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Influence of Coronary Bypass Surgery on Subsequent Outcome of Patients Resuscitated From Out of Hospital Cardiac Arrest

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The effect of coronary bypass surgery on recurrent cardiac arrest was estimated in 265 patients resuscitated from out of hospital cardiac arrest between 1970 and 1988. From this cohort, 85 patients (32%) underwent coronary bypass surgery after recovery from cardiac arrest and 180 patients (68%) were treated medically. A multivariate Cox analysis was used to estimate the effect of coronary bypass surgery on subsequent survival after adjusting for effects of age, prior cardiac history, ejection fraction, year of the event, history of angina, antiarrhythmic drug use and whether the arrest was related to acute myocardial infarction.

The use of coronary bypass surgery had a significant effect in reducing the incidence of subsequent cardiac arrest during follow-up study (risk ratio [RR] 0.48, 95% confidence interval [CI] 0.24 to 0.97, $p < 0.04$). There was also a trend consistent with a reduction in total cardiac mortality (RR 0.65, 95% CI 0.39 to 1.10, $p = 0.10$). These findings suggest that coronary bypass surgery may reduce the incidence of sudden death in suitable patients resuscitated from an episode of ventricular fibrillation.

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Sudden cardiac death is a major medical problem in the United States, affecting approximately 300,000 persons annually (1,2). With the advent of prehospital emergency care systems, a small proportion of these patients have been resuscitated and correlates of successful outcome have been elucidated (3,4). Approximately 75% of resuscitated patients have significant underlying coronary artery disease (5). However, <25% show typical evidence of acute Q wave myocardial infarction at the time of the event (2,4,5). Whereas the majority of sudden deaths are apparently due to ventricular fibrillation, the role of transient myocardial ischemia in precipitating this arrhythmia is unclear.

Coronary artery bypass graft surgery has been shown (6–11) to lower the mortality rate in patients with chronic stable angina, particularly in those with significant obstruction in two or three major coronary arteries. Its benefit appears to be realized primarily by reducing the incidence of sudden unexpected death rather than by preventing myocardial infarction. Its role in preventing recurrent episodes of cardiac arrest in patients who have been resuscitated after ventricular fibrillation has not been well studied. Although reports (12) have been favorable, no large trials evaluating coronary bypass surgery for this condition have been reported. The purpose of this study was to estimate the possible effect of coronary bypass surgery on the subsequent outcome of patients who have been resuscitated from an episode of unexpected cardiac arrest.

Methods

Study patients. The relation between coronary artery bypass surgery and subsequent survival was evaluated in 265 patients drawn from 1,211 consecutive patients resuscitated from a first episode of out of hospital cardiac arrest due to ventricular fibrillation between 1970 and 1987. The group was selected from a Seattle registry of patients in whom prehospital resuscitation for ventricular fibrillation had been attempted by paramedics. This registry has been maintained since 1970. Data for this study were collected after patients gave signed written consent to release of medical records.

Figure 1 describes the entire cohort, which included all patients discharged from the hospital after resuscitation who had 1) no appreciable neurologic morbidity (1,079 of 1,211); 2) documented or suspected underlying coronary artery disease (795 of 1,079); 3) a quantitative measure of left ventricular ejection fraction by contrast or radionuclide ventriculography obtained between 7 and 365 days after cardiac arrest (298 of 795; 15 patients whose ejection fraction was measured within the year before the cardiac arrest and who did not have arrest-related myocardial infarction were

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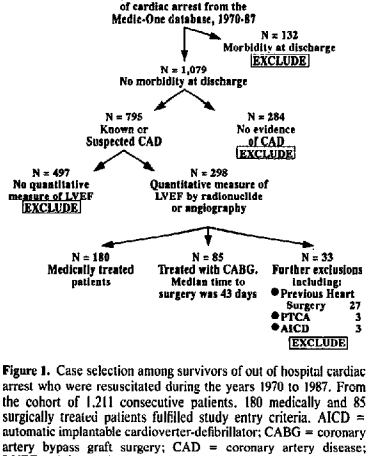

Figure 1. Case selection among survivors of out of hospital cardiac arrest who were resuscitated during the years 1970 to 1987. From the cohort of 1,211 consecutive patients, 180 medically and 85 surgically treated patients fulfilled study entry criteria. AICD = automatic implantable cardioverter-defibrillator; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; PTCA = percutaneous transluminal coronary angioplasty.

included); 4) no history of coronary surgery performed before the index cardiac arrest (271 of 298); and 5) no operative procedure (coronary angioplasty, placement of an implantable defibrillator, valve surgery) other than coronary bypass surgery performed after the index cardiac arrest (265 of 298). The resultant cohort included 265 patients or 22% of the 1,211 survivors of cardiac arrest. Eighty-five (32%) had a coronary artery bypass operation and 180 (68%) were treated medically. Assignment to surgery was by choice of both the physician and the patient and not by protocol.

Clinical data. Baseline patient characteristics were determined through physician review of medical records of the hospital stay after cardiac resuscitation. The data included interpretation of electrocardiograms, cardiac diagnoses, presence or absence of acute Q wave myocardial infarction in association with the cardiac arrest and presence or absence of myocardial necrosis (creatine kinase MB isoenzyme >5%). Data on survival, new hospital admissions, cardiac procedures, medical treatments and smoking status were obtained annually. When available, additional medical records were reviewed to ensure accurate clinical information of subsequent hospital stays during the follow-up period.

Statistical analysis. Univariate covariates included age, gender, year of cardiac arrest, ejection fraction, acute myocardial infarction and history of congestive heart failure, or myocardial infarction. The relation of these covariates to the

Table 1. Baseline Characteristics of 265 Survivors of Out of Hospital Cardiac Arrest

Covariate	Surgical Group (n = 85)	Medical Group (n = 180)	p Value
Age (yr)*	61.5 ± 9.9	60 ± 10.7	NS
No [%] male*	78 [92]	149 [88]	NS
Year of cardiac arrest*	1981 ± 4.1	1980 ± 3.7	<0.01
Ejection fraction*	51.7 ± 14.7	41.2 ± 18.1	<0.001
Hospital days*	17 ± 11.5	14.9 ± 7.3	NS
Acute infarct with cardiac arrest (no. [%])	14 [17]	55 [32]	<0.01
History of heart failure (no. [%])	9 [11]	45 [25]	<0.01
History of myocardial infarction (no. [%])	36 [42]	77 [43]	NS
History of angina (no. [%])	49 [58]	63 [35]	<0.01
Cigarette smoker after follow-up (no. [%])	8 [15]	14 [21]	NS
Use of antiarrhythmic agents after follow-up (no. [%])	24 [29]	91 [54]	<0.001

*Values are mean values ± SD.

use of coronary bypass surgery was described by a *t* test for continuous variables. The separate variance estimate *t* statistic was used for unequal variance. Chi-square analysis or a Fisher exact test was used to compare discrete variables. All p values <0.15 were reported.

Survival time was calculated from the index cardiac arrest. Outcomes examined were the occurrence of recurrent cardiac arrest and total mortality. Those few patients who were resuscitated a second time were counted as dead in calculating total mortality statistics. Age, gender and statistically significant univariate covariates were entered into a stepwise multivariate Cox analysis. Coronary bypass surgery was then added as a time-dependent covariate to determine whether it contributed significantly after adjustment for the other covariates (13). The multivariate Cox analysis was completed with 83 surgically treated patients and 158 medically treated patients who had known values for all covariates.

For illustrative purposes, the expected survival distribution of the surgery cohort was plotted by using the results of multivariate analysis, which excluded coronary bypass surgery as a covariate (under the null assumption that surgery had no effect on outcome). This result was compared with the observed survival distribution as estimated by the method of Kaplan and Meier (14).

Results

Baseline characteristics of the patients. Table 1 compares the demographic and clinical characteristics of the medically and surgically treated groups. There was no difference between groups in gender, age, history of infarction, smoking status or number of hospital days after cardiac arrest. However, patients who were treated with coronary bypass surgery had a higher ejection fraction (51.7 ± 14.7% vs. 41.2

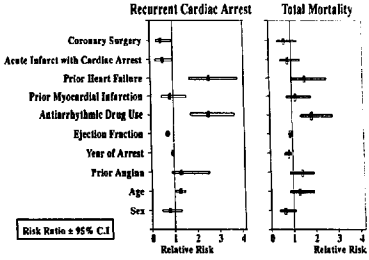

Figure 2. The multivariate relation between clinical characteristics and subsequent cardiac arrest (**left**) and total mortality rate (**right**). The relative risk ratio and 95% confidence intervals (C.I.) are shown. After adjustment for each of the other significant characteristics, the use of coronary bypass surgery was associated with a significantly decreased risk of sudden death ($p < 0.04$).

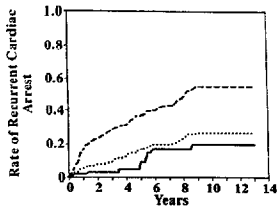

Figure 3. Observed rates of recurrent cardiac arrest for surgically (**solid line**) and medically (**dashed line**) treated patients. An estimate of the beneficial effect of surgery is demonstrated by comparing the observed rate of recurrent cardiac arrest in the surgically treated group with the expected rate of recurrent arrest in this same group (**dotted line**) as derived from a Cox model in which coronary bypass surgery had no effect on the incidence of subsequent cardiac arrest ($p < 0.04$).

± 18.1%, $p < 0.001$), were less likely to have had a remote history of heart failure (11% vs. 25%, $p < 0.01$) and were less likely to have had evidence of an acute myocardial infarction at the time of the cardiac arrest (17% vs. 32%, $p < 0.01$). Also, compared with the medically treated group, patients undergoing bypass surgery were more often drawn from the later years of the 18-year enrollment period. The median date of enrollment in the surgically treated group was 1982 compared with 1980 in the medically treated group. A greater proportion of medically treated patients reported using antiarrhythmic drugs at last follow-up study (54% vs. 29%, $p < 0.001$), whereas the incidence of angina before the index cardiac arrest was higher in the surgically treated patients than in the medically treated patients (58% vs. 35%, $p < 0.01$).

Coronary bypass surgery was usually performed within 1 year after recovery from the cardiac arrest. The median time to operation was 43 days. Thirty-four patients (40%) underwent operation during the hospital stay after resuscitation and 90% of the operations were performed within 8 months (range 2 to 4,050 days). The operative mortality rate was 2.3%.

Outcome related to baseline characteristics and bypass surgery. The follow-up period averaged 4.9 ± 3.7 years. During this time, 11 (13%) of the patients who had coronary bypass surgery and 76 (42%) of the medically treated patients had a second cardiac arrest. There were 46 other (nonarrhythmic) deaths, 11 in the surgically treated group and 35 in the medically treated group. Thus, in all, 22 (26%) of the patients with coronary bypass surgery and 111 (62%) of the medically treated patients died or had a second nonfatal cardiac arrest.

Figure 2 shows the multivariate relation between clinical characteristics and the occurrence of subsequent cardiac arrest and the total mortality rate. Prior heart failure, use of antiarrhythmic drugs and lower left ventricular ejection fraction were each independently related to an increased likelihood of cardiac arrest during the follow-up period. Conversely, three findings were related to a decreased likelihood of subsequent cardiac arrest: 1) study enrollment in more recent years, 2) the association of cardiac arrest with the occurrence of acute myocardial infarction, and 3) the use of coronary bypass surgery (risk ratio [RR] 0.48, 95% confidence interval [CI] 0.24 to 0.91, $p < 0.04$). Patients who underwent bypass surgery had a 52% lower risk of subsequent cardiac arrest after adjustment for other possible confounding factors. There was a nonsignificant association between surgery and lower total mortality (RR 0.65, 95% CI 0.39 to 1.10, $p = 0.10$).

The predictive effect of coronary bypass surgery is shown in Figure 3. The observed rates of subsequent cardiac arrest are shown for the medically and surgically treated groups, as well as an estimate of the rate of subsequent cardiac arrest for the surgically treated group. This estimated rate of cardiac arrest was determined by removing the benefit of surgery from the survival calculations. A significant difference was seen between the observed and estimated rates of recurrent cardiac arrest for the surgically treated group, illustrating the potential benefit of coronary bypass surgery ($p < 0.04$). Likewise, Figure 4 shows the observed total mortality rate for both the medically and surgically treated groups, as well as an estimate of the mortality rate for the surgically treated group had they not had coronary bypass surgery.

Discussion

Clinical implications. In the past 2 decades of monitoring the effects of prehospital emergency cardiac care on the

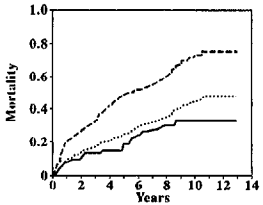

Figure 4. Total mortality rate for surgically (**solid line**) and medically (**dashed line**) treated patients. An estimate of the beneficial effect of surgery is demonstrated by comparing the observed mortality rate in the surgically treated group with the expected mortality rate in this same group (**dotted line**) as derived from a Cox model that assumed that coronary bypass surgery had no effect on the subsequent total all-cause mortality rate. An apparent overall trend toward improved survival in patients treated surgically did not achieve statistical significance ($p = 0.1$).

outcome of victims of out of hospital cardiac arrest, there has been an opportunity to better characterize clinically important risk factors and to examine the effects of treatment. Because these patients were treated in all the area-wide hospitals, therapy was not standardized but instead represents typical clinical practice in the era just before the more routine application of implantable cardioverter-defibrillators. Observational studies (2–5, 15–17) in these patients have shown that certain clinical features (for example, cardiac arrest occurring in the setting of acute myocardial infarction, prior history of heart failure, age, use of antiarrhythmic agents and ejection fraction) are each related to subsequent outcome, particularly the occurrence of subsequent cardiac arrest. In this study, statistical methods were used in an attempt to control for the influence of those factors that are known to affect outcome. The results suggest that coronary bypass surgery reduces the incidence of subsequent cardiac arrest. We also observed a trend for a reduction in total mortality.

Previous studies. This finding is consistent with data from other controlled trials (8–13) that have shown a lower risk of cardiac arrest after coronary bypass surgery in patients with stable angina pectoris. However, in survivors of cardiac arrest, only limited data are available to evaluate the effect of surgery. Kelly et al. (18) followed up 50 survivors of sudden death for a mean of 39 months after electrophysiologic testing and coronary bypass surgery. In this select group of patients, the 5-year cardiac survival rate was estimated to be 98%, but because of patient selection criteria, this estimate is probably not applicable to all patients resuscitated from ventricular fibrillation. Tresch et al. (19) compared outcomes in 52 survivors of cardiac arrest in a nonrandomized but prospective study. Twenty-four patients were treated with coronary bypass surgery and 28 were treated with various medical regimens. After an average follow-up period of 38 months, the rate of recurrent cardiac arrest was 13% in the surgically treated group compared with 18% in the medically treated group. However, because of the small number of patients and the short follow-up period, this difference did not achieve statistical significance. This present study is the first with a large enough sample to show an effect of coronary bypass surgery on subsequent sudden death rates.

Limitations. Although the findings are controlled to the greatest possible extent for potential confounding factors and are consistent with the effect of coronary bypass surgery in patients with unstable angina, there are several possible shortcomings inherent in this analysis. Characteristics that could favorably bias the surgically treated group include a higher left ventricular ejection fraction and more contemporary treatment. A potential bias favoring the medically treated cohort is the stronger association between cardiac arrest and acute myocardial infarction occurring in this group, a factor known to favorably influence subsequent survival (3). Confounding variables with unknown effects include greater use of antiarrhythmic drugs in the medically treated patients and a greater rate of prearrest angina in the surgically treated group. All of these differences in baseline clinical characteristics were adjusted before assessing the effect of coronary bypass surgery. Potential bias introduced in the follow-up data by either coronary angioplasty or automatic implantable cardioverter-defibrillator placement was eliminated by excluding the small number of patients receiving these procedures during the study period.

Because our cohort included only those patients discharged from the hospital, selection bias could occur if potential surgical cases were eliminated from the index cardiac arrest as a result of surgical death during the hospital stay. Review of a random sample of 25% of all patients who died in the hospital >6 days after resuscitation ($n = 493$) did not identify any cases of surgical death. Thus, early surgical mortality rates were extremely low and would be unlikely to affect the results.

Because of the long period required for case acquisition and follow-up data in this study, several technologic advances have occurred that might affect both patient management and outcome. The recent advance of electrophysiologic testing and the use of automatic implantable cardioverter-defibrillators have had an impact on the management of resuscitated patients. However, it was not until the mid-1980s that electrophysiologic testing became routine for suitable patients; hence, the complementary role of programmed stimulation with coronary bypass surgery could not be explored in this analysis.

Conclusions. The role of transient myocardial ischemia in sudden death has been speculative for many years. Most survivors of cardiac arrest have significant coronary artery disease, leading many clinicians to advise coronary bypass surgery in survivors who have correctable lesions. The findings in this study support the hypothesis that transient ischemia may change the myocardial substrate to facilitate

the emergence of ventricular fibrillation and that revascularization probably decreases this phenomenon. We conclude that coronary bypass surgery in selected survivors of cardiac arrest has the potential to reduce the incidence of recurrent cardiac arrest.

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