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ACC/AHA Guidelines for Coronary Artery Bypass Graft Surgery

A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery)

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This document is available on the websites of the ACC (*www.acc.org*) and the AHA (*www.americanheart.org*). Reprints of this document (the complete guidelines) are available for $5 each by calling 800-253-4636 (US only) or writing the American College of Cardiology, Educational Services, 9111 Old Georgetown Road, Bethesda, MD 20814-1699. Ask for reprint No. 71-0174. To obtain a reprint of the shorter version (executive summary and recommendations) published in the September 28, 1999, issue of *Circulation*, ask for reprint No. 71-0173. To purchase additional reprints (specify version and reprint number): up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 214-706-1466, fax 214-691-6342, or E-mail pubauth@heart.org.

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PREAMBLE

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures

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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.

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

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

The executive summary and recommendations are published in the September 28, 1999, issue of *Circulation*. The full text is published in the October 1999 issue of the *Journal of the American College of Cardiology*. Reprints of the full text and the executive summary are available from both organizations.

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

I. INTRODUCTION

The ACC/AHA Task Force on Practice Guidelines was formed to 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 published in 1991, there has been considerable 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 Committee was charged with revising the guidelines published in 1991 (1). The Committee reviewed pertinent publications, including abstracts, through a computerized search of the English literature since 1989 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 10 years is beyond the scope of this document. However, evidence tables were developed and extensively reviewed by an expert in meta-analysis. 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 recent 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 IX), the relative levels of evidence favoring the Class I, II, and III indications were noted.

The ACC/AHA classifications I, II, and III are used to summarize indications as follows:

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

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

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

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

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

The Committee consists of acknowledged experts in cardiac surgery, interventional cardiology, general cardiology, internal medicine, and family practice. The Committee

included representatives from the American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP), as well as the Society for Thoracic Surgery (STS). Both academic and private practice sectors were represented. The document was reviewed by 3 outside observers nominated by the ACC and 3 outside reviewers nominated by the AHA, as well as outside reviewers nominated by AAFP, ACP, STS, the American College of Surgery, and the Society of Cardiovascular Anesthesiologists. This document will be reviewed annually after publication by the Task Force to determine whether a revision is necessary. The guidelines will be considered current unless the Task Force revises them or withdraws them from distribution.

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 transluminal coronary angioplasty (PTCA), 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 doctors can use in combination with other types of knowledge and patient preferences to make rational decisions about treatment.

II. 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).

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 VI, have led to an expected 30-day mortality of <1% in patients receiving elective coronary bypass who are <65 years of age and who have no severe LV dysfunction or congestive heart failure (CHF). Even in otherwise uncomplicated patients aged <65 years and with an ejection fraction (EF) of 0.25 to 0.35, first-time coronary bypass has an operative risk of <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 recently presented the prospect of further reductions in perioperative morbidity.

III. OUTCOMES

A. Hospital Outcomes

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.

2. Predicting Hospital Mortality. 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 datasets 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 datasets. A review of 7 large datasets, representing >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 (ie, urgency of operation, age, prior heart surgery, sex, LVEF, percent stenosis of the left main coronary artery, and number of major coronary arteries with >70% stenosis) were found to be predictive of mortality after CABG in all 7 datasets. 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: PTCA during index admission; recent (<1 week) MI; history of angina, ventricular arrhythmia, CHF, or mitral regurgitation (MR); comorbidities including diabetes, cerebrovascular disease, peripheral vascular disease (PVD), chronic obstructive pulmonary disease (COPD), and creat-

Table 1. Relative Mortality Risk: Core CABG Variables for 6 Datasets

	NNE (21)	VA (22)	STS (16)	NYS (23)	CC (24)	AGH (25)
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	1.05	1.04	1.05	NA
Sex, F	1.2	NA	1.5	1.52	1.63	1.48
Prior heart surgery	3.6	3.2	3.0 3.5 (Mult reops)	3.73	1.72	1.39
LMD (70%)	NS	NA	1.3	1.43 (>90%)	NA	NA
No. of diseased vessels						
1	1.0	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	1.0	1.0	1.0	1.0	1.0	1.0
Urgent	2.1	2.4	1.2	1.42 (USA)	NA	3.5
Emergent	4.4	3.8	2.0	3.98	5.07	7.14
Salvage	NA	NA	6.7	NA	NA	29.9
Ejection fraction						
0.60	1.0	NA	. . .	1.0 (>40%)	NA	. . .
0.50–0.59	1.4	NA	. . .	. . .	NA	. . .
0.40–0.49	1.6	NA	. . .	. . .	NA	. . .
0.30–0.39	1.9 (<40%)	NA	. . .	1.63	NA	2.89 (<30%)
0.20–0.29	NA	NA	. . .	2.21	NA	. . .
<0.20	NA	NA	. . .	4.06	NA	. . .

NNE, Northern New England Cardiovascular Disease Study Group; VA, Veterans Affairs cardiac surgical database; STS, Society for Thoracic Surgery national cardiac surgical database; NYS, New York State cardiac surgery reporting system; 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 >50 years.

*Urgent indicates patients are required to stay in 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.

inine 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 (15).

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 1 compares the relative risk of the 7 core variables identified by Jones et al (18) to be most predictive of mortality as reported by 6 datasets.

Age has consistently predicted mortality after CABG (16,26), with advancing age associated with higher mortality. Assuming that age <65 years carries a relative risk of 1, Tu et al (27) 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 <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 experienced a longer hospitalization and higher hospital mortality, although their long-term survival more closely matched 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 when compared with the general population (28,29), age itself should not exclude a patient from being offered treatment with CABG, assuming that there is no prohibitive comorbidity.

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 (30), smaller diameter of coronary arteries (31), increased age, and comorbidity status (32) have all been suggested as explanations for this increased risk. Despite the increased risk, long-term results appear similar to those of males (33).

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 ≈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 (34). Despite the significant

increased risk, long-term results after reoperative CABG are encouraging (35).

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 (36), most authors have found this approach to carry excessive mortality (37–39). Fibrinolytic therapy and/or PTCA 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 (ie, ventricular septal defect or papillary muscle rupture).

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 (40), the presence of PVD (41), renal insufficiency (42), and COPD have all been shown to have a negative impact on outcome after CABG.

A nonoperative 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 (43,44). Hospital mortality after CABG has also been reported to be lower when the IMA is used (45).

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 2 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. Morbidity Associated With CABG: Adverse Cerebral Outcomes. 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 (46–48). Neurological derangement after CABG has been attributed to hypoxia, emboli, hemorrhage, and metabolic abnormalities (49,50). 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 (51) 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 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 (51). Predictors of both types of cerebral complications included advanced age, especially age >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 (28,52).

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 (53). 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 (54). Duda et al (54) 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. Other authors recommended ascending aortic replacement under circulatory arrest as the best means of minimizing this complication (55,56).

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 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

Table 2. Northern New England Cardiovascular Disease Study Group: Preoperative Estimation of Risk of Mortality, Cerebrovascular Accident (CVA), and Mediastinitis (for Use Only in Isolated CABG Surgery)

Preoperative Estimation of Risk of Mortality, Cerebrovascular Accident, and Mediastinitis			
For use **only** in isolated CABG surgery			
Directions: Locate outcome of interest, eg, mortality. Use the score in that column for each relevant preoperative 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	2	3.5	
Age 70-79	3	5	
Age ≥80	5	6	
Female sex	1.5		
EF<40%	1.5	1.5	2
Urgent surgery	2	1.5	1.5
Emergency surgery	5	2	3.5
Prior CABG	5	1.5	
PVD	2	2	
Diabetes			1.5
Dialysis or creatinine ≥2	4	2	2.5
COPD	1.5		3.5
Obesity (BMI 31-36)			2.5
Severe obesity (BMI ≥37)			3.5
Total Score			
Perioperative Risk			
Total Score	**Mortality %**	**CVA %**	**Mediastinitis %**
0	0.4	0.3	0.4
1	0.5	0.4	0.5
2	0.7	0.7	0.6
3	0.9	0.9	0.7
4	1.3	1.1	1.1
5	1.7	1.5	1.5
6	2.2	1.9	1.9
7	3.3	2.8	3.0
8	3.9	3.5	3.5
9	6.1	4.5	5.8
10	7.7	≥6.5	≥6.5
11	10.6		
12	13.7		
13	17.7		
14	≥28.3		

Calculation of Mortality Risk: An 80-year-old female with an EF<40% who is having elective CABG surgery, has had no prior CABG surgery, and has no other risk factors. Her total score = 5(age≥80) + 1.5(Female) + 1.5(EF<40%) = 8. Because her total score = 8, her predicted risk of mortality = 3.9%.

Definitions:

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

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.

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.

Diabetes: Currently treated with oral medications or insulin.

Dialysis or creatinine ≥2: Peritoneal or hemodialysis dependent renal failure or creatinine ≥2 mg/dL.

COPD (Chronic obstructive pulmonary disease): Treated with bronchodilators or steroids.

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 ≥37.

Example: A patient 5'7" and weighing 200 lbs is classified as obese. If the patient weighed 236 lbs or more, he/she would be classified as 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"	158-184	≥189	**5'8"**	203-236	≥244
5'1"	164-190	≥195	**5'9"**	209-243	≥250
5'2"	169-196	≥202	**5'10"**	215-250	≥258
5'3"	175-203	≥208	**5'11**	222-258	≥265
5'4"	180-209	≥215	**6'0"**	228-265	≥272
5'5"	186-217	≥222	**6'1"**	235-273	≥280
5'6"	191-222	≥228	**6'2"**	241-280	≥287
5'7"	198-229	≥236	**6'3"**	248-288	≥296

Data set and definitions for dependent variables:

The regression models that generated the scores for these prediction rules were based on 7290 patients receiving isolated CABG surgery between 1996 and 1998. The dependent variables and observed event rates are as follows: in-hospital mortality (2.93%); cerebrovascular accident, defined as a new focal neurological event persisting at least 24 hours (1.58%); and mediastinitis during the index admission, defined by positive deep culture and/or Gram stain and/or radiographic findings indicating infection and requiring re-operation (1.19%).

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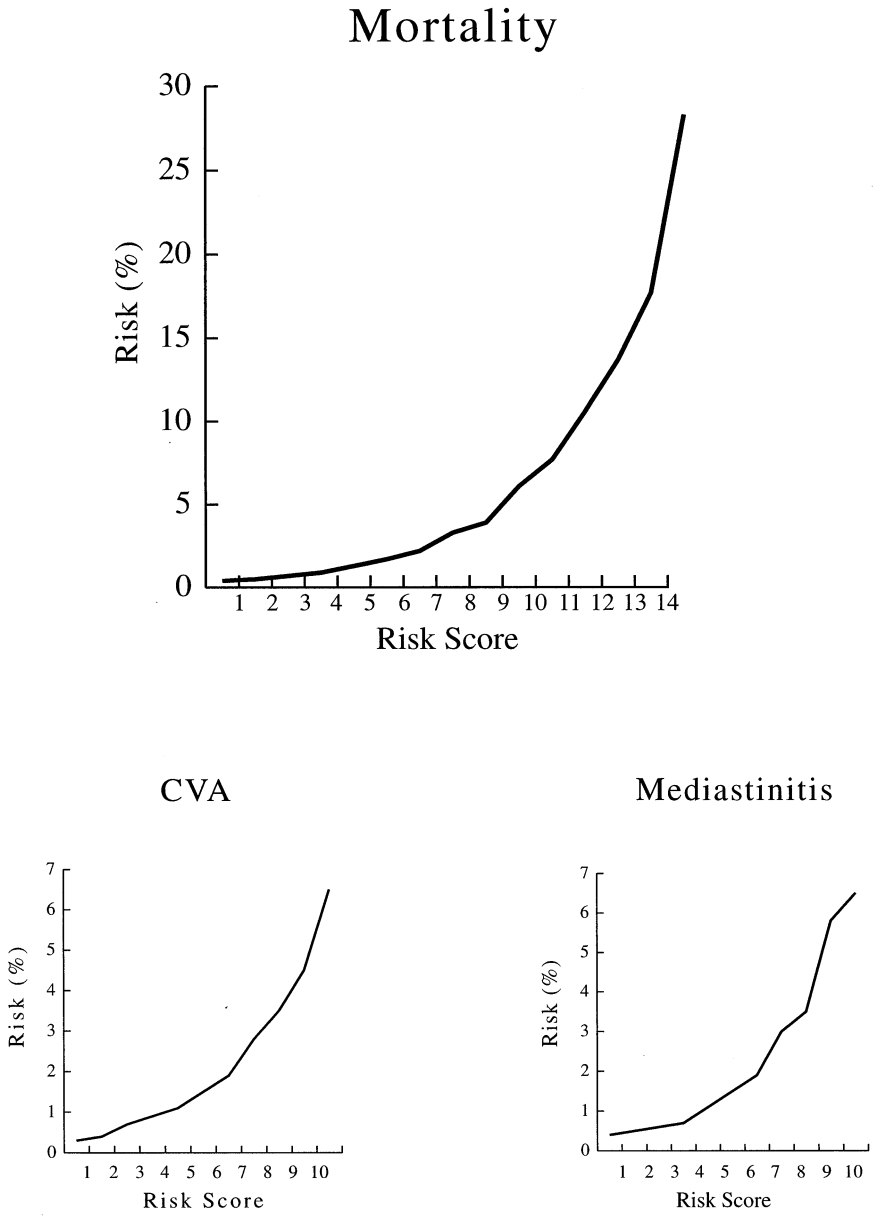


Figure 1. Event curves.

atrial fibrillation), hypertension, prior CABG, PVD, or CHF. Because aortic atherosclerosis is not a predictor of type 2 complications, encephalopathic changes may be related to the brain's microcirculation and are more likely to occur after periods of hypotension or inadequate perfusion.

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 IV, A1.

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% (57,58). Studies have consistently associated obesity and reoperation with this complication, while other risk factors such as use of 1 or 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 (59). In 1 report of 6,459 patients undergoing CABG at a

single institution, Milano et al (60) 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) (61). 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 (60,62), especially in patients requiring insulin (59). 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 ≤200 mg/dL by the continuous, intravenous infusion of insulin has been shown to significantly reduce the incidence of deep sternal wound infection in diabetic patients (63,64).

Prior cardiac surgery is another factor associated with the development of mediastinitis (60,61,65). Reoperation requires additional dissection, longer perfusion times, more bleeding, and 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 1 or more IMAs for bypass conduits and excessive use of electrocautery for hemostasis (60,66). 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 (61,62), while several others have shown no correlation with the development of mediastinitis (57,60). 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 IV, A4.

5. Morbidity Associated With CABG: Renal Dysfunction. The first major multicenter study of renal dysfunction after CABG surgery has recently been published (67). This study of 2,222 patients who underwent myocardial revascularization with CPB defined postoperative renal dysfunction (PRD) as a postoperative serum creatinine level of ≥2.0 mg/dL or an increase in the serum creatinine level of ≥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 between 1.4 and 2.0 mg/dL). The risk of PRD in patients <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 3. 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 (68–70).

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 (71–73). This conclusion has been supported by a recent study of 31 patients who underwent CABG with a baseline serum creatinine level ≥1.6 mg/dL in the 6 months before surgery and who did not require preoperative dialysis (74). 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 ≥2.6 mg/dL, 42% of survivors required chronic hemodialysis, whereas none of the surviving patients with a creatinine level ≤2.6 mg/dL required chronic dialysis. This study suggests that patients >70 years old with a creatinine level ≥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 recent report that correlated acute renal failure sufficient to require dialysis and operative mortality after cardiac surgery (75). 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

TABLE 3. Risk of Postoperative Renal Dysfunction (PRD) After Coronary Artery Bypass Graft Surgery

No. of Risk Factors	Combinations of Preoperative Risk Factors for PRD				Risk of PRD in Various Clinical Strata Depending on Risk Factors and Age		
	CHF	Reop	DM	Creat >1.4	<70 y	70–79 y	≥80 y
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)	0.0% (n=1)
	−	+	−	−	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)	0% (n=0)
	−	+	−	+	20.0% (n=25)	30.8% (n=13)	0% (n=0)
	−	+	+	−	37.6% (n=8)	33.3% (n=3)	0% (n=1)
	+	−	−	+	47.4% (n=19)	7.7% (n=26)	44.4% (n=9)
	+	−	+	−	25.9% (n=27)	18.2% (n=11)	0% (n=0)
	+	+	−	−	31.6% (n=19)	7.1% (n=14)	100.0% (n=1)
3	−	+	+	+	100% (n=1)	100% (n=1)	0% (n=0)
	+	−	+	+	8.3% (n=12)	25% (n=4)	0% (n=1)
	+	+	−	+	0.0% (n=2)	33.3% (n=9)	0% (n=2)
	+	+	+	−	33.3% (n=3)	0% (n=0)	0% (n=0)
4	+	+	+	+	50.0% (n=2)	0% (n=0)	0% (n=0)

CHF indicates prior congestive heart failure; Reop, redo coronary bypass operation; DM, type 1 diabetes mellitus; Creat >1.4, preoperative serum creatinine level >1.4 mg/dL; n, observed number of patients within each clinical stratum; −, risk factor absent; and +, risk factor present. Reproduced with permission from (67).

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

B. 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 1991 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 III, C, 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 4) (76). Other studies have identified predictors for the recurrence of angina and for postoperative MI (Table 5). 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 (77). From this encouraging result with the use of a single arterial graft has sprung

Table 4. Multivariate Analysis Predictors of Late Overall and Late Cardiac Mortality

Predictor	Risk Ratio	95% CI	*P*
Late overall mortality			
Diabetes	2.94	1.81–4.77	< 0.001
Advancing age	1.10	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; EF, rejection fraction; and IMA, internal mammary artery.

Table 5. Multivariate Analysis Predictors for Anginal Recurrence, Late MI, and Any Cardiac Event

Predictor	Risk Ratio	95% CI	*P*
Angina 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.

the arterial arborization of today, with reports of multiple and "complete" arterial grafting (78–81). This is discussed further in Sections IV, B, and VI, B.

C. 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 (ie, number of vessels with anatomically significant disease and whether or not the major epicardial 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 enrolled patients between 1972 and 1984, at which time the predominant medical therapy was the use of β-blockers and nitrates.

There are several important limitations of the randomized trials in view of current practice (Table 6). 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. 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 recent 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).

1. Overview. There were 3 major randomized trials (82–84) and several smaller ones (85–87). These studies addressed similar clinical questions and, as shown in Figures 2 and 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' follow-up (88) (Table 7). Extension of survival is a useful 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. 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

Table 6. Limitations of Randomized Trials in View of Current Practice

Patient Selection	Surgical Factors	Medical/Nonsurgical Therapy
Patients ≤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	β-Blockers used in only half of patients
	Aspirin not routinely given early postoperatively	ACE inhibitors not used
		Coronary angioplasty not widespread

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

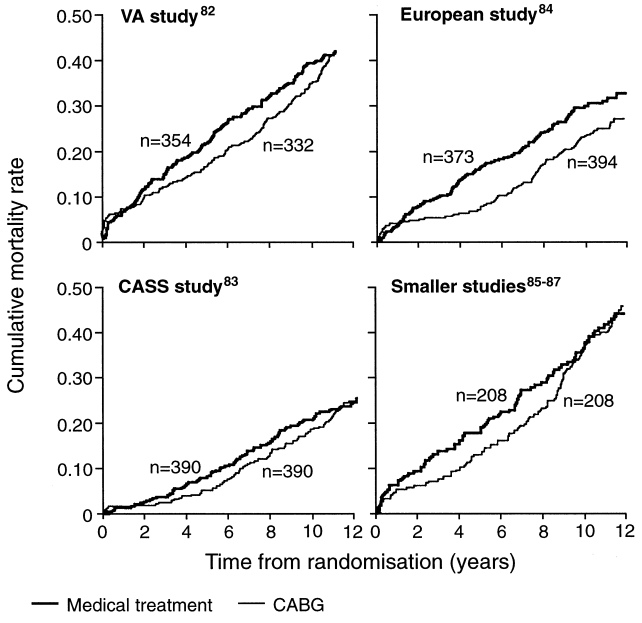


Figure 2. Survival curves of the three large studies and the four small studies combined. Reproduced with permission from (88).

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 7) (88). Two clinical scoring systems had 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 (88) developed a stepwise logistic regression analysis-based risk score that included clinical and angiographic variables as well as EF (Tables 7 through 9). 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%) (Tables 7 through 9) 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 (Tables 7 through 9). Specifically, the mean age of randomized patients was 50.8 years, there were very few patients >65 years, 96.8% were male, and only 19.7% had an LVEF <0.50 (88). 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 (89–91) and other studies (92–94) 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.

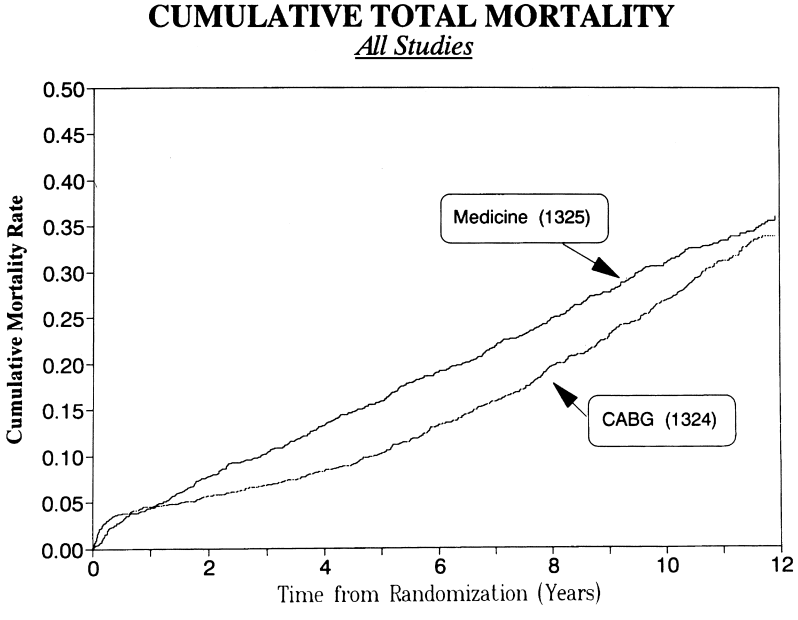


Figure 3. Cumulative total mortality. Reproduced with permission from (88).

TABLE 7. 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 (82)	332	354	58	79	0.74 (0.50–1.08)	118	141	0.83 (0.61–1.14)
European (84)	394	373	30	63	0.40 (0.26–0.64)	91	109	0.72 (0.52–0.99)
CASS (83)	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 (10.2%)	210 (15.8%)	0.61 (0.48–0.77) $P<0.0001$	350 (26.4%)	404 (30.5%)	0.83 (0.70–0.98) $P=0.03$

CABG indicates coronary artery bypass graft; CI, confidence interval; VA, Veterans Administration; and 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. Reproduced with permission from (88).

2. Location and Severity of Stenoses.

a. 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 >50% as judged by contrast angiography. The median survival for surgically treated patients is 13.3 years versus 6.6 years in medically treated patients (95,96).

Left main equivalent disease, defined as severe (≥70%) 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 (95). 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 (88). 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 (95,97,98).

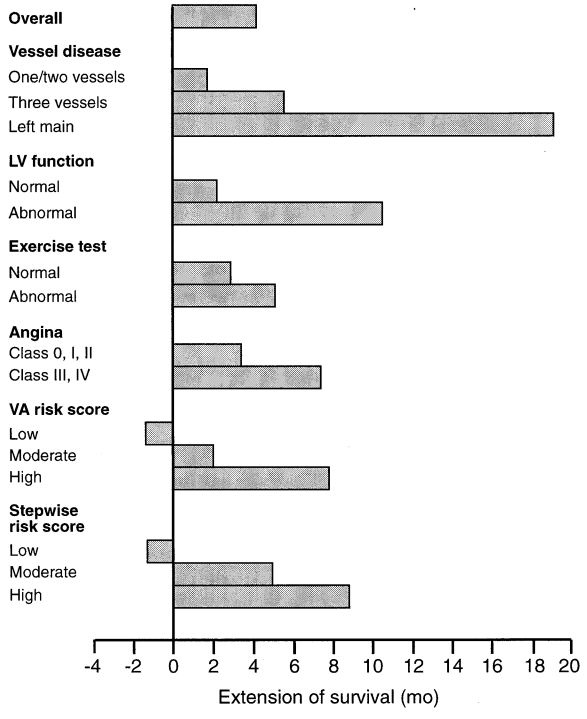


Figure 4. Extension of survival after 10 years of follow up in various subgroups from a meta-analysis of 7 randomized studies. Reproduced with permission from (88).

b. Three-Vessel Disease

Significant CAD is defined variably in the major studies. CASS originally reported results with significant stenosis defined as ≥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 (88), the 50% criterion defined significant disease for all vessels.

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 (84,88,99–103). 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 (88).

c. Proximal LAD Disease

Proximal LAD CAD (>50% stenosis) is an important contributor to outcome. In patients with proximal LAD disease, the relative risk reduction of CABG at 5 years is 42% and at 10 years, 22%. In LAD disease without proximal involvement, the relative risk reduction at 5 years is 34% and at 10 years, 10%. In the presence of depressed LV function, the absolute benefit of surgery is greater because of the risk of this population (84,104).

TABLE 8. Subgroup Results at 5 Years

Subgroup	Overall Numbers		Mortality Rates, %		Odds 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	12.0	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)	0.10
Normal	60	585	9.0	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 (82–83). †Excludes (84). ‡Excludes (84–87). §Excludes (83). Reproduced with permission from (88).

d. LV Function

LV systolic function remains an important predictor of which patients are likely to benefit from surgery (100–102,105). In patients with a normal EF, surgical revascularization 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 (100–102,106,107). 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 <0.35. Thus,

TABLE 9. 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	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. Modified with permission from (88).
*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 of >50% in the left anterior descending coronary artery) + (0.29 × right coronary artery lesion >50%) + (0.43 × history of diabetes) + (0.37 × history of hypertension).

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 V, I.

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 (108), and this as well as other subsets will be discussed in Section V.

e. Symptoms/Quality of Life

More attention has been paid recently 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 (88), no overall beneficial impact of CABG on subsequent MI could be demonstrated. This likely reflects 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 (99). At 10 years, however, these differences were no longer significant. Patients treated surgically and medically used similar amounts of long-acting nitrates and β-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 (109–116).

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 <0.35) (109,111–117). Perhaps because of the symptomatic relief associated with surgical revascularization, the "crossover" from medical treatment to surgery may be of greater significance 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.

f. 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 decreased long-term 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.

g. 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 $\approx$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 $>$20%). Clinical and angiographic markers of risk, including severity of CAD, LV dysfunction, and myocardial ischemia, can identify patients in various risk strata.

D. 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. Recent clinical trials comparing PTCA and CABG have further defined the relative advantages and disadvantages of these treatments.

1. Overview of Randomized Trials. Nine randomized, clinical trials comparing PTCA and CABG have been published (Table 10). 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 ≈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 ≈4,000 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 ≈2,000 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, the Bypass Angioplasty Revascularization Investigation (BARI), comes closest to fulfilling these criteria and will be discussed in detail (118).

In this trial, 1792 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 (118). 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%, $P < 0.05$), 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 repeated revascularization procedures (Table 10). Thirty-one percent of patients initially assigned to PTCA underwent CABG during the trial (118). 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 generalizability of the conclusions. The findings are not applicable to all patients with multivessel coronary disease for 2 reasons. First, only ≈5% of screened patients with multivessel disease were enrolled in the trials (119,120). In the BARI trial, >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 4110 patients had multivessel disease suitable for both PTCA and CABG, and only half of these (7% of those screened) were enrolled in the randomized trial (121). 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 (122). 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 (122).

The age range (mean age varied from 56 to 61 years) and sex distribution (≈20% female) were similar in most trials, although the Medicine, Angioplasty, or Surgery Study (MASS) trial had 42% women (123). 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 10). Several trials were conducted in single centers, whereas RITA, the German Angioplasty Bypass-surgery Investigation (GABI), the Coronary Angioplasty versus Bypass Vascularization 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

TABLE 10. CABG vs PTCA: Randomized Controlled Trials

				Acute Outcome, %			Late Outcome, %						
Trial*	Age, y (% Female)	CAD	N	Death: CABG PTCA	QW-MI: CABG PTCA	Hosp CABG	Death	QW-MI	Angina	RR Total/PTCA/ CABG, %	Primary End Point	Primary End Point, %	F/U, y
BARI (118)	61 (26%)	MV	1792	1.3	4.6	…	10.7	19.6	…	8/7/1	D	10.7	5
				1.1	2.1	6.3	13.7	21.3	…	54/34/31		13.7	
EAST (120)	61 (26%)	MV	392	1.0	10.3	…	6.2	19.6	12	13/13/1	D+MI+T	27.3	3
				1.0	3.0†	10.1	7.1	16.6	20	54/41/22		28.8	
GABI (146)	… (20%)	MV	359	2.5	8.0	…	6.5	9.4	26	6/5/1	A	26	1
				1.1	2.3†	8.5	2.6	4.5	29	44/27/21		29	
Toulouse (147)	67 (23%)	MV	152	1.3	6.6	…	10.5	1.3	5.3	9/9/0	A	5.2	5
				1.3	3.9	3.9	13.2	5.3	21.1†	29/15/15		21.1†	
RITA (127)	57 (19%)	SV+	1011	1.2	2.4	…	3.6	5.2	21.5	4/3/1	D+MI	8.6	2.5§
		MV‡		0.8	3.5	4.5	3.1	6.7	31.3	31/18/19		9.8	
ERACI (132)	58 (13%)	MV	127	4.6	6.2	…	4.7	7.8	3.2	6/3/3	D+MI+A+RR	23	1
				1.5	6.3	1.5	9.5	7.8	4.8	37/14/22		53†	
MASS (123)	56 (42%)	SV	142	1.4	1.4	…	…	…	2	0/0/0	D+MI+RR	3	3
		(LAD)		1.4	0	11	…	…	18	22/29/14		24†	
Lausanne (133)	56 (20%)	SV	134	0	0	…	1.5	1.5	5	3/3/0	D+MI+RR	7.6	2§
		(LAD)		0	0	2.9	0	2.9	6	25/12/13		36.8†	
CABRI (137)	60 (22%)	MV	1054	1.3	…	…	2.7	3.5	10.1	9/6/1	D	2.7	1
				1.3	…	…	3.9	4.9	13.9†	36/21/18		3.9	
Weighted	60 (23%)			1.3	4.1	…	6.5	11.3	10.4	7.3			
average				1.0	2.3	5.9	7.7	11.0	15.5	42.3			

CABG indicates coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; CAD, coronary artery disease; QW, Q wave; MI, myocardial infarction; Hosp CABG, required CABG after PTCA 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, Randomised 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; MV, multivessel; D, death; T, thallium defect; A, angina; SV, single vessel; and LAD, left anterior descending coronary artery.

*$P < 0.05$ comparing CABG and PTCA cohorts. †$P < 0.05$ comparing CABG and PTCA cohorts. ‡Included total occlusion. §Planned 5-year follow-up (interim results).

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 >40% of BARI and Estudio Randomizado Argentino de Angioplastia vs Cirugia (ERACI) patients. The incidence of diabetes mellitus varied from 10% to 12% (Toulouse, Goy, ERACI, GABI, and CABRI) to >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 10). 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 (123). Overall, all of the trials except BARI were underpowered and lacked sufficient follow-up.

2. Results of Randomized Trials

a. 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 10). A statistically significant increase in MI rate was present only in GABI and EAST and in two meta-analyses including many of the trials (119,124). 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 (124).

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 (125,126). The lengths of stay in RITA were 4 and 12 days for PTCA and CABG, respectively (127). Patients having PTCA returned to work sooner and were able to exercise more at 1 month (128). The extent of revascularization achieved with CABG was higher than with PTCA (118,120). In the EAST trial, the percentage of revascularizable segments successfully treated was 99% for CABG versus 75% for PTCA (120). 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 (120,129).

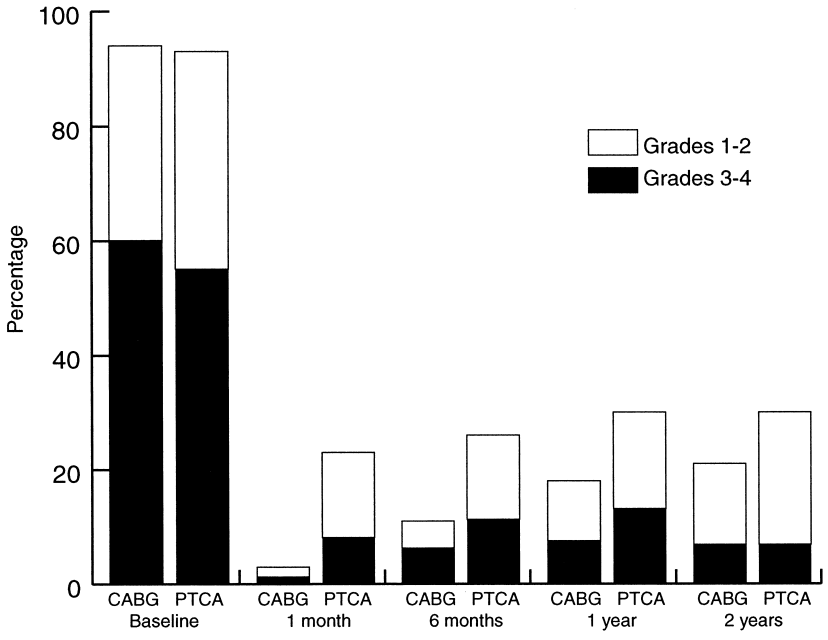
b. Long-Term Outcome

There was no significant difference in survival in any of the nine randomized trials that compared PTCA and CABG at follow-up periods ranging from 1 to 5 years (Table 10). BARI was the largest trial with the longest follow-up. Survival was 89.3% after CABG and 86.3% after PTCA (118). Although this 2.9% absolute difference was not statistically significant, the 95% confidence interval was wide (−0.2% to 6.0%), and this study did not establish with certainty the equivalence of these strategies (130). In fact, the results are consistent with the level of clinically important difference in mortality stated in the protocol (>2.5% absolute difference) in favor of CABG. A secondary analysis of 5-year cardiac mortality demonstrated a significant survival advantage with CABG (95.1% versus 92% in patients assigned to PTCA), but this difference was not apparent in nondiabetics (131). The combined end point of cardiac mortality and MI was similar at 5 years with both treatments (131).

Similarly, 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 10) (119,124). 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) (127). Large thallium defects (assessed in EAST) were slightly more common in PTCA patients at 3 years (120). The relative risk for angina with PTCA tended to be higher early but decreased with longer follow-up (124) (Figure 5).

The most striking difference between the treatments was in the need for subsequent procedures. The rate was four- to tenfold higher for PTCA in every trial (Table 10). 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 (123,132,133). Eight percent of CABG patients required additional revascularization within 5 years in BARI, compared with 54% of PTCA patients (118). Additional procedures were needed earlier in PTCA patients and included PTCA only (23.2%), CABG only (20.5%), or both (10.8%) (118).

Several studies have compared quality of life and cost (125,128,134,135). In RITA, physical activity and employment were similar for both procedures after 3 years (128). 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 (125). Emotional health and employment were also similar in this study and others (125,128,134). The early cost benefit of PTCA decreased during follow-up owing to the more frequent need for repeated procedures and hospitalization approaching the cost of CABG (124,125,134,135). There appeared to be a greater cost benefit to PTCA in patients with 2-vessel disease (125). In BARI, it was estimated that the slight survival advantage of CABG would cost $26,117/y of added life (125).



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	297
PTCA	509	491	491	433	310

Figure 5. Freedom from angina in the Randomized Intervention Treatment of Angina (RITA) trial. Reproduced with permission from (127).

c. 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 (118). However, 3-year cardiac mortality was higher with PTCA in several high-risk groups (in unstable angina and non–Q wave MI, PTCA 8.8% versus CABG 4.9%; in CHF, PTCA 27.7% versus 16.4% with CABG) (131). The ERACI trial included a high proportion (83%) of patients with unstable angina, and there was no difference in survival at 1 year (132).

Data from thrombolytic 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 BARI (118,136). This subgroup of 353 patients (19% of total) were 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 nondiabetics and were also higher for CABG than for PTCA (136).

All-cause mortality and cardiac mortality were both higher in diabetics treated with PTCA (34.7% versus 19.1% and 20.6% versus 5.8%, respectively) (136) (Figure 6). 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 diabetic patients was found in a post hoc analysis of 122 diabetic patients in CABRI (137), but no difference was found for diabetics in EAST (120).

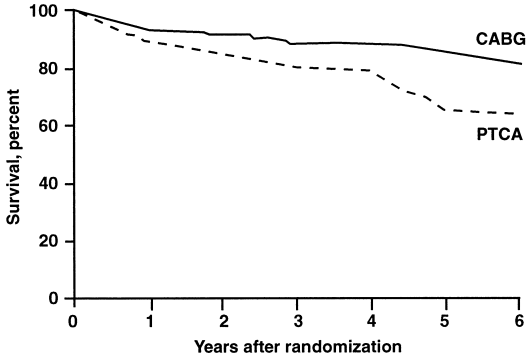


Figure 6. Improved survival with CABG versus PTCA in diabetes mellitus. Results from the Bypass Angioplasty Revascularization Investigation (BARI) showing that patients with multivessel coronary disease who were being treated for diabetes at baseline had a significantly better survival after coronary revascularization with coronary artery bypass graft (solid curve) than with percutaneous transluminal coronary angioplasty (dashed curve) (P = 0.003). Modified with permission from (136).

A separate meta-analysis of the randomized trials for single-vessel disease has also been performed (124). As expected, the overall risk for events is 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 (124).

d. Results From Nonrandomized Trials and Registries

Much of the debate relating to the finding for a survival advantage of CABG in treated diabetic patients is based on the results of nonrandomized trials and registries. Treated diabetics in the BARI registry who refused randomization and selected their form of revascularization did not fare worse with PTCA (138). In a retrospective cohort study comparing PTCA and CABG for diabetic patients with multivessel disease and similar age, sex, EF, and severity of angina, there was also no difference in survival after 6 years (139). However, in one comparison of CABG and PTCA in a nonrandomized, observational database, insulin-requiring diabetics had a lower long-term survival after treatment with multivessel PTCA (140). 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 (141).

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 (142). In this nonrandomized trial, CABG provided superior relief of exercise-induced as well as ambulatory ischemia compared with PTCA (143).

A more compelling report was recently published by Hannan et al (144), 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 survival benefit for patients receiving CABG when proximal LAD stenosis was >70%, regardless of whether 1-, 2-, or 3-vessel disease was present (Figures 7A and 7B and Table 11). 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 PTCA patients.

e. 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 is the cost and length of hospitalization. Patients may return to work sooner after PTCA 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 possibly in patients with treated diabetes mellitus, for whom CABG may be superior. Contrariwise, data from large registries, particularly that 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 PTCA.

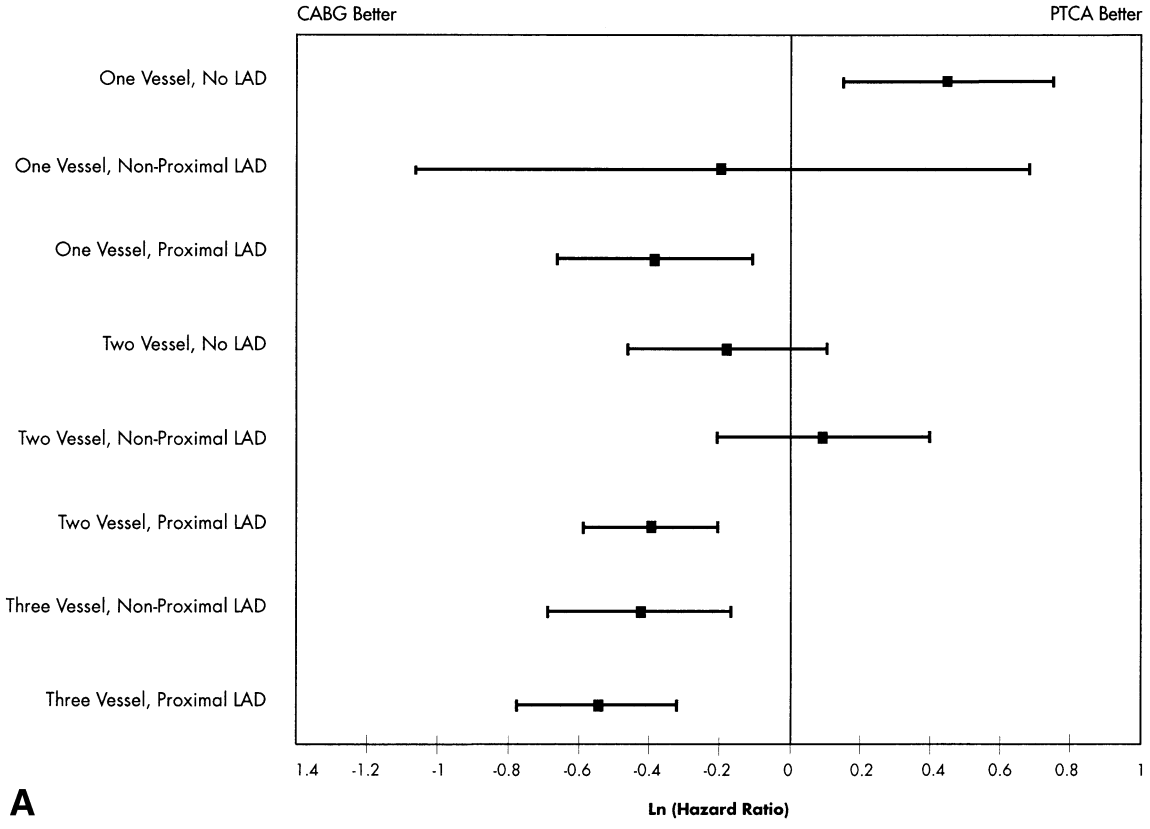
Several important caveats and limitations to these conclusions must be discussed. Since completion of the trials, the influence of new technology, particularly on PTCA, has been considerable. Intracoronary stents are now used in 50% or more of percutaneous coronary interventions and have reduced the need for both urgent CABG and subsequent procedures by as much as 50% (145). Continuing advances in PTCA and stent designs, including the use of brachytherapy (local radiation), will likely further reduce the need for repeated procedures. Medical management of atherosclerosis, both before and after revascularization, has continued to evolve, with greater use of β-blockers and angiotensin-converting enzyme inhibitors after MI and the introduction of statins and other lipid-lowering agents. The recent 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 recent changes in patient management that may influence these conclusions include the use of platelet glycoprotein IIb/IIIa 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.

IV. MANAGEMENT STRATEGIES

A. 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 (148). 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



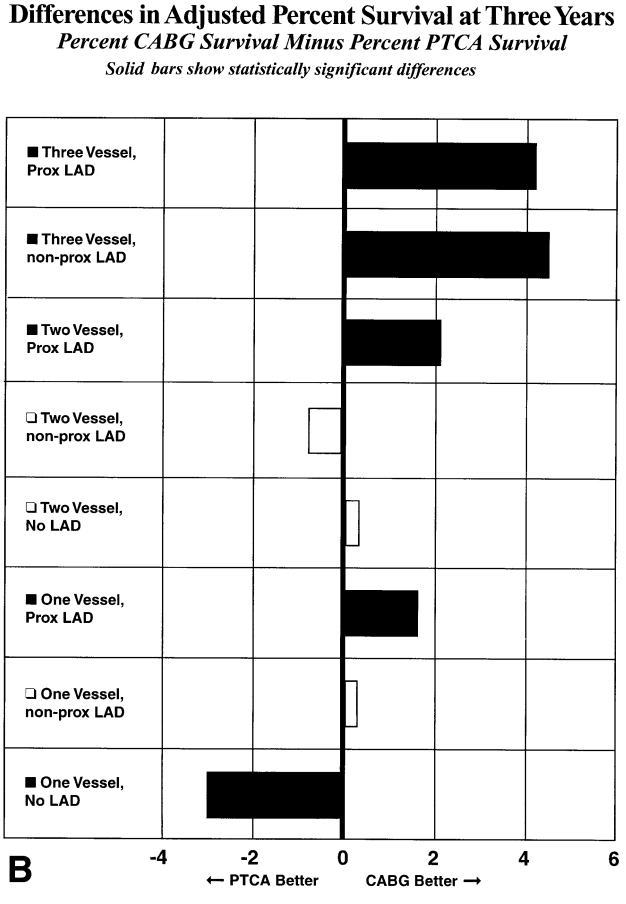


Figure 7. A, 95% Confidence interval for ln (adjusted hazard ratio) of PTCA patient death: CABG patient death within a three-year period (excluding patients with myocardial infarction [MI] <24 h before the procedure). For sample size within each anatomic cohort, see Table 10. (Reprinted with permission from [144].) B, Differences in adjusted percent survival at 3 years: percent CABG survival minus percent PTCA survival. Solid bars show statistically significant differences.

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TABLE 11. Three-Year Survival by Treatment in Each Anatomic Subgroup

Coronary Anatomy Group		Patients, n	Survival		*P*
			Observed, %	Adjusted, %	
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. Reprinted with permission from New York State registry as published in (144).

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.

1. Reducing the Risk of Brain Dysfunction After Coronary Bypass. As discussed in Section IV, A, 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 (149–151). Postoperative stroke is the second most common cause of operative mortality (after low cardiac output state) (152). The incidence of stroke after coronary operation is related to increased age (Figure 8A) (153), which parallels the accelerated involvement of the aorta and great vessels with atherosclerotic plaque (Figure 8B) (152). 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 Section III, A3, 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.

a. 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).

(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, $P < 0.05$) (51), reflecting the role of aortic atheroembolism as the cause of ischemic stroke (157–161). 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 (162). 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 (163). This risk is particularly increased in patients beyond 75 to 80 years old (53) (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 blast effect of the flow from the aortic cannula (156,164). Preoperative, noninvasive testing for detection of the high-risk patient has limited sensitivity. Computed tomography identifies most severely involved aortas but underestimates mild to moderate involvement compared with echocardiography (159,165). TEE is useful for aortic arch examination, but evaluation of the ascending aorta is somewhat limited by the intervening trachea (166). The intraoperative assessment of ascending aortic atheroma by epiaortic imaging (in which the imaging

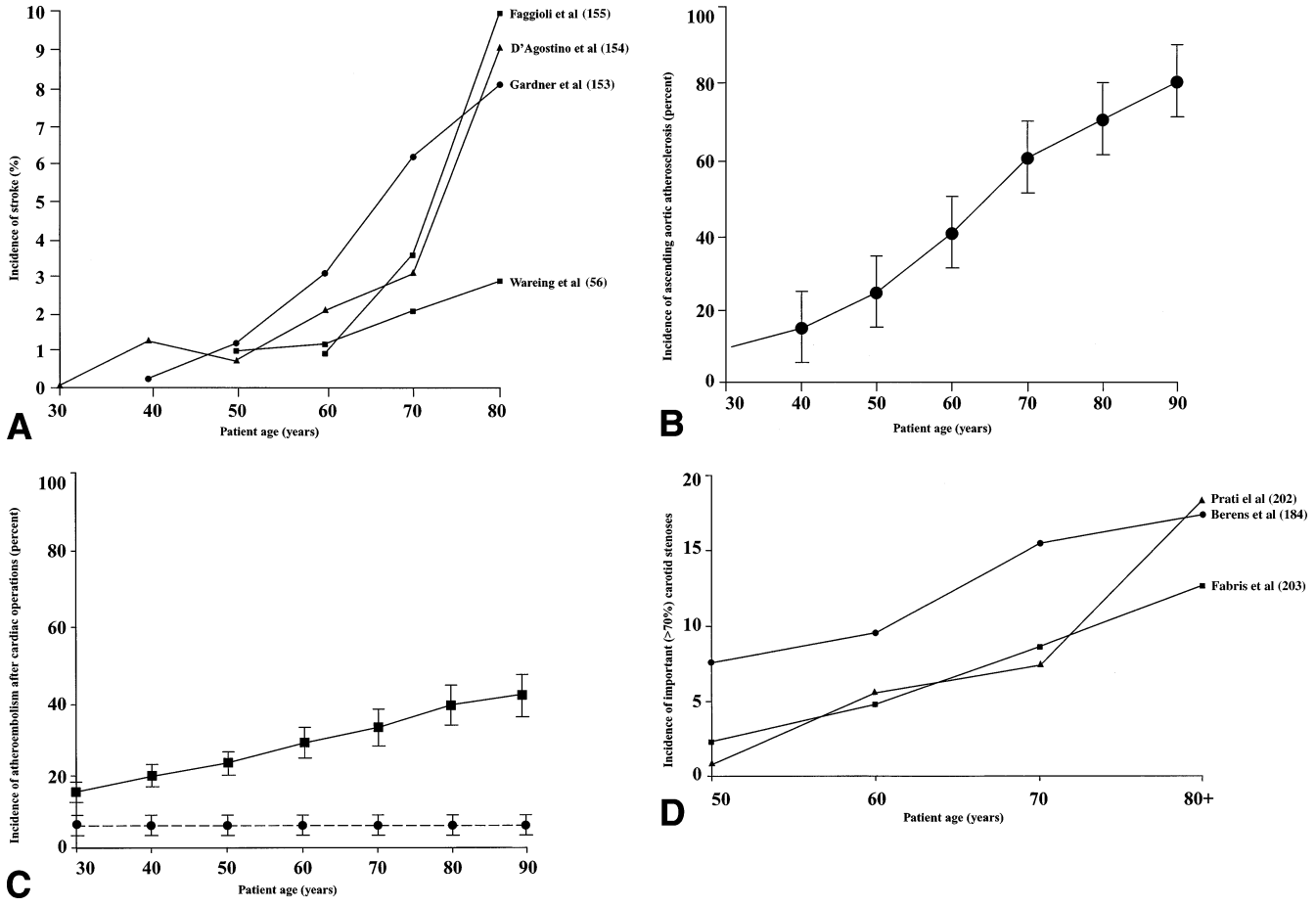

Figure 8. A, Incidence of permanent, focal, central nervous system injury after coronary bypass is strongly correlated with increasing age (56,153–155). B, Ascending aortic atherosclerosis is a powerful marker of increased risk for perioperative stroke in the coronary bypass population and increases 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 and 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 (184,202,203). Reproduced with permission from (156).

probe is placed directly on the aorta) is superior to both TEE and direct palpation (166).

Nevertheless, TEE identification of a mobile arch atheroma in coronary bypass patients was associated with a 33% stroke rate versus 2.7% in patients with nonmobile plaque ($P = 0.01$) (167). Intraoperative palpation is notorious for its underestimation of the high-risk aorta (166). Palpation detected only one third of atherosclerotic lesions identified by epivascular echocardiography (165). The aortic pattern with the highest risk is the protruding or mobile aortic arch plaque, and this eludes intraoperative palpation in 80% of cases (168). Intraoperative epivascular echocardiography represents an important advance and is now used in many centers for intraoperative diagnosis and stroke risk reduction (165,169). 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 echocardiographic imaging appears to reduce the risk of postoperative stroke (56,170). Twelve hundred of 1,334 consecutive open heart patients (88% with coronary disease) underwent screening intraoperative epivascular echocardiography. These findings led to a change in intraoperative technique in 19.3% of patients. In patients with ≤3-mm wall thickening, standard techniques were used. When the aorta demonstrated a >3-mm thickening, the cannulation, clamp, or proximal sites were changed, or a no-clamp fibrillatory arrest strategy (171) 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 echocardiography showed no or mild atherosclerotic disease, the stroke incidence was low, 1.1% (56,171).

In a smaller study of epivascular echo-directed management, 195 consecutive coronary bypass patients 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 ($P < 0.02$) (54).

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 (163,172).

Preoperative risk assessment may identify a small population of patients with such extensive aortic atherosclerosis and poor outlook that 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 with certain morphologies that are associated with only a 20% chance at 4 years of freedom from peripheral embolism, MI, recurrent stroke, or death (161). 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 >20%), alternative forms of revascularization should be considered. These include off-bypass surgery; minimally invasive direct CABG (MID-CAB) without CPB, with or without concomitant PTCA; and exclusive percutaneous revascularization. These techniques may provide the benefit of revascularization in such high-risk patients while minimizing the perioperative risk of stroke.

(2) Atrial Fibrillation and Postoperative Stroke

Chronic atrial fibrillation is a hazard for perioperative stroke as a result of cardioarterial 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 (173–175), with the peak incidence on the second to third postoperative day (176). It is associated with a 2- to 3-fold increase in postoperative risk for stroke (177,178). 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 β-blockers. Identifying at-risk patients and directing treatment to these patients (see Section IV, A5) 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 procedures may also reduce the incidence of postoperative atrial fibrillation (179).

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. 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. If the atrial fibrillation persists, anticoagulation with Coumadin on an outpatient basis may be necessary, with further attempts at cardioversion determined by the individual patient profile.

(3) Recent Anterior MI, LV Mural Thrombus, and Stroke Risk

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 (180) identified LV thrombus in 38 of 124 anterior-infarct patients (31%) and in none of 74 patients with inferior infarcts ($P < 0.001$). Early thrombolytic therapy was not uniformly protective against LV thrombus, and 30% occurred after discharge. Such patients are at risk for perioperative mechanical dislodgement and systemic embolization of the LV clot. Preoperative screening with echocardiography may demonstrate the clot and allow delay of the operation for long-term anticoagulation and reevaluation by echocardiography to ensure resolution or organization of the thrombus before operation. Also, long-term (3 to 6 months) anticoagulation appears prudent for the patient with persistent anterior wall-motion abnormalities after coronary bypass. LV thrombus may recur in patients receiving short-term (2 months) anticoagulation. Apical akinesis at 10 days after infarction was a strong predictor for subsequent thrombus formation, which conferred an increased risk for subsequent stroke (181).

(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 cardiopulmonary bypass (182).

It is generally believed that a delay of 4 weeks or more is prudent if coronary anatomy and symptoms permit.

(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 (183).

(6) Carotid Disease and Neurological Risk Reduction

The problem, rationale, and strategy for concurrent treatment. Carotid disease is significantly associated with a type 1 neurological outcome ($P = 0.001$) (51). Hemodynamically significant carotid stenoses are associated with as many as 30% of early postoperative coronary bypass strokes (154). 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 (155). The trend for coronary surgery to be performed in an ever-increasingly elderly population underscores the importance of the issue (Figure 8D). The prevalence of significant carotid disease in the current cardiac surgical 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 (184,185). Perioperative stroke risk is ≤2% when carotid stenoses are <50%, 10% when stenoses are 50% to 80%, and 11% to 18.8% in patients with stenoses >80% (56,186). 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 (187,188).

Conversely, the leading cause of short- and long-term risk for patients having surgical treatment of carotid disease is the associated coronary disease (189–192). Coronary bypass is the most effective treatment for many of these patients. In the proper hands, prophylactic carotid endarterectomy is superior to conservative therapy for prevention of stroke in symptomatic or asymptomatic patients with high-grade carotid stenoses (193–195).

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 neurological sequelae (155,187,189,196) (Figure 9). Carotid endarterectomy done before or concomitant with coronary bypass carries a low mortality (3.5%), reduces early postoperative stroke risk to <4%, and confers a 10-year freedom from stroke of 88% to 96% (187,196,197). Special interest in this problem among caregivers and careful collaboration between the carotid and coronary surgical teams are keys to success. Also, stroke and mortality rates after carotid endarterectomy are inversely related to institutional volume (198,199).

Who should undergo carotid screening? The absence of symptoms referable to carotid disease is not reassuring: a carotid stenosis of ≥75% in an *asymptomatic* patient is an independent predictor of stroke risk immediately after coronary bypass (OR of 9.87, $P < 0.005$) (154,155). 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%) (200).

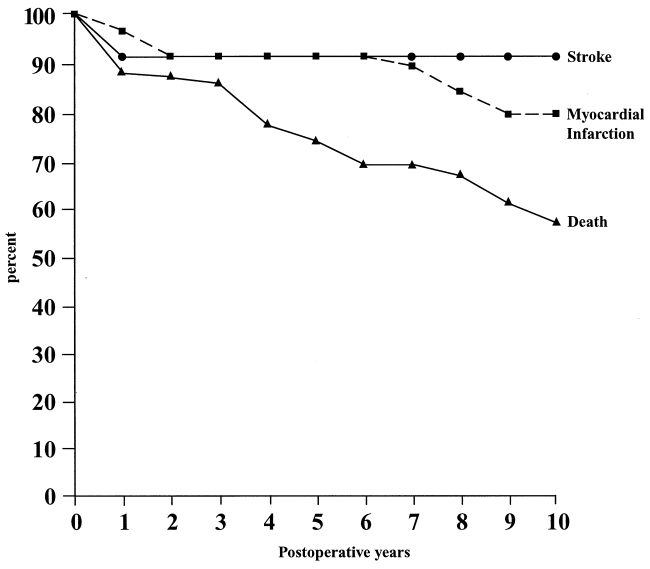

Figure 9. Contemporaneous surgical treatment of carotid and coronary disease is associated with an excellent long-term outcome. The graph shows freedom from stroke, myocardial infarction, and death over time. Reproduced with permission from (196).

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 ($P < 0.05$) (184). If all patients with at least one 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.

Surgical tactics to reduce the risk for concurrent carotid/coronary disease. 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 special attention to prevent postoperative myocardial ischemia. Coronary bypass 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 (196) of 7 published series, each with ≥100 patients, published from the mid-1980s to the mid-1990s had an overall mortality of 4% and 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 (201). 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 (196).

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 a stroke risk of 14% when carotid operation followed rather than preceded (2.8%, $P < 0.05$) coronary bypass, whereas mortality rates were similar (204). It is generally accepted that cerebral revascularization should precede coronary revascularization when significant carotid disease is known, except in the uncommon situation of the truly emergency coronary bypass 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. Recent multicenter trials have shown an advantage of surgical over medical management for significant carotid stenosis in either symptomatic or asymptomatic patients (193,205–207). 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 coronary bypass is in concordance with *Guidelines for Carotid Endarterectomy: A Multidisciplinary Consensus Statement From the Ad Hoc Committee, American Heart Association [Special Report]* (208). The success of this long-term strategy is predicated on assembling a team that can achieve excellent near-term carotid and coronary surgical results (198,199,209–211).

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 14). 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.

b. Type 2 Neurological Injury

Type 2 neurological complications occur in 3.0% of patients and are correlated with a 10% post-coronary bypass mortality rate, an average of 7 days in the intensive care unit and 20 days in hospital, and at least an additional $6150 of in-hospital charges. Forty percent of these patients incur additional costs as a result of the need for transitional care after hospital discharge (51,148).

Abnormal neurocognitive function is frequently present preoperatively in the coronary bypass population (212). 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 (46). This deficit usually improves over time, such that by 2 months' follow-up, there is little to no difference between patients having undergone major operations without extracorporeal circulation compared with coronary bypass patients with extracorporeal circulation. Both groups frequently show subtle neurological and neuropsychological impairment (213–216).

(1) Reducing the Risk of Microembolization

Microembolization is a major contributor to postoperative cerebral dysfunction after coronary bypass (217,218). 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 (217,219,220). 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 (221). These vacuolated vascular abnormalities have also been seen after catheter manipulation of the ascending aorta, suggesting an atheroembolic etiology. Small gaseous or lipid 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 (222). The use of a 40-μm 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 (183,223,224).

(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 (225,226). 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%, $P = 0.047$) (227).

(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 recent 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 (228–231). Hyperglycemia may also amplify the impairment caused by an acute neurological event, emphasizing the importance of meticulous perioperative glucose monitoring and control (231).

Cerebral edema that may be present in patients immediately after extracorporeal circulation (232) 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 (233–235).

2. Reducing the Risk of Perioperative Myocardial Dysfunction. Most modern myocardial protection techniques allow the coronary bypass patient 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 (236,237). There is no substitute for a well-orchestrated, technically sound, expeditious operation to minimize risk.

a. Myocardial Protection for the Patient With Satisfactory Preoperative Cardiac Function

The wide latitude of techniques associated with excellent results for the majority of coronary bypass patients is testimony to the fact that there is no "ideal" or universally applicable myocardial protection technique (238). 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 elective coronary bypass patients demonstrated a low, perioperative MI rate (1.4% warm versus 0.8% cold, NS), IABP use (warm 1.4% versus cold, 2.0%, NS), and mortality (1.0% warm versus 1.6% cold, NS) with either technique (236). 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 (239–242). Certain techniques, however, offer a wider margin of safety for special patient subsets.

b. Myocardial Protection for Acutely Depressed Cardiac Function

In contrast to the patient with normal myocardial function, it is easier to demonstrate benefit from specialized protocols (243,244) in the patient with an acutely injured ventricle. One multicenter study of emergency coronary bypass 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 coronary bypass series (245). Preoperative regional wall-motion abnormalities improved after bypass in 87% of these patients despite an average of >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 coronary bypass after failed angioplasty. There

was a significant *reduction in MI* with the sanguineous technique (65% infarcts with crystalloid versus 26% for blood, $P < 0.007$) (246). Multivariate analysis confirmed normothermic blood cardioplegia as an independent predictor of freedom from infarct in this study ($P < 0.005$). 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 (247). Multivariate analysis confirmed that crystalloid cardioplegia ($P = 0.008$) was a significant, independent predictor of postoperative morbidity when compared with warm blood cardioplegia (248).

c. Protection for Chronically Dysfunctional Myocardium

Severe LV dysfunction is an important risk factor for patients undergoing coronary bypass (249). Efforts to document reduction of risk in this cohort are confounded by incomplete data on the prevalence of reversibly ischemic systolic dysfunction (hibernating myocardium) and the contribution of improved function from revascularization of myocardium as opposed to myocardial protection strategies (250). There is an emerging consensus, however, that for the chronically impaired ventricle, there is an added margin of safety provided by blood cardioplegic techniques (250–252). Its theoretical advantages include superior buffering capacity, rheological considerations at the capillary level, and free-radical control when compared with crystalloid cardioplegia.

d. Adjuncts to Myocardial Protection

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 of $\leq$0.25 demonstrated a 4-fold reduction in 30-day mortality in patients treated with IABP. Thirty-day mortality was 2.7% in patients who received a prophylactic IABP placed preoperatively versus 11.9% for patients not receiving a balloon ($P < 0.005$). IABP use was also associated with a shorter hospital stay and lower hospital charges (253). A recent, randomized trial confirmed the benefit of preoperative IABP support in high-risk patients. Placement of the IABP immediately before operation afforded similar protection to that accompanying placement the day before bypass surgery (254,255).

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 (256–260). 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 (12,261). Less appreciated is the reduction in immediate, operative mortality associated with the use of the mammary artery as opposed to saphenous revascularization. Its use may thus be considered an adjunct to myocardial protection. Its use should be encouraged in the elderly (262,263), the emergent/acutely ischemic patient (264), and other subgroups that previously were thought not to receive its immediate and long-term benefit. The large, coronary bypass database available to the STS (265) 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 ($P < 0.005$), sex ($P < 0.005$), priority of operation ($P < 0.005$), normal ($P < 0.01$) or reduced ($P < 0.005$) LV function, diabetics ($P < 0.005$), obese patients ($P < 0.005$), history of previous infarct ($P < 0.005$), previous PTCA ($P < 0.001$), and any pattern of coronary anatomy ($P < 0.005$). Multivariate analysis also confirmed use of the IMA as an independent predictor of operative survival ($P < 0.0025$). 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 >70 years of age.

e. Reoperative Patients

For patients undergoing repeated CABG surgery who previously have had a left IMA-to-LAD graft, a concern has been the inadvertent transection of the graft during sternotomy. However, one report from a high-volume center showed that experienced surgeons rarely encountered this complication (<3%) (266). 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 (266). A risk-neutralizing 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.

f. Inferior Infarct With Right Ventricular Involvement

Right ventricular (RV) failure secondary to an ischemic RV (either infarction or stunning) presents a particularly hazardous situation (267). 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 (268–272). 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 (273). 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 (274). 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 (275). 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 (276).

The best defense is an index of suspicion and recognition of the RV dysfunction by physical examination (277,278), electrocardiography (right precordial leads), echocardiography, or radionuclide-gated blood pool study (273,278–280). If early PTCA of the right coronary artery is indicated, this should be performed. It is best to delay surgery for ≥4 weeks to allow recovery of RV function.

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 (281,282). Numerous strategies have been shown to blunt this counterproductive immune response (281). 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 (283–287). 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 intensive care unit (288–292). Although there is no demonstration of an increased risk for infection in studies to date, it may be prudent to avoid the use of steroid in diabetic patients (291). 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 (293). 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 (283).

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 (281). However, there are insufficient data at present to make a strong recommendation for the routine use of this relatively expensive drug (283) (Table 14) (287,294).

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 (281,295–297). 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 (281,298–302). 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 guidelines are not at hand.

4. Reducing the Risk of Perioperative Infection. Multiple opportunities exist for infection risk neutralization in coronary bypass patients. 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 (303,304), clipping rather than shaving the skin (305–308), avoidance of hair removal (61), reduction of operating room traffic, laminar-flow ventilation, shorter operations, minimal electrocautery (66), avoidance of bone wax (309), use of double-gloving barrier techniques for the operating team (310–314), and routine use of an easily constructed pleuropericardial flap (315) have all been shown to be of value in reducing postoperative infection (63).

Several newer strategies that are easily integrated into practice deserve consideration. Diabetes mellitus afflicts 1 of 5 coronary bypass patients and is an independent risk factor for wound infection (316). The risk for deep sternal wound infection is halved by aggressive perioperative glucose control by using a continuous, intravenous, insulin infusion

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TABLE 12. Prophylactic Antimicrobials for Coronary Artery Bypass Graft Surgery (322, 421–423)

Cephalosporins	Equivalent Efficacy IV Dosing Regimens Dose and Interval	Cost per Dose	Comments
Cefuroxime	1.5 g preoperatively 1.5 g after CPB 1.5 g Q12×48	$6.33/1.5 g	First-line agents; low toxicity; pharmacokinetics vary; shorter prophylaxis duration <24 h may be equally efficacious for cefuroxime
Cefamandole, cefazolin	1 g preoperatively 1 g at sternotomy 1 g after CPB 1 g Q6×48 (Initial dose to be given 30–60 minutes before skin incision)	$6.27/g $0.90/g	
Vancomycin	1 g Q12/h/until lines/tubes out At least 2 doses (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.

(0.9% deep sternal wound infection) versus intermittent subcutaneous insulin treatment (1.9%, $P = 0.04$) (63).

Homologous blood transfusions after coronary bypass 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 (317,318). A retrospective study of 238 coronary bypass patients demonstrated this immunosuppressive effect of transfusion. Wound and remote infections occurred in 4% of patients who received ≤2 U of red blood cells, in 7% of those transfused with 3 to 5 U, and in 22% in those having received ≥6 U (317). Leukodepletion strategies have been shown to blunt the immunosuppressive effect of blood transfusion in surgical patients (318). 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 (319). A single-center prospective trial of 3 transfusion protocols in 914 cardiac surgical patients showed a significant reduction for patients receiving leukocyte-depleted blood (17.9%) as opposed to nonfiltered blood (23.5%, $P = 0.04$) for all infections (respiratory, urinary tract, bacteremia, and wound) (318). 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% ($P = 0.019$) (318). The reduction in the postoperative rate of noncardiac causes of death (ie, multisystem failure) in leukocyte-depleted/transfused patients compared with patients receiving nonfiltered blood was highly significant ($P = 0.001$) (318). 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 (320). Prophylactic antimicrobial efficacy is dependent on adequate drug tissue levels before microbial exposure (321,322). 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 12) (323). Institution- or surgeon-specific selection is appropriate within this class (323). Data suggest that a 1-day course of intravenous antimicrobials is as efficacious as the traditional 48-hour (or longer) regimens (324–327). There is little evidence that prolonging (≥2 days) the antimicrobial prophylaxis even in high-risk patients provides any benefit (328). A 1-day course of antimicrobial prophylaxis is

safe and effective (329). There are insufficient data to suggest that aminoglycosides add substantial benefit to the antimicrobial prophylactic regimen (323). Usual cephalosporin pharmacokinetics mandates administration within 30 minutes of incision and redosing if the operation exceeds 3 hours (321,330).

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 recent multiinstitutional 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 coronary bypass patients. One year later, compliance was even worse at 20% (331). 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 (322,332). 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. 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 death (333,334). A recent 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 (335).

5. Prevention of Postoperative Dysrhythmias. Postoperative atrial fibrillation increases the length of stay up to 5 days (336), increases the charges by as much as $10,055 (336), and is associated with a 2- to 3-fold increase in postoperative stroke (177,178).

The causal and temporal relationship among atrial fibrillation after coronary bypass, the incidence of new left atrial thrombus, and the potential for cardioarterial embolus and stroke remains ill-defined. However, if atrial fibrillation after coronary bypass persists into a second day, warfarin anticoagulation with a goal international normalized ratio of 2.0 should be considered (337).

Withdrawal of β-blockers in the perioperative period doubles the incidence of postoperative atrial fibrillation after coronary bypass. One series showed that 40 of 105 patients who had withdrawal of β-blockers developed postoperative atrial fibrillation compared with 18 of 105 patients who had early postoperative reinstitution of β-blocker ($P = 0.02$). Virtually every study of β-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 β-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 ($P = 0.001$) (338) (Table 13) (339).

A recent, prospective study of propafenone versus atenolol for prevention of postcardiotomy supraventricular tachyarrhythmias showed no significant difference between the 2 drugs (339). Both groups had a low incidence of postoperation atrial fibrillation (12% for propafenone versus 11% for atenolol, $P = 0.89$). This result identifies a less negatively inotropic drug (propafenone) as an alternative to β-blockers in patients in whom underlying LV dysfunction is an important concern (340) or for patients whose active bronchospasm makes β-blocker use less attractive.

Low-dose sotalol also appears to be effective for reduction of atrial fibrillation after coronary bypass. In a prospective, double-blind, randomized, placebo-controlled study, the placebo group had an incidence of supraventricular arrhythmias of 43% compared with 26% for sotalol ($P = 0.0012$, or a 43% reduction) (341).

Amiodarone administered beginning 1 week preoperatively halves the incidence of postcardiotomy atrial fibrillation (53% placebo to 25%, $P = 0.003$), reduces hospital costs ($26,000 to $18,000, $P = 0.03$), and shortens the length of stay (8 to 6.5 days, $P = 0.04$) (342). This represents another option for elective surgical patients who have contraindications to β-blocker therapy.

Digoxin and calcium channel blockers (verapamil has been the most extensively studied) have no consistent benefit for prophylaxis of supraventricular arrhythmias after coronary bypass operation (Table 13) (341). Currently, preoperative or early postoperative administration of β-blockers is considered standard therapy to prevent atrial fibrillation after coronary bypass surgery.

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 coronary bypass. 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 (343).

TABLE 13. Pharmacological Strategies for Prevention of Atrial Fibrillation (AF) After Coronary Artery Bypass Graft Surgery (177, 178, 424–442)

Treatment	Timing	Dose/Route	AF Incidence, %	Comments	Evidence/Reference
FRONTLINE STRATEGIES					
Resumption of patient's preoperative β-blocker	Postoperative resumption	Same as preoperative	β-Blocker stopped; 38.1% Continued $P=0.02$ 17.1% β-Blocker stopped; 28% Continued $P=0.01$ 6%	Resumption of β-blocker reduced AF by 45% Nearly 5-fold decrease in incidence; if no longer needed after revascularization, may taper as outpatient	randomized trial Ali, et al. (440) randomized trial Silverman, et al. (441)
• β-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 Matangi, et al. (442)
• Almost all β-blockers evaluated	Postoperatively	Varies	Significantly reduced vs placebo	Odds ratio 0.17; confidence interval 0.03–0.98 in favor of β-blocker over controls in meta-analysis	randomized trials reviews, Myhre et al. (443), Lauer & Eagle (444) metanalysis Andrews, et al. (341)
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	randomized trial Lamb, et al. (338)
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	Nystrom, et al. (433)
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 Fanning, et al. (445)
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 Daoud, et al. (342)

TABLE 13. Continued

Treatment	Timing	Dose/Route	AF Incidence, %	Comments	Evidence/Reference
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, Hohnloser, et al. (424)
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 Merrick, et al. (339)
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 Klemperer, et al. (431)
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 digoxin = 139/min control = 161/min *P* = 0.02	prospective trials Johnson, et al. (427) Tyras, et al. (428) metanalysis Andrews, et al. (341)
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 Davison, et al. (429) Williams et al. (446) Smith, et al. (430) metanalysis Andrews, et al. (341)

Cardiac surgical patients account for 10% of blood transfusions in the United States (344). 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 (345). Predisposing risk factors for transfusion after coronary bypass include advancing age, lower preoperative red blood cell volume, preoperative aspirin therapy, priority of operation, duration of CPB, recent thrombolytic therapy, reoperative coronary bypass, and differences in heparin management (346–352). 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 (353).

Aspirin, a very common preoperative medication in coronary bypass patients, decreases platelet aggregation and increases postoperative blood loss. The magnitude of this effect has been confirmed in prospective, controlled trials (354). Preoperative aspirin is associated with increased risk for transfusion, prolonged wound closure time, and a 4-fold increase in early reoperation for bleeding (355). 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.

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, primary coronary bypass patients, those on aspirin, and in particular the reoperative bypass population (356,357). Aprotinin does not appear to decrease early graft patency after coronary bypass despite its benefit in reducing postoperative bleeding and need for blood transfusion (358,359). Mechanical strategies to reduce the need for homologous blood have been only marginally successful.

Both ε-aminocaproic acid and an analogue, tranexamic acid, have antifibrinolytic activity. Both have been demonstrated to decrease mediastinal drainage after cardiac operation (360–363). Demonstration of a reduction in transfusion requirements has been inconsistent, however (361). 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 (359,364). The concept of risk stratification for transfusion requirements has been validated (365) and suggests more rational approaches of risk reduction strategies to minimize blood requirements (365).

Efforts to synthesize multiple blood-conservation methods have proven successful in reducing transfusion (366). The most fully evolved protocol using multiple mechanical and pharmacological means achieved a remarkable series of 100 consecutive, selected coronary bypass patients without transfusion (367). Intrinsic to this strategy was the concept of varying risk for transfusion and an individualized, algorithm-driven approach for the elective coronary bypass patient. 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 (25). Comparison was made with a consecutive series of concurrent patients with the same transfusion criteria. The multimodality conservation patients had no transfusion compared with 38% of the concurrent control group who received an average of 2.2 ± 6.7 U of blood. Mediastinal drainage for the conservation group was half that of the control group (370 ± 180 versus 660 ± 270 mL, $P = 0.001$) (367). 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 <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, $P = 0.001$). 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 ($P < 0.01$) 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, $P < 0.01$) (368).

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 ($P < 0.05$) was noted (369).

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 (364,368).

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 (370).

7. General Management Considerations. Acuity 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 V, K. Smoking cessation and improvement of chronic bronchitis before elective coronary operation lessen the risk for perioperative pulmonary complications (281). 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 (371). If the patient's coronary anatomy and clinical course permit, a concerted effort at weight reduction is appropriate and operation is deferred.

B. Maximizing Postoperative Benefit

1. Antiplatelet Therapy for SVG Patency. 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 (355). 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 (372–374). The benefit of postoperative aspirin on SVG patency is lost when started >48 hours after surgery (375). Dosing regimens ranging from 100 mg once per day to 325 mg 3 times 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 (376).

Ticlopidine is efficacious (377) 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 was rare and similar to that of aspirin in a recent controlled trial (378). 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 (379).

Current evidence suggests that dipyridamole adds nothing to the aspirin effect for saphenous graft patency (355). Warfarin has shown no consistent benefit in maintaining saphenous graft patency (380) and may be associated with an increased risk for bleeding compared with antiplatelet therapy for this application (381).

In summary, aspirin is the drug of choice for prophylaxis against early saphenous graft thrombotic closure and should be considered a standard of care for the first postoperative year (Table 14). In general, patients are continued on aspirin indefinitely, given its benefit in the secondary prevention of acute MI.

2. Pharmacological Management of Hyperlipidemia. The Cholesterol Lowering Atherosclerosis Study was the first angiographic study to provide clear evidence of a treatment effect on human atherosclerotic lesions (382). This study was conducted with 162 middle-aged, nonsmoking men who had recently undergone coronary bypass and were treated with placebo or combined colestipol hydrochloride and niacin therapy. Serial angiograms demonstrated a significant reduction of progression of atherosclerosis ($P < 0.001$) in the treated group. Specifically, there was a reduction in the number of new native coronary ($P < 0.03$) and graft ($P < 0.04$) lesions and the slowed progression of existing native coronary ($P < 0.04$) and graft ($P < 0.03$) stenoses in the treatment group.

The efficacy of statin treatment in the postbypass patient has been demonstrated 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 low density lipoprotein <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 low density lipoprotein <140 mg/dL) ($P < 0.001$; Post CABG Trial 1997). 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, $P = 0.03$). These results, along with those from a number of both primary and secondary prevention trials, strongly support aggressive attempts to screen for and treat elevated low density lipoprotein cholesterol levels in patients receiving coronary bypass surgery. Patients already taking 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors preoperatively should have them resumed postoperatively. Patients with unknown lipid levels should be screened and treated if low density lipoprotein >100.

Hyperhomocystinemia, recognized as an independent risk factor for coronary disease, is reduced by the administration of oral folic acid along with vitamins B_6 and B_{12}. In the sole study of its relationship to coronary bypass grafting,

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TABLE 14. 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 ≥80%
Perioperative			
Antimicrobials	I	Prophylactic antimicrobials	Table 12
Antifibrinolytics	IIa	Aprotinin in selected groups	Significant reduction in blood transfusion requirement
Antiarrhythmics	I	β-Blockers to prevent postoperative atrial fibrillation	Propafenone or amiodarone are alternatives if contraindication to β-blocker (Table 13)
Anti-inflammatory drugs	IIa	Minimize diffuse inflammatory response to cardiopulmonary bypass	
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 >100 mg/dL	3-Hydroxy-3-methylglutaryl/coenzyme A reductase inhibitors preferred if elevated low-density lipoprotein is major aberration
Smoking cessation	I	Smoking cessation education, and offer counseling and pharmacotherapies	

there was no association with early graft attrition found, but the angiographic follow-up was only through 1 year (383).

In summary, all patients should be considered candidates for pharmacological low density lipoprotein reduction after CABG if their low density lipoprotein level exceeds 100 (Table 14).

3. Hormonal Manipulation. More than 30 observational studies have shown a reduced mortality for coronary disease in postmenopausal women on hormone replacement therapy. The American Heart Association and the American Fertility Society have reached a consensus that hormone replacement therapy lowers mortality in women with moderate or severe coronary disease (384). The one long-term observational study that focused on hormone replacement therapy in postmenopausal women after coronary bypass demonstrated a marked reduction in all-cause mortality (385). A stepwise proportional-hazards analysis confirmed a significant reduction in relative risk with hormone replacement therapy. Eighty-one percent of women using hormone replacement therapy were alive 10 years after coronary bypass compared with only 65% who were not on hormone replacement therapy ($P = 0.0001$). Benefit was realized even when hormone replacement therapy began after coronary bypass.

The recently completed Heart and Estrogen/progestin Replacement Study trial (386), a randomized comparison of placebo and estrogen plus progestin, examined hormonal manipulation for the secondary prevention of coronary disease in postmenopausal women. Treatment had a beneficial effect on low density lipoprotein cholesterol level, with an 11% reduction ($P \leq 0.001$), and a 10% increase in high density lipoprotein cholesterol level ($P \leq 0.001$). However, there was no beneficial effect on the overall rate of coronary heart disease events. The question remains open as to whether unopposed (without progestin) estrogen replacement therapy in this patient population is beneficial. This study included patients having had coronary bypass, but a subgroup analysis for this subset was not reported.

In summary, hormone replacement therapy should be considered in postmenopausal women after CABG when, in the physician's judgment, the potential coronary benefit is not offset by a perceived risk for uterine and/or breast cancer.

4. Smoking Cessation. Smoking is the single, most important cause of preventable premature mortality in the United States (387). 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) ($P = 0.018$) (388). Cessation of smoking after coronary bypass improves the postoperative survival of successful quitters to that of postbypass patients who have

never smoked; persistent smokers have significantly more MIs and reoperations (389). 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' (390).

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 (391).

Depression is an important complicating factor in smoking and may account for a significant number of cessation failures (392,393). Behavioral treatments alone are not as effective as drug therapy (394).

The nicotine transdermal patch is effective in smoking cessation treatment. The average cost per year of life saved ranges from $965 to $2360 (387). 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 (395). Nicotine gum added to transcutaneous patch therapy significantly increased abstinence rates above that of the active patch alone at 52 weeks (396).

A sustained-release form of bupropion, an antidepressant similar to the selective serotonin reuptake inhibitors, 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 ($P < 0.001$) (393). The results at 1 year parallel those seen with nicotine replacement strategies.

In summary, all smokers should receive educational counseling and be offered smoking cessation therapy after coronary bypass. Pharmacological therapy including nicotine replacement and bupropion should be offered to patients indicating a willingness to quit.

5. Cardiac Rehabilitation. Cardiac rehabilitation including early ambulation during hospitalization, outpatient prescriptive exercise training, family education (397), and sexual counseling (398) have been shown to reduce mortality (399,400). 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 ($P = 0.0001$), a slight (2%) but significant ($P = 0.05$) increase in high density lipoprotein cholesterol, and a 6% reduction in body fat ($P = 0.002$) (401). 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 (402). 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, $P = 0.02$), *unemployed* patients (63% of those declining versus 45% of the participants, $P = 0.02$), those with a *lower* income and educational level (both $P = 0.001$), and *those with a greater functional impairment* ($P = 0.001$) (403). 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 (404,405). Despite the fact women have a generally higher risk profile and a relatively lower functional capacity than men at initiation of a rehabilitation period (406), 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%, $P < 0.001$) (407). 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 (408).

In a long-range trial focused exclusively on a coronary bypass population, postoperative patients were randomized to standard posthospital care (n = 109) or standard care plus rehabilitation (n = 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, $P = 0.005$), perceived better health ($P = 0.03$), and a perceived better overall life situation ($P = 0.02$). A larger proportion of the rehabilitated patients were working at 3 years ($P = 0.02$). This difference disappeared with longer follow-up (409). Patients who sustained an infarct followed by coronary bypass had greater improvement in exercise tolerance after rehabilitation (change in exercise capacity 2.8 ± 1.4 metabolic equivalents) than did those having infarct alone (0.8 ± 2, $P < 0.02$). Improvement was sustained to 2 years (410).

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 $\pm$ 3911 versus $1936 $\pm$ 5459, $P = 0.022$) (411).

The coronary bypass patient is more likely to resume sexual activity and to a greater degree than is the postinfarct patient. 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 (412).

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

6. Emotional Dysfunction and Psychosocial Considerations. The 2 most important independent psychosocial predictors of death in a multivariate analysis of elderly postoperative coronary bypass patients are a lack of social participation and religious strength (413). Social isolation is

associated with increased mortality and coronary disease (414), and successful treatment may improve outcome (415). Depression is generally poorly recognized by the cardiac specialist (401). 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 (416). 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 per se and depression. 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 (417).

Eighteen percent of patients are depressed after major cardiac events, including coronary bypass (401). 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) (401).

7. Rapid Sustained Recovery After Operation. Rapid recovery and early discharge, the "fast-track" approach, for the coronary bypass patient should become the standard *goal* of care. The shortest postoperative stays in the hospital are followed by the fewest rehospitalizations (418). 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 (419,420).

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.

V. SPECIAL PATIENT SUBSETS

A. 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 (447). 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 (448). 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 (449,450). In Figure 10, operative mortality (%) is shown as a function of age. A near-linear slope changes abruptly at age 75. Similarly, in Figure 11 the OR for operative mortality is shown as a function of age (26). The effects of these factors on patient outcomes and institutional resources have significant

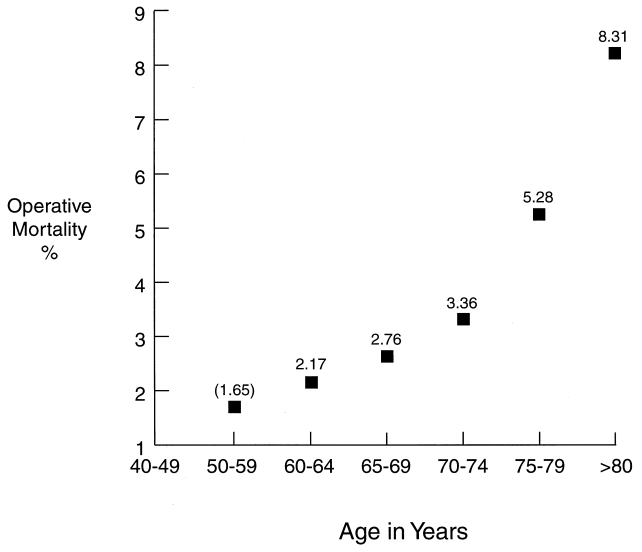

Figure 10. Operative mortality (%) for CABG in various age cohorts (26).

implications for peer review, quality assurance screening, institutional reporting to external sources, and reimbursement (449).

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 (448) 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 <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 <0.20). Other correlates of increased risk include increasing age; recent MI (<30 days), especially in the presence of unstable angina, left main disease, or 3-vessel disease; emergent or urgent coronary bypass; reoperation; reduced renal function; cerebrovascular disease; COPD; a smoking history; obesity; and female sex (37,451–458). A higher operative mortality occurs for all identified risk factors in patients aged 75 years or older than for those <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 <0.20 up to a 10-fold increase (26,459,460). Predictors of postoperative low cardiac output syndrome are, in descending order of importance, LVEF <0.20, repeated operation, emergency operation, female sex, diabetes mellitus, age >70 years, left main disease, recent MI, and/or 3-vessel disease (461). The greatest risk is in the acutely ill, elderly patient for whom the CABG operation may be the best of several high-risk options (462).

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 (262,454,455,463). Obesity has been identified as a risk factor for infection in patients receiving bilateral IMA grafts (464). 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 (45,263,265,465). CABG without cardiopulmonary pump assistance may be advantageous in high-risk patients, particularly those with an LVEF <0.35 (466,467).

Postoperative atrial fibrillation is a particular problem in elderly patients undergoing CABG. Correlates of postoperative atrial fibrillation include age >70 (especially age >80), male sex, postoperative pulmonary complications, ventilation time >24 hours, return to the intensive care unit, and use of the IABP. Atrial fibrillation contributes to a substantially prolonged hospital stay (9.3 ± 19 versus 15.3 ± 28 days) (336). Patients with preoperative chronic renal failure are at a particular risk, as they tend to be older and have additional comorbidity (74). Interventions to prevent atrial fibrillation are discussed in Section IV.

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 (468). 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

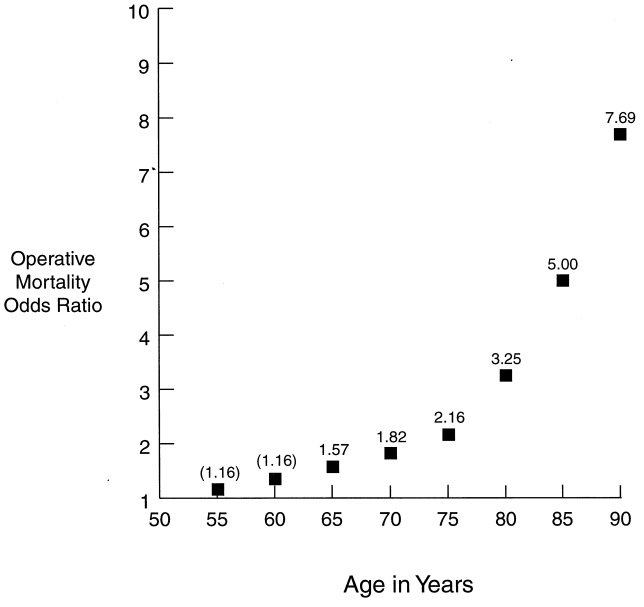

Figure 11. Operative mortality odds ratio (26).

(469–471). 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) (472).

Peterson et al (473) 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 (14.3 versus 21.4 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 (471,473,474). 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 (475). 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 (476).

In operations combining valve surgery and CABG, independent predictors for late survival included NYHA Class IV, age >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 (477–480).

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 sustained improvement and 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 (454,481–483).

B. 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 (33,484–487). 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 (486,488–497). 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 (487,488).

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 (498). Others have argued that smaller coronary arteries in women may contribute to higher risk (31). IMA grafts have been reported to be used less often in women, possibly contributing to a higher mortality (492,494). Kurlansky et al (81) 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 (486) 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 intensive care unit length of stay (499,500). Comparable findings were reported for coronary bypass surgery in black male and female patients (501).

However, analysis from the CASS found a higher operative mortality for women (OR 2) (501) as did Jaglal et al (502), even when comorbidities were adjusted for appropriately. They suggested that the excessive mortality was due to late treatment (502). Farrer et al (503) 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 (504).

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 (81,494,498). Women appear particularly vulnerable to postoperative

CHF, low cardiac output syndrome (33,488,494), and blood loss (491). Although postoperative depression is common in women and men, its occurrence in women has been reported to be more common (≈60%) and more commonly unrecognized (103). Nonetheless, at 6 months postoperatively, men and women report similar psychosocial recovery (490) (see Section IV).

In the CASS, 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 (505).

Over time, changes in the clinical characteristics of women undergoing coronary bypass surgery 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 emergent 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 (497). 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 (506).

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

C. CABG in Patients With Diabetes

Coronary heart disease is the leading cause of death among adult diabetics and accounts for ≈3 times as many deaths among diabetics as among nondiabetics (507). Not only is the frequency of acute MI increased in diabetic patients (508,509) but also its treatment is more complicated than in the nondiabetic patient. Diabetic patients 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 diabetics have a greater frequency of CHF, shock, arrhythmias, and recurrent MI than do nondiabetics. Similarly, diabetic patients with unstable angina have a higher mortality than do nondiabetic patients. A recent prospective study indicated a 3-month mortality of 8.6% and 1-year mortality of 16.7% in diabetics versus 2.5% and 8.6%, respectively, in nondiabetics (510).

CABG surgery in elderly diabetics (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 diabetic and nondiabetic patients (511). Nevertheless, a recent study from Sweden has indicated that diabetic patients of all ages have a mortality rate during the 2-year period after CABG that is about twice that of nondiabetic patients. Thirty-day mortality after CABG was 6.7% in diabetic patients, and subsequent mortality between day 30 and 2 years was 7.8% compared with 3% and 3.6%, respectively, in nondiabetic patients (512).

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) (118). 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%, $P = 0.0003$), which was confined to those patients receiving at least one IMA graft. Thus, although mortality after CABG surgery may be increased in diabetics, CABG surgery when indicated appears to provide a better chance for survival than does medical therapy or PTCA.

Diabetic patients 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 (374,513). 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 (374). 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 (374,514). This approach is supported by a study that randomized 26 patients with >75% stenosis in at least one coronary artery and relatively normal LV function to either revascularization or medical therapy with aspirin and a calcium channel blocker (513). 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.

D. 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 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 a rise in alveolar dead space secondary to decreased 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 (515). Postoperatively, early extubation is desirable, appears safe, and does not increase postoperative cardiac or pulmonary morbidity, especially if the total bypass time is <100 minutes (516,517). 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 postoperatively.

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 a near-direct relation to the severity of the degree of pulmonary dysfunction (451,518–520). 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 (518).

The parameter most commonly reported by authors in estimating the degree of pulmonary dysfunction is the forced expiratory volume per second (FEV_1). There is little consistency in the literature defining the level of abnormality for moderate to severe COPD. Values for FEV_1 range from <70% to <50% of the normal predicted value and/or an FEV_1 of <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 (515,518,519), 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 (519), who compared 37 patients with COPD who were undergoing CABG surgery to 37 matched control patients without COPD. They defined COPD in clinical terms (ie, 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 ± 0.032 versus 2.33 ± 0.49 L [<60% of control value]) and a lower arterial oxygen tension. This group had a significantly higher rate of preoperative atrial and ventricular arrhythmias. Postoperatively, they remained in the intensive care unit 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 (519). Kroenke et al (518) reported the results of 107 operations in 89 patients with severe COPD, defined as an FEV_1 <50% of predicted and an FEV_1 to forced vital capacity ratio of <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 (518).

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 (521). Wahl et al (521) 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 <70% and total lung capacity <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 (521). Similar findings were reported by Goyal et al (522) 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 (523,524).

A history of COPD and >2 days on a mechanical ventilator postoperatively have been reported as risk factors for nosocomial pneumonia in postoperative coronary bypass patients (525) and have been documented as a risk factor for mediastinitis (526,527). 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 abnormality, many patients may be successfully carried through the operative procedure.

E. CABG in Patients With End-Stage Renal Disease

The latest available data indicate that during 1995, >257,000 Americans were treated for ESRD, with substantial associated morbidity and mortality (528). Data from the US Renal Data System (USRDS) have established that the mortality rate of dialysis patients in the United States is high compared with that of other industrialized nations (528). The basis for this difference is not well understood, but case mix appears to be of great importance, with a major factor being cardiovascular disease (529). Previous data from the USRDS have indicated a 41% prevalence of cardiovascular disease among dialysis patients, with the mortality risk for these patients being 22% greater than for those free of disease (530). MI and other cardiac disorders constitute the leading causes of death in the ESRD population, and death rates due to cardiac disease increase dramatically with age in these patients. With growing numbers of older patients undergoing renal replacement therapy, the number of patients with ESRD who present with CAD amenable to surgical revascularization is likely to increase.

Cardiovascular disease is the single best predictor of mortality in patients with ESRD, as it accounts for almost 54% of deaths (528). 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 >60 years. In addition to the foregoing, patients with ESRD 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, dialysis patients can be treated with either PTCA or CABG. The indications for these procedures are similar to those in non-ESRD subjects with coronary disease. Coronary revascularization with surgery 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 (531). 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 (532). In addition, infection and sepsis have been identified as significant causes of morbidity and mortality in patients with ESRD undergoing cardiac surgical procedures (532). 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 coronary bypass grafting.

Both the mortality with CABG and the complication rate with PTCA appear to be increased in patients with ESRD (533,534). An additional problem is that the success rate with PTCA is less satisfactory in this setting. In one small series, for example, the angina recurrence rate was 75% and the restenosis rate was 81%, and subsequent restenosis occurred in 11 of 12 vessels after repeated PTCA (none of these patients had stents) (535). There also is evidence that the risk of cardiac events in dialysis patients is higher after PTCA than after CABG (533,536). Thus, CABG is the preferred approach in the treatment of severe coronary disease in patients with ESRD, as confirmed in a more recent study indicating that dialysis patients undergoing PTCA have a higher risk of subsequent angina, MI, and cardiovascular death than do those undergoing CABG (537).

In one recent large series, CABG was associated with significant improvement in cardiac symptoms and overall functional status in patients with ESRD on dialysis (538). In fact, the patients in this series represent a subgroup of patients with severely debilitating symptoms of coronary disease along with many associated risk factors other than renal failure. Nevertheless, overall 30-day mortality for the group was 9%, and the reduction in cardiac symptoms was excellent, both at discharge and during follow-up. Thus, CABG in dialysis patients may be associated with an acceptable mortality, with a significant increase in the

quality of life for long-term survivors. Each of the 19 hospital survivors in this series returned to routine maintenance dialysis therapy and enjoyed symptomatic improvement. However, because this retrospective study lacked the matched control groups of prospective randomized studies, this study cannot definitively compare coronary bypass grafting with other therapies for patients with ESRD and coronary disease.

Thus, the primary question remaining to be answered is whether freedom from cardiac-related events is improved by surgical revascularization in dialysis patients. Unfortunately, alternatives to revascularization often are limited in patients with severe coronary symptoms refractory to medical therapy, and long-term results of PTCA have been relatively poor in ESRD patients (537). More definitive demonstration of the relative costs and benefits of CABG in this patient population awaits future studies, particularly in patients who present for elective revascularization.

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.

F. Valve Disease

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 ≈25% in patients with atypical chest pain and to ≈20% in those without chest pain (539–546). 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 (539–546). 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 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 involving the papillary muscles, and the dilemma is when it is 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 to 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 rare 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.

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 >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 >70 years, female sex, advanced NYHA class, poor LV function, and multiple valve procedures (547). 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% (548).

The results of combined aortic valve and coronary disease have led to the recommendation to graft significantly obstructed vessels (≥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 (549). 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 >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 whether or not the reoperative risk of late AVR after previous CABG is

Table 15. Risk for First, Second, and Third Reoperation for CABG

	CASS, %	Portland, %	Mayo, Secondary, %	Cleveland Clinic, Secondary, %	Mayo, Tertiary, %	Cleveland Clinic, Tertiary, %
Hospital mortality	3.1	2.0	2.8	3.4	11.9	7.0 (0–14)
Perioperative MI	5.8	4.2	7.5	7.2	8.9	
Reoperation/bleeding	2.9	4.6	4.7	6.8	6.0	
Wound infection	1.9	0.6	1.9	1.6	3.0	
Neurological complication	0.8	1.2	0.9	2.1	4.5	
Overall survival, %						
5 Years	95	90	94	90	75	84
10 Years	89	75	89	75	48	66
Event-free survival, %						
5 Years		78	63	76		74
10 Years		50	26	48		
Angina-free survival, %						
5 Years			28	52		
10 Years		64				

CABG indicates coronary artery bypass graft; CASS, Coronary Artery Surgery Study; and MI, myocardial infarction.
References for each study are as follows: CASS (557,558); Portland (559); Mayo—secondary (560); Mayo—tertiary (555); Cleveland Clinic—secondary (561); and Cleveland Clinic—tertiary (554).

significantly increased. Sundt et al (550) 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 (551) 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 (552). 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.

G. Reoperation

Reoperation for CAD is responsible for as many as 15% to 18% of all CABGs in some centers. The STS National Database, which has collected data since 1987, reports an incidence of 8.6% to 10.4% with a total patient enrollment of 594,059. At least 2 factors explain this discrepancy. First, enrollment in the STS National Database is voluntary. This means that not all cases are required to be sent to the data center. It simply reports the incidence of reoperations of those patients enrolled. To the extent that centers may only be enrolling first-CABG cases, the data may underestimate the true incidence. Second, nationwide the incidence of reoperations varies among centers, with tertiary care centers receiving reoperation referrals that were not deemed appropriate at primary (or community) centers. As has been well documented in the early years of CABG, the predominant reason that reoperation is necessary is the development of vein-graft atherosclerosis. Although there is disease progression in native vessels and the development of new disease in previously ungrafted coronary arteries, these do not approach the frequency and clinical importance of late SVG disease.

The operative mortality of reoperations for CABG is distinctly higher than the mortality of first-time operations. Reoperative mortality increases with the urgency or severity of symptoms, age >65 years, <1 year between first and second operations, and low EF (34) (Table 15) (553–555). The highest risk seems to be associated with a short time interval between the first operation and the subsequent need for reoperation. Christenson et al (34) reported a reoperative mortality risk of 18% in a group of patients who underwent reoperation <1 year after their first CABG. This figure was compared with an 8% mortality in those patients who had an operation-free time of >1 year. The presence of diabetes was greater in the group undergoing operation in <1 year.

Third- and fourth-time coronary bypass operations are becoming more frequent with longer follow-up. Occlusion or stenosis of prior placed grafts was the principal reason for reoperation in >90% of the patients. It was also noted that the risk of left main disease and/or triple-vessel disease was more prevalent in the multiple-reoperation patient group (555). Second- or third-time reoperations for CABG are associated with a higher incidence of perioperative complications, including reoperation for bleeding, perioperative MI, and neurological and pulmonary problems (Table 15).

The 5- and 10-year survival after reoperation for CAD is reported at 77% and 48%, respectively (554,555). These late results provide significant reason to recommend patients for reoperation provided that the severity of symptoms and anticipated benefit justify the risk. It has been argued that once the patient's symptoms present, it is better to proceed with prompt revascularization rather than delay the procedure, during which time the condition may progress and lead to an emergency operation, which carries a much higher perioperative risk (554,556).

One intriguing aspect of the reoperation question is what effect arterial grafts will have on the incidence and risks of reoperation. One recent report (555), comparing the effect

on late events of single versus bilateral IMAs used for coronary revascularization, demonstrated a reduction in late events, including reoperation, with the use of both IMAs. This finding, however, was not independent of the presence of diabetes. This implies that patients with diabetes were unlikely to have had bilateral IMAs used, presumably owing to the fear of increased incidence of sternal wound infection with the use of both IMAs. Also, the incidence of reoperation is increased when an IMA is not used at the first operation. The future of coronary artery surgery is being rewritten in light of arterial coronary grafting. To date, there are sparse data to guide recommendations advocating multiple arterial grafting, though advocated by many. However, it is accepted that superior results occur with use of the left MA, especially when grafted to the LAD.

H. 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 (562). CAD is the leading cause of both early and late mortality in patients undergoing peripheral vascular reconstruction (563). MI is responsible for about half of all postoperative deaths in patients undergoing abdominal aortic aneurysm resection (564,565), extracranial revascularization (190,566), or lower-extremity revascularization (565,567). Long-term survival after successful vascular reconstruction is limited by the high incidence of subsequent cardiac death (568). On the other hand, the presence of PVD is a strong, independent predictor of long-term mortality in patients with stable chronic angina (569). After successful myocardial revascularization, patients with PVD are at substantially increased risk for in-hospital (570) and long-term (41) mortality.

The importance of preoperative cardiac evaluation was demonstrated by Hertzer et al (563) in a study of 1,000 patients with PVD: abdominal aortic aneurysm, cerebrovascular disease, or lower-extremity ischemia. All 1,000 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 (569) 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 (41,570). 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.

I. Poor LV Function

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 surgery compared with patients with normal LV function. Both low EF and clinical heart failure are predictive of higher operative mortality rates with CABG (571). 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 $\geq$0.50 to 6.7% in patients with an EF $<$0.19 (572). An operative mortality of 6.6% in patients with an EF $<$0.35 in comparison with 2.6% in patients with an EF $>$0.50 was recently reported (573). Compared with patients with an EF of 0.40 or higher, patients whose EF was $<$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 $\approx$5% in excellent centers in

patients of a younger age, with fewer symptoms, and having no comorbid conditions, to >30% in patients who were older, with severe ventricular dysfunction, and having several comorbid conditions (571). 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 <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 <0.25, respectively (574). 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 5,824 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 <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 (90). 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 (90,571,575,576). Patient selection is crucial for achieving the beneficial effects of myocardial revascularization in this subset of patients and is discussed in Section IX.

J. Transplantation Patients

Cardiac transplantation is an accepted treatment for end-stage heart failure, with >30,000 cardiac transplantations performed worldwide to date (577). Allograft CAD is the leading cause of death after the first year of transplantation (578–580). 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 posttransplantation with a yearly attrition rate of 15% to 20% (581,582). 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 (581). 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 (583). 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 (583–585). Treatment of hyperlipidemia with pravastatin (586) or weekly low density lipoprotein apheresis (587) 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 had been reported with coronary angioplasty and directional coronary atherectomy in selected patients with discrete and proximal coronary lesions (588,589). 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 (590,591). In a recent 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 (592). The safety and efficacy of coronary bypass grafting were recently reported in 31 renal transplant patients who underwent isolated coronary bypass surgery (593). 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 (593). 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 (594).

K. CABG in Acute Coronary Syndromes

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, and for the purposes of this document, a clinical definition encompassing progressive, rest, and postinfarction angina and Q-wave and non–Q wave MI will be used to examine the effects of surgery.

The effectiveness of CABG for unstable angina was first demonstrated in a randomized Veterans Administration trial comparing medical therapy with CABG initiated in 1976 (595). 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 (106), in those with 3-vessel disease (596), and in those with LV dysfunction presenting with electrocardiographic changes (597). 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 (111). 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, thrombolytics, and PTCA.

There have been no randomized trials specifically comparing CABG and PTCA 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 non-Q wave MI. There was no difference in 5-year overall survival for these patients treated with either CABG (88.8%) or PTCA (86.1%, P = NS) (118). 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 diabetic patients (131).

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 (120). 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 (127). There was a particularly high incidence of unstable angina (83%) in the small ERACI trial (132). These patients had mostly complex lesions (50% type B2 and 13% type C), which are associated with greater angioplasty complications (598). However, in-hospital mortality was higher with CABG (4.6% versus 1.5%), and 3-year survival and freedom from Q-wave MI were similar for both forms of revascularization (132).

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 (393).

Several early studies performed before 1990 demonstrated an increased surgical mortality ranging from 4.6% to 7.3% in patients with unstable angina (395,599–601). More recent studies have confirmed this finding (602,603). In the series of Louagie et al (602), 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 recent study examining early revascularization versus conservative therapy for patients with non–Q wave MI had a much higher 30-day surgical mortality (12%) in patients undergoing early CABG compared with those managed conservatively (5%) (398).

In patients with postinfarct angina, a higher mortality has been observed, particularly with early operation after Q-wave infarction (390,599,604). Braxton et al (606) compared 116 patients operated on within 6 weeks of MI with 255 patients without prior MI. Mortality was highest (50%) in 6 patients with Q-wave infarcts undergoing surgery <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 16.

Table 16. Factors Associated With Adverse Outcome During Coronary Artery Bypass Grafting for Unstable Angina

Factor	Relative Risk of Mortality (Range)
Clinical	
Recent MI: <24 h (605), <48 h (606), <30 d (457)	2.1–18
Female (457,602,604,605)	1.4–1.7
Reoperation (457,602,604,605)	2.9–5.8
Age (457,458,604,607)	2.9–5.3*
IDDM (607)	8.3†
Angiographic/hemodynamic	
No. of diseased vessels (602,604)	. . .
LV dysfunction (457,458,604)	1.9–2.3 (EF 0.20–0.39) 5.9–10.7 (EF < 0.20)
Hypotension (458,605)	6.5–7.8
Surgical	
Aortic cross-clamp time (602,607)	2.25‡
Urgent surgery (604,605)	1.8–1.9
Bypass time (607)	. . .
IABP support (607)	4.1

MI indicates myocardial infarction; IDDM, insulin-dependent diabetes mellitus; LV, left ventricular; IABP, intra-aortic balloon pump; and EF, ejection fraction.
*Age >70 years. †Relative risk for perioperative MI. ‡Relative risk major of adverse outcome ≥100 vs <100 minutes.

The use of CABG for primary reperfusion during Q-wave MI has largely been superseded by thrombolysis 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-Q wave MI, and during acute MI is increased severalfold relative to patients with stable angina, although the risk is not necessarily higher than that of medical therapy for these patients.

VI. IMPACT OF EVOLVING TECHNOLOGY

A. Less-Invasive CABG

Technical modifications of traditional CABG have been developed in the last several years in an attempt to decrease the morbidity of the operation, either by using limited

incisions or by eliminating the use of CPB. These techniques were greatly advanced by Bennett's suggestion in 1994 at the International Symposium on Myocardial Protection in Chicago (608) that CABG could be performed through a small left thoracotomy with the aid of a thoracoscope on a beating heart. Less-invasive CABG surgery can be divided into 3 categories: 1) Off-bypass coronary artery bypass is performed through a standard median sternotomy and generally with a smaller skin incision. A local stabilization device is used to immobilize the target vessels, and anastomoses are performed without the use of CPB. 2) Minimally invasive direct coronary artery bypass (MID-CAB) is performed through a left anterior thoracotomy without CPB, with or without thoracoscopic techniques. 3) Port-access coronary artery bypass is performed with femoral-femoral CPB and cardioplegic arrest with limited incisions.

The potential benefits of off-pump CABG are the avoidance of CPB and potentially a smaller skin incision and less retraction of the sternum during median sternotomy. CPB is associated with a 1% to 5% incidence of stroke and other complications including myocardial stunning, pulmonary edema, bleeding, renal insufficiency, and systemic thromboembolism (609).

CABG 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 advent of CPB. However, CABG on a beating heart was still practiced in several countries, where much experience was accumulated (610,611). Off-pump coronary bypass is performed on a beating heart by the reduction of cardiac motion with a variety of pharmacological agents and mechanical devices. These include slowing the heart with β-blockers and calcium channel blockers, creating a temporary cardiac arrest with adenosine (612), or vagal simulation (613). Various techniques for elevation of the heart have been developed, thereby allowing some access to the vessels on the lateral side of the inferior surface of the heart in addition to the vessels on the anterior surface. Because this technique is performed through a full median sternotomy, it would be considered slightly more invasive than the anterior thoracotomy approach described in the next paragraph.

The term "MID-CAB" should be reserved for performance of CABG without median sternotomy and without the use of CPB. In general, this is performed through a left anterior thoracotomy, which exposes the heart through the fourth intercostal space with access to the LAD and diagonal branches (and occasionally, anterior marginal vessels). The right coronary artery may also be approached through a right anterior thoracotomy in a similar manner.

At the Second Utrecht Minimally Invasive Coronary Artery Bypass Grafting workshop, >3,000 performed cases of CABG on a beating heart with 4,400 anastomoses were reported (614). More than 1,000 cases were done with minithoracotomy (ie, the MID-CAB procedure). The mean number of anastomoses per patient ranged from 1.0 to 2.0 grafts. Forty-nine percent of these patients had single-vessel disease, 28% had 2-vessel disease, and 13% had 3-vessel disease. Hospital stay was reduced from an average of 8 days for conventional CABG to 4 days. Patients returned to work and social activities after 2 to 3 weeks.

Calafiore and colleagues (615) recently reported their experience of 366 patients undergoing single-vessel left IMA-to-LAD anastomosis via a small, left anterior thoracotomy. Half of the patients had single LAD disease and the rest had LAD as a part of multivessel disease. The 30-day mortality rate was 0.8%, 23-month actuarial survival rate was 98%, and event-free survival was 88% (91% in patients with single-vessel disease versus 86% in those with multivessel disease, $P = 0.006$). Graft patency rate was 93% by angiography or Doppler examination. Five percent and 2% of patients, respectively, required operative revision for malfunctioning grafts during early (<30 days) and late (>30 days) periods. Forty percent of the patients were extubated in the operating room or 1 hour postoperatively. Mean intensive care unit and hospital stays were 4.2 and 53 hours, respectively.

Although this and other early reports (614,616–618) of clinical results are encouraging, they should be viewed with caution. The number of anastomoses performed on a beating heart is usually 1 and occasionally 2. The subset of patients with single-vessel CAD who require coronary revascularization is relatively small. Most clinical reports of MID-CAB procedures have included patients with multivessel disease. Incomplete revascularization in patients with multivessel occlusive CAD has been shown to be associated with increased cardiac events and death (117,619). Preliminary reports of MID-CAB experience have demonstrated the benefits of rapid recovery, a shorter hospital stay, less perioperative morbidity, a faster return to routine activities, and cost reduction (620). Clearly, the long-term efficacy of MID-CAB procedures remains to be determined, particularly with regard to long-term graft patency. The techniques and indication for the MID-CAB procedure continue to evolve, and its ultimate role in the surgical armamentarium of coronary artery revascularization is being clarified.

The third emerging technique in less-invasive cardiac surgery is the closed-chest, port-access, video-assisted CABG operation developed at Stanford, Calif (621). 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. A recent published report showed excellent perioperative safety and graft patency in animal experiments with the port-access technique in the performance of a left IMA-to-LAD anastomosis (622). Clinical trials are currently ongoing. 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.

B. Arterial and Alternate Conduits

The choice of graft conduits is crucially important in CABG because short- and long-term graft patency is closely associated with cardiac morbidity and mortality. The standard choice of graft conduits in the past 15 years has been the in situ IMA and greater saphenous veins. In the early 1980s, the SVG was shown to be prone to progressive intimal proliferation and atherosclerotic changes (623). In 1985, Barner et al (624) reported superior IMA graft patency in comparison with SVGs in 1000 patients over a 12-year period. At 1 year, IMA grafts and SVGs had comparable patency rates of 95% and 93%, respectively. However, at 5 and 10 years, IMA grafts were shown to have a superior patency rate of 88% and 83%, respectively, compared with a patency rate of 74% and 41% in SVGs. In addition, the use of a single IMA graft was associated with a low perioperative complication rate. A large, long-term follow-up study comparing patients receiving left IMA-to-LAD and supplemental vein grafts with patients receiving SVGs only demonstrated a significantly lower rate of recurrent angina and MI, a lower incidence of reoperation or PTCA, and higher actuarial 10-year survival among patients with IMA grafts (625). The routine use of the left IMA for LAD grafting with supplemental SVGs to other coronary artery lesions is generally accepted as the standard grafting method.

Circumstances may exist in which the autologous IMA and/or greater saphenous vein is absent or unsuitable as a result of intrinsic venous disease, prior myocardial revascularization, varicose vein ligation, and previous peripheral artery reconstruction. In these circumstances, alternative coronary conduits must be used. Alternative conduits include autologous venous and arterial grafts, preserved nonautologous venous and arterial grafts, and synthetic grafts. When the greater SVG is not available, the lesser saphenous vein and upper-extremity veins, mainly the cephalic and basilic vein, can be used. Long-term patency of upper-extremity vein conduits is poorer than that of the SVG. The choices for autologous arterial conduits, in addition to the left IMA, are the right IMA, radial artery, right gastroepiploic artery, inferior epigastric artery, and very rarely, the subscapular, intercostal, splenic, left gastric, and gastroduodenal artery.

Barner in 1974 (626) first reported the results of the use of bilateral IMAs as conduits for coronary revascularization. Despite the short- and long-term superior patency rates for IMA conduits in comparison with SVGs, early enthusiasm was deterred by the high rate of postoperative complications associated with the use of bilateral IMA grafts. Problems included postoperative bleeding, prolonged ventilatory support, and sternal wound infection (627). Several subsequent large series, however, have demonstrated the safety and efficacy of the use of bilateral IMA grafts during both the perioperative period and with long-term follow-up. The only remaining caveat, however, is a higher rate of sternal wound infection associated with bilateral IMA grafting (628–630). By statistical analysis, patients who were obese, diabetic, and required prolonged ventilatory support were identified to have an increased risk of sternal wound complications after bilateral IMA grafting. The long-term clinical benefits of bilateral IMA grafting compared with single IMA grafting include lower rates of recurrent angina pectoris, MI, and need for reoperation and a trend toward better survival (79,631,632). Use of the right IMA as a free graft or sequential graft has been shown to have excellent short- and long-term results (633,634).

The use of the radial artery as a conduit for coronary bypass grafting was first reported by Carpentier et al (635) in 1973. Its use was quickly abandoned when occlusion rates up to 30% were reported (636,637). 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 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 recent experiences with radial artery grafting. Brodman et al (638) 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 (639) recently 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 (640,641). 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% (642–644), but long-term results have not been published. The inferior epigastric artery free graft has been used for CABG since 1990 (645,646). 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 (647). Short-term patency rates of up to 98% have been reported (648). Long-term results are not available.

Cryopreserved homologous SVGs and glutaraldehyde-treated homologous umbilical veins grafts have been used for clinical aortocoronary bypass surgery (649,650). 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 an ≈50% 1-year patency (651,652). 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 (653–655). The patency of polytetrafluoroethylene grafts is also limited and has been reported to be ≈60% at 1 year (656,657).

C. 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 (658).

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 (659,660). New refinements in stent design and adjunctive pharmacological therapy are further improving patient outcomes after stenting. Directional coronary atherectomy has also been shown to reduce restenosis compared with conventional PTCA, but its role relative to stents is not yet clear (661). Several new devices, such as transluminal extraction catheter (InterVentional Technologies, Inc., San Diego, CA) and 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 rotablation has expanded the types of lesions (eg, calcified or long lesions) that can be treated without surgery (662).

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 (663), gene therapy, and local radiation therapy (664).

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 (665–668), and within 10 years, about half of all vein grafts are totally occluded or have severe atherosclerotic disease (77,669,670). 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 (671–673). 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 (557,674,675). 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 (676–679). 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 non–Q wave MI (680,681). The transluminal extraction catheter, another atherectomy device, may reduce the incidence of distal embolization (682,683).

Intracoronary stents are now commonly used in the management of SVG stenosis. A recent 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 (684). 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, repeated 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.

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 centers (685–688). Typically, 1 to 4 days after initial MID-CAB for the left IMA-to-LAD grafting, 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 (686). 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. Thus, the theoretical benefits of combining procedures must be matched by scientific proof of efficacy before this strategy is likely to become commonplace.

D. Transmyocardial Revascularization

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 (689). Early attempts to use these connections to supply the ischemic myocardium included implantation of the left IMA directly into the heart muscle (690) and direct-needle acupuncture to the ischemic myocardium to create communicating channels (691,692). Sen and colleagues (691,692) 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 (693,694). 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 lased channels and thus lead to improved channel patency (695). Long-term channel patency on histological examination has been reported in animal experiments and in sporadic clinical case reports (695–697). 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, PTCA, or heart transplantation. These patients often have diffuse, small-vessel disease and are not appropriate candidates for another PTCA or CABG. The use of TMLR for the management of cardiac allograft vasculopathy has also been reported (698,699).

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 recently reported by Horvath and colleagues (700). 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 (701). In the TMLR group, 72% of patients improved by at least two 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.

Early studies suggest that TMLR is a promising, new surgical technique for alleviating angina symptoms and improving quality of life in a small and select group of patients for whom conventional revascularization is not an option. However, the mechanisms for the demonstrated clinical benefits of TMLR are poorly understood. Whether or not lased channels remain patent for a long period of time after TMLR is a subject of active investigation. Animal experiments have shown that cardiac afferent nerve fibers are destroyed during laser revascularization (702). This raises

the concern that angina relief may be due to denervation of the heart rather than relief of ischemia. It has been hypothesized that the benefit may be secondary to angiogenesis induced by the laser injury. Clearly, further basic science and clinical research is needed to clarify the mechanism of action of TMLR. Nonetheless, TMLR is a possible therapeutic option for a difficult subset of patients. The techniques of TMLR are amenable to percutaneous methods, and indeed, such systems are currently under investigation. In addition, trials are under way wherein TMLR is combined with bypass surgery; the premise is to improve coronary inflow to areas adjacent to those on which TMLR has been performed.

VII. INSTITUTIONAL AND OPERATOR COMPETENCE

A. Volume Considerations

Owing to the recent 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 datasets were proposed as a means of risk adjustment to compare outcomes between hospitals of high and low volume (703,704). These studies found a relationship between mortality after CABG and the volume of procedures performed annually. A cutoff at ≈200 cases defined high- and low-volume institutions. A relative risk of ≈0.44 (1.29 to 0.65, 95% confidence interval) was found in high-volume institutions. The ability of administrative datasets to accurately stratify risk has since been questioned, particularly because of their inability to distinguish preoperative comorbidity data from postprocedure complications data (705–707).

Since 1986, in response to these criticisms, primary cardiac surgical datasets have appeared with sufficient power to address this question. Hannan et al (708) reported that in New York State, after adjusting for case mix, the high-volume institutions that performed >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) (709). 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 (709) postulated that this was due in part to the outmigration of older, low-volume surgeons and the inmigration 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 (710). 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 (<100 cases annually).

A report of the STS National Cardiac Database reviewed 124,793 patients operated on by >1200 surgeons in >600 institutions. Only in institutions performing <100 cases annually (n = 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) (711).

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 (712). This observation was not confirmed in the STS report, as Clark (711) found no protective relationship in high-volume institutions (>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 (713) 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 (713) 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 fewer 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 (eg, 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 <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.

B. 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 (714) 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 (714) 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 (22) 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 (715), a group from the Cleveland Clinic, suggested that the reduction in mortality noted in New York State was caused by an outmigration of high-risk patients due to the increased scrutiny provoked by public release of mortality data. Despite this criticism, Hannan et al (714) found no consistent bias against selecting high-risk patients in the state of New York. Ghali et al (716) 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 (717) 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. Peterson et al 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 are indeed effective in improving mortality rates after CABG.

Although outcome tracking has resulted in fewer deaths after CABG, many would suggest that public dissemination of this information has fallen short in helping to inform consumers. 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 (718). When clinicians in Pennsylvania and New York State 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 (719,720). In California, data reflecting diagnosis-related group mortality rates were distributed to hospitals and criticized for being excessively complex, poorly displayed, and not linked to process information that would allow institutions to respond meaningfully to the data.

In conclusion, 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 outmigration 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.

VIII. ECONOMIC ISSUES

A. Cost-Effectiveness of CABG

CABG represents a major investment for society, with an initial hospital cost of ≈$30,000 applied to >300,000 patients annually in the United States alone (≈10 billion dollars) (125). It is most appropriate to consider the cost of CABG surgery compared with other medical treatment modalities with regard to cost-effectiveness. Definitive data for such a comparison are sparse, and multiple assumptions must be made. The most reasonable system of analysis appears to be an estimation of the dollars spent per quality-adjusted life-year gained ($/QALY). In general, a cost-effectiveness of $20,000 to $40,000/QALY is consistent with other medical programs funded by society, such as

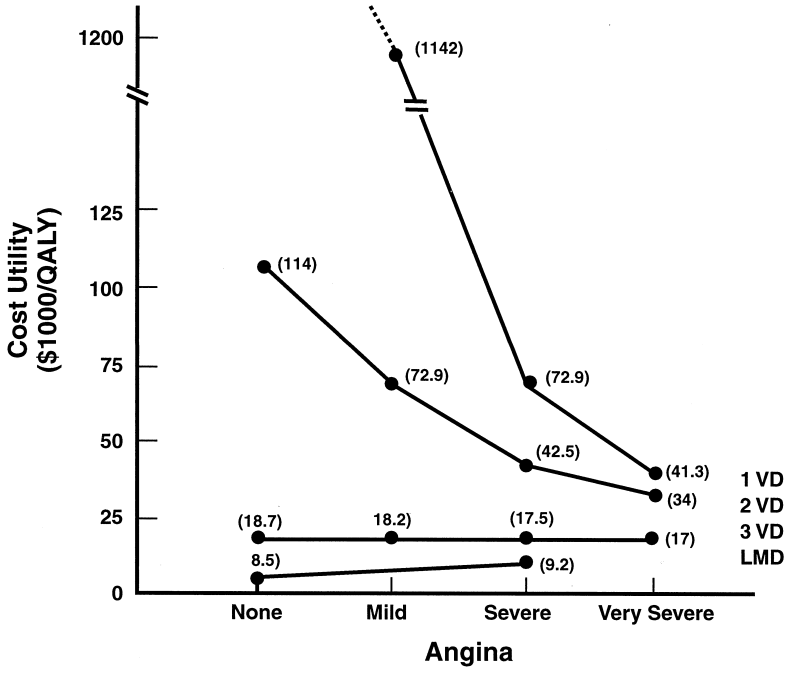

Figure 12. Cost utility. VD = vessel disease; LMD = left main disease. Modified with permission from (721).

hemodialysis and treatment of hypertension. A cost of <$20,000/QALY would be considered particularly cost-effective, while a cost >$60,000/QALY would be considered expensive (721).

A widely quoted analysis of the cost-effectiveness of CABG surgery was compiled by Weinstein and Stason (722) 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 whom 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 17. Cost-effectiveness for coronary bypass in patients with left main disease is exceptionally good at $9,000/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 survival 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.

Table 17. Cost per Quality-Adjusted Life-Year ($/QALY) of Revascularization Compared With Medical Therapy*

CABG for left main stenosis, with or without angina	9,000
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	9,000
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 (721).

B. 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 (ie, 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 $9,000/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 (723).

A direct comparison of the cost of angioplasty and coronary bypass surgery for selected patients with multivessel disease (ie, 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 ≈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 (134). 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 (135). 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 (125). 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 $2,700 more than the cost of initial angioplasty (an ≈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 <$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 has shown that there is a significant cost gradient for angioplasty as the extent of disease increases (related to repeated procedures whose instance may be reduced by stents), which is not apparent for coronary bypass (Figure 13) (724).

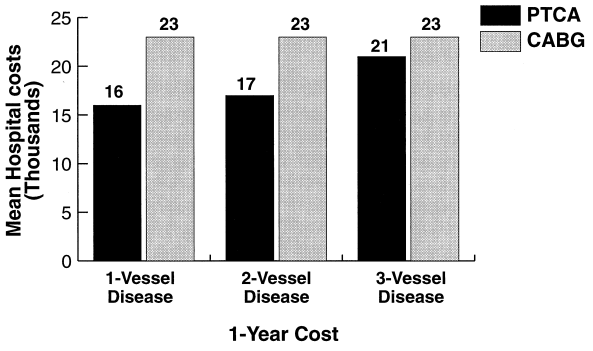

Figure 13. Percentage of 1-year costs for PTCA and CABG. Reproduced with permission from (724).

C. 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.

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 (620). 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.

IX. INDICATIONS

A. Introduction

1. Quality of Life. 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 indication 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 (725). 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.

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 <66 years, without CHF, and an EF>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 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 VIII, the procedure is cost-effective as well.

2. Survival. The second important indication 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.

B. Clinical Subsets

1. Asymptomatic or Mild Angina. 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 III. 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 III, C, 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 III, C and listed in Table 6.

Indications for CABG in Asymptomatic or Mild Angina

Class I

1. **Significant left main coronary artery stenosis.**
2. **Left main equivalent: significant (≥70%) stenosis of the proximal LAD and proximal left circumflex artery.**
3. **Three-vessel disease. (Survival benefit is greater in patients with abnormal LV function; eg, EF <0.50.)**

Class IIa

Proximal LAD stenosis with 1- or 2-vessel disease.*

Class IIb

One- or 2-vessel disease not involving the proximal LAD.†

Class III

See text.

2. Stable Angina. For patients with stable angina, the indication 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

*Becomes Class I if extensive ischemia documented by noninvasive study and/or LVEF <50%.

†If large area of viable myocardium and high-risk criteria or noninvasive testing, becomes Class I.

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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.

Indications for CABG in Stable Angina

Class I

1. **Significant left main coronary artery stenosis.**
2. **Left main equivalent: significant (≥70%) stenosis of the proximal LAD and proximal left circumflex artery.**
3. **Three-vessel disease. (Survival benefit is greater when LVEF <0.50.)**
4. **Two-vessel disease with significant proximal LAD stenosis and either EF <0.50 or demonstrable ischemia on noninvasive testing.**
5. **One- or 2-vessel CAD without significant proximal LAD stenosis, but with a large area of viable myocardium and high-risk criteria on noninvasive testing.**
6. **Disabling angina despite maximal noninvasive therapy, when surgery can be performed with acceptable risk. If angina is not typical, objective evidence of ischemia should be obtained.**

Class IIa

1. **Proximal LAD stenosis with 1-vessel disease.***
2. **One- or 2-vessel CAD without significant proximal LAD stenosis, but with a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing.**

Class III

1. **One- or 2-vessel disease not involving significant proximal LAD stenosis, in patients who have mild symptoms that are unlikely due to myocardial ischemia or who have not received an adequate trial of medical therapy and**
   (A) Have only a small area of viable myocardium or
   (B) Have no demonstrable ischemia on noninvasive testing.
2. **Borderline coronary stenoses (50% to 60% diameter in locations other than the left main coronary artery) and no demonstrable ischemia on noninvasive testing.**
3. **Insignificant coronary stenosis (<50% diameter reduction).**

3. Unstable Angina/Non–Q Wave MI. 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 non–Q wave MI 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 V, K). 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.

Indications for CABG in Unstable Angina/Non–Q Wave MI

Class I

1. **Significant left main coronary artery stenosis.**
2. **Left main equivalent: significant (≥70%) stenosis of the proximal LAD and proximal left circumflex artery.**
3. **Ongoing ischemia not responsive to maximal nonsurgical therapy.**

Class IIa

Proximal LAD stenosis with 1- or 2-vessel disease.*

Class IIb

One- or 2-vessel disease not involving the proximal LAD.†

Class III

See text.

4. ST-Segment Elevation (Q-Wave) MI. Although early coronary bypass surgery as a primary reperfusion strategy in patients suffering from an ST-segment elevation infarction has been reported, the widespread use of intravenous thrombolytic therapy for this purpose and more recently, primary angioplasty, has largely superseded 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 thrombolytic 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

*Becomes Class I if extensive ischemia documented by noninvasive study and/or LVEF <50%.

†If large area of viable myocardium and high-risk criteria on noninvasive testing, becomes Class I.

Table 18. Coronary Artery Bypass Graft Surgery Mortality in Patients With Acute Myocardial Infarction (MI)

	Mortality % (n/N)			Relative Risk		
	Q-Wave MI	Non–Q-Wave MI	Total Mortality	IABP	Inotropes	Perioperative
Group						
<48 Hours	50 (3/6)	0 (0/1)	18	9.3	3.5	3.0
3–5 Days	0 (0/7)	16 (1/6)	3.3	14.6	1.5	1.2
6–42 Days	10 (4/45	1.9 (1/51)	2.2	5.99	1.8	1.4

IABP indicates intra-aortic balloon pump.

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 thrombolysis, angioplasty, or both. As with angioplasty, the risks of bypass operation in patients in the midst of an acute ST-segment elevation infarction 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 subclassifying 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 >10 IU/L. Non–Q wave infarction is defined as ST-segment and T-wave abnormalities that do not progress to pathological Q waves but show abnormal elevations of CPK-MB isoenzyme of >10 IU/L (606). 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 other than default 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), and anatomy unsuitable for other forms of therapy. The literature is somewhat vague regarding the categories for surgical intervention. Some of the reports address Q-wave versus non–Q wave infarctions while others address the recency of MI to operation (ie, <6 hours, 6 hours to 2 days, 2 to 14 days, 2 to 6 weeks, and >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 (606) studied the comparative effect of operating on patients with a Q-wave MI and non–Q wave MI versus a control group. Table 18 illustrates the mortality and relative risks. Excluding the patients who require emergency operation for mechanical complications of an acute MI, the patients undergoing CABG within 48 hours of the Q-wave MI will carry a significantly increased operative mortality approaching 50%. The data imply that for such patients, there is little to be gained by waiting >48 hours in most circumstances. The implication is also made that symptomatic patients with a non–Q wave MI may undergo surgical revascularization at any time with no significant increase in mortality over elective patients (606). This is substantiated in a recent article by Goodman et al (603), wherein MI after thrombolytic therapy was evaluated in relation to events with Q-wave versus non–Q wave MIs. The non–Q wave MI was more likely to be nonanterior, distally located, and have better global and regional LV function. In the setting of thrombolysis after MI, patients with a non–Q wave MI 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 Q-wave and non–Q wave MIs should also translate into operative risk for these 2 patient cohorts and verifies the worse operative risk with surgery in the early Q-wave period.

Creswell et al (601) 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 <6 hours had an operative mortality of 8.4% and those who underwent operation >6 hours, 4.3% ($P = 0.02$) (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

Table 19. Coronary Artery Bypass Graft Surgery Mortality After Acute Myocardial Infarction (MI): Effect of Delaying Operation

Outcome	<6 Hours	6–48 Hours	2–14 Days	2–6 Weeks	>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%

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

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 (599). In this series, 641 of 3,397 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 >8% of total CPK, CPK >3 times normal; CPK-MB >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 (38,456,600,726) suggests that unless patients are in cardiogenic shock or have mechanical complications of acute MI, early CABG can be performed with little of 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 (727–734). 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 (727) 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.

Indications for CABG in ST-Segment Elevation (Q–Wave) MI

Class I

None.

Class IIa

Ongoing ischemia/infarction not responsive to maximal nonsurgical therapy.

Class IIb

1. **Progressive LV pump failure with coronary stenosis compromising viable myocardium *outside* the initial infarct area.**
2. **Primary reperfusion in the early hours (≤6 to 12 hours) of an evolving ST-segment elevation MI.**

Class III

Primary reperfusion late (≥12 hours) in an evolving ST-segment elevation MI without ongoing ischemia.

5. Poor LV Function. As discussed in Section V, I, 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 (735). There should be demonstration of substantial regions of myocardial viability that would benefit from revascularization (736). Such areas must be perfused by coronary arteries of sufficient size and location to be reasonable targets for bypass surgery (737).

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 <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 (735–737).

Indications for CABG in Patients With Poor LV Function

Class I

1. **Significant left main coronary artery stenosis.**
2. **Left main equivalent: significant (≥70%) stenosis of the proximal LAD and proximal left circumflex artery.**
3. **Proximal LAD stenosis with 2- or 3-vessel disease.**

Class IIa

Poor LV function, with significant viable noncontracting revascularizable myocardium and without any of the above anatomic patterns.

Class III

Poor LV function, without evidence of intermittent ischemia and without evidence of significant revascularizable viable myocardium.

6. Life-Threatening Ventricular Arrhythmias. 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 (738–740). It is particularly effective when an ischemic etiology for the arrhythmia can be documented, for instance, with exercise (741). 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 (742). Similarly, continued inducibility or clinical recurrence of ventricular tachycardia after CABG usually requires defibrillator implantation.

Indications for CABG in Life-Threatening Ventricular Arrhythmias

Class I

1. **Left main coronary artery stenosis.**
2. **Three-vessel coronary disease.**

Class IIa

1. **Bypassable 1- or 2-vessel disease causing life-threatening ventricular arrhythmias.‡**
2. **Proximal LAD disease with 1- or 2-vessel disease.‡**

Class III

Ventricular tachycardia with scar and no evidence of ischemia.

7. CABG After Failed PTCA. 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 (743,744), as well as anatomic factors such as complex lesion characteristics, extent of multivessel disease, and the absence of collaterals (743–746). Finally, outcome also depends on the total ischemic time and may be adversely affected by a delay in transport to the operating room (743,744,747,748). 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 guide wire 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 (743,749). 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 (659,750). Among patients who require emergency bypass after a failed angioplasty in the current era, the rate of complications remains substantial (751–753). This probably

‡Becomes Class I if arrhythmia is resuscitated sudden cardiac death or sustained ventricular tachycardia.

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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.

Indications for CABG After Failed PTCA

Class I

1. **Ongoing ischemia or threatened occlusion with significant myocardium at risk.**
2. **Hemodynamic compromise.**

Class IIa

1. **Foreign body in crucial anatomic position.**
2. **Hemodynamic compromise in patients with impairment of the coagulation system and without previous sternotomy.**

Class IIb

Hemodynamic compromise in patients with impairment of the coagulation system and with previous sternotomy.

Class III

1. **Absence of ischemia.**
2. **Inability to revascularize due to target anatomy or no-reflow state.**

8. Patients With Previous CABG. Reoperation after previous CABG can be successfully performed, but the risk of hospital mortality is increased ≈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 IV, A2 and V, G). 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 relative utility of percutaneous techniques in this situation is increased, particularly if these techniques can be applied to the native vessels. The application of percutaneous techniques to vein-graft stenosis is markedly inferior to the results obtainable in the native vessels.

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.

Indications for CABG in Patients With Previous CABG

Class I

Disabling angina despite maximal noninvasive therapy. (If angina is not typical, then objective evidence of ischemia should be obtained.)

Class IIa

Bypassable distal vessel(s) with a large area of threatened myocardium by noninvasive studies.

Class IIb

Ischemia in the non-LAD distribution with a patent IMA graft to the LAD supplying functioning myocardium, without an aggressive attempt at medical management and/or percutaneous revascularization.

Class III

See text.

X. AREAS IN NEED OF FUTURE RESEARCH

The last 30 years of progress in CABG surgery have been most impressive. Many challenges remain, however, as analysis of current results reveals areas of patient selection and perioperative management strategies that are poorly defined by currently available data. Several patient subsets particularly stand out as areas in need of further investigation. It appears that diabetic patients offer an unusual challenge, since the results of coronary artery bypass in this group of patients are distinctly inferior to the results in nondiabetic patients. Perhaps more compulsive management of perioperative and postoperative glucose levels will improve this problem. There are current data suggesting that coronary bypass may be superior to percutaneous techniques in these patients, but stents were not used extensively in the BARI trial. There is an absence of data on minority patients with regard to CABG surgery, an important area of future investigation. Appropriate management of patients with acute coronary syndromes is an evolving situation. Improvements in percutaneous techniques, including the use of drugs that inhibit platelet function, has dramatically altered management in this situation. At the same time, CABG offers an opportunity for controlled reperfusion and perhaps the best opportunity for resuscitation of infarcting myocardium. The management of patients with end-stage coronary disease, particularly patients who have had multiple stenting procedures and/or multiple coronary bypass procedures, is becoming an increasingly difficult problem. The success of coronary bypass in younger patients has led to the increasing consideration of CABG in elderly and very elderly patients. These patients were systematically excluded from the randomized trials of coronary bypass versus medical therapy and versus percutaneous techniques. Data on optimal management of this increasingly important and large patient subset are scarce.

Many areas of perioperative management are also evolving and need refinement and evaluation. The use of multiple arterial conduits appears to offer benefit, but the long-term efficacy and benefit of radial artery grafts and second IMA grafts are incompletely defined. Techniques for less-invasive CABG are rapidly changing, and video-assisted technology and robotic operative tools may lead to even more dramatic changes in the near future. TMLR appears to offer clinical benefit, but the mechanism of this benefit is very poorly understood. This technique may be implementable via percutaneous techniques. Gene therapy holds promise as a technique for stimulation of the development of new vasculature in ischemic myocardium. Much of the morbidity and mortality of coronary bypass is related to the use of CPB. There are developing pharmacological and mechanical methods for reducing the sequelae of CPB (drugs that reduce coagulation and inflammatory complications, such as aprotinin or aminocaproic acid, and leukocyte depletion to diminish the early inflammatory response). The management of patients with very poor LV function is also evolving, as preoperative application of mechanical assistance with an IABP appears to be useful. Operative techniques such as ventricular remodeling (in the case of a scarred myocardium or a grossly dilated LV) or mitral repair in the case of chronic ischemic MR, are techniques that warrant further study.

Modification of risk factors after CABG is perhaps the most promising but also the most difficult area for future improvement in long-term results. It remains discouraging that attempts at smoking cessation have achieved only a 20% success rate. One would hope that the near certainty of future problems with coronary disease would be a strong motivational factor in this effort. Psychological problems of anxiety and depression appear to be associated with, if not causally related to, CAD and its progression. The pharmacological management of these disorders is becoming increasingly effective. Progress in the management of serum lipids, including reduction of cholesterol and other lipid levels in patients with "average" levels, appears to offer promise in decreasing the progression of coronary disease.

From the perspective of resource utilization by society, cost analysis of medical therapy, percutaneous therapy, and surgical therapy of coronary disease remains a current and compellingly important area of research. Evolving techniques will mean that these data and data analysis will need to be repeatedly revisited in future years. As one attempts to quantify the value of coronary bypass surgery, a recurrent reevaluation of patient benefit is also obviously necessary. Indeed, the future of coronary bypass depends on a quantitative demonstration of patient benefit and value to society, as the various opportunities for delivery of sophisticated medical care are increasingly competitive for the limited resources available.

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