Long-term Survival of Patients With Coronary Artery Disease During the 1970s*

A Cohort Study

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Study objective: This study was undertaken to determine the effects of altered risk factors and treatment modalities on the short- and long-term survival of patients with documented coronary artery disease whose conditions were diagnosed from 1972 through 1982.

Study design: The study was a retrospective database analysis of clinical, angiographic, and follow-up information.

Setting: Data from all patients referred for cardiac catheterization at the Baptist Memorial Hospital, Memphis, Tenn, were studied.

Patients: Risk factors and survival of patients who underwent cardiac catheterization from 1972 through 1982 and who were followed up for at least 5 years were evaluated. Cohort A included 1,821 patients studied from 1972 through 1977; cohort B included 5,369 patients studied between 1977 and the end of 1982. Each cohort was subdivided based on type of therapy (medical or surgical) that the patients received.

Measurements and results: The 30-day (short-term) and 5-year (long-term) survival rates were compared by life table methods. Short-term survival improved significantly in both medical (from 94.9% to 97.5%, p<0.001) and surgical (from 95.5% to 97.6%, p<0.001) groups from cohort A to cohort B. Long-term survival, however, did not differ significantly between the two cohorts. In the medical group, 5-year survival in cohort A was 86.3% and in cohort B it was 86.9% (p=NS); in the surgical group, in cohort A it was 89.1% while in cohort B it was 89.4% (p=NS). Prevalence of both cigarette smoking and hypercholesterolemia declined significantly from cohort A to cohort B in both surgical and medical groups. However, advanced age, female gender, and previous myocardial infarction were significantly more common in cohort B than in cohort A for both treatment groups.

Conclusions: These results indicate that during the study period, a significant decline in short-term mortality occurred for patients with angiographically documented coronary artery disease. Long-term survival did not, however, improve possibly due to a complex interplay between factors that promote coronary artery disease, e.g., cigarette abuse and hypercholesterolemia, and factors that determine survival, e.g., increases in age and history of prior infarction and advances in medical and surgical therapy.

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Key words: cardiovascular disease epidemiology; coronary artery disease; survival studies

Cardiovascular mortality has declined significantly over the past two decades.1 For example, in the Framingham Heart Study, cumulative 10-year mortality from cardiovascular disease for men who were aged 50 to 59 years in 1970 was 43% lower than for those in this age range in 1950.2 During that period, the case fatality rate fell by 60% and, for those free of disease at entry into the study, cumulative incidence of cardiovascular disease fell by 19%.2 This decline has been attributed to several factors, including changes in life-style, reduced prevalence of risk factors for coronary artery disease, improved medical therapy, and advances in surgical techniques for myocardial revascularization.1,3

In this report, we describe the changes in risk factors, angiographic abnormalities, and survival of patients referred for coronary angiography from the first half to the second half of the 1970s. This patient base differs in key ways from large studies of the general population, such as in the Framingham Study,2 the Worcester Heart Attack Study,4,5 the Minnesota Heart Study,6 and others. Herein, we will examine changes in risk factors and outcomes in the subset of patients with symptomatic ischemic heart disease documented to be present by coronary angiography. Hence, the question we will examine is: “During the period from 1972 through 1982, did short- and long-term outcome improve for patients with angiographically documented coronary disease as they did for the general population?”

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Long-term Survival of Patients with Coronary Artery Disease in the 1970s (Ramanathan et al)
METHODS

Patient Selection

The database for this study was the Cardiac Disease Registry of the Baptist Memorial Hospital, Memphis, Tenn. This computerized registry contains clinical, hemodynamic, and angiographic information abstracted at the time of cardiac catheterization from the patients’ charts and the procedure reports. Follow-up information was obtained from questionnaires mailed annually to either the patient or the referring physician within 1 month of the catheterization anniversary date. Significant coronary stenosis was defined as the presence of 70% or greater reduction in luminal diameter of a major epicardial coronary artery, as determined by manual calipers.

From this group of patients, those who underwent the procedure between the years 1972 to 1982 and who were followed up for 5 years or longer were selected (Fig 1). Those with normal coronary angiograms, or with congenital, valvular, primary myocardial, and pericardial diseases, or who died as a result of the angiographic procedure (n=5) were excluded. The patients were then divided into two cohorts, based on the year in which they underwent catheterization. Patients who underwent cardiac catheterization from January 1, 1972 through December 31, 1976 formed one cohort (cohort A), and those from January 1, 1977 through December 31, 1982 formed the second cohort (cohort B).

Patients in each cohort were further divided into two groups, based on the type of treatment they received after angiography. The medical group consisted of patients with coronary artery disease who underwent medical therapy; the surgical group consisted of patients who underwent coronary artery bypass grafting. The type of therapy was determined by the patient’s primary physician.

Presence of risk factors was determined at the time of admission to the hospital for coronary angiography. Hypertension was considered present if systolic pressure was 160 mm Hg or greater, diastolic pressure was 90 mm Hg or greater, or if the patient was receiving therapy for hypertension. A serum cholesterol level of or greater than 240 mg/dL was considered to indicate hypercholesterolemia. Diagnoses of diabetes mellitus and cigarette abuse were made based on recorded histories.

Statistical Analysis

Univariate analysis included Mantel-Haenszel χ² tests for dichotomous characteristics to compare the characteristics of the two cohorts for each treatment group. Characteristics with continuous measures were dichotomized as follows: age, <65 and ≥65 years of age; serum cholesterol, <240 mg/dL and ≥240 mg/dL; and ejection fraction, <50% and ≥50%.

Life table methods using the Lee-Desu statistic were used to compare long-term survival in the two cohorts over a 5-year period after cardiac catheterization. Life table techniques were also applied to the data stratified by baseline characteristics to adjust for differences in patient survival due to variations in age, gender, etc. Multivariate analyses included the Cox proportional hazard model to test the actual effect of time (cohorts) on survival, after adjusting for other risk factors that may affect survival.

RESULTS

A total of 13,071 patients underwent coronary arteriography between 1972 and 1982 (Fig 1). Patients with congenital, valvular, primary myocardial, and pericardial disease, with normal coronary arteries, or with procedure-related mortality were excluded. Thus, a total of 7,190 patients were included in this study.

Cohort A consisted of 1,821 patients undergoing angiography before the beginning of 1972 and the end of 1976. Of these, 626 patients who underwent medical therapy and 965 patients who underwent surgical therapy had adequate follow-up. Cohort B included 5,369 patients studied from the beginning of 1977 through the end of 1982; 2,367 patients who underwent medical therapy and 2,203 patients who underwent surgical therapy had follow-up and were further analyzed. The percentages of patients unavailable for follow-up were similar for both cohorts.

Risk Factor Analysis of Cohort A and Cohort B

The prevalence of risk factors for coronary artery disease in each cohort was determined and compared (Table 1).

Age: There was a significantly greater number of patients aged 65 years or older in cohort B than in cohort A. This was true for both medical and surgical groups.

Gender: There was also a significantly greater number of women in cohort B than in cohort A. This

Table 1—Baseline Characteristics and Risk Factors

<table>
<thead>
<tr>
<th>Medical Group, %</th>
<th>Surgical Group, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cohort A</td>
</tr>
<tr>
<td></td>
<td>Cohort A</td>
</tr>
<tr>
<td>Age &gt;65 yr</td>
<td>8.8</td>
</tr>
<tr>
<td>Women</td>
<td>25.5</td>
</tr>
<tr>
<td>Smokers</td>
<td>75.2</td>
</tr>
<tr>
<td>Elevated cholesterol level</td>
<td>39.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36.4</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12.7</td>
</tr>
<tr>
<td>Previous MI*</td>
<td>25.5</td>
</tr>
</tbody>
</table>

*MI=myocardial infarction.
†p<0.001.
†p<0.05.
Table 2—Changes in Angiographic Characteristics

<table>
<thead>
<tr>
<th>Medical Group, %</th>
<th>Surgical Group, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cohort A</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td></td>
</tr>
<tr>
<td>&lt;50%</td>
<td>20.8</td>
</tr>
<tr>
<td>Mild disease*</td>
<td>31.1</td>
</tr>
<tr>
<td>1-Vessel disease</td>
<td>27.3</td>
</tr>
<tr>
<td>2-Vessel disease</td>
<td>19.9</td>
</tr>
<tr>
<td>3-Vessel disease</td>
<td>16.4</td>
</tr>
<tr>
<td>Left main disease</td>
<td>5.4</td>
</tr>
</tbody>
</table>

*Mild disease = <70% coronary stenosis.
†p<0.05.
* p<0.001.

difference also existed for both medical and surgical groups.

Hypertension: There was no significant difference in the prevalence of hypertension between the two cohorts in either the medical or the surgical groups.

Diabetes Mellitus: The prevalence of diabetes mellitus did not differ significantly between the two cohorts.

Cigarette Smoking: There were significantly fewer smokers in cohort B compared with cohort A for both the medial and the surgical groups.

Hypercholesterolemia: Both medical and surgical groups in cohort A had greater numbers of patients with hypercholesterolemia than did the corresponding groups of cohort B.

Previous Myocardial Infarction: In both medical and surgical groups, a significantly greater number of patients in cohort B had prior myocardial infarction than did subjects in cohort A.

Angiographic Characteristics of Cohorts A and B

Angiographic features of patients in the two cohorts are presented in Table 2.

Ejection Fraction: There was a significantly smaller percentage of patients with an ejection fraction less than 50% in cohort B, medical group, than in cohort A, medical group (20.8% vs 15.1%, p<0.05).

However, there was no significant difference between the two cohorts for patients treated surgically.

Extent of Coronary Artery Disease: A significantly greater percentage of patients in cohort B had single-vessel coronary disease than in cohort A for both treatment groups. Three-vessel coronary disease was, in contrast, significantly less prevalent in cohort B than in cohort A for medical and surgical groups. The prevalence of two-vessel and left main disease were not different in the two cohorts.

Mortality Rates for Cohorts A and B

Early and long-term survival statistics for the two groups were compared (Tables 3 and 4, Figs 2 through 4).

Early Mortality: Early (30-day) mortality was lower in cohort B, medical group (2.5%) than for cohort A, medical group (5.1%, p<0.001). In the surgical groups, short-term mortality also declined significantly from 4.5% in cohort A to 2.4% in cohort B (p<0.01).

Five-Year Survival: The 5-year survival for cohort

Table 3—Five-Year Survival Stratified by Risk Factors and Angiographic Characteristics

<table>
<thead>
<tr>
<th>Medical Group, %</th>
<th>Surgical Group, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cohort A</td>
</tr>
<tr>
<td>Age &gt;65 yr</td>
<td>75.9</td>
</tr>
<tr>
<td>Women</td>
<td>91.4</td>
</tr>
<tr>
<td>Elevated cholesterol level</td>
<td>85.6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>86.6</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>75.0</td>
</tr>
<tr>
<td>Ejection fraction &lt;50%</td>
<td>63.9</td>
</tr>
<tr>
<td>1-Vessel disease</td>
<td>93.9</td>
</tr>
<tr>
<td>2-Vessel disease</td>
<td>86.0</td>
</tr>
<tr>
<td>3-Vessel disease</td>
<td>67.6</td>
</tr>
<tr>
<td>Left-main disease</td>
<td>48.9</td>
</tr>
</tbody>
</table>

*p<0.05.
A was 88% and for cohort B was 88% (Fig 2). When groups based on the treatment received were examined, there were also no significant differences in survival. Cohort A, medical group, 5-year survival was 86.3% and for cohort B, medial group, 5-year survival was 86.9% (p=0.62). Cohort A, surgical group, had a 5-year survival of 89.1%, while in cohort B, surgical group, long-term survival was 89.4% (p=0.15).

Long-Term Survival in Patients Stratified for Risk Factors and Angiographic Characteristics: We stratified the patients in both cohorts and treatment groups based on risk factors and angiographic features (Table 3). Factors considered were age, gender, history of cigarette smoking, presence of hypertension, elevated cholesterol level, ejection fraction less than 50%, and the number of vessels involved.

Survival in several stratified subsets improved between cohort A and cohort B. However, the only significant difference in 5-year survival was between the cohort A, medical group and cohort B, medical group for patients with single-vessel coronary artery disease. Cohort A, medical group demonstrated significantly better survival than cohort B, medical group (93.9% vs 87.9% p<0.01). No subsets could be identified among the groups treated with surgery in which long-term survival significantly improved over the study period.

The survival curves for patients with ejection fractions of 50% or less are plotted in Figure 3. Survival for patients treated surgically did not differ at any point (1 to 5 years) between cohorts. For medical groups, however, survival at 1 year was significantly better for those in cohort B than in cohort A. However, by the second year after angiography, the curves converged so that longer-term survival was no longer significantly different.

Comparison of 5-Year Survival for Patients Aged 65 Years or Older: There were more patients aged 65 years or older in both the medical and surgical groups of cohort B than in cohort A. Survival curves for the subset of patients 65 years of age or older are depicted in Figure 4. They demonstrate that 1-year survival for both medical and surgical groups improved significantly from cohort A to cohort B. However, survival rates after 2 years or longer were not significantly different. When older patients were then sub-stratified based on sex, ejection fraction, and age, the differences in survival were no longer significant.
Table 5—Multivariate Model, Including Cohorts as a Variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\chi^2$</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>148.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>113.49</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>22.54</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19.15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medical groups</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>105.08</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>62.12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender</td>
<td>8.74</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4.77</td>
<td>0.029</td>
</tr>
<tr>
<td>Surgical group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>57.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>45.61</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11.79</td>
<td>0.0006</td>
</tr>
<tr>
<td>Smoking</td>
<td>8.79</td>
<td>0.003</td>
</tr>
</tbody>
</table>

The number of vessels stenosed, no significant differences in 5-year survival were noted between the two cohorts (Table 4).

Multivariate Analysis: Multivariate analysis, based on the stepwise Cox proportional hazard model, was used to determine the independent statistical importance of the year of angiography for 5-year survival (Table 5). Independent variables included in the model were age in years, race, gender, presence or absence of smoking history, presence or absence of hypertension, presence or absence of diabetes mellitus, presence or absence of hypercholesterolemia, ejection fraction (as percent), and the patient’s cohort (A or B). The cohort was used as a proxy for year of angiography.

For the study population as a whole, the variables that were significant independent predictors of survival were ejection fraction, age, smoking history, and diabetes history. The cohort was not selected as a significant variable. When the medical and surgical groups were independently analyzed, cohorts were also not selected as a significant variable in the stepwise model.

Medical Treatment in Cohorts A and B

The classes of medical therapies prescribed for patients in cohort A and cohort B were compared (Fig 5). In both medical and surgical groups, fewer patients in cohort B received nitrate therapy than in cohort A; in contrast, a higher percentage of patients in cohort B received therapy with $\beta$-adrenergic or with calcium channel blocking agents or antiplatelet drugs than did patients in cohort A.

Discussion

The decline in cardiovascular mortality that has been documented in the United States has been attributed to several interactive factors. Modification of life-style and risk factors, and more effective therapy of hypertension and hyperlipidemia reduce the prevalence of ischemic heart disease and retard the extent of coronary atherosclerosis. Advances in medical technology, eg, widespread implementation of coronary care units and prehospital care, and in drug therapy have in most (but not all) studies reduced case fatality rates. Similarly, surgical revascularization in appropriately selected patients improves survival, while advances in surgical techniques have reduced the operative mortality and increased the efficacy of the procedures.

The present effort to study the correlates of the declining mortality rate differs in several ways from prior studies of this phenomenon. First, the patients who were evaluated all had documented coronary artery disease and a clinical syndrome suggesting myocardial ischemia. This is in contrast to large population studies such as the Framingham Heart Study and others that examined groups with and without clinical evidence of disease. Because we examined outcomes only in patients with significant ischemic heart disease, effects of primary prevention interventions to prevent disease are excluded. Effects of primary and secondary preventive measures to limit the extent of disease, however, remain possible.

Second, in our study, the extent of coronary artery
disease and the state of left ventricular function were known from angiographic studies. In general population studies, these variables are not known. Both the extent of coronary atherosclerosis and level of ventricular function\textsuperscript{12,13} are major, independent determinants of survival that cannot be accurately determined from clinical presentations. Thus, specific knowledge of the variables allows better stratification of patients into subgroups for analysis of survival.

Results of this study showed several phenomena. First, the prevalence of several risk factors for ischemic heart disease fell significantly from the first cohort to the second. Goldman and Cook\textsuperscript{1} attributed 60\% of the decline in cardiovascular mortality to this effect. In our population, significant reductions in hypercholesterolemia and cigarette abuse were observed (Table 1).

Similar observations have been published by others. The Lipid Research Clinics\textsuperscript{14} and other studies\textsuperscript{15} suggest that mean cholesterol levels in the general population during the period of study may have fallen by as much as 7\%. Similarly, in the Framingham study,\textsuperscript{2} 56\% of patients aged 50 to 59 years in 1950 smoked cigarettes whereas only 34\% of those aged 50 to 59 years in 1970 did so.

Reductions in the prevalence of these risk factors would be expected to improve survival by limiting the development and extent of coronary disease. Patients with hyperlipidemia have a greater likelihood of developing ischemic heart disease, have more extensive atherosclerosis, and have reduced survival rates than do those who have normal cholesterol levels.\textsuperscript{16,17} Similarly, cigarette smoking is associated with higher incidence and greater extent of coronary atherosclerosis and reduced survival.\textsuperscript{18,19} The increased risk imposed by elevated cholesterol levels may be greater in those with cardiac disease (as in our patients) than in those without.\textsuperscript{20} Conversely, reversing these risk factors improves outcome.\textsuperscript{21,22}

Second, short-term postcatheterization survival improved for patients treated by either medical or surgical approaches. Thirty-day mortality fell from 5.1\% to 2.5\% for patients treated medically and from 4.5\% to 2.4\% for those undergoing surgical revascularization. These results are similar to those reported for short-term survival after acute myocardial infarction. For example, the case fatality rate during the hospital phase of acute myocardial infarction fell from 22.1\% in 1975 to 17.4\% in 1981 in the Worcester Heart Attack Study.\textsuperscript{4} Reductions were also reported in many other studies, such as the Minnesota Heart Study,\textsuperscript{6} the study of DuPont employees,\textsuperscript{20} and the Rochester, Minnesota study.\textsuperscript{11} In contrast, Goldman et al\textsuperscript{7} reported no change in short-term mortality in Boston from 1973 to 1974 to 1978 to 1979. Although these reports focused on acute infarction, the relevant issues are likely to be similar to those in our population for short-term survival.

We, as have others, attribute this improved short-term survival to the advances in medical and surgical therapies that occurred during the 1970s. Goldman and Cook\textsuperscript{1} attributed 13.5\% of the reduction in mortality to coronary care units and an additional 4\% to prehospital care. Advances in surgical techniques also led to reduced mortality.\textsuperscript{9,10}

Changes in medical therapy have also improved outcome. As shown in Figure 5, patients in cohort B—whether treated with or without surgical revascularization—were more likely than were patients in cohort A to receive drugs that improve survival, eg, \( \beta \)-blockers, calcium channel antagonists, and antplatelet agents. \( \beta \)-Blockers have been shown, in many studies, to increase early and long-term survival.\textsuperscript{24,25} Similar conclusions have been presented for calcium channel antagonists.\textsuperscript{26,27}

An additional factor that may have played an important role is “lead-time bias.”\textsuperscript{28} More aggressive referral for angiography earlier during the natural history of coronary disease\textsuperscript{29} would result in less severely ill patients being studied who would, in turn, be expected to have a better outcome. Thus, the statistical length of survival of a population sample may be increased without a real change in natural history.\textsuperscript{2} The role for this is suggested, for example, by the greater prevalence of single-vessel disease in cohort B than in cohort A.

Finally, long-term survival did not improve from one cohort to the second. Five-year survival did not improve significantly for either medical or surgical subgroups (Fig 2). In addition, no subgroup of patients defined by clinical variables such as age or gender or on angiographic findings could be defined in which long-term survival improved (Tables 3 through 5). Finally, the day of angiographic study—corresponding to cohort—was not selected as a significant predictor of long-term survival by multivariate regression techniques (Table 5).

Other reports vary in regard to this outcome. In a study similar to ours of patients referred for cardiac catheterization, Pryor et al\textsuperscript{3} reported progressive increases in 2-year survival between 1967 to 1984. For patients treated surgically, the year of study was an independent predictor of improved outcome, but for those treated medically, normalization for clinical status obliterated the observed improvement. Loop et al\textsuperscript{9} reported improved 5-year survival in patients operated on in 1971 to 1973 compared with those undergoing surgery in 1967 to 1970. Similarly, Rahimtoola et al\textsuperscript{10} reported better 4-year survival in those undergoing surgery in 1974 to 1979 compared with those operated on between 1969 to 1973.

Again, other relatively comparable data are from
studies of long-term survival after acute infarction. Gomez-Marin et al.\(^\text{30}\) reported that 4-year survival for men was 35% better in 1980 than in 1970 and was 27% better for women in 1980 than in 1970. Numerous other studies, in contrast, reported no improvement in long-term survival after acute infarction during the 1970s. These include studies of populations in Baltimore,\(^\text{31}\) Rochester, Minn,\(^\text{11}\) New York,\(^\text{32}\) and Worcester, Mass.\(^\text{4,5}\)

Reasons why long-term survival in our study did not improve remain speculative. Advances in medical and surgical therapy that occurred during the 1970s might reasonably be expected to have improved long-term survival, but they did not. One explanation relates to the presence of countervailing forces acting on survival. Patients in cohort B studied between 1977 and 1982 were older, had a higher prevalence of prior myocardial infarction, and had a higher proportion of women that did cohort A evaluated between 1972 and 1977 (Table 1). Each of these factors might be anticipated to reduce long-term survival. Older age is associated with reduced long-term survival in general\(^\text{33,34}\) as well as reduced survival after coronary artery surgery.\(^\text{35,36}\) Women have also been reported to have higher perioperative mortality rates than do men\(^\text{37,38}\) and, in some studies, reduced long-term survival\(^\text{39}\) and less complete revascularization.\(^\text{40}\) And, finally, the prevalence of prior infarction may be associated with regional left ventricular dysfunction and reduced revascularization capability that may reduce survival. These variables may then counteract the beneficial effects of altered risk factors and improved medical and surgical therapies to result in no significant change in overall survival.\(^\text{41}\) Thus, the relative outcomes of the two cohorts reflect the complex interaction of many factors, some of which improve and some of which impede long-term survival.

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Qualifying Examination Date: November 9, 1995

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