Twenty-Year Survival After Coronary Artery Surgery
An Institutional Perspective From Emory University

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Background—Coronary artery bypass graft (CABG) surgery has been performed frequently for symptomatic coronary atherosclerotic heart disease for more than 30 years. However, uncertainty exists regarding the relationship between long-term survival after CABG and readily available clinical correlates of mortality.

Methods and Results—We studied outcome at 20 years by age, sex, and other variables in 3939 patients who had CABG surgery from 1973 to 1979 in the Emory University System of Healthcare. Twenty-year survival, freedom from myocardial infarction, and freedom from repeat CABG were 35.6% (95% confidence interval [CI], 33.9% to 37.3%), 66.6% (95% CI, 64.6% to 68.6%), and 59.1% (95% CI, 56.9% to 61.5%). Multivariate correlates of late mortality were age (hazard ratio [HR], 1.46 per 10 years), female sex (HR, 1.21), hypertension (HR, 1.44), angina class (HR, 1.07 per class increase of 1), prior CABG (HR, 1.72), ejection fraction (HR, 1.07 per 10-point decrease), number of vessels diseased (HR, 1.11 per 1-vessel increase), and weight (HR, 1.04 per 10 kg). Twenty-year survival by age was 55%, 38%, 22%, and 11% for age <50, 50 to 59, 60 to 69, and >70 years at the time of initial surgery. Survival at 20 years after surgery with and without hypertension was 27% and 41%, respectively. Similarly, 20-year survival was 37% and 29% for men and women.

Conclusions—Symptomatic coronary atherosclerotic heart disease requiring surgical revascularization is progressive with continuing events and mortality. Clinical correlates of mortality significantly impact survival over time and may help identify long-term benefits after CABG. (Circulation. 2003;107:1271-1277.)

Key Words: coronary disease ■ surgery ■ survival ■ mortality

Coronary atherosclerotic heart disease remains the number one cause of death, disability, and economic loss among industrialized nations. Although the primary focus of care for patients with atherosclerosis is prevention of disease progression by risk factor modification, management strategies for symptomatic patients include both pharmacological therapy and revascularization by either percutaneous coronary intervention or coronary artery bypass graft (CABG) surgery. CABG surgery was introduced nearly 35 years ago, and it has become clear that this operation relieves angina pectoris and likely improves quality of life. Long-term survival after CABG surgery in prospectively evaluated patient groups has been ≈33% at 15 years and 20% at 22 years, although the numbers of patients reported is limited. Because CABG is one of the most commonly performed and costly surgical interventions performed today, it is important to understand the impact of age and associated patient-specific disease characteristics on survival.

This study describes survival and the natural course of disease in a patient population undergoing coronary artery surgery for standard indications from 1973 to 1979, with both short and long-term follow-up. This is the largest such cohort of patients from one institution reported to date that assesses the impact of age and associated disease correlates (hypertension, congestive heart failure, diabetes mellitus, prior myocardial infarction, and angina severity) on survival over such a long time span. We found age was the most significant contributor to mortality over time. As the number of associated mortality correlates increased, long-term survival decreased dramatically.

Methods

Definitions
Single-vessel disease was defined as ≥50% diameter luminal narrowing in either the left anterior descending, left circumflex, or right coronary artery or a major branch or branches. Double-vessel disease was the presence of ≥50% diameter luminal narrowing in 2 of the 3 major epicardial vessel systems. Three-vessel disease was the presence of ≥50% diameter luminal narrowing in all 3 major epicardial vessel systems or in the left anterior descending and proximal...
Table 1. Clinical Characteristics by Sex

<table>
<thead>
<tr>
<th></th>
<th>Women (n=627)</th>
<th>Men (n=3312)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>57±9</td>
<td>54±9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systemic hypertension, n (%)</td>
<td>226 (50.9) (n=444)</td>
<td>809 (34.8) (n=2325)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior MI, n (%)</td>
<td>227 (50) (n=454)</td>
<td>1334 (54.8) (n=2436)</td>
<td>0.07</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>84 (19.1) (n=440)</td>
<td>261 (11.3) (n=2302)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart failure, n (%)</td>
<td>28 (6.7) (n=417)</td>
<td>104 (4.8) (n=2156)</td>
<td>0.14</td>
</tr>
<tr>
<td>Class III/IV angina, n (%)</td>
<td>127 (58) (n=219)</td>
<td>493 (51.7) (n=954)</td>
<td>0.11</td>
</tr>
<tr>
<td>Prior CABG, n (%)</td>
<td>7 (1.1)</td>
<td>24 (0.7)</td>
<td>0.44</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>65±13</td>
<td>81±12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>62±13</td>
<td>58±13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1-Vessel disease, n (%)</td>
<td>152 (28.0)</td>
<td>561 (19.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2-Vessel disease, n (%)</td>
<td>180 (33.2)</td>
<td>929 (32.8)</td>
<td>0.9</td>
</tr>
<tr>
<td>3-Vessel disease, n (%)</td>
<td>155 (28.6)</td>
<td>1028 (36.3)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Left main disease, n (%)</td>
<td>55 (10.1)</td>
<td>313 (11.1)</td>
<td>0.58</td>
</tr>
<tr>
<td>Elective surgery, n (%)</td>
<td>568 (91)</td>
<td>3046 (92)</td>
<td>0.28</td>
</tr>
<tr>
<td>Q-wave MI, n (%)</td>
<td>21 (3.7) (n=624)</td>
<td>152 (4.68) (n=3249)</td>
<td>0.18</td>
</tr>
<tr>
<td>Death in hospital, n (%)</td>
<td>7 (1.12)</td>
<td>32 (0.98) (n=3273)</td>
<td>0.91</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>10.07±9.72</td>
<td>8.9±6.58</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Values are mean±SD or n (%). MI indicates myocardial infarction.

Patient Follow-Up

Follow-up information was obtained from patients or referring physicians. Follow-up status for each end point was also assessed at each subsequent hospital admission. Patients not readmitted were contacted by telephone or letter approximately every 5 years. Follow-up was available on 3905 of 3939 patients (99%). The median length of follow-up was 14.2 years and, in survivors, 20 years. Information obtained included occurrence of myocardial infarction since the initial CABG, subsequent need for an additional revascularization procedure (percutaneous coronary intervention or CABG), death (cardiac plus noncardiac), and recurrent angina. All follow-up information was recorded on standardized forms and entered into the computerized database. All repeat procedures performed at Emory University Hospitals were confirmed from the database. Myocardial infarctions during follow-up were ascertained largely from the patients, and there may be inherent under-reporting and over-reporting.

Statistical Analyses

Data are expressed as proportions or as mean±SD. Differences in categorical variables were analyzed by χ² or Fisher’s exact tests, and differences in continuous variables were analyzed by ANOVA. Multivariate correlates of long-term survival were determined by Cox model analysis. Missing data were filled in using the method of Harrel. Discrimination of the multivariate analysis for in-hospital and long-term mortality models were examined using the C index. Validation and calibration of models were tested by the methods of Harrel. Potential nonlinear effects of each of the continuous predictor variables were checked using restricted cubic splines. Interaction terms were examined. Statistical modeling and testing were performed in S-Plus.

Results

Clinical Characteristics and Outcome by Sex

Baseline clinical and angiographic characteristics of the 3939 patients studied are presented in Table 1. Women, who represented 16% of the study population, were older (57±9 versus 54±9 years) and had a higher prevalence of hypertension and diabetes and more severe angina. However, women had fewer prior myocardial infarctions, better ejection fractions, and more single-vessel and less triple-vessel coronary artery disease. The presence of clinical congestive heart failure, double-vessel coronary artery disease, and left main disease was essentially the same among in both men and women. There was no difference noted in the acuteness of the procedure. There was little difference in in-hospital outcome, with Q-wave myocardial infarctions and death (1.12% for women, 0.98% for men) nearly equal in the 2 groups; length of stay was longer among women (10.1±9.7 versus 8.9±6.6 days; P=0.0002).

Circumflex arteries in left-dominant patients. Left main disease was the presence of ≥50% diameter luminal narrowing in the left main coronary artery. An emergent procedure was a procedure performed in the setting of acute ischemia or infarction. Myocardial infarction as a complication after the procedure was determined by the development of new Q waves. Variables defined by patient history were hypertension, diabetes, severity of angina, congestive heart failure, prior myocardial infarction, and myocardial infarction during follow-up. Angina was classified by the Canadian Cardiovascular Society Classification. Congestive failure was classified by New York Heart Association criteria.
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Clinical Characteristics by Age Group

Patients stratified by age are shown in Table 2. Patients age 50 to 59 years represented the largest number of patients (1692 patients; 43%), and the fewest were >70 years (143 patients; 3.6%) at the time of initial operation. At each increasing age group of 10 years (<50, 50 to 60, 60 to 70, and ≥70 years), men outnumbered women, although the proportion of women in each age group increased with each decade, as did the prevalence of hypertension, diabetes, heart failure, class III/IV angina, and left main coronary artery disease.

Hospital Outcome by Age Group

Table 3 shows surgical status and early clinical outcome grouped according to age. The prevalence of elective, emergent, and urgent CABG, as well as post-surgical Q-wave myocardial infarction, was roughly preserved across age categories. Only death in the hospital and length of stay significantly increased with age. Mortality rates rose most dramatically across the age groups (0.09% for ages <50 years to 2.11% for ages ≥70 years). Older patients also had longer hospital stays. No significant age-adjusted effects were seen among elective, emergent, or urgent CABG procedures.

Correlates of Long-Term Mortality

Consistent with prior studies assessing clinical correlates of late outcome among patients undergoing surgery 20 years ago,11,12 we found age (Table 4) was the most powerful contributor to decreased survival probability in our model (hazard ratio, 1.46 per decade of life); the younger the patient at the time of operation, the higher the likelihood of long-term survival. Hypertension, female sex, and prior coronary surgery were also powerful contributors to decreased survival likelihood. Other risk factors included higher initial angina class, reduced ejection fraction, number of vessels diseased, and increased weight. Although the presence of diabetes or heart failure contributed univariately to mortality risk, neither showed independent statistical significance. The ability of the model to discriminate was at best moderate, with a c index of 0.631 (validated at 0.630). The calibration of the model was excellent (data not shown). A separate model was also developed with all patients surviving beyond 5 years censored at 5 years. In this model, sex and weight were no longer independent risk factors. Otherwise, the model was similar, with the same correlates and similar hazard ratios, 95% confidence intervals, and probability values.

Survival by Correlates

Overall survival at 1, 5, 10, 15, and 20 years was 97.6% (95% CI, 97.1 to 98.0), 91.9% (95% CI, 91.5% to 92.4%), 78.4% (95% CI, 77.1% to 79.8%), 56.5% (95% CI, 54.8% to 58.2%) and 36.6% (95% CI, 34.9% to 38.4%), respectively.
Survival curves by age begin to diverge around 7 years after surgery, and divergence increases significantly at 10 years and beyond. Ten years after surgery, percent survival in each age group was 85%, 80%, 74%, and 56% for ages <50, 50 to 60, 60 to 70, and >70 years at the time of initial operation. Twenty years after surgery, percent survival was 51%, 38%, 22%, and 11% for age <50, 50 to 60, 60 to 70, and >70 years, respectively.

Survival to 20 years was 29% in women and 37% in men (P<0.0001; Figure 2). Survival in patients without hypertension was 41%, and in patients with hypertension, 27% (P<0.0001). Survival to 20 years was 40% for patients with ejection fractions >50%, 25% for ejection fractions 35% to 50%, and 17% for patients with ejection fractions <35% (P<0.0001; Figure 3).

**Freedom From Events**

Overall 20-year freedom from myocardial infarction and freedom from repeat CABG were 66.6% (95% CI, 64.6% to 68.6%) and 59.1% (95% CI, 56.9% to 61.5%), respectively.

Freedom from subsequent myocardial infarction was 57% at <50 years, 68% at 50 to 60 years, 74% at 60 to 70 years, and 77% at >70 years. The inverse age relationship is probably related to the higher mortality with increasing age. Freedom from subsequent CABG is shown in Figure 4. Like the analysis of freedom from subsequent myocardial infarction, freedom from either surgical or percutaneous revascularization was greatest among older age groups. Ten years after initial CABG surgery, 79%, 87%, 94%, and 99% of patients aged <50, 50 to 60, 60 to 70, and >70 years, respectively, were free from repeat CABG. At 20 years, 47%, 58%, 74%, and 92% of patients aged <50, 50 to 60, 60 to 70, and >70 years were free from repeat CABG. Twenty-year freedom from percutaneous coronary intervention was 69%, 73%, 80%, and 91%, respectively, for patients aged <50, 50 to 60, 60 to 70, and >70 years.

**Discussion**

In the present study, we showed in a large sample of 3939 patients that there are continuing events over the 20 years after coronary surgery. Mortality at 20 years is high. The ability to determine who is at especially high risk was at best moderate, with a C index of 0.63. Variables that have often been shown to predict mortality, such as age and ejection fraction, were predictive in this population. Others, especially diabetes, were not independently predictive. This may reflect the fact that this study was drawn from a population 20 years ago and the spectrum of patients undergoing coronary surgery today may be somewhat different.

Several studies have considered long-term survival to 20 years after coronary surgery. Laurie et al.11 studied the outcome of 1698 patients undergoing CABG between 1968 and 1975. Survival at 20 years was 40% for 1-vessel, 26% for 2-vessel, 20% for 3-vessel, and 25% for left main disease. Independent correlates of survival were age at operation, extent of coronary disease, left ventricular function, history of
stroke, and preoperative heart failure. In a much smaller study, Ulicny et al.12 studied the 20-year outcome of 100 patients undergoing CABG between 1970 and 1972. The 5-, 10-, 15-, and 20-year survival rates were 89.8%, 68.4%, 53.1%, and 40.8%, respectively. Myers et al.5 evaluated 15-year follow-up after CABG in 8221 patients from the Coronary Artery Surgery Study (CASS) registry, with a mean follow-up of 15 years. Survival was 90% at 5 years, 74% at 10 years, and 56% at 15 years. Female sex, small body surface, ischemic symptoms, and emergency status predicted early mortality. Heavier weight, prior myocardial infarction, diabetes, smoking, left main and left anterior descending artery stenosis, and use of vein grafts only increased late mortality.

Registries and randomized trials of patients undergoing CABG have provided a great deal of information regarding continued patient benefit from this intervention in appropriately selected patients.13–17 Patients with left main disease and 3-vessel disease have improved survival compared with patients treated medically.2–4 Technical improvements have resulted in reduced perioperative mortality, myocardial infarction, and stroke, as well as better long-term survival and improved graft patency with internal thoracic artery grafting and improved myocardial protection.18,19 More recently, off-pump surgery has resulted in shorter lengths of stay and possibly improved outcome.20 Despite these improvements, the disease remains chronic and unremitting. Clearly, risk factor control must remain a cornerstone of long-term therapy.

Figure 2. Twenty-year survival after coronary surgery by sex.

Figure 3. Twenty-year survival after coronary surgery by ejection fraction.
The dramatic impact of age on survival in cohorts of patients undergoing surgical and percutaneous revascularization has been extremely consistent. However, the impact of associated mortality correlates on survival varies considerably. One would expect that the effect of age on mortality might be partially accounted for by other risk factors associated with the aging process, such as higher prevalence of diabetes mellitus, 3-vessel coronary artery disease, systemic hypertension, and congestive heart failure. Diabetics have a higher rate of myocardial infarction and need for additional revascularization procedures and a lower (although acceptable) survival after successful CABG. The number of coronary arteries severely narrowed has been shown to increase in-hospital and long-term mortality. A history of hypertension and heart failure has also been associated with adverse early and long-term outcomes after CABG.

Study Limitations
This study has some limitations. We used multivariate analysis to reduce confounding in determining the increased risk associated with several variables. However, there may be additional risk factors that affect outcome that we have not controlled for that could have influenced our results. One of these is the influence of the period of observation, because patients included in this study were operated on >20 years ago, and outcomes reflect the surgical and medical approaches prevalent at that time. There have been substantial improvements in surgical techniques and preoperative and postoperative care that have reduced perioperative mortality and morbidity. Routine use of internal mammary grafts were not common at that time, and their use has likely increased graft conduit patency and subsequent survival, both short and long term. Furthermore, the additive benefit of routine antiplatelet and lipid-lowering therapy in this patient population would also likely have improved the benefits of CABG surgery significantly. Our in-hospital complication rates were excellent for that time period, as are the long-term outcomes compared with other reports.

Conclusions
Finally, these data serve to remind clinicians that symptomatic coronary atherosclerotic heart disease requiring revascularization is progressive, with continuing events and mortality. Age and associated clinical disease characteristics (survival risk factors) heavily impact survival after CABG. Hypertension, hyperlipidemia, and other modifiable diseases should be treated aggressively because they are associated with decreased survival over time. Furthermore, the long-term benefits of surgical coronary revascularization were short lived among those patients with multiple clinical correlates for decreased survival, including older age, even among a surgical population that was significantly healthier than today’s coronary surgery population.

References


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