has been reached prior to CABG surgery, attention should be directed to elevated triglycerides and low high-density lipoprotein cholesterol (HDL-C). These dyslipidemias, especially when combined with an elevated fasting glucose, central obesity, and hypertension, constitute the cardiovascular metabolic syndrome, a syndrome that along with diabetes, is associated with excess cardiovascular mortality and morbidity. These patients should be treated with diet, weight control, daily exercise, and drug therapy designed to increase HDL-C and decrease triglycerides. The recommendations of ATP-III should serve as a guideline (399). Those patients with the insulin resistance syndrome or diabetes often need additional therapy with ACE inhibitors or angiotensin receptor blockers to protect their renal function.

Patients with a strong family history of coronary disease and patients undergoing CABG surgery with completely normal or low lipid levels without recent illness or lipid-lowering therapy should be screened for elevated novel risk factors such as homocysteine, lipoprotein(a), hs–C-reactive protein, and fibrinogen (402).

### 4.2.3. Hormonal Manipulation

**Class III**

**Initiation of hormone therapy is not recommended for women undergoing CABG surgery. *(Level of Evidence: B)***

Although more than 30 observational studies have shown a reduced mortality for coronary disease in postmenopausal women on hormone replacement therapy, hormone therapy (HT) is no longer recommended for women undergoing CABG surgery.

The Heart and Estrogen/Progestin Replacement Study (HERS) randomized postmenopausal women less than 80 years of age with CAD to placebo (1a,405) or estrogen/progestin HT (1a,397). Forty-two percent of the patients underwent CABG surgery (405). The primary end point was nonfatal MI and CAD deaths. The patients were followed up for 4.1 years. There was no statistical difference in the primary end points, but there were more cardiovascular disease deaths in the patients receiving HT (71 versus 58). There were significantly more patients with deep vein thrombosis (*P* equals 0.004) and any thromboembolic events (*P* equals 0.002) in the women receiving HT.

The reason for the marked discrepancy between the observational studies and this large controlled trial probably relates to the fact that although HT does offer long-term protection from cardiovascular disease, it increases the risk of clotting. Therefore, patients with MI undergoing PCI or CABG surgery should not be started on HT. Patients on HT should have therapy discontinued if undergoing surgery or prolonged bed rest secondary to an illness such as a stroke.

### 4.2.4. Smoking Cessation

**Class I**

1. **All smokers should receive educational counseling and be offered smoking cessation therapy after CABG. *(Level of Evidence: B)***
2. **Pharmacological therapy including nicotine replacement and bupropion should be offered to select patients indicating a willingness to quit. *(Level of Evidence: B)***

Smoking is the single most important cause of preventable premature mortality in the United States (406). There is strong evidence from the CASS that smoking cessation after coronary bypass is rewarded by less recurrent angina, improved function, fewer hospital admissions, maintenance of employment, and improved survival (84% survival for quitters versus 68% for persistent smokers at 10 years for those randomized to operation) (*P* equals 0.018) (407). Cessation of smoking after coronary bypass improves the postoperative survival of successful quitters to that of post-bypass patients who have never smoked; persistent smokers have significantly more MIs and reoperations (408). As expected, smoking leads to angiographically detected deterioration over time: only 39% of smokers' saphenous grafts are disease-free at 5 years compared with 52% of nonsmokers (409).

Failure to attempt cessation and recidivism are the difficult issues. Treatment individualized to the patient is crucial. Smoking is an addictive disorder and should be treated as such and not as an indication of self-destructiveness or weak willpower (410).

Depression is an important complicating factor in smoking and may account for a significant number of cessation failures (411,412). Behavioral treatments alone are not as effective as drug therapy (413).

The nicotine transdermal patch is effective in smoking cessation treatment. The average cost per year of life saved ranges from $965 to $2360 (406). A transdermal nicotine patch in conjunction with a behavioral modification program sustained continuous abstinence for 20% of patients receiving the patch versus 9% for those receiving behavioral modification alone (414). Nicotine gum added to transcutaneous patch therapy significantly increased abstinence rates above that of the active patch alone at 52 weeks (415).

A sustained-release form of the antidepressant bupropion is effective for smoking cessation in a dose-related fashion. The agent reduces the nicotine craving and anxiety of smokers who quit. Three hundred milligrams per day led to a 44% smoke-free rate at 7 weeks and 23% at 1 year, double that of the placebo group (*P* less than 0.001) (412). The results at 1 year parallel those seen with nicotine replacement strategies. As with any drug, the patient started on bupropion should be monitored for adverse side effects.

In summary, all smokers should receive educational counseling and be offered smoking cessation therapy, including pharmacological therapy if appropriate, after coronary

bypass (Table 16) (416). Pharmacological therapy including nicotine replacement and bupropion should be offered to patients indicating a willingness to quit.

## 4.2.5. Cardiac Rehabilitation

**Class I**

**Cardiac rehabilitation should be offered to all eligible patients after CABG. *(Level of Evidence: B)***

Cardiac rehabilitation including early ambulation during hospitalization, outpatient prescriptive exercise training, family education (417), and sexual counseling (418) have been shown to reduce mortality (419,420). Cardiac rehabilitation beginning 4 to 8 weeks after coronary bypass and consisting of 3-times-weekly educational and exercise sessions for 3 months is associated with a 35% increase in exercise tolerance (*P* equals 0.0001), a slight (2%) but significant (*P* equals 0.05) increase in HDL-C, and a 6% reduction in body fat (*P* equals 0.002) (421). Exercise training is a valuable adjunct to dietary modification of fat and total caloric intake in maximizing the reduction of body fat while minimizing the reduction of lean body mass (422). A significant hurdle appears to be *initiation* of rehabilitation. In a prospective study of recruitment for a comprehensive cardiac rehabilitation program for patients having just undergone coronary bypass, only 52 of 393 elected to participate. Participation was lower for women (26% of nonparticipants versus 12% of enrolled, *P* equals 0.02), unemployed patients (63% of those declining versus 45% of the participants, *P* equals 0.02), those with a lower income and educational level (both *P* equals 0.001), and those with a greater functional impairment (*P* equals 0.001) (423). If the barriers to enrollment can be overcome, benefits seem to accrue to all special groups studied. The benefits of cardiac rehabilitation extend to the elderly and to women (424,425). Despite the fact women have a generally higher risk profile and a relatively lower functional capacity than men at initiation of a rehabilitation period (426), there were similar compliance and completion rates, and women achieved a similar or greater improvement in functional capacity (women increased peak metabolic equivalents by 30%, men by 16%, *P* less than 0.001) (427). Medically indigent patients appear to have rehabilitation compliance and benefit rates on par with insured/private-pay patients if rehabilitation is initiated and appropriately structured (428).

In a long-range trial focused exclusively on a coronary bypass population, postoperative patients were randomized to standard posthospital care (n equals 109) or standard care plus rehabilitation (n equals 119). At 5 years, the groups were similar on measures of symptoms, medication use, exercise capacity, and depression scores. However, rehabilitated patients reported more freedom of physical mobility (Nottingham Health Profile, *P* equals 0.005), perceived better health (*P* equals 0.03), and a perceived better overall life situation (*P* equals 0.02). A larger proportion of the rehabilitated patients were working at 3 years (*P* equals 0.02). This difference disappeared with longer follow-up (429). Patients who sustained an infarct followed by coronary bypass had greater improvement in exercise tolerance after rehabilitation (change in exercise capacity 2.8 plus or minus 1.4 metabolic equivalents) than did those having infarct alone (0.8 plus or minus 2, *P* less than 0.02). Improvement was sustained to 2 years (430).

In addition to benefiting a sense of well-being, there is an economic benefit that accrues from participation in cardiac rehabilitation programs. During a 3-year follow-up (mean of 21 months) after coronary events (58% of events were coronary bypass operations), per capita hospitalization charges were $739 lower for rehabilitated patients compared with nonparticipants ($1197 plus or minus $3911 versus $1936 plus or minus $5459, *P* equals 0.022) (431).

After CABG, the patient is more likely to resume sexual activity and to a greater degree than is the patient postinfarct. Anticipatory and proactive advice by the physician or surgeon on the safety of resumption of sexual activity as the patient reengages in other daily activities is beneficial (432).

In summary, cardiac rehabilitation should be offered to all eligible patients after coronary bypass surgery.

**Table 16.** Smoking Cessation for the Primary Care Clinician

Strategy 1. Ask—systematically identify all tobacco users at every visit.
- Implement an office-wide system that ensures that for EVERY patient at EVERY clinic visit tobacco-use status is queried and documented.

Strategy 2. Advise—strongly urge all smokers to quit.
- In a clear, strong, and personalized manner, urge every smoker to quit.
- Ask every smoker if he or she is willing to make a quit attempt at this time.

Strategy 3. Assist—aid the patient in quitting.
- Help the patient with a quitting plan.
- Encourage nicotine replacement therapy or bupropion except in special circumstances.
- Give key advice on successful quitting.
- Provide supplementary materials.

Strategy 4. Arrange—schedule follow-up contact
- Schedule follow-up contact, either in person or via telephone.

From the ACC/AHA 2002 Guideline Update on the Management of Patients With Stable Angina that was modified from Fiore MC, Bailey WC, Cohen JJ, et al. Smoking Cessation. Clinical Practice Guideline Number 18. AHCPR publication No. 96-0692. Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, U.S. Department of Health and Human Services, 1996.

## 4.2.6. Emotional Dysfunction and Psychosocial Considerations

The 2 most important independent psychosocial predictors of death in a multivariate analysis of elderly patients post-CABG are a lack of social participation and religious strength (433). Social isolation is associated with increased mortality and coronary disease (434), and successful treatment may improve outcomes (435). Depression is generally poorly recognized by the cardiac specialist (421). Mood for

up to 1 year after coronary bypass is correlated most strongly with mood before coronary bypass. The prevalent opinion that depression is a common result of coronary bypass is challenged by several reports (436). Half of patients who were depressed before operation were not depressed afterward, and only 9% of patients experienced new depression postoperatively. The overall prevalence of depression at 1 month and 1 year was 33%, which was similar to that in reports of patients undergoing other major operations. Some have argued that preoperative screening simply sensitizes the healthcare team and family to postoperative mood problems, rather than there being a more direct pathophysiological association of coronary bypass and depression per se. Coronary disease and psychiatric disorders are highly prevalent and frequently concurrent. Anxiety and depression are often encountered around the time of coronary bypass operation. Anxiety may intensify the autonomic manifestations of coronary disease and complicate patient care. Realization of one's mortality, physical limitations, limitations of sexual activity, survival guilt after successful operation, and development of nihilism regarding modification of risk factors play a role in recovery. Denial has adaptive value during hospitalization and can enhance care, but its persistence in the early home convalescence may be counterproductive. Clinical depression is correlated with subsequent mortality (437).

Eighteen percent of patients are depressed after major cardiac events, including coronary bypass (421). Cardiac rehabilitation has a highly beneficial effect on these patients, whether moderately or severely depressed. In a prospective but uncontrolled study of 3 months of rehabilitation on measures of depression, anxiety, hostility, somatization, mental health, energy, general health, bodily pain, functional status, well-being, and a total quality of life score, patients were improved from 20% to 57% ($P$ value for the scores ranged from 0.001 to 0.004) (421).

### 4.2.7. Rapid Sustained Recovery After Operation

Rapid recovery and early discharge, the "fast-track" approach, for the patient post-CABG should become the standard goal of care. The shortest postoperative stays in the hospital are followed by the fewest rehospitalizations (438). There is very little evidence of a rise in morbidity, mortality, or readmission rates in systems employing fast-track protocols. Longer initial hospitalizations generally are recognized not to prevent rehospitalizations. Prevention or prompt correction of noncardiac disorders allows rapid recovery after coronary operations. Important components of the fast-track system are patient selection, patient and family education, short-acting narcotic or inhalational anesthetic agents allowing early extubation and transfer from the intensive care setting, prophylactic antiarrhythmic therapy, dietary considerations, early ambulation, early outpatient follow-up by telephone, and a dedicated fast-track coordinator (439,440).

### 4.2.8. Communication Between Caregivers

A primary care physician frequently refers patients who undergo CABG to a cardiologist and/or surgeon. Maintaining appropriate and timely communication between treating physicians regarding care of the patient is crucial. The primary care physician's request for referral may well be verbal but should also be documented in writing and accompanied by relevant medical information. Ideally, the primary care physician follows the patient with the other treating physicians during the perioperative course in the hospital if circumstances and geography permit. The referral physician(s) needs to provide written reports of findings and recommendations to the primary care physician, including a copy of the discharge summary from the hospital. Discharge medications that are likely to be required for the long term should be clearly identified. The decision about the degree of responsibility for postoperative care and prevention strategies needs to be made by mutual agreement among the patient, the primary care physician, the cardiologist, and the surgeon in each individual case. The primary care physician can emphasize and continue to implement secondary prevention strategies, frequently begun by the cardiologist and surgeon, since most of these strategies involve lifestyle changes or pharmacological therapies over an extended period of time.

## 5. SPECIAL PATIENT SUBSETS

### *5.1. CABG in the Elderly: Age 70 and Older*

The evolution in surgical techniques and changing demographics and patient selection for CABG surgery have led to its application in older and sicker patients with more complex disease (441). Nearly all reports during the past 10 years define "elderly" in the context of coronary surgery as age 70 years or older. However, the definition of elderly in the literature has gradually increased from 65 years or older to 80 years or older. The greatest increase in numbers has occurred in the oldest group, persons 85 years or older (442). This group has a higher incidence of left main disease, multivessel disease, LV dysfunction, and reoperation as the indication for surgery, and for many, concomitant valvular surgery. These patients generally have more comorbid conditions, including diabetes, hypertension, COPD, PVD, and renal disease. This combination of more advanced coronary disease and worse comorbidity leads to increased fatal and nonfatal complications. Higher rates of intraoperative or postoperative MI, low-output syndrome, stroke, gastrointestinal complications, wound infection, renal failure, and use of an IABP may occur (443,444). In Figure 10, operative mortality (%) is shown as a function of age. A near-linear slope increases abruptly at age 75. Similarly, in Figure 11 the OR for operative mortality is shown as a function of age (21). The effects of these factors on patient outcomes and institutional resources have significant implications for peer review, quality assurance screening, institutional reporting to external sources, and reimbursement (443).

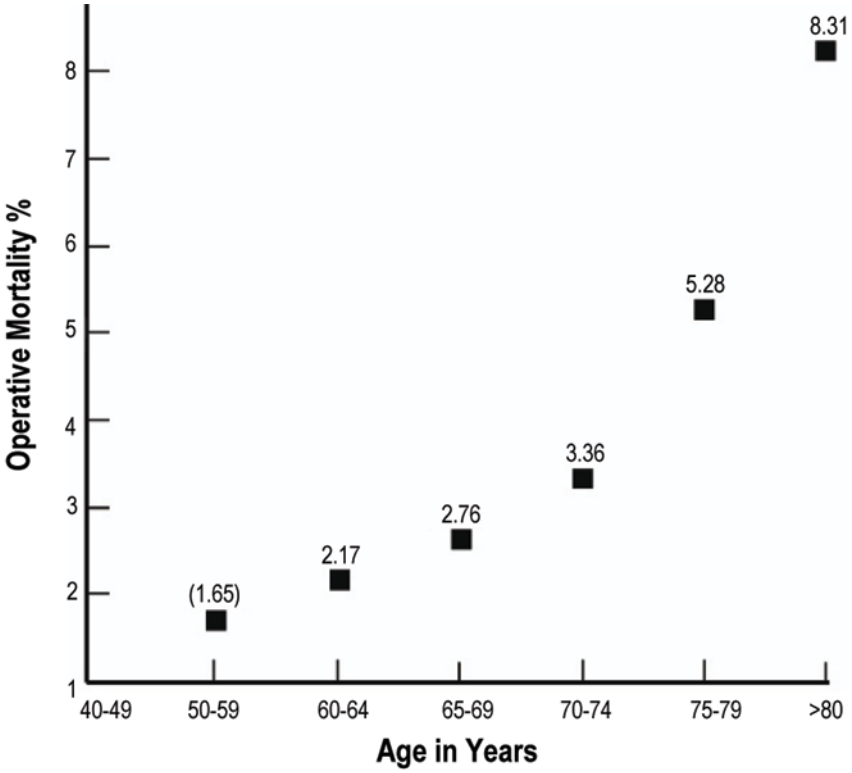


**Figure 10.** Operative mortality (%) for CABG in various age cohorts. Data derived from Hannan et al. Am Heart J. 1994;128:1184-91 (21).

Operative mortality in the elderly has ranged from 5% to 20% during the past 20 years for isolated CABG, averaging 8.9%. In a large study from Ontario, Canada, Ivanov et al (442) found a 34% reduction in risk-adjusted operative mortality (1982 to 1996) while confirming a time-related increase in the prevalence of older patients and an increase in the preoperative risk profile in these patients. They reported an overall mortality of less than 5% for elderly patients, with a 3% mortality for low- and medium-risk patients.

Preoperative predictors of hospital mortality and morbidity (30 days) in elderly patients include a near-linear relation to New York Heart Association (NYHA) class and/or reduced LVEF (particularly if less than 0.20). Other correlates of increased risk include increasing age; recent MI (less than 30 days), especially in the presence of unstable angina, left main disease, or 3-vessel disease; emergency or urgent coronary bypass; reoperation; reduced renal function; cerebrovascular disease; COPD; a smoking history; obesity; and female sex (21,445-452). A higher operative mortality occurs for all identified risk factors in patients aged 75 years or older than for those less than 65 years old. However, in particular, emergency surgery confers up to a 10-fold increase in risk (3.5% to 35%), urgent surgery a 3-fold increase (3.5% to 15%), hemodynamic instability a 3- to 10-fold increase, and an LVEF less than 0.20 up to a 10-fold increase (21,453,454). Predictors of postoperative low cardiac output syndrome are, in descending order of importance, LVEF less than 0.20, repeat operation, emergency operation, female sex, diabetes mellitus, age greater than 70 years, left main disease, recent MI, and/or 3-vessel disease (455). The greatest risk is in the acutely ill, elderly patient for whom the CABG operation may be the best of several high-risk options (456).

Operative factors that have been reported to adversely influence hospital mortality in the elderly include the use of bilateral IMA grafts, prolonged pump time and/or cross-clamp time, an increased number of grafts required, right IMA grafting, and any postoperative complication (448,449,457,458). Obesity has been identified as a risk factor for infection in patients receiving bilateral IMA grafts (457). Contrariwise, improved hospital mortality and long-term survival have been reported when the left IMA is used along with 1 or more vein grafts as opposed to vein grafting alone. Thus, use of the left IMA as a conduit appears to be a predictor of improved early and late survival (41,42,276,459). CABG without cardiopulmonary pump assistance may be advantageous in high-risk patients, particularly those with an LVEF less than 0.35 (460,461).

Postoperative atrial fibrillation is a particular problem in elderly patients undergoing CABG. Correlates of postoperative atrial fibrillation include age greater than 70 (especially age greater than 80), male sex, postoperative pulmonary complications, ventilation time greater than 24 hours, return to the intensive care unit, and use of the IABP. Atrial fibrillation contributes to a substantially prolonged hospital stay (9.3 plus or minus 19 versus 15.3 plus or minus 28 days) (351). Patients with preoperative chronic renal failure are at a particular risk, as they tend to be older and have additional comorbidity (71). Interventions to prevent atrial fibrillation are discussed in Section 4.1.5.

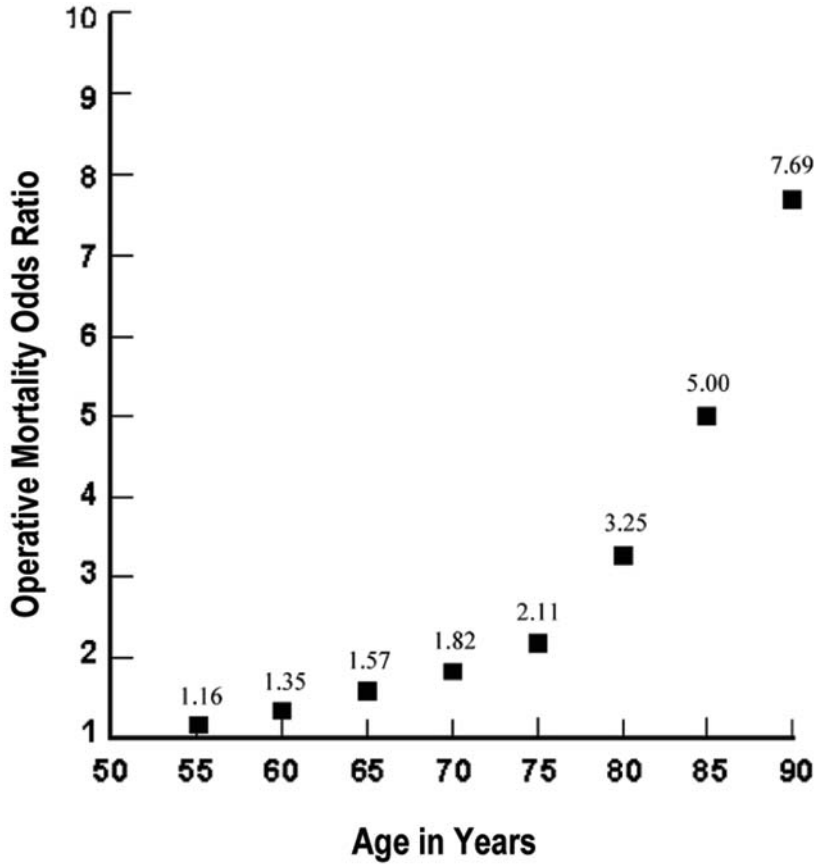


**Figure 11.** Operative mortality odds ratio (relative to odds for 50-year-old patients). Data derived from Hannan et al. Am Heart J. 1994;128:1184-91(21).

It should be emphasized that long-term survival and functional improvement can be achieved in the elderly patient despite severe cardiovascular disease and an urgent indication for surgery (462). The 5-year survival of such patients who recover from surgery is comparable to that of the general population matched for age, sex, and race (463,465). Preoperative variables that are correlated with poor long-term survival in elderly patients include the presence of atrial fibrillation, smoking, PVD, and poor renal function (low creatinine clearance). An unsatisfactory functional outcome has been influenced by hypertension, cerebrovascular insufficiency, and poor renal function (low creatinine clearance) (466).

Peterson et al (467) analyzed the Medicare database to assess long-term survival in patients 80 years and older and found it comparable to the general population of octogenarians. This group was hospitalized significantly longer than those aged 70 or younger (21.4 versus 14.3 days) and had a higher hospital mortality (11.5% versus 4.4%) and higher 3-year mortality (28.8% versus 18.1%). Hospital costs and charges were also higher. Similar findings are reported by others, with actuarial survival including hospital death at 80 months of 32.8% versus 37.6% for age-, sex-, and race-matched populations. These authors concluded that advanced age alone should not be a contraindication to CABG if it had been determined that long-term benefits outweighed the procedural risk (465,467,468). Although hospitalization may be longer for elderly patients, physiological, psychological, and social recovery patterns through the first 6 weeks postoperatively have been reported to be similar to those of a younger age group (469). Age 70 and older is an independent risk factor for stroke after CABG, adversely affecting hospital mortality, prolonging the hospital stay, and negatively impacting late death (470).

In operations combining valve surgery and CABG, independent predictors for reduced late survival included NYHA Class IV, age greater than 70 years, male sex, decreased LVEF, extent of CAD and use of a small prosthetic valve, but not necessarily the presence of CAD per se (471-474).

In summary, the patient aged 70 years or older who may be a candidate for CABG surgery has, on average, a higher risk for mortality and morbidity from the operative procedure in a direct relation to age, LV function, extent of coronary disease, comorbid conditions, and whether or not the procedure is emergent, urgent, or a reoperation. Nonetheless, functional recovery and an improvement in quality of life may be achieved in the large majority of such patients.

The patient and physician together should explore the potential benefits of improved quality of life with the attendant risks of the procedure versus alternative therapy, taking into account baseline functional capacities and patient preferences. Age alone should not be a contraindication to CABG surgery if it is thought that long-term benefits outweigh the procedural risk (448,475-477).

### *5.2. CABG in Women*

Early studies provided evidence that female sex was an independent risk factor for higher in-hospital mortality and morbidity than in males, but that long-term survival and functional recovery were similar to those in males undergoing CABG surgery (29,478-481). More recent studies have suggested that on average, women have a disadvantageous preoperative clinical profile that may account for much of this perceived difference. This includes the fact that women present for treatment at an older age, with poorer LV function, more frequently with unstable angina pectoris, NYHA Class IV heart failure, 3-vessel and left main disease, and more comorbid conditions including hypothyroidism, renal disease, diabetes mellitus, hypertension, and PVD (25,480-489). Based on these differences, it has been inferred that women may be under-referred or referred late for treatment and/or coronary angiography. These findings are not universal, as significant differences exist in clinical practice between institutions (481,482).

A variety of factors may account for the perception that female sex is an independent risk factor for in-hospital mortality and morbidity after CABG surgery. For example, Israeli women were reported to have a 3.2-fold higher hospital mortality than men, but women also received a higher number of SVGs, suggesting more diffuse disease. When this consideration was adjusted for, mortality was found to be similar (490). Others have argued that smaller coronary arteries in women may contribute to higher risk (26). IMA grafts have been reported to be used less often in women, possibly contributing to a higher mortality (25,486). Kurlansky et al (78) reported favorable results in 327 women with bilateral IMA grafts plus supplemental vein grafts, with a hospital mortality of 3% to 4%, low postoperative morbidity, excellent functional improvement, and enhanced long-term survival. Five-year survival of 90.5% and of 65.6% at 10 years was achieved, with 94% of patients reaching NYHA Class I and 4.5% NYHA Class II. Hammar et al (480) reported that when age and body surface area were taken into account, the relative operative risk between men and women became similar. Others have also found no differences in operative mortality, total postoperative morbidity, and ICU length of stay (491,492). Comparable findings were reported for coronary bypass surgery in black male and female patients (493).

However, analysis from the CASS registry found a higher operative mortality for women (493) as did Jaglal et al (494), even when comorbidities were adjusted for appropriately. They suggested that the excessive mortality was due to late treatment (494). Farrer et al (495) found that women had more severe symptoms with a similar severity of coronary disease as defined by angiography when compared with men, suggesting a referral bias with referral occurring later in the course of the disease. Whether these perceived biases are real and whether they are practitioner or patient related or have a biological explanation is not known. They serve as a challenge for future investigation (496).

Postoperative complications in women mirror those seen in all patients undergoing CABG surgery. These include MI, stroke, reoperation for bleeding, pulmonary insufficiency, renal insufficiency, sternal wound infection (perhaps related to obesity), CHF, rhythm other than normal sinus rhythm, and low cardiac output syndrome (25,78,490). Women appear particularly vulnerable to postoperative CHF, low cardiac output syndrome (25,29,482), and blood loss (485). Although postoperative depression is common in women and men, its occurrence in women has been reported to be more common (about 60%) and more commonly unrecognized (484). Nonetheless, at 6 months postoperatively, men and women report similar psychosocial recovery (100) (see Section 4).

In the CASS registry, although a higher operative mortality for women was found, the subsequent 15-year postoperative survival and benefits were similar to those for men. Greater absolute benefit was achieved in those with the highest risk in both male and female groups. For women, independent risk factors for poorer long-term survival included older age, prior MI, prior CABG, and diabetes mellitus (497).

Over time, changes in the clinical characteristics of women undergoing CABG mirror those of the changing characteristics of the general population. One study compared female patients operated on between 1974 and 1979 to a group receiving surgery between 1988 and 1999 and showed that operative mortality had increased from 1.3% to 5.8%. This rise was attributed to an older cohort of women, more emergency or urgent operations, an increased incidence of depressed LV function, diabetes mellitus, and more 3-vessel and left main disease, all suggesting that the female population undergoing coronary bypass surgery had changed (498). In another report, women aged 70 or older were found to be at no greater risk for operative mortality and postoperative complications than men of similar age (499).

Another study based on the STS national database examined more than 300 000 patients undergoing CABG after 1994. Women were found to have a significantly higher operative mortality for all risk factors examined even when normalized for size (body surface area). A logistic risk model was used to determine the net impact of all risk factors. The model showed that in risk-matched patients, female gender was an independent risk factor of operative mortality in low- and moderate-risk subsets but not in high-risk populations (28).

In conclusion, it appears that in-hospital mortality and morbidity and long-term survival are related more to risk factors and patient characteristics than to sex. Coronary bypass surgery should therefore not be delayed or denied to women who have the appropriate indications for revascularization.

### *5.3. CABG in Patients With Diabetes*

Coronary artery disease is the leading cause of death among adult patients with diabetes and accounts for about 3 times

as many deaths among patients with diabetes as among patients without diabetes (500). Not only is the frequency of acute MI increased in patients with diabetes (501,502) but also its treatment is more complicated than in the patients without diabetes. Patients with diabetes with acute MI, regardless of the level of control of their diabetes before hospital admission, exhibit significantly higher mortality and morbidity, with fatality rates as high as 25% in the first year after infarction in some series. Several factors contribute to this increase in mortality. The size of the infarct tends to be greater, and patients with diabetes have a greater frequency of CHF, shock, arrhythmias, and recurrent MI than do patients without diabetes. Similarly, patients with diabetes with unstable angina have a higher mortality than do patients without diabetes. A prospective study indicated a 3-month mortality of 8.6% and 1-year mortality of 16.7% in patients with diabetes versus 2.5% and 8.6%, respectively, in patients without diabetes (503).

CABG surgery in elderly patients with diabetes (age 65 or greater) has been reported to result in a reduction in mortality of 44% in CASS. The relative survival benefit of CABG versus medical therapy was comparable in patients with and without diabetes (503a). Nevertheless, a study from Sweden has indicated that patients with diabetes of all ages have a mortality rate during the 2-year period after CABG that is about twice that of patients without diabetes. Thirty-day mortality after CABG was 6.7% in patients with diabetes, and subsequent mortality between day 30 and 2 years was 7.8% compared with 3% and 3.6%, respectively, in patients without diabetes (504).

Despite increased morbidity and mortality after coronary revascularization, results from the BARI trial showed that patients with multivessel coronary disease who were being treated for diabetes at baseline had a significantly better survival after coronary revascularization with CABG than with PTCA (Figure 6) (117). In this study, patients were followed up for an average of 5.4 years. Better survival with CABG was due to reduced cardiac mortality (5.8% versus 20.6%, *P* equals 0.0003), which was confined to those patients receiving at least one IMA graft. Thus, although mortality after CABG surgery may be increased in patients with diabetes, CABG surgery when indicated appears to provide a better chance for survival than does medical therapy or PCI.

Large randomized trials have now reached 7 to 8 year follow-up (131,130). These updated studies generally show that 7 to 8 year survival is superior for patients with diabetes undergoing CABG compared with patients with diabetes undergoing PTCA (131,130). In the BARI trial, the protective effect of CABG was only seen in insulin-dependent patients with diabetes (505) who had an IMA graft (131). There was virtually no difference in survival among patients without diabetes.

Patients with diabetes who are candidates for renal transplantation may have a particularly strong indication for CABG surgery. Approximately 20% to 30% of these patients have significant CAD, which may be asymptomatic or unassociated with conventional cardiovascular risk factors (390,506). One study assessed the incidence of coronary disease via angiography (which was performed independently of the presence of risk factors or suggestive symptoms) in 105 consecutive dialysis patients with diabetes (390). Angiographic evidence of significant coronary disease was found in 38 (36%) patients, only 9 of whom experienced prior symptoms of angina. The degree of hypercholesterolemia, hypertension, and smoking history did not differ between those with and without documented coronary disease. Thus, noninvasive testing and, if indicated, cardiac catheterization should be performed before renal transplantation, because conventional clinical predictors of disease are unreliable and active intervention may improve patient outcomes (390,507). This approach is supported by a study that randomized 26 patients with greater than 75% stenosis in at least 1 coronary artery and relatively normal LV function to either revascularization or medical therapy with aspirin and a calcium channel blocker (506). Both the incidence of cardiovascular end points (2 of 13 versus 10 of 13) and mortality rate (0 of 13 versus 4 of 13) were lower in the revascularized patients.

### *5.4. CABG in Patients With Pulmonary Disease, COPD, or Respiratory Insufficiency*

For many years, it has been recognized that patients undergoing cardiac surgery develop variable degrees of respiratory insufficiency postoperatively. In these patients, higher concentrations of oxygen are required to achieve adequate arterial oxygen tension, primarily as a consequence of intrapulmonary shunting. Scattered regions of atelectasis and alveolar collapse may occur, resulting in some air spaces receiving pulmonary blood flow that are not being ventilated. Other contributing factors may occur. Impaired capillary endothelial integrity may be followed by an increase in interstitial fluid and alveolar edema. Anesthetic agents and vasodilators may affect pulmonary vasoconstriction. Other causes of gas exchange abnormalities after cardiac surgery include central effects from anesthesia and narcotics as well as CNS embolization of air or blood clots. Impairment of carbon dioxide elimination may develop from either a rise in alveolar dead space or a decrease in ventilatory drive from the effects of general anesthesia and/or narcotics. Inadequate tidal volume from neuromuscular weakness may occur. Changes in the mechanics of breathing may occur postoperatively as a result of inhalation anesthetics and/or muscle-paralyzing agents. Pain from the chest incision and thoracic or mediastinal chest tubes may result in diminished excursion of the chest and diaphragm. Obesity and rare phrenic nerve injury may also play a role (508). Postoperatively, early extubation is desirable, appears safe, and does not increase postoperative cardiac or pulmonary morbidity, especially if the total bypass time is less than 100 minutes (509,510). However, longer periods of mechanical ventilatory support postoperatively may be necessary in patients who develop acute adult respiratory distress syndrome or who have evidence of severe pulmonary insufficiency postopera-

tively. In such patients, ventilation with lower tidal volumes (6 mL/kg) should be considered (511).

Preoperatively, it is important to identify patients with significant restrictive or obstructive pulmonary disease. The former includes patients with pulmonary venous congestion, large pleural effusions, and a large, dilated heart compressing the lungs, all of which may result in a reduction of lung compliance. Restrictive lung disease is also found in patients with interstitial lung disease including pulmonary fibrosis, sarcoidosis, pneumoconiosis, and collagen vascular diseases. The most common cause of preoperative pulmonary dysfunction, however, is COPD. Patients with mild COPD and few or mild symptoms generally do well through cardiac surgery. However, patients with moderate to severe obstructive pulmonary disease who are undergoing coronary bypass grafting, especially those in an older age group, are at an increased risk for operative mortality and postoperative complications in relation to the severity of their degree of pulmonary dysfunction (445,512-514). Identification of these higher-risk patients is important because preoperative measures to improve respiratory function may diminish postoperative complications. These measures include the use of antibiotic therapy for lung infections, bronchodilator therapy, cessation of smoking, preoperative incentive spirometry, deep-breathing exercises, and chest physiotherapy. Such measures frequently permit patients with obstructive pulmonary disease to safely undergo cardiac surgery (512).

The parameter most commonly reported by authors in estimating the degree of pulmonary dysfunction is the forced expiratory volume in the first second ($FEV_1$). However, there is little consistency in the literature defining the level of abnormality for moderate to severe COPD, with values for $FEV_1$ ranging from less than 70% to less than 50% of the normal predicted value and/or an $FEV_1$ of less than 1.5 L. Others measure arterial oxygen tension and carbon dioxide tension. Any degree of hypercapnia above a normal range places the patient at least in a moderate-risk category (508,512,513), as does the need for oxygen at home before surgery. $FEV_1$ levels as low as 1.0 L would not necessarily disqualify a candidate for CABG surgery. Clinical evaluation of lung function is likely as important as most spirometric studies. This sentiment is reflected by Cohen et al (513), who compared 37 patients with COPD who were undergoing CABG surgery to 37 matched control patients without COPD. They defined COPD in clinical terms (i.e., age, smoking history, presence of preoperative arrhythmias, history of hospitalization for shortness of breath, and evidence of COPD on X-ray film). Those with COPD had lower values for $FEV_1$ (1.36 plus or minus 0.032 versus 2.33 plus or minus 0.49 L) and a lower arterial oxygen tension. This group had a significantly higher rate of preoperative atrial and ventricular arrhythmias. Postoperatively, they remained in the ICU longer, had a longer intubation period and more frequent reintubations, had more postoperative atrial and ventricular arrhythmias and complications, and remained in the hospital twice as long. By 16 months postoperatively, 5 of the COPD patients had died, with deaths related to arrhythmias. None was functionally improved after coronary bypass surgery. These investigators concluded that clinical COPD is a significant factor for morbidity and mortality, in large part due to more frequent postoperative arrhythmias. Subsequent long-term clinical benefits were significantly reduced (513). Kroenke et al (512) reported the results of 107 operations in 89 patients with severe COPD, defined as an $FEV_1$ less than 50% of predicted and an $FEV_1$ to forced vital capacity ratio of less than 70%. In this diverse group, 10 patients underwent CABG surgery. Pulmonary complications occurred postoperatively in 29% of all patients and were significantly related to the type and duration of surgery. Mortality clustered primarily around the time of CABG (5 of 10 patients) compared with only 1 death in 97 noncoronary operations. In this study, noncardiac surgery (as opposed to CABG) was accompanied by an acceptable operative risk in patients, even in the presence of severe COPD (512).

Severe, reversible, restrictive pulmonary function abnormalities, which appear not to be caused by advanced age or preexisting COPD, have been reported to follow coronary bypass surgery in the early postoperative period. In the early postoperative period, these changes may delay ventilator weaning in the first 72 hours, but full recovery is expected (515). Wahl et al (515) compared pulmonary function in a group of patients older than age 70 with a group with COPD, defined as a ratio of $FEV_1$ to forced vital capacity of less than 70% and total lung capacity less than 80% of predicted, and a normal group in the preoperative and postoperative periods. All 3 groups demonstrated comparable decreases in $FEV_1$, total lung capacity, and forced vital capacity postoperatively. Partial recovery occurred by day 7 and returned to preoperative levels by 3 months (515). Similar findings were reported by Goyal et al (516) after CABG with saphenous veins, IMAs, or a combination. Others have reported more severe abnormalities of pulmonary gas exchange and pulmonary function through 72 hours postoperatively in patients receiving left IMA grafts, with normality returning by hospital discharge (517,518).

A history of COPD and greater than 2 days on a mechanical ventilator postoperatively have been reported as risk factors for nosocomial pneumonia in patients post-CABG (519) and have been documented as a risk factor for mediastinitis (520,521). Moderate to severe degrees of obstructive pulmonary disease preoperatively, whether defined by clinical or laboratory parameters, represent a significant risk factor for early mortality and/or postoperative morbidity in patients undergoing CABG. However, with careful preoperative assessment and treatment of the underlying pulmonary abnormalities, many patients may be successfully carried through the operative procedure.

### *5.5. CABG in Patients With End-Stage Renal Disease*

Cardiovascular disease is the single best predictor of mortality in patients with end-stage renal disease (ESRD), as it accounts for almost 54% of deaths (522). The high rate of

cardiac morbidity and mortality is occurring at a time when the prevalence of coronary disease is declining in the general population and is related in part to the changing nature of new patients being started on dialysis. At present, more than one third of such patients have diabetes mellitus, and the average patient age at initiation of dialysis is greater than 60 years. In addition to the foregoing, patients with ESRD usually have a number of other risk factors for cardiovascular mortality, including hypertension, LV hypertrophy, myocardial dysfunction, abnormal lipid metabolism, anemia, and increased plasma homocystine levels.

When indicated, patients on dialysis can be treated with CABG. The indications for CABG are similar to those in patients without ESRD with coronary disease. Coronary revascularization with CABG or PTCA is associated with better survival than is standard medical therapy in several specific settings. These include patients with a modest decrease in LV function, significant left main coronary disease, 3-vessel disease, and unstable angina (523). Although these patients also are at increased risk for operative morbidity and mortality, they are at even higher risk when treated with conservative medical management.

It should be noted that patients with chronic renal failure clearly differ in several respects from other patients who undergo surgical coronary revascularization. Patients with ESRD often have multiple comorbid disorders, including hypertension and diabetes mellitus, each with its own complications and associated impact on both short- and long-term survival (524). In addition, infection and sepsis have been identified as significant causes of morbidity and mortality in patients with ESRD undergoing cardiac surgical procedures (524). As a result of these factors and others such as perioperative volume and electrolyte disturbances, patients with chronic renal failure are at increased risk for complications after CABG.

Patients with ESRD have an increased risk with CABG. The Northern New England Cardiovascular Disease Study Group reported that after adjusting for known risk factors in multivariate analysis, dialysis-dependent patients with renal failure were 3.1 times more likely to die after CABG (adjusted OR 3.1, 95% confidence interval 2.1 to 4.7; *P* less than 0.001) (525). Dialysis-dependent patients with renal failure also had a substantially increased risk of postoperative mediastinitis (3.6% versus 1.2%) and postoperative stroke (4.3% versus 1.7%) (525). CABG surgery in patients on dialysis may be associated with an acceptable mortality, with a significant increase in the quality of life for long-term survivors.

In summary, coronary bypass grafting may be performed for selected patients with ESRD who are dialysis dependent, with increased but acceptable risks of perioperative morbidity and mortality. Early after revascularization, patients may expect relief from coronary symptoms with coincident improvement in overall functional status. However, long-term survival remains relatively limited in this patient population, suggesting a need for further investigations to establish the relative costs and benefits of revascularization in patients with dialysis-dependent ESRD.

### *5.6. Valve Disease*

**Class I**

**Patients undergoing CABG who have severe aortic stenosis (mean gradient greater than or equal to 50 mm Hg or Doppler velocity greater than or equal to 4 m/s) who meet the criteria for valve replacement should have concomitant aortic valve replacement. *(Level of Evidence: B)***

**Class IIa**

1. **For a preoperative diagnosis of clinically significant mitral regurgitation, concomitant mitral correction at the time of coronary bypass is probably indicated. *(Level of Evidence: B)***
2. **In patients undergoing CABG who have moderate aortic stenosis and are at acceptable risk for aortic valve replacement (mean gradient 30 to 50 mm Hg or Doppler velocity 3 to 4 m/s) concomitant aortic valve replacement is probably indicated. *(Level of Evidence: B)***

**Class IIb**

**Patients undergoing CABG who have mild aortic stenosis (mean gradient less than 30 mm Hg or Doppler velocity less than 3 m/s) may be considered candidates for aortic valve replacement if risk of the combined procedure is acceptable. *(Level of Evidence: C)***

The coexistence of CAD and valvular disease will vary throughout the population, dependent on which disease initiates the patient's symptoms, their age, sex, and clinical risk factors. The incidence of aortic valve disease in patients undergoing CABG is much less than the incidence of CAD in patients undergoing valve replacement. In general, the incidence of CAD in patients with typical angina who are undergoing aortic valve replacement (AVR) is 40% to 50% and drops to about 25% in patients with atypical chest pain and to about 20% in those without chest pain (526-533). The incidence of CAD is generally less in patients with aortic regurgitation than aortic stenosis owing to the younger patient population presenting with aortic regurgitation (526-533). The incidence of CAD in patients with mitral stenosis is small, owing to the fact that this lesion is more frequently seen in middle-aged women.

There is a distinctive relationship between mitral regurgitation (MR) and CAD, especially when the mitral valve is structurally normal but functionally regurgitant. This MR is usually caused by ischemia. The quandary this presents is when the MR requires correction at the time of CABG. The question is easily answered if there are structural abnormalities in the mitral apparatus. Mitral repair is indicated in the majority of such circumstances, although occasional patients require valve replacement. The structurally normal mitral valve may be regurgitant due to reversible ischemia involv-

ing the papillary muscles, and the dilemma is, "When is it necessary to inspect the mitral valve for correction?" Intraoperative TEE has brought dramatic refinement to this question by providing a functional and quantitative assessment before and after CPB. When the MR is grade 1 to 2, this may decrease during anesthesia induction and/or with complete revascularization, thus eliminating the need to inspect the valve during cross-clamping of the aorta. An added finding by echocardiography or direct inspection at the time of operation is the presence of an enlarged left atrium, which generally signifies chronicity of the MR and adds justification to the consideration of mitral valve repair. This strategy is further assessed by a final post-CPB TEE in the operating room. If, under this circumstance, the MR is unacceptable, reinstitution of CPB can be performed and the MR corrected. For instance, if the MR is grade 3 to 4, it is necessary to inspect the valve and correct the mechanical lesion. It is important to stress that in this situation, it is imperative that an intraoperative TEE be performed to see whether the MR is grade 3 to 4, to assess the reparability of the valve, and to assess success of the repair. The study by Aklog and associates (534) concluded that CABG surgery alone for moderate ischemic MR leaves many patients with significant residual MR. These authors conclude that a preoperative diagnosis of moderate MR may warrant concomitant mitral annuloplasty (534).

For situations in which patients are undergoing mitral valve surgery and have "incidental" CAD and nonischemic mitral valve disease, the approach has been to perform CABG on vessels with greater than 50% stenosis at the same operation. There are far fewer data on this topic than that of AVR and CAD, but conventional wisdom has promoted this policy, and there have not been reports of significant increases in operative mortality.

The discussion of combined procedures revolves around overall operative risk, which is dependent on several variables. The most notable of these are age greater than 70 years, female sex, advanced NYHA class, poor LV function, and multiple valve procedures (535). There is also a difference in early and late mortality when the valve lesion is aortic versus mitral and when the mitral lesion is ischemic. The simple addition of MR to a coronary bypass without valve correction increases the operative mortality to 3% to 5%. The operative mortality of rheumatic mitral valve disease and CAD varies from 3% to 20% (536). The addition of a valve operation to CABG is also associated with a substantial increase in the risk of stroke (536a).

The results of combined aortic valve and coronary disease have led to the recommendation to graft obstructed vessels (greater than or equal to 50%) when an AVR is performed. The operative mortality for patients undergoing AVR who have ungrafted CAD approaches 10%, while those patients having AVR and concomitant CABG for CAD have an operative mortality approaching that of AVR alone (537). It is generally accepted that the risk of adding CABG to a valve replacement or repair will increase the operative mortality over that of an isolated valve procedure. The additional variables of age greater than 70 or 80 years and poor LVEF will further increase this risk.

Another aspect of this combined condition is the patient with prior CABG who now requires a valve replacement or repair. There is inconclusive evidence that the reoperative risk of late AVR after previous CABG is significantly increased. Sundt et al (538) stated that the operative risk for AVR alone was 6.3%, whereas the risk of AVR after previous CABG was 7.4%. Odell et al (539) found the risk of reoperative AVR with prior CABG to be 12%. A report from the same institution identified an operative risk of 3.7% (11 of 297) for isolated AVR (540). The discrepancy may be due to sample size, in that the article by Sundt et al reviewed 52 patients, whereas Odell et al reported on 145 patients undergoing reoperation for AVR with prior CABG.

### *5.7. Reoperation*

Patients who have undergone CABG may present with recurrent ischemic syndromes and be considered for reoperation. The voluntary STS National Database has reported an incidence of reoperation of 8.6% to 10.4% in isolated bypass operations since 1987, and in centers experienced with reoperations, the percentage of isolated bypass operations constituting reoperations may be 20% to 25%. Reoperative candidates represent a distinct subgroup of bypass surgery patients. Segments of myocardium may be supplied by patent arterial grafts (at risk for damage during reoperation) or by atherosclerotic vein grafts. Vein graft atherosclerosis is a pathology that is different from native-vessel CAD and it is more prone to cause embolization and thrombosis. In addition, reoperative candidates are older and often have far advanced coronary and noncoronary atherosclerosis. Left ventricular function is commonly abnormal, and conduits to perform bypass grafts may be lacking (541).

The mortality rate for reoperation is greater than that for primary surgery, although in experienced centers that risk differential has narrowed with time. Advanced age, abnormal LV function, number of atherosclerotic vein grafts, the number of previous bypass operations, and emergency status are specific variables that have been consistently associated with an increased in-hospital risk associated with reoperation. Emergency operation, in particular, substantially increases the risk of reoperation. Third and fourth bypass operations are increasing in frequency and have all the difficulties associated with a second operation, only more so. They have been associated with an increased mortality rate, an increased risk of hospital complications, and increased cost (541).

However, despite the difficulties of reoperation, it is often the best treatment strategy for many patients with recurrent ischemic syndromes. No randomized studies comparing treatment options for patients with previous bypass surgery exist. However, an observational study of patients receiving coronary angiograms after bypass surgery has shown that for patients with late (greater than or equal to 5 years after operation) stenoses in vein grafts, there is a high risk of subsequent cardiac events and a relatively high risk of death. A

subsequent observational comparative study showed that reoperation improved the survival rate and symptom status of patients with late vein graft stenoses, particularly if an atherosclerotic vein graft subtended the LAD coronary artery. Further studies have identified a positive stress test as a factor that incrementally defines a group of patients at high risk without repeat surgery. Percutaneous procedures have often been effective in the treatment of patients with native coronary stenoses but have been particularly ineffective in the treatment of atherosclerotic vein graft stenoses. These considerations combined with late survival rates after reoperation of 90% to 95% at 5 years, and more than 75% at 10 years, indicate that reoperation can be a sound form of treatment for patients with severe symptoms or survival jeopardy (541).

As the impact of vein graft atherosclerosis on graft failure was appreciated in the early 1980s, it appeared as though the need for coronary reoperation might become overwhelming, but a number of factors decrease the reoperation rate. One is the use of arterial grafts. Despite the lack of randomized data observational studies clearly indicate that use of the left IMA to LAD graft decreases reoperation rate. Studies also indicate that the strategy of bilateral IMA grafting may further decrease the reoperation rate. Second, vein graft failure may be delayed by pharmacological treatment. Early vein graft patency rates are clearly improved by perioperative treatment with platelet inhibitors, and the use of postoperative statin therapy decreases late vein graft failure rate and the incidence of late clinical events. Finally, the availability of percutaneous treatments may further delay the need for reoperation (541).

### *5.8. Concomitant PVD*

The coexistence of CAD and PVD is well known. It is estimated that the prevalence of serious, angiographic CAD ranges from 37% to 78% in patients undergoing operation for PVD (542). CAD is the leading cause of both early and late mortality in patients undergoing peripheral vascular reconstruction (543). MI is responsible for about half of all postoperative deaths in patients undergoing abdominal aortic aneurysm resection (544,545), extracranial revascularization (199,546), or lower-extremity revascularization (545,547). Long-term survival after successful vascular reconstruction is limited by the high incidence of subsequent cardiac death (548). On the other hand, the presence of PVD is a strong, independent predictor of long-term mortality in patients with stable chronic angina (549). After successful myocardial revascularization, patients with PVD are at substantially increased risk for in-hospital (37) and long-term (550) mortality.

The importance of preoperative cardiac evaluation was demonstrated by Hertzer et al (543) in a study of 1000 patients with PVD: abdominal aortic aneurysm, cerebrovascular disease, or lower-extremity ischemia. All 1000 patients underwent coronary angiography. Severe, surgically correctable CAD was found in 25% of the patients; 34% of the patients suspected to have CAD on clinical grounds were found to have severe, surgically correctable CAD; 14% of the patients not suspected to have CAD were found to have severe, surgically correctable CAD. The early postoperative mortality rate after the peripheral vascular procedures was lower in patients who had preliminary CABG compared with those who did not. The long-term beneficial effect of preliminary CABG in patients undergoing peripheral vascular reconstruction was reported by Eagle et al (549) in their retrospective cohort analysis of 1834 patients with combined CAD and PVD. Nine hundred eighty-six patients received CABG and 848 patients were treated medically. In a mean follow-up of 10.4 years, 1100 deaths occurred and 80% were due to cardiovascular causes. The group treated with surgical coronary revascularization had significant survival benefits at 4, 8, 12, and 16 years compared with patients treated with medical therapy alone. Subgroup analysis suggested that the long-term survival benefits of surgical coronary revascularization were particularly seen in patients with 3-vessel CAD and depressed LVEFs.

The predictive value of PVD for short- and long-term clinical outcomes of patients receiving CABG was also examined by the Northern New England Cardiovascular Disease Study Group (37,550). In-hospital mortality rates with CABG in patients with PVDs were 7.7%, a 2.4-fold higher incidence than in patients without PVD (3.2%). After adjusting for higher comorbidity scores associated with patients with PVD, patients with PVD were 73% more likely to die in hospital after CABG. The excess risk of in-hospital mortality associated with PVD was particularly notable in patients with lower-extremity occlusive disease (adjusted OR 2.03). The presence of cerebrovascular disease had a small but nonsignificant effect on CABG-related in-hospital deaths (adjusted OR 1.13).

Excess mortality rates in patients with PVD were due primarily to an increased incidence of heart failure and dysrhythmias rather than cerebrovascular accidents or peripheral arterial complications. The difference in mortality rate was also apparent at long-term follow-up. Five-year mortality after CABG was substantially higher in patients with PVD than in those without PVD, with a crude hazard ratio of 2.77 and an adjusted hazard ratio of 2.01 after multivariate adjustment for comorbid conditions. Significantly elevated adjusted hazard ratios occurred in patients with overt cerebrovascular disease, clinical and subclinical lower-extremity occlusive disease, abdominal aortic aneurysm, and combined PVDs. Asymptomatic carotid bruit or stenosis conferred a small, nonsignificant increased adjusted hazard ratio of 1.47. In summary, the presence of clinical and subclinical PVD is a strong predictor of increased in-hospital and long-term mortality rate in patients undergoing CABG.

### *5.9. Poor LV Function*

See Section 9.2.5 for recommendations.

LV function is an important predictor of early and late mortality after coronary artery surgery. LV dysfunction is associated with an increased risk of perioperative and long-term mortality in patients undergoing coronary bypass sur-

gery compared with patients with normal LV function. Both low EF and clinical heart failure are predictive of higher operative mortality rates with CABG (551). In 6630 patients who underwent isolated CABG surgery in the CASS registry, the average operative mortality was 2.3%, ranging from 1.9% in patients with an EF greater than or equal to 0.50 to 6.7% in patients with an EF less than 0.19 (552). An operative mortality of 6.6% in patients with an EF less than 0.35 in comparison with 2.6% in patients with an EF greater than 0.50 was reported (553). Compared with patients with an EF of 0.40 or higher, patients whose EF was less than 0.20 or between 0.20 and 0.39 had 3.4 and 1.5 times higher perioperative mortality rates, respectively (17). Reports of perioperative mortality rate varied widely, ranging from about 5% in excellent centers in patients of a younger age, with fewer symptoms, and having no comorbid conditions, to greater than 30% in patients who were older, with severe ventricular dysfunction, and having several comorbid conditions (551). A trend toward lower operative mortality rates in recent years compared with those in early years has been reported, perhaps due to better myocardial protection techniques and perioperative management in the contemporary period.

Analysis of patients with an EF less than 0.35 from the CASS registry showed 5-year survival rates of 73%, 70%, and 62% in patients with an EF from 0.31 to 0.35, 0.26 to 0.30, and less than 0.25, respectively (554). A comparison between surgically treated and medically treated groups revealed the greatest surgical benefit in patients with an EF of 0.25 or less. The medically treated patients had a 5-year survival rate of 43% compared with 63% for those treated with coronary bypass surgery. A comparison study of 5824 patients who underwent medical or surgical therapy for ischemic heart disease in the Duke University Cardiovascular Database showed that patients with the worst LV function (EF less than 0.35) had the greatest 10-year survival benefit from bypass surgery (46% versus 27%). Patients with an EF of 0.35 to 0.50 had a 10-year survival rate of 62% in the surgical group versus 50% in the medical group (87). Patients with severe LV dysfunction have increased perioperative and long-term mortality compared with patients with normal LV function. However, the beneficial effects of myocardial revascularization in patients with ischemic heart disease and severe LV dysfunction are clearly evident when compared with medically treated patients in terms of symptom relief, exercise tolerance, and long-term survival (87,551,555,556). Coronary artery bypass graft surgery is recommended in patients with severe multivessel disease and poor ventricular function but with a large amount of viable myocardium. Patient selection is crucial for achieving the beneficial effects of myocardial revascularization in this subset of patients and is discussed in Section 9.

## *5.10. Transplantation Patients*

Cardiac transplantation is an accepted treatment for end-stage heart failure, with greater than 30 000 cardiac transplantations performed worldwide to date (557). Allograft CAD is the leading cause of death after the first year of transplantation (558-560). This type of occlusive CAD is diffuse, often rapidly progressive, and affects a substantial number of heart transplant recipients. The incidence of angiographic transplant vasculopathy is estimated at 40% to 45% at 3 to 5 years after transplantation with a yearly attrition rate of 15% to 20% (561,562). Angina pectoris is rarely the presenting symptom in patients with allograft CAD owing to the lack of afferent autonomic innervation, although partial reinnervation of the allograft can occur. Silent MI, heart failure due to loss of allograft function, and sudden cardiac death are the common signs of cardiac allograft vasculopathy (561). Analysis of coronary angiograms of affected cardiac allografts has revealed unique morphological features consisting of diffuse, concentric narrowing in middle and distal vessels with distal vessel obliteration and a paucity of calcium deposition (563). The underlying pathophysiology of allograft vasculopathy is largely unknown, but it is likely a common final pathway of a constellation of immunologic and nonimmunologic injuries, namely chronic rejection, cytomegalovirus infection, hyperlipidemia, and older donor age (563-565). Treatment of hyperlipidemia with pravastatin (566) or weekly LDL apheresis (567) has been reported to lower the incidence of coronary vasculopathy or even lead to regression. Currently, retransplantation is the only definitive therapy for advanced allograft vasculopathy. Good results have been reported with PCI and directional coronary atherectomy in selected patients with discrete and proximal coronary focal lesions (568-569a). In general, coronary bypass surgery is not an option because of the diffuse type of coronary disease in patients with cardiac allograft vasculopathy. Isolated cases of successful coronary bypass grafting have been reported (570,571). In a report of 5 patients who underwent CABG for cardiac allograft vasculopathy, 3 patients died during the perioperative period and 1 died at 50 days.

It is well known that ESRD is associated with an increased risk of CAD (572). The safety and efficacy of coronary bypass grafting were reported in 31 renal transplant patients who underwent isolated coronary bypass surgery (573). Perioperative mortality was 3.2%, and no renal allograft function was impaired. Overall, 1- and 5-year survival rates for patients undergoing open heart surgery were 88% and 85%, respectively (573). The safety and efficacy of CABG were also reported in a small series of 3 patients with transplanted livers, with no deaths or hepatic decompensation and good improvement of cardiac symptoms (574). (See Section 5.5. on ESRD.)

## *5.11. CABG in Acute Coronary Syndromes*

**Class I**

**If clinical circumstances permit, clopidogrel should be withheld for 5 days before performance of CABG surgery. *(Level of Evidence: B)***

The acute coronary syndromes represent a continuum from severe angina to acute MI. Various classifications are based

on the presence or absence of Q waves associated with evidence for myocardial necrosis, the elevation or depression of ST segments on the electrocardiogram, and clinical definitions based on the pattern of angina. Historically, a clinical definition encompassing progressive, rest, and postinfarction angina and Q-wave and non–Q-wave MI has been used to examine the effects of surgery. More recent nomenclature defines the spectrum of acute coronary syndromes from unstable angina to non–ST-segment elevation MI (NSTEMI) to ST-segment elevation MI (STEMI). Where appropriate, we use the new classification in this document, recognizing, however, that many of the cited trials categorized the patient subgroups according to the older nomenclature.

The effectiveness of CABG for unstable angina was first demonstrated in a randomized Veterans Administration trial comparing medical therapy with CABG initiated in 1976 (575). Although there was no overall difference in survival between medically and surgically treated patients, an improvement in survival with CABG occurred in patients in the lowest tertile of EF (0.3 to 0.58) at 3, 5, and 8 years of follow-up (105), in those with 3-vessel disease (576), and in those with LV dysfunction presenting with electrocardiographic changes (577). At 5 years of follow-up, surgically treated patients had less angina and improved exercise tolerance and required fewer antianginal medications than did the medically treated patients (110). It is difficult to interpret the results of this study because surgical and medical therapies have both evolved substantially, including the routine use of modern techniques for myocardial preservation, arterial bypass conduits, aspirin, fibrinolytics, and PCI.

There have been no randomized trials specifically comparing CABG and PCI in patients with unstable angina and multivessel CAD. The BARI trial prespecified a comparison subgroup based on the severity of angina. In this trial, 7% of patients had unstable angina or NSTEMI. There was no difference in 5-year overall survival for these patients treated with either CABG (88.8%) or PTCA (86.1%, *P* equals NS) (117). However, there was an increased cardiac mortality in patients treated with PTCA (8.8%) compared with CABG (4.9%), and this difference was entirely due to a difference in outcomes in treated patients with diabetes (129).

In contrast, EAST included a large proportion (60%) of randomized patients with Canadian Cardiovascular Society Class IV angina, and there was no difference in mortality at 3 years (119). Similarly, 59% of enrollees in RITA had rest angina, and this study demonstrated no significant differences in death or MI at 2.5 years of follow-up (126). There was a particularly high incidence of unstable angina (83%) in the small ERACI trial (133). These patients had mostly complex lesions (50% type B2 and 13% type C), which are associated with greater angioplasty complications (578). However, in-hospital mortality was higher with CABG (4.6% versus 1.5%), and 3-year survival and freedom from STEMI were similar for both forms of revascularization (133).

No studies have addressed the important subset of patients with unstable angina after prior CABG. The culprit lesion in these patients is often located in a vein graft, where both angioplasty and reoperative CABG have less success (412).

Several early studies performed before 1990 demonstrated an increased surgical mortality ranging from 4.6% to 7.3% in patients with unstable angina (414,579-581). More studies have confirmed this finding (582,583). In the series of Louagie et al (582), 474 patients admitted with prolonged rest angina and requiring surgery during the same hospitalization had an operative mortality of 6.8% and a perioperative MI rate of 7.2%, and 19% required placement of an IABP. A study examining early revascularization versus conservative therapy for patients with NSTEMI had a much higher 30-day surgical mortality (12%) in patients undergoing early CABG compared with those managed conservatively (5%) (418).

In patients with post-infarct angina, a higher mortality has been observed, particularly with early operation after STEMI (409,579,584). Braxton et al (585) compared 116 patients operated on within 6 weeks of MI with 255 patients without prior MI. Mortality was highest (50%) in 6 patients with STEMI undergoing surgery less than 48 hours after infarction versus 7.7% in 52 patients undergoing surgery 3 to 42 days after infarction and versus 2% to 3% when CABG was performed even later and in patients without prior infarction. Factors associated with adverse outcomes during CABG for unstable angina are listed in Table 17.

A new issue that has arisen concerns the risk of CABG in patients with acute coronary syndrome treated with new and

**Table 17.** Factors Associated With Adverse Outcome During Coronary Artery Bypass Grafting for Unstable Angina

| Factor (Reference) | Relative Risk of Mortality (Range) |
|---|---|
| **Clinical** | |
| Recent MI: less than 24 h (777), less than 48 h (585), less than 30 d (451) | 2.1-1.8 |
| Female (451,582,584,777) | 1.4-1.7 |
| Age (451,452,584,779) | 2.9-5.3* |
| IDDM (779) | 8.3† |
| **Angiographic/hemodynamic** | |
| No. of diseased vessels (582,584) | 1.9-2.3 (EF 0.20-0.39) |
| LV dysfunction (451,452,584) | 5.9-10.7 (EF less than 0.20) |
| Hypotension (452,777) | 6.5-7.8 |
| **Surgical** | |
| Aortic cross-clamp time (582,779) | 2.25‡ |
| Urgent surgery (584,777) | 1.8-1.9 |
| Bypass time (779) | ... |
| IABP support (779) | 4.1 |

MI indicates myocardial infarction; IDDM, insulin-dependent diabetes mellitus; LV, left ventricular; IABP, intra-aortic balloon pump; and EF, ejection fraction.

*Age greater than 70 years.

†Relative risk for perioperative MI.

‡Relative risk of major adverse outcome greater than or equal to 100 versus less than 100 minutes.

more potent antithrombotic and antiplatelet therapies. Several studies have demonstrated a greater risk for postoperative hemorrhage in patients treated with low-molecular-weight heparin (586), abciximab (587), and clopidogrel (588). It is important to understand the pharmacokinetics of these agents to reduce the risk. For instance, no increased bleeding was observed when the short-acting glycoprotein IIb/IIIa inhibitor eptifibatide was discontinued at least 2 hours before bypass (589), when platelet transfusions were appropriately administered after abciximab (590), and when clopidogrel was withheld for 5 days before surgery (588). In some instances, the need for urgent surgery supercedes the risk.

The use of CABG for primary reperfusion during STEMI has largely been superseded by fibrinolysis and primary PTCA. Early coronary bypass for acute infarction may be appropriate in patients with residual ongoing ischemia despite nonsurgical therapy and if other conditions warrant urgent surgery, including left main or 3-vessel disease, associated valve disease, mechanical complications, and anatomy unsuitable for other forms of therapy.

In conclusion, CABG offers a survival advantage compared with medical therapy in patients with unstable angina and LV dysfunction, particularly in those with 3-vessel disease. Currently, there is no convincing survival advantage for surgery over PTCA in patients with unstable angina suitable for treatment with either technique. However, the risk of CABG in patients with unstable angina, postinfarction angina, early after non-STEMI, and during acute MI is increased several fold relative to patients with stable angina, although the risk is not necessarily higher than that of medical therapy for these patients.

# 6. IMPACT OF EVOLVING TECHNOLOGY

## *6.1. Less-Invasive CABG*

Patients presenting for CABG are older, have more comorbid conditions, and as a group have a higher predicted risk of mortality than their historical predecessors. Despite these trends, clinical outcomes after CABG have continued to improve (591,592).

Before 1995, the vast majority of CABG procedures used a midline sternotomy incision, CPB, and global cardioplegic arrest. Cardiopulmonary bypass has adverse effects on many organ systems and elicits a systemic inflammatory response. Some have sought to minimize the invasiveness of CABG through the elimination of CPB or through the use of smaller incisions or both.

Coronary artery bypass graft surgery on a beating heart without CPB was first reported by Kolessov in 1967, who was technically challenged by the motion of the heart, and access to the posterior surface of the heart was not possible (10). The technique was largely abandoned in the United States after the refinement of CPB. However, CABG on a beating heart was still practiced in several countries, where much experience was accumulated (593,594). These procedures were primarily reserved for patients needing LAD or right coronary artery (RCA) bypass because techniques for safe access to the lateral and posterior wall arteries had not developed.

Single LAD bypass on the beating heart through a small anterolateral thoracotomy (MID-CAB) was reintroduced in the mid-1990s (595-597). Target coronary artery stabilization was initially achieved with pharmacologically induced bradycardia or intermittent temporary asystole, with small bolus infusions of adenosine. Early angiographic anastomotic patency rates were inferior to those achieved with conventional CPB-CABG and prompted the development of various styles of mechanical stabilizers to limit target artery motion. Patency rates improved with experience and with the use of mechanical stabilization (598).

Surgeons uncommonly are referred patients with single-vessel LAD disease, but the results of MID-CAB fostered interest in the development of techniques for multivessel OPCAB. Building on the experience of Benetti and Bufolo, surgeons developed methods to safely access lateral wall and posterior wall vessels. With mechanical coronary artery stabilizers, devices for clearing the anastomotic field of blood, intracoronary shunts, and techniques and devices for cardiac positioning, many centers were able to report sizeable series in which the large majority of CABG procedures were achieved without CPB (599-602).

Several retrospective studies have suggested that OPCAB may reduce morbidity and/or mortality. Nearly all reports have demonstrated reductions in the need for transfusion of blood products, shorter ICU stays, and shorter postoperative lengths of stay. Some of these studies have also suggested that hospital costs are reduced (603-605).

Hernandez et al (606) reported on the experience of the Northern New England Cardiovascular Disease Study Group comparing 1741 OPCAB and 6126 contemporaneous CPB patients. The groups differed somewhat in preoperative risk factors, but their predicted risk of mortality was the same. They found no differences in crude rates of mortality, stroke, mediastinitis, or return to the operating room for bleeding. OPCAB patients had a reduced need for IABP support, less atrial fibrillation, and shorter median postoperative lengths of stay.

Magee et al (607) reviewed all multivessel CABG procedures from 2 large institutions from January 1998 through July 2000. They entered 8449 patients (1983 OPCAB, 6466 CPB) into a multivariate logistic regression analysis to evaluate the impact of CPB on mortality, independent of other risk factors known to affect mortality. They also used propensity scoring to computer match pairs of OPCAB and CPB patients in an attempt to remove selection bias from the analysis. CPB was associated with increased mortality compared with OPCAB by univariate analysis (CPB 3.5%, OPCAB 1.8 %) even though the OPCAB group had a higher predicted mortality. CPB was associated with increased mortality by multiple regression analysis (OR 1.79, 95% confidence interval 1.24 to 2.67). The combined computer-matched groups based on OPCAB-selection propensity

score also demonstrated an increased risk of mortality for CPB (OR 1.9, 95% confidence interval 1.2 to 3.1).

Plomondon et al (608) reviewed CABG-only procedures from the Veterans Affairs Continuous Improvement in Cardiac Surgery Program records from October 1997 through March 1999. Nine centers were identified that had completed at least 8% of their CABG procedures as OPCAB and were designated as study hospitals. OPCAB patients (n equals 680) from these hospitals were then compared with CPB patients (n equals 1733) for mortality or morbidity. Predicted mortality was higher in the OPCAB group (OPCAB 4.4%; CPB 3.9%; *P* equals 0.0022), as was predicted morbidity (OPCAB 13.2%; CPB 11.9%; *P* equals 0.0008). OPCAB patients experienced lower mortality (OPCAB 2.7%; CPB 4.0%) and lower morbidity (OPCAB 8.8%; CPB 14%; *P* equals 0.001). Multivariable OR for OPCAB versus CPB groups, after risk adjustment for patient risk factors, were computed. For mortality, the OR for OPCAB was 0.56 (95% confidence interval, 0.32 to 0.93, *P* equals 0.033), and for morbidity the OR was 0.52 (95% confidence interval, 0.38 to 0.70, *P* less than 0.0001). Observed-to expected ratios for mortality and morbidity were less than 1.0 for OPCAB patients and more than 1.0 for CPB patients. The authors concluded that in centers experienced in beating heart coronary bypass, an off-pump approach for CABG was associated with lower risk-adjusted morbidity and mortality.

Cleveland et al (609) reported on the largest multicenter report to date. They retrieved data from the STS National Cardiac Surgery Database from a 2-year period of time (January 1998 through December 1999) and identified 126 centers experienced in OPCAB. There were 11 717 (9.9%) OPCAB patients and 106 423 (90.1%) CPB patients. The OPCAB patients were older, were more likely female, and were less likely to be diabetic than the CPB subjects. The OPCAB group also had more patients with preexisting COPD, dialysis-dependent renal failure, and cerebrovascular disease than the CPB group. The CPB patients were more likely to have 3-vessel disease, and more of them were in need of urgent or emergency CABG. Predicted mortality was similar (OPCAB 2.88%; CPB 2.87%). The observed risk-adjusted mortality in the OPCAB group was 2.31%, and that of the CPB group was 2.93% (*P* less than 0.0001). The risk-adjusted rate of major morbidity in the OPCAB group was 10.62% compared with 14.15% in the CPB group (*P* less than 0.0001). When complications were examined individually, the OPCAB group had fewer strokes (OPCAB 1.25%; CPB 1.99%; *P* less than 0.001), less postoperative renal failure (OPCAB 3.85%; CPB 4.26%; *P* equals 0.036), and fewer patients with postoperative cardiac arrest (OPCAB 1.42%; CPB 1.74%; *P* equals 0.010), and fewer patients returned to the operating room for bleeding (OPCAB 2.07%; CPB 2.80%; *P* less than 0.001). Additionally, in patients with pre-existing COPD or cerebrovascular disease, OPCAB patients were less likely to require prolonged mechanical ventilation or to have stroke or coma, respectively.

Three randomized, prospective trials have been reported comparing OPCAB and CPB CABG. None of these trials were large enough to demonstrate any differences in operative mortality or the occurrence of postoperative stroke.

Angelini et al (610) pooled data from 2 separate randomized trials. OPCAB patients were shown to have reduced morbidity (e.g., transfusion, chest infection). At midterm follow-up there were no differences between groups with regard to cardiac death or cardiac events.

van Dijk et al (611) randomized relatively low-risk patients (n equals 281) to OPCAB or CPB CABG. Completeness of revascularization was equivalent between groups. OPCAB patients required fewer intraoperative transfusions and had lower levels of cardiac-specific enzyme release. At 1 month, no differences were noted in rates of cardiac death or cardiac-related events.

Puskas et al (612) randomized 201 patients to OPCAB or CPB CABG. No patients were excluded on the basis of coronary artery anatomy, LV dysfunction, or any comorbidity. Intended target vessels were identified and recorded preoperatively before randomization. OPCAB patients required fewer transfusions, had less release of cardiac-specific enzymes, had shorter times to extubation, had shorter ICU and postoperative lengths of stay, and had lower hospital costs. Levels of revascularization were identical between groups.

Patients with significant comorbidity have been reported to have been revascularized by OPCAB techniques. The elderly, patients with prior CABG, patients with left main CAD, and those with impaired myocardial, renal, or pulmonary function have all been reported to have been safely and effectively approached without CPB.

Larger randomized trials will be necessary to delineate which patients benefit from the avoidance of CPB and what the magnitude of that benefit actually is.

The third emerging technique in less-invasive cardiac surgery is the closed-chest, port-access, video-assisted CABG operation developed at Stanford, Calif (613). CPB and cardioplegia of a globally arrested heart are integral parts of this technology. Vascular access for CPB is achieved via the femoral artery and vein. A triple-lumen catheter with an inflatable balloon at its distal end is used to achieve endovascular aortic occlusion, cardioplegia delivery, and LV decompression. With CPB and cardioplegic arrest, CABG can be performed on a still and decompressed heart, through several small ports and with the aid of a videoscope. In comparison with the MID-CAB approach, the port-access technique allows access to different areas of the heart, thus facilitating more complete revascularization, and the motionless heart allows for accurate anastomosis. The proposed advantage of this approach compared with conventional CABG is the avoidance of median sternotomy, with the resultant diminished incisional pain and faster recovery. The potential morbidity of the port-access technique stems from the multiple port sites, limited thoracotomy, and groin dissection for femoral-femoral bypass. The short- and long-term safety, benefits, and efficacy of the minimally invasive port-access

approach must be compared with the conventional operation in an appropriately controlled clinical trial. As in any new technology, vigorous scientific scrutiny must be applied before any conclusions can be made.

### 6.1.1. Robotics

Investigational work continues in the development of robotic coronary bypass. Closed-chest multiarterial bypass on the beating heart would offer the maximum benefit via the least invasive approach. CPB and thoracotomy would be avoided, and the durability of arterial CABG would be preserved.

Boyd et al (614) described 4 levels of robotically assisted coronary bypass currently being investigated.

1. Voice-activated robotic control of an intrathoracic camera placed through a port and used for video-assisted manual endoscopic harvesting of the IMA with standard endoscopic instruments. A manual beating heart anastomosis is then completed through a small thoracotomy.
2. Video-assisted port-access telerobotic conduit harvesting, in which the surgeon works from a computer-enhanced remote console to harvest the IMA with port-access telemanipulators (robotic arms). A manual beating heart anastomosis is then completed through a small thoracotomy.
3. Computer-assisted endoscopic coronary artery anastomoses in which the conduit is harvested manually via standard sternotomy and the coronary anastomosis is constructed on the arrested or beating heart from the computer-enhanced master console through telemanipulators passed via ports.
4. Totally endoscopic coronary bypass during which conduit harvesting and preparation, target coronary artery identification and preparation, vascular control, and the anastomosis are all accomplished from the computer-enhanced console via port-access telemanipulators without any chest incision.

Successful application of all 4 of these strategies has been reported from specialized centers (615-618). The major obstacle to a totally endoscopic CABG has been the technical difficulty in the construction of an accurate anastomosis. Considerable effort is under way to develop technology for a facilitated anastomotic device, perhaps avoiding the need for a sutured anastomosis. Robotically assisted coronary artery bypass must be considered a work in progress at this time.

## *6.2. Arterial and Alternate Conduits*

**Class I**

**In every patient undergoing CABG, the left IMA should be given primary consideration for revascularization of the LAD artery.** ***(Level of Evidence: B)***

The benefits of bypass surgery are related to patent bypass grafts, and short- and long-term graft patency is associated with cardiac morbidity and mortality. The most commonly used bypass grafts have been the in situ IMA and segments of greater saphenous vein (SVG) used as aorta-to-coronary grafts. By the early 1980s, serial angiographic studies of vein grafts made it apparent that SVGs could develop intrinsic pathological changes, intimal fibroplasia and vein graft atherosclerosis, that were progressive and compromised long-term graft patency rates. Late vein graft patency rates ranged from 70% to 80% at 5 postoperative years to 40-60% at 10 postoperative years. Fortunately, similar serial studies showed that IMA grafts had early patency rates of greater than 90%, but more importantly, they showed that late attrition of IMA grafts is extremely uncommon, resulting in a late patency rate of in situ IMA grafts of 90% or more at 10 postoperative years. The clinical importance of the left IMA-to-LAD graft was emphasized by a long-term follow-up study that compared patients with left IMA-LAD grafts and supplemental vein grafts to patients receiving only vein grafts. The patients receiving left IMA-to-LAD grafts had a better survival rate, fewer reoperations, and fewer cardiac events at a 10-year follow-up.

In the modern era, it can be expected that vein graft patency rates will be improved over the earlier studies. Randomized trials have shown that perioperative treatment of patients with platelet inhibitors improves bypass graft patency rates at 1 postoperative year. Prospective angiographic studies from the BARI trial documented an 87% 1-year vein graft patency rate compared with 98% for IMA grafts. Furthermore, aggressive treatment with statins appears to decrease vein graft attrition rate. However, although the interventions have decreased vein graft failure, it has not been eliminated. The prospective study of SVG patency rates noted a 66% patency rate at 10 postoperative years.

If 1 IMA graft is good, might 2 be better? The use of the right IMA in addition to the left IMA (bilateral IMA, or BIMA, grafting) for bypass grafting has been employed as a surgical strategy since the early years of bypass surgery. Despite the apparent logic of using 2 grafts anticipated to have excellent long-term patency rates, evidence that BIMA grafting (or any other extension of arterial grafting) provides incremental clinical benefit over the left IMA-to-LAD graft in associated vein graft strategy (single IMA, or SIMA, grafting) has been difficult to document for a variety of reasons. First, there are no randomized studies concerning this issue. Second, too few institutions have used BIMA grafting to provide enough patients to allow detailed analysis. Third, survival rates after SIMA grafting are favorable for the first postoperative decade, meaning that particularly long-term follow-up studies are necessary to allow any differences to become apparent. Fourth, patient selection can confound the analysis of outcomes. In general, studies of BIMA grafting have excluded patients undergoing emergency operation and those with previous bypass surgery and have included decreased numbers of patients with diabetes. However, there

are now several nonrandomized, risk-adjusted, comparative studies that show improved long-term outcomes for patients receiving BIMA grafts in terms of fewer reoperations and improved late survival rates. BIMA grafting has not become a routine strategy even for elective patients for multiple reasons, including increased operative difficulty, increased operative time, and the risk of wound complications. Most studies have shown an increase in the risk of wound complications with BIMA grafting, usually in patients with diabetes. The use of techniques for skeletonizing the IMAs during preparation, thus minimizing the decrement in sternal blood supply, may decrease the incidence of sternal complications, but even modern studies of BIMA grafting have shown an increased risk of wound complications in obese diabetic patients.

The use of the radial artery as a conduit for coronary bypass grafting was first reported by Carpentier et al (619) in 1973. Its use was quickly abandoned when occlusion rates up to 30% were reported (620,621). Interest in its use was revived in 1989 when radial artery grafts were found to be patent in patients who had undergone their coronary artery surgery 13 to 18 years earlier. The radial artery is a thick muscular artery with an average diameter of 2.5 mm and an average length of 20 cm. It is prone to spasm when mechanically stimulated, and perioperative calcium channel blockers or long-acting nitrates are often used to reduce this complication. The technique of minimal manipulation and en bloc dissection of the radial artery with its surrounding satellite veins and fatty tissue is thought to account for the superior results in experiences with radial artery grafting. Brodman et al (622) reported a 95% 12-week patency rate in 175 patients receiving 229 radial artery grafts (54 patients had bilateral radial artery grafts). Perioperative MI and mortality rates were similar to those of conventional bypass surgery. There was no reported hand ischemia, wound hematoma, or infection. A 2.6% incidence of transient forearm dysesthesia, which resolved over 1 day to 4 weeks after surgery, was reported. Acar et al (623) reported an 84% 5-year radial artery graft patency rate in 100 consecutive patients receiving the radial artery as a conduit for coronary revascularization. In the same group of patients, the left IMA graft patency rate was 90% at 5 years. Thus, the radial artery appears to be a safe and reliable arterial conduit for coronary revascularization on the basis of these early clinical experiences.

Use of the in situ right gastroepiploic artery as a conduit for CABG was first reported in 1987 (624,625). This artery can be harvested by extending the median sternotomy incision toward the umbilicus and dissecting the artery along the greater curvature of the stomach. A pedicle length of 15 cm or more can be achieved by mobilizing the artery to the origin of the gastroduodenal artery. It can be grafted to the right or circumflex coronary artery by routing it in a retrogastric fashion or to the LAD in an antegastric fashion. Early graft patency ranged from 90% to 100% (626-628), but long-term results have not been published. The inferior epigastric artery free graft has been used for CABG since 1990 (629,630). This artery can be harvested by retracting the rectus muscle via a paramedian incision. A length of 6 to 16 cm can be dissected from its origin from the external iliac artery (631). Short-term patency rates of up to 98% have been reported (632). Long-term results are not available.

Cryopreserved homologous SVGs and glutaraldehyde-treated homologous umbilical veins grafts have been used for clinical aortocoronary bypass surgery (633,634). Graft patency was reported to be only 50% at 3 to 13 months. These grafts should not be used unless other conduits are unavailable. Similarly, the bovine IMA has been used, again with about 50% 1-year patency (635,636). Synthetic grafts that have been used for aortocoronary bypass include Dacron grafts and polytetrafluoroethylene grafts. Only a few successful cases of Dacron graft use have been reported, and these were in patients in whom the graft was used as an interposition between the ascending aorta and the proximal end of a coronary artery with resultant high flow (637-639). The patency of polytetrafluoroethylene grafts is also limited and has been reported to be about 60% at 1 year (640,641).

### *6.3. Percutaneous Technology*

Technological improvements have had a great impact on PTCA and have included new medications and devices that have reduced both the acute and long-term complications of percutaneous coronary interventions. The most significant medication advance has been the introduction of new platelet inhibitors, which have reduced the incidence of MI and death during angioplasty and related interventions (642).

In the area of devices, intracoronary stents have reduced complications, including the need for emergency surgery, as well as the need for repeated interventions due to restenosis (643,644). New refinements in stent design and adjunctive pharmacological therapy are further improving patient outcomes after stenting (645). Directional coronary atherectomy has also been shown to reduce restenosis compared with conventional PTCA, but its role relative to stents is not yet clear (646). Several new devices, such as the transluminal extraction catheter (InterVentional Technologies, Inc., San Diego, CA) and the Angioget thrombectomy catheter (Possis Medical, Inc., Minneapolis, MN), that remove thrombus before intervention either have been approved for use or are undergoing investigation and may reduce complications in some high-risk subsets of patients. Rotational atherectomy or rotational ablation has expanded the types of lesions (eg, calcified or long lesions) that can be treated without surgery (647).

Restenosis remains the greatest weakness of PTCA and is being addressed by mechanical solutions such as stents and directional atherectomy, which improve the intimal lumen diameter, and by pharmacological interventions aimed at preventing intimal hyperplasia. Promising approaches included in this latter category are medications such as probucol and folate (648-650), gene therapy, and local radiation therapy (651-653). Finally, the balance between bypass

surgery and PCI is being further altered as the promise of new technology offered by drug-eluting stents is realized (654).

After CABG surgery, failure of the SVG is a major cause of recurrent cardiac ischemia. Angiographic studies have shown that 16% to 31% of SVGs fail within 1 year (655-658), and within 10 years, about half of all vein grafts are totally occluded or have severe atherosclerotic disease (74,659,660). It is estimated that vein graft failure is responsible for recurrent angina at an annual rate of 4% to 9% in patients after aortocoronary artery bypass grafting (661-663). In these patients, repeated CABG surgery is a satisfactory option. However, in comparison with initial bypass surgery, reoperation is technically more challenging and is associated with higher perioperative morbidity and mortality as well as less symptomatic relief (664-666). As alternatives to repeated bypass surgery, various percutaneous techniques have been developed to treat stenotic vein grafts. These techniques include conventional balloon angioplasty and the use of newer interventional devices such as coronary stents and directional coronary atherectomy.

In general, the results of angioplasty in SVGs are less favorable than in native vessels, with less procedural success and a higher rate of restenosis. Several factors influence the clinical outcome of the procedure: age of the graft, location of the stenosis within the graft, and the discrete (versus diffuse) morphological features of the atherosclerotic plaques (667-670). In a randomized comparison with angioplasty, directional coronary atherectomy was associated with a higher initial success rate and fewer repeated target-vessel interventions at 6 months but more periprocedural complications, most notably distal embolization and NSTEMI (671,672).

Intracoronary stents are now commonly used in the management of SVG stenosis. A multicenter, prospective, randomized trial compared the effects of stent placement with those of balloon angioplasty on clinical and angiographic outcomes in patients with obstructive disease of SVGs (673). Compared with the balloon angioplasty group, stenting of vein graft lesions resulted in a higher rate of procedural efficacy (92% versus 69%) and a greater increase in luminal diameter immediately after the procedure (1.92 versus 1.21 mm) and at 6 months (0.85 versus 0.54 mm). The 6-month outcome in terms of freedom from death, MI, repeat bypass surgery, or revascularization of the targeted vessel was significantly better in the stent group (73% versus 58%). Although the difference in the rate of restenosis between the stent and angioplasty groups did not achieve statistical significance, it appears that stent placement has certain advantages over conventional balloon angioplasty in the initial and short-term angiographic and clinical outcomes. The use of a balloon-occlusion and aspiration device has been shown to reduce the risk of adverse cardiovascular events during SVG interventions by protecting the coronary circulation from distal embolization of atherosclerotic debris (674). More operator-friendly filter-type devices are under investigation and will likely become routine adjuncts for such procedures.

With the increasing use of MID-CAB for left IMA-to-LAD grafting, a combined strategy of MID-CAB and either balloon angioplasty or stent placement ("hybrid revascularization") to achieve complete revascularization in patients with 2-vessel disease has been used in some situations. PTCA is performed on the second diseased vessel, which has included the right coronary artery, the left circumflex artery, and the left main coronary artery. The reverse order of performing PTCA first with subsequent MID-CAB for the left IMA-to-LAD revascularization has also been described (675). The hybrid approach of MID-CAB and percutaneous intervention provides complete revascularization through limited incisions without CPB. It also provides a useful management modality for isolated patients who are at high risk for either procedure alone. This approach highlights the potential complementary role of surgery and PTCA in the management of CAD. However, long-term outcome data for patients undergoing hybrid procedures are not yet available. Also, if coronary stenting is performed, then aspirin and clopidogrel are indicated for at least 30 days, which may affect the timing of coronary surgery. Thus, the theoretical benefits of combining procedures must be matched by scientific proof of efficacy before this strategy is likely to become commonplace.

### *6.4. Transmyocardial Laser Revascularization*

**Class IIa**

**Transmyocardial surgical laser revascularization, either alone or in combination with CABG, is reasonable in patients with angina refractory to medical therapy who are not candidates for PCI or surgical revascularization.** ***(Level of Evidence: A)***

Intracavitary arterial blood in the LV is only millimeters away from ischemic areas of myocardium. Indeed, communicating channels between the cavity and the myocardium occur in reptilian hearts and in fetal hearts during the first 7 weeks of gestation until the coronary arterial system develops. This network of communicating channels between the heart chambers and the coronary arteries, the myocardial sinusoids, the arterial-luminal and venous-luminal connections, were described in a study by Wearn et al in 1933 (676). Early attempts to use these connections to supply the ischemic myocardium included implantation of the left IMA directly into the heart muscle (677) and direct-needle acupuncture to the ischemic myocardium to create communicating channels (678,679). Sen and colleagues (678,679) used direct acupuncture and found that these acupuncture channels were protective from acute infarction after ligation of the LAD. These channels appeared to be open and endothelialized at 8 weeks but appeared to close within several months due to fibrosis and scarring secondary to local tissue injury. This technique was abandoned with the arrival of aortocoronary artery bypass surgery in the late 1960s.

Use of the carbon dioxide laser for transmyocardial revascularization was attempted in the early 1980s by Mirhoseini and coworkers (680,681). A high-energy laser beam was used to create channels from the epicardial to the endocardial surface of an arrested or beating heart, thus allowing oxygenated blood from the LV to perfuse the ischemic myocardium. Brisk bleeding from the channels due to ventricular perforation could be easily controlled with light epicardial pressure. It was postulated that a high-energy laser beam would minimize local tissue injury and prevent premature fibrotic closure of the newly created channels and thus lead to improved channel patency (682). Long-term channel patency on histological examination has been reported in animal experiments and in sporadic clinical case reports (682-684). The principal utility of transmyocardial laser revascularization (TMLR) is directed toward patients with severe angina pectoris refractory to medical therapy and who are unsuitable for surgical revascularization, PCI or heart transplantation. These patients often have diffuse small-vessel disease and are not appropriate candidates for another PCI or CABG. The use of TMLR for the management of cardiac allograft vasculopathy has also been reported (685,686).

The results of a multicenter trial with TMLR as the sole therapy for 200 patients with refractory, end-stage CAD and documented reversible ischemia was reported by Horvath and colleagues (687). The perioperative mortality rate was 9%. Postprocedure angina class according to the Canadian angina classification was significantly decreased from their preoperative status at 3, 6, and 12 months of follow-up. Hospital admissions for angina were decreased from an average of 2.5 admissions in the year before treatment to an average of 0.4 admissions in the year after treatment. The number of perfusion defects in the treated LV free wall was also significantly decreased as assessed by radionuclide perfusion scan or positron emission tomographic scan performed after TMLR. A multicenter randomized, prospective study comparing TMLR with continued medical management demonstrated improved event-free survival in 160 patients with symptomatic, end-stage CAD. In the TMLR group, 72% of patients improved by at least 2 angina classes, while 69% of patients in the medical therapy group had no change of angina class; the remaining 31% experienced greater angina. Survival free of death, unstable angina, or class IV angina at 6 months was 73% for the TMLR group versus 12% in the medical management group. Quality of life indexes also improved in the TMLR group.

Five prospective, controlled, randomized trials have been reported (689-693). In each study, TMLR patients demonstrated a statistically significant improvement in angina compared with patients treated with medical therapy alone. None of the trials demonstrated a significant survival benefit, and only 1 study found a significant improvement in myocardial perfusion (692). One of the studies (689) concluded that TMLR "cannot be advocated." This trial from the United Kingdom was the only one of the randomized studies that was not a multicenter study. Their recommendation came in spite of finding a statistically significant (*P* less than 0.001) improvement in angina for TMLR patients compared with patients receiving medical therapy without TMLR.

Subsequent studies have supported the initial findings of these early reports. Compared with medical therapy, there appears to be consistent and sustained improvement in angina class for at least the first year after TMLR (694-700). Thereafter, the beneficial effects of TMLR decline somewhat (694,695,699), but Horvath et al (694), in a follow-up study to the work cited above, reported that long-term efficacy commonly persists for 5 years. As experience accumulates, it appears that operative mortality is generally less than 5% (696,701,702). The most significant predictors of operative mortality are unstable angina (703) and compromised LV function (699).

# 7. INSTITUTIONAL AND OPERATOR COMPETENCE

## *7.1. Volume Considerations*

Owing to the availability of hospital and physician-specific mortality data and because of the perceived economies of scale in consolidating complex medical procedures into regional centers, considerable attention has been directed to relating outcome after CABG to the number of procedures performed. Before 1986, administrative data sets were proposed as a means of risk adjustment to compare outcomes between hospitals of high and low volume (704,705). These studies found a relationship between mortality after CABG and the volume of procedures performed annually. A cutoff at about 200 cases defined high- and low-volume institutions. High-volume institutions were determined to have superior results. The ability of administrative data sets to accurately stratify risk has since been questioned, particularly because of their inability to distinguish preoperative comorbidity data from postprocedure complications data (706-708).

Since 1986, in response to these criticisms, primary cardiac surgical data sets have appeared with sufficient power to address this question. Hannan et al (709) reported that in New York State, after adjusting for case mix, the high-volume institutions that performed greater than 223 cases annually experienced significantly lower mortality than did institutions performing fewer than 223 cases annually, with a relative risk of 0.74 (0.56 to 0.94, 95% confidence interval). This same relationship was true for individual surgeon volumes, with high-volume surgeons performing more and low-volume surgeons performing fewer than 116 CABG procedures annually. These cutoff points were determined arbitrarily by being above or below the state median, based on data from only 1 year.

The relationship between in-hospital mortality rate and surgical volume was again explored in 1991, when the cutoff for institutional volume was defined at 200 cases annually, and the relative risk, while still significant, was reduced to 0.84 (0.66 to 1.07, 95% confidence interval) (710). This

report represented data collected over 3 years (1989 to 1992). In addition to showing the protective effect of high-volume institutions, the study also showed considerable variation, particularly among the low-volume centers. A further analysis of this patient population revealed that a significant portion of the observed improvement found in the overall risk-adjusted mortality rates in New York State was a disproportionate improvement experienced by the low-volume institutions compared with the high-volume institutions. Hannan et al (710) postulated that this was due in part to the out-migration of older, low-volume surgeons and the in-migration of younger, better-trained surgeons. It is also of interest that the relationship between individual surgeon volume and outcome reported in 1989 and 1991 had disappeared.

The Department of Veterans Affairs Hospitals reported on 24 394 patients operated on between 1987 and 1992 (711). While there appeared to be a significant relationship between volume and mortality rate among the 43 hospitals examined, when adjusted for case mix the relationship disappeared. Again, low-volume hospitals had a higher variation in mortality rates compared with the high-volume institutions. This variation in outcome led the Department of Veterans Affairs to routinely review low-volume institutions (fewer than 100 cases annually).

A report of the STS National Cardiac Database reviewed 124 793 patients operated on by more than 1200 surgeons in more than 600 institutions. Only in institutions performing fewer than 100 cases annually (n equals 18) was the observed mortality rate of 5.0% significantly higher than the expected rate of 3.0% (2.9% to 3.2%, 95% confidence interval) (712).

Dudley et al (713) reviewed the literature linking high and low volumes to better and worse outcomes for a variety of procedures including CABG. By relying on the highest-quality studies, they were able to assign ORs for adjusted in-hospital mortality comparing high-volume hospitals and low-volume hospitals (fewer than 500 cases annually). By applying this model to the California Office of Statewide Health Planning and Development Database, they projected that there were between 124 and 372 potentially avoidable deaths in the state of California in 1997. The authors cautioned against drawing too firm a conclusion from these findings because of the inherent limitations of observational data, the possibility of inadequate risk adjustment, and the absence of a direct cause and effect relationship between volume and outcome.

Birkmeyer et al (714) reviewed Medicare claims data for 6 cardiovascular and 8 cancer-related procedures. Although they found that a volume/outcome effect was seen in all 14 procedures studied, the degree of difference in adjusted in-hospital and 30-day mortality between very-low-volume (fewer than 230 cases annually) and very-high-volume hospitals (more than 849 cases annually) ranged from a high of 12% in pancreatic resections to a low of 0.2% for carotid endarterectomies. They found that the range of adjusted mortality rates for CABG between very-low- and very-high-volume hospitals was 1.3%, which suggests that the relationship was modest at best.

The question of whether high-volume institutions performed significantly better than did moderate-volume institutions was addressed in a study from Canada. The Adult Cardiac Care Network of Ontario suggested that concentrating CABG into high-volume regional centers has explained their low observed mortality rate and the lack of variation between centers (715). This observation was not confirmed in the STS report, as Clark (712) found no protective relationship in high-volume institutions (greater than 900 cases/y).

Criticism of these reports revolves primarily around the adequacy of case-mix adjustment and the limitations of observational studies. Sowden et al (716) performed a meta-analysis of studies relating volume to outcome and found that the stronger the relationship between volume and outcome, the less case mix was accounted for. They postulated that owing to the observational nature of these studies, confounding accounted for most of the difference between high and low volume, and as confounding was reduced by improved risk stratification, the volume-outcome relationship disappeared. Sowden et al (716) also found that the volume-outcome relationship diminished over time, suggesting that low-volume institutions had “improved” faster than had high-volume institutions.

In summary, studies suggest that survival after CABG is negatively affected when carried out in institutions that perform less than a threshold number of cases annually. Similar conclusions have been drawn regarding individual surgeon volumes. In states where reporting of outcomes is an accepted practice (e.g., New York State), the relationship between low volumes at either an institutional or individual level seems to have diminished over time. This observation strengthens the argument for outcome tracking and supports a posture of close monitoring of institutions or individuals that perform less than 100 cases annually. It must be remembered that these same studies also found a wide variation in risk-adjusted mortality rates in low-volume situations; ie, some institutions and practitioners maintained excellent outcomes despite relatively low volumes. Therefore, credentialing policies based on conclusions drawn from these data must be made with caution.

### *7.2. Report Cards and Quality Improvement*

Mortality rates after CABG have declined since the 1987 release by the Health Care Financing Administration of hospital-specific mortality data. The Northern New England Cardiovascular Disease Study Group reported a 24% decline in regional mortality from 1987 to 1993 (13). Hannan et al (717) reported that the actual mortality rate in New York State declined from 3.52% in 1989 to 2.78% in 1992 while the risk-adjusted rate decreased from 4.17% to 2.45% during the same period. The STS National Cardiac Surgical Database reported that the risk-adjusted mortality rate for

CABG declined from 3.76% to 3.50% between 1990 and 1994 (16).

There are numerous potential explanations for this reduction in mortality after CABG. Some authors suggest that the feedback of outcome data associated with either an organized or implicit effort at quality improvement has been principally responsible for this decline. O'Connor et al (13) reported that a combination of regular feedback of mortality data, associated with open discussion and visitation between competing cardiac surgical programs in Maine, New Hampshire, and Vermont, was directly responsible for the 24% reduction in mortality observed there. Hannan et al (717) reported that the simple fact that outcomes were tracked and reported back to institutions led implicitly to improvement efforts that accounted for the New York State decline in mortality rate. Grover et al (718) reported on a program of data feedback and regular audit of programs by members of the Audit Committee of the Veterans Affairs Cardiac Surgery Consultants Committee that led to a decrease in observed versus risk-adjusted mortality rates within the Veterans Administration cardiac surgical system. Omoigui et al (719), a group from the Cleveland Clinic, suggested that the reduction in mortality noted in New York State was caused by an out-migration of high-risk patients due to the increased scrutiny provoked by public release of mortality data. Despite this criticism, Hannan et al (717) found no consistent bias against selecting high-risk patients in the state of New York. Ghali et al (720) suggested that the reduction seen in both northern New England and New York State would have happened regardless of quality improvement efforts, as similar improvement was found in Massachusetts where there was neither a statewide, organized improvement effort nor dissemination of mortality data. Peterson et al (721) examined Medicare data on both the total amount of improvement and the ultimate risk-adjusted mortality rate and found that New York State and northern New England showed both the lowest overall mortality rates as well as the greatest improvements of any other state or region in the country.

Although it appears clear that outcome tracking has resulted in fewer deaths after CABG, Chassin (722) would suggest that it is the public dissemination of this information that has been responsible for driving that improvement. While the 1987 Health Care Financing Administration report of CABG mortality data received widespread media attention, most newspapers focused on outlier hospitals and thus provided little guidance to consumers (723). Peterson et al (721) concluded that reporting of outcomes, whether voluntary and anonymous (northern New England) or mandatory and public (New York State), coupled with initiatives in quality improvement is indeed effective in improving mortality rates after CABG.

Besides driving improvement efforts, many suggested that public reporting of mortality data would initiate market forces that would drive patients to high-volume "centers of excellence." Yet, when clinicians and patients in Pennsylvania (724,725) and clinicians in New York State (726) were asked to assess how much the statewide reporting of outcome data influenced their referral practices, surprisingly few admitted that these efforts had any effect at all (724,726). Shahian (727) found that in the State of Massachusetts, patients preferred hospital reputation, traditional referral patterns and geographic proximity over published outcomes as determinants for selecting a cardiac surgical provider. Finlayson (728) studied a Veterans Administration population and found that patients anticipating high-risk surgical procedures would accept a 2-fold to 6-fold increase risk of mortality to receive their care close to home.

An excellent review of the impact of outcomes reporting on cardiac surgery has been provided by Shahian et al (729). Outcome reporting in the form of risk-adjusted mortality rates after CABG has been effective in reducing mortality rates nationwide. While distortion of data (gaming) and out-migration of patients have been reported, it is doubtful that these practices have had a meaningful effect on this improvement. However, public release of hospital and physician-specific mortality rates has not been shown to drive this improvement and has failed to effectively guide consumers or alter clinicians' referral practices.

### *7.3. Hospital Environment*

The context within which coronary surgery is performed will ultimately influence the outcome experienced by patients. Because of the highly technical nature of the procedure and the narrow clinical margin of the patient population, strategies to ensure consistent care have evolved. These strategies include establishing specialized cardiac surgical centers (heart hospitals), forming multidisciplinary clinical teams within hospitals, and creating and implementing clinical pathways, care maps, algorithms, and protocols.

Appropriately implemented clinical guidelines have been shown to improve the processes of clinical care in 90% of cases and show measurable improvement of outcome in 20% of cases (730). Successful application of clinical guidelines require they be accompanied by unambiguous statement of purpose, that clinicians for whom they are intended have some role in their creation or implementation, and that forcing functions, such as clinical pathways, algorithms, or protocols, be tied to the guidelines (731,732).

Whereas clinical practice guidelines describe an ideal treatment strategy for a particular disease process, clinical pathways (a.k.a. critical pathways, care maps) represent the optimal sequence of timing of interventions for a particular diagnosis or procedure. Well-designed clinical pathways ensure care is delivered as prescribed by a practice guideline while optimizing resource utilization, minimizing chance of error, and allowing for the reinvention of these standards within the context of local culture. They are typically created for patient populations that are large in number, relatively homogeneous in appearance, and consume large amounts of resources and have thus been found ideal for the CABG population (732,733).

# 8. ECONOMIC ISSUES

## *8.1. Cost-Effectiveness of CABG*

CABG represents a major investment for society, with an initial hospital cost of around $30 000 applied to more than 300 000 patients annually in the United States alone (around 10 billion dollars) (124). It is most appropriate to consider the cost of CABG surgery compared with other medical treatment modalities with regard to cost-effectiveness. Definitive data for such a comparison are sparse, and multiple assumptions must be made. The most reasonable system of analysis appears to be an estimation of the dollars spent per quality-adjusted life-year gained ($/QALY). In general, a cost-effectiveness of $20 000 to $40 000/QALY is consistent with other medical programs funded by society, such as hemodialysis and treatment of hypertension. A cost of less than $20 000/QALY would be considered particularly cost-effective, whereas a cost greater than $60 000/QALY would be considered expensive (734).

A widely quoted analysis of the cost-effectiveness of CABG surgery was compiled by Weinstein and Stason (735) in 1982 utilizing data gathered from the then-available randomized trials comparing medical therapy with coronary artery bypass. The cost of coronary bypass is relatively constant, whether it is conducted for left main disease or for single-vessel disease. Cost-effectiveness is excellent when the procedure is applied to patient subgroups for which the benefit in terms of survival or relief of symptoms compared with medical therapy is great (as it would be, for example, in a patient with severe angina and triple-vessel disease). The cost-effectiveness of CABG becomes inordinately poor, however, when the benefit in terms of survival is marginal and there are few symptoms in the preoperative patient. These conclusions are depicted in Figure 12, and examples are presented in Table 18. Cost-effectiveness for coronary bypass in patients with left main disease is exceptionally good at $9000/QALY. It is similarly quite attractive in patients with 3-vessel disease, at $18 000/QALY. If one considers the cost-effectiveness of coronary bypass in 2-vessel disease, Weinstein and Stason found that the presence or absence of LAD disease was very important. Because CABG surgery is particularly effective in relieving angina, its cost-effectiveness, even in patients with single-vessel disease, is not prohibitive if that patient has severe angina. In the patient without angina or with only mild angina, however, the cost of coronary bypass per QALY was prohibitive in this analysis, exceeding $100 000 for patients with 2-vessel or 1-vessel disease.

It is not surprising that coronary bypass surgery is cost-effective in exactly those groups of patients in whom sur-

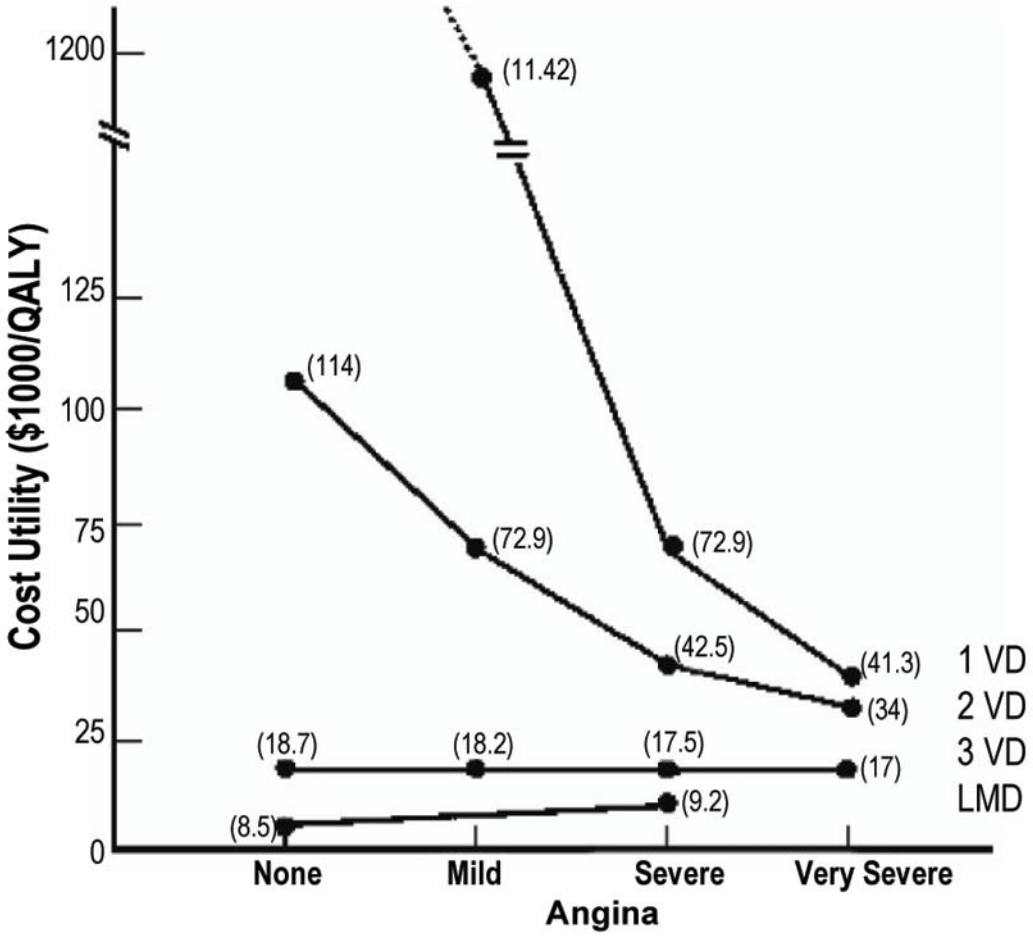


**Figure 12.** Cost utility. VD = vessel disease; LMD = left main disease; QALY=quality-adjusted life-year. Modified with permission from Elsevier Science Inc. (Kupersmith et al. Prog Cardiovas Dis. 1995;37:307-56) (734).

**Table 18.** Cost per Quality-Adjusted Life-Year ($/QALY) of Revascularization Compared With Medical Therapy*

| | |
|---|---|
| CABG for left main stenosis, with or without angina | 9000 |
| CABG for 3VD with or without angina | 18 000 |
| CABG for 2VD with severe angina and LAD stenosis | 22 000 |
| CABG for 2VD with severe angina, no LAD disease | 61 000 |
| CABG for 2VD, no angina, with LAD stenosis | 27 000 |
| CABG for 2VD, no angina, no LAD disease | 680 000 |
| CABG for 1VD, severe angina | 73 000 |
| PTCA for 1VD, severe angina | 9000 |
| PTCA for LAD stenosis, mild angina | 92 000 |

CABG indicates coronary artery bypass graft; 1, 2, or 3VD, 1-, 2-, or 3-vessel disease; LAD, left anterior descending coronary artery; and PTCA, percutaneous transluminal coronary angioplasty.

*Adjusted to 1993 dollars from multiple sources in a review by Kupersmith et al. Prog Cardiovas Dis. 1995;37:307-56 (734).

vival and/or symptomatic benefit is demonstrable. Most important, within these subsets the cost-effectiveness of coronary bypass compares favorably with other generally accepted medical therapies.

### *8.2. Cost Comparison With Angioplasty*

The cost-effectiveness of angioplasty is dependent on the preangioplasty symptoms of the patient in the same way that CABG surgery is so dependent, particularly in subgroups in whom revascularization cannot be shown to have a survival benefit compared with medical therapy (i.e., in single-vessel disease). Because it relieves angina, angioplasty for single-vessel-disease patients with severe angina is estimated to have a cost-effectiveness of $9000/QALY. In patients with only mild angina, however, angioplasty in the setting of LAD single-vessel disease is estimated to have a poor cost-effectiveness of $92 000/QALY (736).

A direct comparison of the cost of angioplasty and coronary bypass surgery for selected patients with multivessel disease (i.e., those patients for whom either therapeutic modality was considered appropriate) has been made in the randomized trials of angioplasty versus CABG. In general, the cost analyses of randomized trials have revealed that the initial cost of angioplasty is about 50% to 65% of the initial cost of bypass surgery. The incremental cost of repeated procedures during the follow-up period has led to a cumulative cost of angioplasty that approaches the cumulative cost of bypass surgery at 3 years. The EAST found that the 3-year inpatient cost of angioplasty was 94% of that of bypass surgery (135). The RITA trial, which included a large number of patients with single-vessel disease, found that the 2-year cumulative cost of angioplasty was 80% of the cost of coronary bypass (136). The BARI trial conducted a prospectively designed analysis of the comparative cost of the 2 procedures from a subgroup of the participating centers, comprising a total of 934 of the 1829 patients enrolled (124). The mean initial hospital cost of angioplasty was 65% of that of surgery, but after 5 years the cumulative cost of initial surgical therapy was only $2700 more than the cost of initial angioplasty (around a 5% difference). Because the surgical cohort had a higher overall 5-year survival, the cost of this survival benefit could be calculated. It was found to be $26 000/y of survival benefit for surgical therapy of 2- and 3-vessel disease (in patients for whom either angioplasty or surgery was considered appropriate initial therapy). As considered in the previous section, this incremental cost for double- and triple-vessel disease is within the range of costs for generally accepted therapies. It is notable that this cost of incremental benefit does not consider the benefit of coronary bypass in terms of relief of angina during the follow-up interval, which was demonstrated in each of these 3 trials (BARI, EAST, and RITA). If this factor were included, the cost-effectiveness of CABG for incremental benefit in these selected patients with multivessel disease ($/QALY) would be less than $26 000.

Previous considerations of both patient benefit and cost-effectiveness have suggested that angioplasty is less effective for patients with more advanced disease. Data gathered at Duke University have shown that there is a significant cost gradient for angioplasty as the extent of disease increases (related to repeated procedures whose incidence may be reduced by stents), which is not apparent for coronary bypass (Figure 13) (737).

The use of drug-eluting stents in percutaneous revascularization will require a re-evaluation of cost-effectiveness considerations. The initial procedure is considerably more expensive (equaling the cost of CABG in many patients with multivessel disease), but the recurring cost of reintervention for restenosis will be dramatically reduced. Cost-effectiveness will depend on pricing of stents, utilization rates of the more expensive stents, and efficacy. All of these factors are evolving rapidly.

### *8.3. Cost Reduction in Coronary Bypass*

Estimates presented in the previous portion of this section suggest that coronary bypass has been cost-effective in the last 2 decades. Initiatives to decrease the length of stay by using clinical pathways and standardized fast-track protocols have reduced hospital costs. Indeed, the estimates made by Weinstein and Stason are distinctly dated: improvements in outcomes and shortened lengths of hospitalization are likely to have considerably improved the cost-effectiveness of CABG (and angioplasty) since 1982.

Studies from the 1980s suggested that by concentrating CABG procedures into high-volume institutions, the overall cost of providing coronary surgical revascularization would be reduced owing to efficiencies of scale (738-740). Shahian et al (741) studied this question and found no relationship between either hospital size or annual CABG case volume and cost of performing bypass surgery.

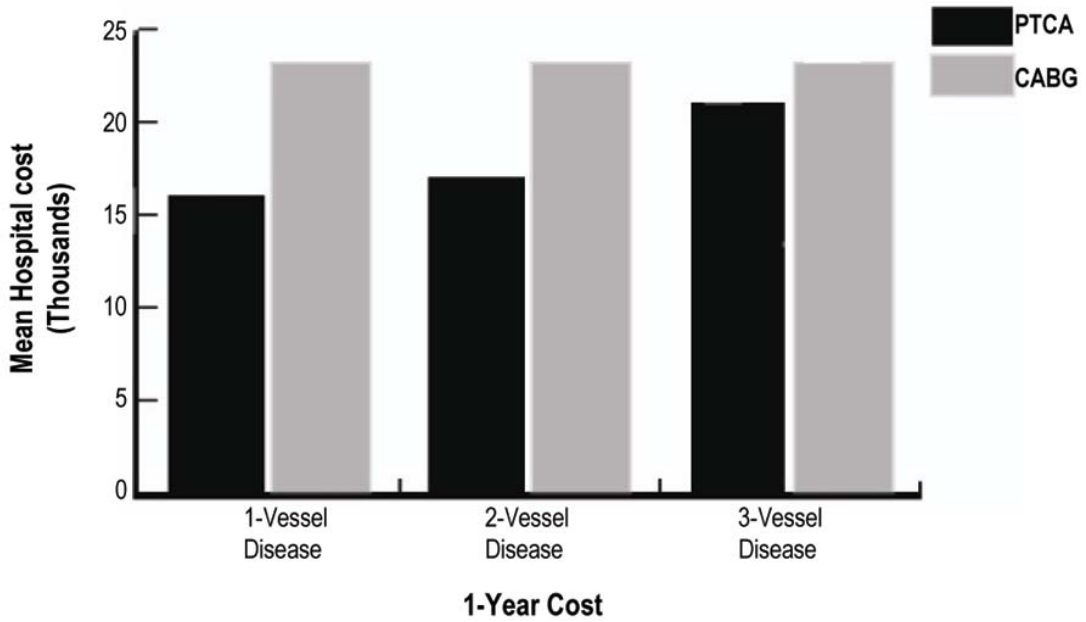


**Figure 13.** Percentage of 1-year costs for PTCA and CABG. PTCA indicates percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft. Reprinted with permission from the Society of Thoracic Surgeons (Mark. Ann Thorac Surg 1996;61:S12-5) (737).

A major innovation has been the introduction of off-bypass CABG, which has reduced the postprocedure length of stay to between 2 and 3 days. In some centers, this has led to a total 3-month cost for single-vessel coronary bypass that is not significantly different from the total 3-month cost for angioplasty of single-vessel disease (742). Considering the favorable long-term patency of an IMA graft to the LAD, the cost reductions possible with off-bypass CABG may improve the relative cost-effectiveness of coronary bypass compared with either medical therapy or percutaneous techniques, particularly for symptomatic, proximal LAD disease.

# 9. INDICATIONS

## *9.1. Introduction*

The CABG operation is indicated both for the relief of symptoms and for the prolongation of life. The 1991 Guidelines focused on survival relative to medical therapy as the pivotal recommendation for operation. In addition to extension of the length of life, this operation is an important therapeutic tool for the relief of disabling symptoms.

The 1991 Guidelines state that "the evidence is complete that the coronary artery bypass operation relieves angina in most patients." The results of the randomized trials of CABG versus PTCA have confirmed and extended this conclusion (743,744). Not only did CABG effectively relieve angina in the symptomatic patients enrolled in the randomized trials, but also freedom from angina and from antianginal medications was superior in the CABG cohorts compared with PTCA cohorts. Bypass surgery also relieved angina better than coronary stents in a randomized trial comparing the 2 forms of therapy (137).

The benefit realized from the use of CABG to relieve disabling symptoms must be balanced against the risk of the operation and tempered by the potential activity level of the individual patient. This risk may be very low in selected groups of patients. In a series of 1386 patients with single- and double-vessel disease aged less than 66 years, without CHF, and an EF greater than 0.35 from the early 1980s at Emory University, a hospital mortality of 0.07% (1 patient) was reported. Not only did these young, healthy patients have a very low risk, but their potential for renewal of an active lifestyle was exceptionally high. CABG in patients such as these for relief of disabling angina after failure of medical therapy is an attractive option, even if no survival benefit can be predicted. If, on the other hand, one were to consider a 78-year-old patient with limiting arthritis and Class II angina, then the potential benefit of CABG will be considerably less and the risk comparably greater. In this case, the attractiveness of PTCA or continued medical therapy as the appropriate therapy is enhanced.

Some caution must be expressed in the use of CABG for relief of symptoms. CABG treats the manifestations of CAD, not the disease process. As coronary disease progresses, therefore, angina often returns. The hazard function for return of angina is low for the first 5 years after operation and then begins to rise, seemingly related to late closure of bypass conduits. So long as the patient and the healthcare practitioner understand that angina may return after 5 to 10 years, the application of CABG for the relief of angina rather than for survival benefit is appropriate, particularly in low-risk patients. If preoperative symptoms are disabling, there is a high probability for a return to a fully functional lifestyle and, as discussed in Section 8, the procedure is cost-effective as well.

The second important recommendation for CABG, after relief of symptoms, is prolongation of life. The randomized trials of CABG versus medical therapy have defined patient subsets whose survival is enhanced. These patients tend to be those with advanced coronary disease: notably left main disease and triple-vessel disease (or double-vessel disease including a proximal LAD stenosis) combined with LV dysfunction. The survival benefit of CABG was examined in detail in the 1991 Guidelines and will be applied to specific patient subgroups in the following sections.

The explosive growth of PCI in the last decade mandates a careful examination of CABG survival versus PCI survival. Large randomized trials generally show that 7 to 8 year survival is superior for patients with diabetes undergoing CABG compared with patients with diabetes undergoing PTCA (131,130). Among patients without diabetes, there appears to be little difference in survival.

Only short-term results of stent revascularization are available at this time; however, similar trends favoring surgery in patients with diabetes are emerging. Definitive conclusions regarding stent procedures await maturation of ongoing clinical trials.

## *9.2. Clinical Subsets*

### 9.2.1. Asymptomatic or Mild Angina

**Class I**

1. **CABG should be performed in patients with asymptomatic or mild angina who have significant left main coronary artery stenosis. *(Level of Evidence: A)***
2. **CABG should be performed in patients with asymptomatic or mild angina who have left main equivalent: significant (greater than or equal to 70%) stenosis of the proximal LAD and proximal left circumflex artery. *(Level of Evidence: A)***
3. **CABG is useful in patients with asymptomatic ischemia or mild angina who have 3-vessel disease. (Survival benefit is greater in patients with abnormal LV function; e.g., EF less than 0.50 and/or large areas of demonstrable myocardial ischemia.) *(Level of Evidence: C)***

**Class IIa**

**CABG can be beneficial for patients with asymptomatic or mild angina who have proximal LAD stenosis with 1- or 2-vessel disease. (This recommendation becomes a Class I if extensive ischemia is documented by noninvasive study and/or LVEF is less than 0.50.) *(Level of Evidence: A)***

**Class IIb**

**CABG may be considered for patients with asymptomatic or mild angina who have 1- or 2-vessel disease not involving the proximal LAD (If a large area of viable myocardium and high-risk criteria are met on noninvasive testing, this recommendation becomes Class I). *(Level of Evidence: B)***

For patients with no symptoms or mild angina, the appropriateness of coronary bypass surgical therapy is based on survival advantage therapy compared with nonsurgical therapy. The relative appropriateness of percutaneous versus surgical therapy is discussed in Section 3.3. To identify anatomic subsets in which coronary bypass is beneficial, definition of "important" coronary stenosis is necessary. For this and all subsequent sections, coronary stenosis will be defined as a 50% or greater reduction of lumen diameter. This is the degree of narrowing defined as important in the majority of randomized trials that have examined the relationship of coronary anatomy and survival after CABG. It is important to note that the level of angina in this category is not considered an indication for surgery. Moderate or severe angina would represent symptoms that many patients find unacceptable despite adequate medical therapy. Contrariwise, in this category, patients are either completely asymptomatic or have acceptable symptoms such that bypass surgery for symptom relief is not the issue.

The indication for bypass surgery in this category relates to the extent of coronary disease, the demonstration of objective signs or symptoms of this disease, and consideration for the risk of nonmedical therapy, which may include either bypass surgery or angioplasty. As stated in Section 3.2, the data on which these classifications are assigned are based on 3 randomized controlled trials, several smaller randomized trials, a subsequent meta-analysis of these data, and several observational studies. The limitations of these data are discussed in Section 3.2 and listed in Table 7.

### 9.2.2. Stable Angina

**Class I**

1. **CABG is recommended for patients with stable angina who have significant left main coronary artery stenosis. *(Level of Evidence: A)***
2. **CABG is recommended for patients with stable angina who have left main equivalent: Significant (greater than or equal to 70%) stenosis of the proximal LAD and proximal left circumflex artery. *(Level of Evidence: A)***
3. **CABG is recommended for patients with stable angina who have 3-vessel disease. (Survival benefit is greater when LVEF is less than 0.50.) *(Level of Evidence: A)***
4. **CABG is recommended in patients with stable angina who have 2-vessel disease with significant proximal LAD stenosis and either EF less than 0.50 or demonstrable ischemia on noninvasive testing. *(Level of Evidence: A)***
5. **CABG is beneficial for patients with stable angina who have 1- or 2-vessel CAD without significant proximal LAD stenosis but with a large area of viable myocardium and high-risk criteria on noninvasive testing. *(Level of Evidence: B)***
6. **CABG is beneficial for patients with stable angina who have developed disabling angina despite maxi-**

**mal noninvasive therapy, when surgery can be performed with acceptable risk. If angina is not typical, objective evidence of ischemia should be obtained. *(Level of Evidence: B)***

**Class IIa**

1. **CABG is reasonable in patients with stable angina who have proximal LAD stenosis with 1-vessel disease. (This recommendation becomes Class I if extensive ischemia is documented by noninvasive study and/or LVEF is less than 0.50). *(Level of Evidence: A)***
2. **CABG may be useful for patients with stable angina who have 1- or 2-vessel CAD without significant proximal LAD stenosis but who have a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing. *(Level of Evidence: B)***

**Class III**

1. **CABG is not recommended for patients with stable angina who have 1- or 2-vessel disease not involving significant proximal LAD stenosis, patients who have mild symptoms that are unlikely due to myocardial ischemia, or patients who have not received an adequate trial of medical therapy and**
   a. **have only a small area of viable myocardium or *(Level of Evidence: B)***
   b. **have no demonstrable ischemia on noninvasive testing. *(Level of Evidence: B)***
2. **CABG is not recommended for patients with stable angina who have borderline coronary stenoses (50% to 60% diameter in locations other than the left main coronary artery) and no demonstrable ischemia on noninvasive testing. *(Level of Evidence: B)***
3. **CABG is not recommended for patients with stable angina who have insignificant coronary stenosis (less than 50% diameter reduction). *(Level of Evidence: B)***

For patients with stable angina, the recommenation for CABG is based both on the likelihood of improving survival and on the likelihood of relief of lifestyle-limiting symptoms. Based on the 3 large, prospective, randomized trials comparing medical with surgical therapy and multiple observational studies, the patient factors most influencing a decision to recommend CABG include the presence of severe proximal multivessel coronary disease, LV dysfunction, a strongly positive stress test, and comorbid conditions such as PVD and diabetes. Additional factors that are of critical importance relate to the perceived immediate risk of bypass surgery and the long-term prognosis, particularly whether the patient's potential improvement in longevity or quality of life due to a successful bypass operation justifies the short-term risk.

### 9.2.3. Unstable Angina/Non–ST-Segment Elevation MI (NSTEMI)

**Class I**

1. **CABG should be performed for patients with unstable angina/NSTEMI with significant left main coronary artery stenosis. *(Level of Evidence: A)***
2. **CABG should be performed for patients with unstable angina/NSTEMI who have left main equivalent: significant (greater than or equal to 70%) stenosis of the proximal LAD and proximal left circumflex artery. *(Level of Evidence: A)***
3. **CABG is recommended for unstable angina/NSTEMI in patients in whom revascularization is not optimal or possible, and who have ongoing ischemia not responsive to maximal nonsurgical therapy. *(Level of Evidence: B)***

**Class IIa**

**CABG is probably indicated for patients with unstable angina/NSTEMI who have proximal LAD stenosis with 1- or 2-vessel disease. *(Level of Evidence: A)***

**Class IIb**

**CABG may be considered in patients with unstable angina/NSTEMI who have 1- or 2-vessel disease not involving the proximal LAD when percutaneous revascularization is not optimal or possible. (If there is a large area of viable myocardium and high-risk criteria are met on noninvasive testing, this recommendation becomes Class I.) *(Level of Evidence: B)***

Indications for coronary bypass surgery in this category relate not only to survival but also to the relief of symptoms. Thus, in general, all of the survival indications listed for the asymptomatic patient or the individual with stable angina apply. However, timing of surgery becomes a critical consideration. Some reports have suggested a high mortality after CABG in patients with acute unstable angina or NSTEMI and have shown that one of the independent predictors of mortality after coronary bypass surgery is the stability of the patient going to operation. Other investigators have not found this association (Section 5.11). In the patient in whom stabilization with aggressive medical therapy may be achieved, it is advisable to stabilize and reduce ongoing ischemia before proceeding to bypass surgery. In this regard, a small randomized trial demonstrated that insertion of an IABP 2 hours or more before CPB can reduce bypass time, intubation time, and length of stay, and improve postoperative cardiac output in high-risk patients (745).

### 9.2.4. ST-Segment Elevation MI (STEMI)

**Class I**

**Emergency or urgent CABG in patients with STEMI should be undertaken in the following circumstances:**

a. **Failed angioplasty with persistent pain or hemodynamic instability in patients with coronary anatomy suitable for surgery. *(Level of Evidence: B)***
b. **Persistent or recurrent ischemia refractory to medical therapy in patients who have coronary anatomy suitable for surgery, who have a significant area of myocardium at risk, and who are not candidates for PCI. *(Level of Evidence: B)***
c. **At the time of surgical repair of postinfarction ventricular septal rupture or mitral valve insufficiency. *(Level of Evidence: B)***

d. **Cardiogenic shock in patients less than 75 years old with ST-segment elevation or left bundle-branch block or posterior MI who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock, unless further support is futile because of patient's wishes or contraindications/unsuitability for further invasive care *(Level of Evidence: A)***
e. **Life-threatening ventricular arrhythmias in the presence of greater than or equal to 50% left main stenosis and/or triple-vessel disease *(Level of Evidence: B)***

**Class IIa**

1. **CABG may be performed as primary reperfusion in patients who have suitable anatomy and who are not candidates for or who have had failed fibrinolysis/PCI and who are in the early hours (6 to 12 hours) of evolving STEMI. *(Level of Evidence: B)***
2. **In patients who have had an STEMI or NSTEMI, CABG mortality is elevated for the first 3 to 7 days after infarction, and the benefit of revascularization must be balanced against this increased risk. Beyond 7 days after infarction, the criteria for revascularization described in previous sections are applicable. *(Level of Evidence: B)***

**Class III**

1. **Emergency CABG should not be performed in patients with persistent angina and a small area of myocardium at risk who are hemodynamically stable. *(Level of Evidence: C)***
2. **Emergency CABG should not be performed in patients with successful epicardial reperfusion but unsuccessful microvascular reperfusion. *(Level of Evidence: C)***

Although early coronary bypass surgery as a primary reperfusion strategy in patients suffering from a STEMI has been reported, the widespread use of intravenous fibrinolytic therapy for this purpose and more primary PCI has largely superceded early application of bypass surgery. Studies have shown that eventual infarct size and the subsequent risk of mortality and/or LV dysfunction are related to the time from the onset of symptoms until coronary reperfusion. Although, on average, coronary bypass surgery requires a longer time to establish coronary reperfusion than either of the nonsurgical techniques, modification of the conditions of reperfusion that is possible with surgical therapy may offer some benefit with regard to eventual infarct size relative to percutaneous or fibrinolytic therapy. Despite this potential benefit of reperfusion modification, coronary bypass is rarely performed for this indication except in special circumstances. The decision to perform surgery requires angiographic demonstration of adequate target vessels in the region of infarction and usually other regions as well. In most circumstances, early coronary bypass for acute infarction is appropriate only in patients with residual ongoing ischemia despite nonsurgical therapy, be it fibrinolysis, PCI, or both. As with PCI, the risks of bypass operation in patients in the midst of a STEMI are substantially higher than are the risks in elective candidates.

To determine the benefits and liabilities of treatment of an acute MI with CABG requires accurately defining the topic. The definition of acute MI is the resultant ischemic muscle injury after reduction or interruption of the coronary artery blood supply. The obvious weakness in this definition is the variability of the tissue damage. This has been addressed by sub-classifying MIs into Q-wave and non–Q-wave types. A Q-wave infarction has been defined as ST-segment changes that progress to new Q waves in addition to a creatine phosphokinase (CPK)-MB isoenzyme elevation of greater than 10 IU/L. Non–Q-wave infarction is defined as ST-segment and T-wave abnormalities (generally NSTEMI) that do not progress to pathological Q waves but show abnormal elevations of CPK-MB isoenzyme of greater than 10 IU/L (585). The decision or appropriateness to recommend surgical revascularization in the face of an acute MI depends on the clinical symptoms and the presence of persistent ischemia despite maximum medical therapy. This is also the algorithm that is used to decide to proceed with catheter-based therapy. It appears that when there is a situation that is not amenable to medical or catheter-based therapy and persistent ischemia is present, CABG is indicated. This is presuming that there is no overwhelming contraindication against operation.

There are specific conditions that will warrant CABG in the face of an acute MI: the presence of left main stenosis, severe 3-vessel disease, associated valve disease (whether secondary to the MI or unrelated) (35a), and anatomy unsuitable for other forms of therapy. The literature is somewhat vague regarding the categories for surgical intervention. Some of the reports address STEMI versus NSTEMI while others address the proximity of MI to operation (i.e., less than 6 hours, 6 hours to 2 days, 2 to 14 days, 2 to 6 weeks, and greater than 6 weeks) or unstable angina versus evolving MI, mechanical complications, acute occlusions, and control patients. It is best to review these separately and try to identify a common recommendation and approach.

Braxton et al (585) studied the comparative effect of operating on patients with STEMI and NSTEMI versus a control group. Excluding the patients who require emergency operation for mechanical complications of an acute MI, the patients undergoing CABG within 48 hours of the STEMI had a significantly increased operative mortality which approached 50%. The data imply that for such patients, there is much to be gained by waiting more than 48 hours in most circumstances. The implication is also made study also suggested that symptomatic patients with a NSTEMI may undergo surgical revascularization at any time with no significant increase in mortality over elective patients (585). This is substantiated in an article by Goodman et al (583), wherein MI after fibrinolytic therapy was evaluated in relation to events with STEMI versus NSTEMI. The NSTEMI was more likely to be nonanterior, distally locat-

ed, and have better global and regional LV function. In the setting of fibrinolysis after MI, patients with a NSTEMI were more likely to have early, complete, and sustained infarct-related artery patency and better LV function. This identification of anatomic and functional differences between STEMI and NSTEMI should also translate into operative risk for these 2 patient cohorts and verifies the worse operative risk with surgery in the early STEMI period.

Creswell et al (581) retrospectively reviewed 2296 patients who underwent CABG after an acute MI. A generalization that was made was that the operative mortality decreased as the time between the acute MI and operation increased. Patients who underwent operation less than 6 hours after MI had an operative mortality of 8.4% and those who underwent operation greater than 6 hours, 4.3% (*P* equals 0.02) (Table 19). Additional findings were that despite the urgency of operation, operative mortality was greater for those patients with a preoperative MI than those without an MI. It is important to note that when the independent risk factors of urgency of operation, increased patient age, renal insufficiency, number of previous MIs, and hypertension were adjusted for, the time interval between MI and CABG was not a significant predictor of death.

A third way to examine the impact of an MI on operative mortality was reported by von Segesser et al (579). In this series, 641 of 3397 patients had stable or unstable angina, respectively, and underwent CABG. These 641 patients were divided into 5 groups. Group A patients had unstable angina that involved the inclusion of 2 of 6 criteria including impending infarction, electrocardiographic ST-segment modifications, minimal increases in CPK values, prolonged angina at rest, angina resistant to intravenous medication, and postinfarction angina. Group B patients were sustaining an evolving MI defined as either a new electrocardiographic Q wave; electrocardiographic ST-segment modifications; and CPK-MB values greater than 8% of total CPK, CPK greater than 3 times normal; CPK-MB greater than 10% of total CPK; or new LV dyskinesis on echocardiography or scintigraphy. Group C patients had mechanical complications of acute MI. Group D patients had an acute coronary occlusion (emergency post-PTCA or angiography), and Group E patients had stable class IV angina (control).

In this series, acute CABG in patients with unstable angina, evolving MI, and acute coronary occlusion demonstrated results comparable to those of CABG in the elective cohort. Late survival in these 3 cohorts was similar to that of the group with stable angina. The worst late survival was in those with mechanical complications, although it was acceptable. The conclusions of this investigation support acute revascularizations in unstable angina and selected patients after acute MI.

A review of other articles dealing with operation after acute MI (34,450,580,746) suggests that unless patients are in cardiogenic shock or have mechanical complications of acute MI, early CABG can be performed with little or no increase in risk of perioperative mortality.

Mechanical complications of acute MI include ventricular septal defect, MR secondary to papillary muscle infarction and/or rupture, and LV free-wall rupture (747-754). There is general agreement that cardiogenic shock associated with a mechanical complication of an MI warrants emergency operation to correct the defect as a life-saving procedure. Although there is less consensus as to the timing of operation for patients with ventricular septal defect or MR after acute MI with hemodynamic stability, most cardiac surgical centers proceed promptly to surgery.

There does not appear to be clear documentation of the best timing for stable patients with a mechanical complication. There has been the argument to delay operation to allow the friable tissue to "mature" and hold sutures; this invokes some Darwinian selection process and prompted Norell et al (747) to approach all of these types of problems acutely. Their results did not demonstrate a statistical difference between acute and subacute operation. It must be stated, however, that the numbers in many of these series were small or included patient enrollment extending over several decades while techniques, understanding of physiology, and philosophy have advanced.

## 9.2.5. Poor LV Function

**Class I**

1. **CABG should be performed in patients with poor LV function who have significant left main coronary artery stenosis. *(Level of Evidence: B)***
2. **CABG should be performed in patients with poor LV function who have left main equivalent: significant (greater than or equal to 70%) stenosis of the proximal LAD and proximal left circumflex artery. *(Level of Evidence: B)***
3. **CABG should be performed in patients with poor LV**

**Table 19.** Coronary Artery Bypass Graft Surgery Mortality After Acute Myocardial Infarction: Effect of Timing of Operation

| Outcome | Less than 6 Hours | 6-48 Hours | 2-14 Days | 2-6 Weeks | Greater than 6 Weeks | No MI |
|---|---|---|---|---|---|---|
| Op mort | 9.1% | 8.3% | 5.2% | 6.5% | 2.9% | 2.1% |
| Periop MI | 9.1% | 9.8% | 2.8% | 2.7% | 4.0% | 3.9% |
| Trans CVA | 0.0% | 3.0% | 1.3% | 0.4% | 0.8% | 0.8% |
| Perm CVA | 9.1% | 3.8% | 2.9% | 1.5% | 2.3% | 1.2% |
| AF | 27.2% | 40.9% | 33.0% | 39.1% | 31.8% | 30.7% |

MI indicates myocardial infarction; Op mort, operative mortality; Periop, perioperative; Trans, transient; CVA, cerebrovascular accident; Perm, permanent; and AF, atrial fibrillation.

**function who have proximal LAD stenosis with 2- or 3-vessel disease.** ***(Level of Evidence: B)***

**Class IIa**

**CABG may be performed in patients with poor LV function with significant viable noncontracting, revascularizable myocardium and without any of the above anatomic patterns.** ***(Level of Evidence: B)***

**Class III**

**CABG should not be performed in patients with poor LV function without evidence of intermittent ischemia and without evidence of significant revascularizable viable myocardium.** ***(Level of Evidence: B)***

As discussed in Section 5.9, increasing evidence suggests that chronic LV dysfunction due to viable but hibernating myocardium in patients with severe multivessel disease is relatively common. Furthermore, observational studies now support the notion that coronary bypass surgery can result in stabilization and often improvement in LV function in selected patients. Operation on a patient with poor LV function is particularly appropriate if the patient has signs or symptoms of intermittent ischemia and minimal or no CHF. On the other hand, if the patient has prominent signs and symptoms of CHF with minimal angina, the decision to operate should be based on objective evidence of hibernating myocardium (755). There should be demonstration of substantial regions of myocardial viability that would benefit from revascularization (756). Such areas must be perfused by coronary arteries of sufficient size and location to be reasonable targets for bypass surgery (757).

The concept of operating on patients with poor LV function for survival advantage comes from the randomized trials that suggested that patients with left main, 3-vessel, and 2-vessel disease and vessel disease involving the proximal LAD with concomitant LV dysfunction on average had a greater survival advantage compared with those on medical therapy. Although the randomized studies did not include large numbers of patients with EFs less than 0.30, subsequent observational data suggest that these patients, although having a higher immediate risk for bypass surgery, may achieve a greater long-term gain in terms of survival advantage, assuming that the concepts discussed above are applied (755-757).

## 9.2.6. Life-Threatening Ventricular Arrhythmias

**Class I**

1. **CABG should be performed in patients with life-threatening ventricular arrhythmias caused by left main coronary artery stenosis.** ***(Level of Evidence: B)***
2. **CABG should be performed in patients with life-threatening ventricular arrhythmias caused by 3-vessel coronary disease.** ***(Level of Evidence: B)***

**Class IIa**

1. **CABG is reasonable in bypassable 1- or 2-vessel disease causing life-threatening ventricular arrhythmias. (This becomes a Class I recommendation if the arrhythmia is resuscitated sudden cardiac death or sustained ventricular tachycardia.)** ***(Level of Evidence: B)***
2. **CABG is reasonable in life-threatening ventricular arrhythmias caused by proximal LAD disease with 1- or 2-vessel disease. (This becomes a Class I recommendation if the arrhythmia is resuscitated sudden cardiac death or sustained ventricular tachycardia).** ***(Level of Evidence: B)***

**Class III**

**CABG is not recommended in ventricular tachycardia with scar and no evidence of ischemia.** ***(Level of Evidence: B)***

The benefits of CABG in patients with ventricular arrhythmias have been studied in survivors of out-of-hospital cardiac arrest and in patients with inducible ventricular tachycardia or fibrillation under electrophysiological study. In general, bypass surgery has been more effective in reducing episodes of ventricular fibrillation than ventricular tachycardia, because the mechanism of the latter arrhythmia usually involves reentry with scarred endocardium rather than ischemia.

In survivors of cardiac arrest who have severe and operable coronary disease, CABG surgery can suppress arrhythmia induction, reduce subsequent cardiac arrest, and result in a good long-term outcome (758-760). It is particularly effective when an ischemic cause of the arrhythmia can be documented, for instance, with exercise (761). However, because coronary revascularization may not alleviate all of the factors that predispose to ventricular arrhythmias, concomitant insertion of an implantable cardioverter-defibrillator may be necessary (762). Similarly, continued inducibility or clinical recurrence of ventricular tachycardia after CABG usually requires defibrillator implantation.

## 9.2.7. CABG After Failed PTCA

**Class I**

1. **CABG should be performed after failed PTCA in the presence of ongoing ischemia or threatened occlusion with significant myocardium at risk.** ***(Level of Evidence: B)***
2. **CABG should be performed after failed PTCA for hemodynamic compromise.** ***(Level of Evidence: B)***

**Class IIa**

1. **It is reasonable to perform CABG after failed PTCA for a foreign body in crucial anatomic position.** ***(Level of Evidence: C)***
2. **CABG can be beneficial after failed PTCA for hemodynamic compromise in patients with impairment of the coagulation system and without previous sternotomy.** ***(Level of Evidence: C)***

**Class IIb**

**CABG can be considered after failed PTCA for hemodynamic compromise in patients with impairment of the coagulation system and with previous sternotomy. *(Level of Evidence: C)***

**Class III**

1. **CABG is not recommended after failed PTCA in the absence of ischemia. *(Level of Evidence: C)***
2. **CABG is not recommended after failed PTCA with inability to revascularize due to target anatomy or no-reflow state. *(Level of Evidence: C)***

The decision to proceed with emergency bypass surgery after a failed PTCA procedure is a complex one. The interventional cardiologist and consulting cardiac surgeon must together decide when the procedure cannot be salvaged by percutaneous techniques, often in the acute setting of ischemia or infarction. Important considerations include the mechanisms of the failed procedure, the potential to correct this situation surgically, the extent of myocardium that is jeopardized, and the overall clinical status of the patient. Threatened compared with acute vessel closure poses a particularly challenging situation, since the physicians must balance further attempts at percutaneous salvage versus moving forward with surgery. Factors that influence the outcome of surgery include patient characteristics such as LV dysfunction, older age, and previous MI (763,764), as well as anatomic factors such as complex lesion characteristics, extent of multivessel disease, and the absence of collaterals (763-766). Finally, outcome also depends on the total ischemic time and may be adversely affected by a delay in transport to the operating room (763,764,767,768). Bypass surgery is clearly the procedure of choice in the setting of hemodynamic compromise or for retrieval of a foreign body, such as a fractured guidewire or undeployed stent in a crucial anatomic position.

Emergency bypass for failed PTCA is understandably associated with a higher rate of death and subsequent MI compared with elective bypass surgery (763,769). It is encouraging to observe the diminishing need for emergency bypass surgery in this situation, owing in large measure to the increasing use and availability of intracoronary stents (643,645). Among patients who require emergency bypass after a failed angioplasty in the current era, the rate of complications remains substantial (770-772). This probably reflects the increased severity of CAD and other comorbidities in patients currently treated with PTCA. Therefore, a coordinated approach and cooperative interaction between the cardiologist, cardiac surgeon, and anesthesia team are necessary to expedite resuscitation, transfer, and revascularization of patients with failed PTCA (773-775).

## 9.2.8. Patients With Previous CABG

**Class I**

1. **Coronary bypass should be performed in patients with prior CABG for disabling angina despite optimal nonsurgical therapy. (If angina is not typical, then objective evidence of ischemia should be obtained.) *(Level of Evidence: B)***
2. **Coronary bypass should be performed in patients with prior CABG without patent bypass grafts but with Class I indications for surgery for native-vessel CAD (significant left main coronary stenosis, left main equivalent, 3-vessel disease). *(Level of Evidence: B)***

**Class IIa**

1. **Coronary bypass is reasonable in patients with prior CABG and bypassable distal vessel(s) with a large area of threatened myocardium by noninvasive studies. *(Level of Evidence: B)***
2. **Coronary bypass is reasonable in patients who have prior CABG if atherosclerotic vein grafts with stenoses greater than 50% supplying the LAD coronary artery or large areas of myocardium are present. *(Level of Evidence: B)***

Reoperation after previous CABG can be successfully performed, but the risk of hospital mortality is increased about 3-fold compared with the primary operation. Moreover, reoperation is associated with a diminished expectation for relief of symptoms and a diminished expectation for prolongation of life compared with the primary operation (see Sections 4.1.2 and 5.7). For this reason, reoperation is generally reserved for relief of disabling symptoms or for compelling evidence of potentially life-threatening areas of myocardium at risk objectively quantified by noninvasive studies. Because many of these patients have had previous myocardial damage, consideration of the consequences of infarction of an area of myocardium demonstrated to be at risk must be weighed against the cumulative effect of the current threatening situation combined with prior damage.

The existence of significant late stenoses (greater than or equal to 5 years after operation) representing atherosclerosis in vein grafts that are greater than 50% stenosed and that supply either the LAD coronary artery or large areas of myocardium represent a potential anatomic indication for operation.

For a patient with previous bypass surgery, percutaneous techniques can be effective in treating native-vessel stenoses and appear to be safe in treating early stenoses in vein grafts. However, the use of percutaneous techniques to treat late atherosclerotic stenoses in vein grafts has been much less successful.

An increasingly common situation is the presence of a functioning IMA graft to the LAD artery, with recurrent ischemia in other regions of the heart. The potential loss of this conduit consequent to a reoperation represents a major negative factor in the long-term therapy of that patient and is cause for additional caution in recommendation of a reoperation.

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**APPENDIX 1.** ACC/AHA Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery—Relationships With Industry

| Committee Member Name | Research Grant | Speakers Bureau/ Honoraria | Stock Ownership | Consultant |
|---|---|---|---|---|
| Dr. Kim A. Eagle | Aventis<br>Pfizer<br>Blue Cross/Blue Shield | None | None | National Institutes of Health<br>Sanofi |
| Dr. Robert A. Guyton | Medtronic, Inc.<br>Qwest Medical, Inc.<br>Chase Medical, Inc. | None | None | None |
| Dr. Ravin Davidoff | None | None | None | None |
| Dr. Fred H. Edwards | None | None | None | None |
| Dr. Gordon A. Ewy | None | Pfizer<br>Merck<br>GlaxoSmithKline<br>Wyeth | None | None |
| Dr. Timothy J. Gardner | None | None | None | None |
| Dr. James C. Hart | Medtronic, Inc.<br>CardioVations | Medtronic, Inc.<br>Novare. | None | Medtronic, Inc<br>St. Jude Medical<br>CardioVations |
| Dr. Howard C. Herrmann | Johnson & Johnson<br>Boston Scientific<br>Pfizer<br>Merck<br>Millennium | Johnson & Johnson<br>Pfizer | Johnson & Johnson | Johnson & Johnson<br>Boston Scientific<br>Merck |
| Dr. L. David Hillis | None | None | None | None |
| Dr. Adolph M. Hutter | None | None | None | None |
| Dr. Bruce Whitney Lytle | None | None | None | None |
| Dr. Robert A. Marlow | None | None | None | None |
| Dr. William C. Nugent | None | None | None | None |
| Dr. Thomas A. Orszulak | None | None | None | None |

This table represents the relationships of committee members with industry that were disclosed at the initial writing committee meeting in March 2002 and updated in conjunction with all meetings and conference calls of the writing committee. It does not necessarily reflect relationships with industry at the time of publication.

**APPENDIX 2.** External Peer Reviewers for the ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery*

| Reviewer Name** | Reviewer Category and Affiliation | Relationships With Industry |
|---|---|---|
| Dr. Robert H. Jones | Official Reviewer – ACC (Board of Trustees) | None |
| Dr. Edward H. Williams | Official Reviewer – ACC (Board of Governors) | None |
| Dr. Loren F. Hiratzka | Official Reviewer – ACC/AHA Task Force on Practice Guidelines | None |
| Dr. Irving L. Kron | Official Reviewer – AHA | None |
| Dr. Irvin B. Krukenkamp | Official Reviewer – AHA | None |
| Dr. E. Magnus Ohman | Official Reviewer – AHA | Stock Holder: Medtronic<br>Research Grants: Berlex, Millennium, BMS, Sanofi-Synthelabo, Merck |
| Dr. John F. Butterworth | Organizational Reviewer – Society of Cardiovascular Anesthesiologists | None |
| Dr. Harry J. D'Agostino, Jr. | Organizational Reviewer – Society of Thoracic Surgeons | None |
| Dr. Constance K. Haan | Organizational Reviewer – Society of Thoracic Surgeons | None |
| Dr. Elliott M. Antman | Content Reviewer – ACC/AHA Task Force on Practice Guidelines | Research Grants: Bristol-Myers Squibb, Sanofi-Synthelabo, Millennium, Merck, Eli Lilly |

This table represents the relationships of peer reviewers with industry that were disclosed at the time of peer review of this guideline. It does not necessarily reflect relationships with industry at the time of publication.
*Participation in the peer review process does not imply endorsement of the document.
**Names are listed in alphabetical order within each category of review.

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