Effect of Diabetes and Associated Conditions on Long-Term Survival After Coronary Artery Bypass Graft Surgery

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Background—The effects of diabetes on short-term results of coronary artery bypass graft (CABG) surgery are known, but less is known about the long-term effects of diabetes and diabetic-related sequelae for patients undergoing this surgery. We studied the 10-year survival of nondiabetic and diabetic patients undergoing CABG surgery.

Methods and Results—A prospective regional cohort study was conducted of 36 641 consecutive isolated CABG patients in northern New England from 1992 through 2001. Patient records were linked to the National Death Index to assess mortality. There were 154 140 person-years of follow-up and 5779 deaths. Kaplan–Meier techniques were used. Survival was stratified into three categories: no diabetes, diabetes without peripheral vascular disease and renal failure, and diabetes with peripheral vascular disease and/or renal failure. The overall annual incidence rate of death was 3.7 deaths per 100 person-years. Annual incidence rates for nondiabetic subjects and diabetic subjects were similar: 3.1 deaths per 100 person-years and 4.4 deaths per 100 person-years, respectively. The annual incidence rate for diabetic subjects with renal failure, peripheral vascular disease, or both was 9.4 deaths per 100 person-years. The log-rank test showed that the survival curves were significantly different (P<0.001).

Conclusion—Patients that have diabetes without the sequelae of renal failure and/or peripheral vascular disease have long-term survival similar to but slightly less than patients without diabetes who undergo CABG surgery. Survival of CABG surgery patients with diabetes is greatly affected by associated comorbidities of peripheral vascular disease and renal failure. This knowledge may help guide the patient as well as the cardiologist and cardiac surgeon in making appropriate decisions in these critically ill patients. (Circulation. 2004;110[suppl II]:II-41–II-44.)

Key Words: diabetes mellitus ■ peripheral vascular disease ■ cardiopulmonary bypass ■ survival ■ renal failure ■ bypass ■ epidemiology

The incidence of diabetes continues to increase in the United States, with current estimates showing 16 million diabetic patients and 26 million patients who are insulin-resistant.1 Diabetes mellitus has been associated with the development of cardiovascular disease.2 In the population of patients undergoing coronary artery bypass grafting (CABG), the incidence of diabetes ranges from 12% to 38%.3–8 Diabetes has been associated with increased morbidity and mortality associated with CABG surgery and is a strong predictor for risk of death7,9 and mediastinitis.10 Renal failure (RF) also has been associated with increased short-term morbidity and mortality with CABG surgery.7,11 Herlitz et al showed that RF in patients with diabetes caused a significant increase in short-term mortality.3 Peripheral vascular disease (PVD) in patients having CABG surgery also has been shown to be an independent predictor of short-term mortality.12

The long-term survival of diabetic patients having CABG surgery is less understood. Varied annual long-term incidence rates have been published with the incidence of death at 5 years ranging from 1.3 deaths per 100 person-years to 6.5 deaths per 100 person-years.3,5,8,9,13,14 CABG appears to have a long-term benefit compared with percutaneous coronary interventions in diabetic patients who require revascularization.8,15,16

A prospective regional cohort study was conducted of 36 641 consecutive patients undergoing CABG in northern New England from 1992 to 2001. These records were linked to the National Death Index to assess long-term mortality. The goal of this study was to evaluate the effect of diabetes and conditions associated with it on the long-term survival of patients undergoing CABG surgery.

Methods

Patients and Setting
The Northern New England Cardiovascular Disease Study Group (NNECDSG) is a voluntary research consortium representing all centers where CABG is performed in Maine, New Hampshire, and

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Vermont, along with the Beth Israel Deaconess Medical Center in Boston, Mass. Since 1987, the NNECDSG has maintained a prospective registry of all patients undergoing cardiac operations in this region. This multicenter study includes 36,641 consecutive patients undergoing isolated CABG from 1992 through 2001.

Data Collection
Patient and procedure information was collected prospectively for all patients. Patient data included age, sex, comorbid conditions (diabetes, PVD, preoperative dialysis-dependent RF, chronic obstructive pulmonary disease [COPD], congestive heart failure, cancers, and liver disease), current cardiac condition (recent [<7 days] myocardial infarction, current congestive heart failure), and previous cardiac surgery. Diabetes was defined as documentation of diabetes (diet-controlled, using oral medication, or using insulin) in the patient medical record or by patient history. PVD was defined as cerebrovascular disease (previous stroke, previous transient ischemic attack or amaurosis fugax, previous carotid surgery, carotid stenosis by history or radiographically documented, or carotid bruit), and lower extremity disease (claudication, previous lower extremity bypass, previous nontraumatic lower extremity amputation, absence of pedal pulses [recorded as absent if nonpalpable], or lower extremity ulcers). Dialysis-dependent RF was defined by the preoperative use of hemodialysis or peritoneal dialysis.

This study focused on the following 5 patient subgroups: (1) patients without diabetes; (2) patients with diabetes alone; (3) patients with diabetes and PVD; (4) patients with diabetes and RF; and (5) patients with diabetes and PVD, RF, or both.

Procedural data available included cardiac catheterization variables (degree of left main coronary artery stenosis, total number of significantly diseased coronary arteries, left ventricular end-diastolic pressure, and ejection fraction) data, and priority of surgery. Cardiac catheterizations were performed using standard methods during the course of regular clinical care. The number of diseased coronary vessels was assessed by use of criteria established by the National Heart, Lung, and Blood Institute Coronary Artery Surgery Study. The priority of a patient’s surgery was defined as emergency, urgent, or elective. Emergency indicated that medical factors relating to the patient’s cardiac disease dictate that the procedure be performed within hours to prevent morbidity or death. Urgent indicated that medical factors require the patient to stay in the hospital for the procedure before discharge. Elective was defined by medical factors that indicated the need for the procedure, but which allowed the patient to be discharged from the hospital with readmission at a later date. Complete definitions of these variables have been previously published.

Outcome
The National Death Index was used to ascertain long-term mortality of patients in the study. The accuracy of the National Death Index is between 92% and 99%.17 The National Death Index had data about vital status of patients through the end of 2001. Registry records were linked to the death data by probabilistic methods based on key identifiers such as patient name, date of birth, social security number, gender, date last known alive, and state of last known residence. The outcome measure for this study was all-cause mortality during this 10-year period.

Statistical Analysis
All analyses were performed using Stata release 7.0 software.18 Standard methods were used to describe the prevalence of comorbid conditions. Survival analyses were performed using Kaplan–Meier techniques. Survival curves were compared using the log-rank statistic.19 Incidence density rates (deaths/person-years) were calculated using Stata survival programs.

Results
Prevalence of Comorbid Conditions
Hypertension was the most frequent comorbid condition in this study with a prevalence of 64.3%. Diabetes occurred in 30.8% of patients, followed by obesity (20.3%), PVD (19.3%), COPD (10.4%), peptic ulcer disease (7.0%), severe obesity (6.1%), cancer (2.5%), and RF (1.4%). Among the 36,641 patients, 25,455 had no diabetes (69.5%), 8194 had diabetes without PVD or RF (22.4%), 2713 (7.4%) had diabetes with PVD, 137 (0.4%) had diabetes with RF, and 142 (0.4%) had diabetes with both PVD and RF (Table).

Survival Outcomes
From 1992 through 2001, there were 5779 deaths among the 36,641 subjects; 154,140 person-years of follow-up were available. Annual incidence rate of death was 3.7 deaths per 100 person-years (Table). Survival among diabetic subjects was significantly worse than among nondiabetic subjects. Annual incidence of death among diabetic subjects was 5.5 deaths per 100 person-years versus 3.1 deaths per 100 person-years among nondiabetic subjects (p log rank test <0.001). However, when patients with diabetes only were compared with those with diabetes and PVD or RF (or both), a marked survival difference was noted between the groups (Table). Patients with diabetes alone had an annual incidence rate of 4.4 deaths per 100 person-years. Annual incidence rate was 8.4 deaths per 100 person-years for diabetic subjects with PVD, 16.3 deaths per 100 person-years for diabetic subjects with RF, and 26.3 deaths per 100 person-years for diabetic subjects with both comorbid conditions. Log rank tests comparing each of these groups to patients with diabetes alone were all statistically significant (p log rank test <0.001) (Figure 1). Adding ≥1 of these comorbidities to diabetes increased risk of death from 2-fold (with PVD) to 6-fold (with both PVD and RF). In patients with diabetes, RF, and PVD, the initial mortality rate was very high and may be related to in-hospital mortality.

Because the numbers of patients with diabetes and RF or diabetes and both RF and PVD were small, we combined all diabetic patients with comorbid conditions for further analysis (Figure 2). This combined group of diabetic patients with RF, PVD, or both (2992 patients) had twice the annual incidence rates death of diabetic subjects without those comorbidities (9.4 deaths per 100 person-years versus 4.4 deaths per 100 person-years) and 3-times the annual mortality of patients without diabetes (9.4 deaths per 100 person-years versus 3.1 deaths per 100 person-years).

Incidence Rates of Death by Diabetes and Associated Conditions

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>N of Deaths</th>
<th>Person-Years Follow-Up</th>
<th>Incidence Rate of Deaths/100 Person-Years</th>
<th>N of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>5779</td>
<td>154,140</td>
<td>3.7</td>
<td>36,641</td>
</tr>
<tr>
<td>No diabetes</td>
<td>3439</td>
<td>111,680</td>
<td>3.1</td>
<td>25,455</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2340</td>
<td>42,460</td>
<td>5.5</td>
<td>11,186</td>
</tr>
<tr>
<td>Diabetes only</td>
<td>1440</td>
<td>32,858</td>
<td>4.4</td>
<td>8,194</td>
</tr>
<tr>
<td>Diabetes and PVD</td>
<td>736</td>
<td>8808</td>
<td>8.4</td>
<td>2,713</td>
</tr>
<tr>
<td>Diabetes and RF</td>
<td>73</td>
<td>448</td>
<td>16.3</td>
<td>137</td>
</tr>
<tr>
<td>Diabetes, RF, and PVD</td>
<td>91</td>
<td>346</td>
<td>26.3</td>
<td>142</td>
</tr>
</tbody>
</table>

PVD indicates peripheral vascular disease; RF, renal failure.
To see whether the long-term survival effect of diabetes as well as diabetes plus PVD/RF continues after hospitalization, we censored the data at 6 months. With this censoring, there still is a similar and significant effect on the long-term survival of diabetic patients with the comorbidities PVD and/or RF. The curves continue to diverge with a significant difference in 10-year mortality.

Discussion

This study used a large, multicenter, regional database to examine the 10-year all-cause mortality among isolated CABG surgery patients who had diabetes with and without comorbidities PVD and RF. The long-term survival of diabetic subjects without these conditions was excellent. The presence of the diabetic comorbidities PVD and RF had a significant impact on both the annual incidences of death and long-term survival. The annual incidence rate of death for nondiabetic subjects was 3.1 deaths per 100 person-years compared with 4.4 deaths per 100 person-years for diabetic subjects without the comorbidities. The presence of PVD nearly increased the annual mortality by 4 times. RF even had a greater effect on mortality, increasing the annual incidence of death ≥5 times that compared with diabetic subjects without the studied comorbidities. The number of diabetic patients in subgroups of RF and PVD each were small and the survival numbers were small as the follow-up interval approached 10 years. When these subgroups were combined to form a larger and more stable group, the significant effect on mortality after CABG surgery remained. In this group, the annual mortality was 3 times that of nondiabetic subjects and twice that of diabetic subjects without the comorbidities RF and PVD.

Comparison With Previous Studies

This study showed an annual incidence rate death in diabetic subjects of 4.4 deaths per 100 person-years without PVD or RF, which was similar to several other published studies (3.1 deaths per 100 person-years to 6.5 deaths per 100 person-years). Calafiore et al reported that diabetes was an independent risk factor for early cardiac death. Once patients survive the first 30 days, long-term survival was not statistically different between diabetic and nondiabetic patients. Mean follow-up in that study was 50 months, which is much shorter than the follow-up of our group of patients. However, Calafiore et al’s study had a similar finding in that chronic RF and PVD were statistically independent predictors for increased mortality.

One of the first studies that looked at the long-term survival of diabetics was performed by Morris. This study looked at 5654 patients followed-up for up to 8 years (mean, 2.5 years). Only 20% of the patients had diabetes in their study. The 5-year survival of all diabetic subjects was 0.80 and for nondiabetic subjects it was 0.91. This corresponds to an annual incidence of death of 4% for diabetic subjects compared with 3.1% in our study. They did not look at PVD or RF in regard to long-term survival. They found that lower ejection fraction, older age, failure to use an internal mammary artery graft, female gender, elective/urgent presentation, number of diseased vessels, and mitral insufficiency were incremental risk factors for long-term survival from CABG surgery.

Study Limitations

Several limitations exist in this study. First, there was no distinction made between diabetic subjects treated with insulin compared with those treated with oral agents. Weintraub et al reported in the EAST trial that the presence of insulin requirements for both the CABG group and the angioplasty group had a significant negative effect on long-term survival. Szabo et al showed that insulin-requiring diabetic subjects had poorer mid-term survival compared with diabetic patients treated with oral agents or diet. O’Keefe showed that diabetic subjects treated with insulin had a worse long-term survival rate compared with those treated with diet alone. Thourani et al published a study showing a survival benefit at 10 years in diabetic patients who were treated without insulin compared with those diabetic subjects treated with insulin. The NNECDSG only began collecting treatment data in the later part of 1996; therefore, it is not presented in this analysis because it would have restricted our analysis time period. Second, we do not collect information on diabetes type, hemoglobin A1c level, or treatment at time of their procedure. The majority of our patients are older than 65, and we have assumed that most of these patients have type 2 diabetes. Patients’ hemoglobin A1c levels are not routinely measured at time of admission; therefore, we do not know how well a patients’ blood sugar is controlled at the time of their procedure. As more evidence is published, this practice may change. Several participating centers have changed their practice in recent years, but the long-term effect of this change in practice was not evaluated in this current study.
Two studies published 10-year follow-up in diabetic patients who had CABG surgery. O’Keefe et al.\(^6\) compared CABG with coronary angioplasty. Only 12% of patients had diabetes in his study compared with 30% in this study. Diabetic patients had an annual incidence of mortality of 4 deaths per 100 person-years, which was similar to ours. The published series of Thourani et al.\(^9\) reported diabetic patients had a 10-year survival rate of 50% compared with 60% in this study.

Liu et al.\(^11\) looked at the short-term morbidity and mortality of dialysis patients undergoing CABG surgery. Twenty-eight percent of the nondialysis patients had diabetes compared with 48% in the dialysis group. The presence of RF provided a 3-fold increase of death (OR = 3.1). Herzog et al.\(^{13}\) looked at the impact that diabetes had on long-term survival of dialysis patients having coronary revascularization with CABG, angioplasty, or coronary artery stenting. Dialysis-dependent diabetic patients had improved long-term survival with CABG surgery compared with angioplasty or stent placement. Four-year survival was 37%, which was similar to our study.

Birkmeyer et al.\(^1\) looked at the effect of PVD on long-term mortality after CABG surgery. After adjustment for other significant comorbidities, the presence of PVD had an odd ratio for death of 2, compared with similar patients without PVD. Our study showed that the presence of PVD in diabetic patients had a similar 2-fold increase in the annual incidence of death compared with diabetic patients without PVD. The theory that diabetes and PVD together is associated with small vessel disease may play a role in the cause of the higher long-term mortality seen in these 2 studies.

**Implications**

This study carries significant long-term implications for diabetic patients undergoing surgical revascularization. Thirty percent of patients undergoing CABG surgery have diabetes as a comorbid condition. Many patients have the associated conditions of PVD and RF. Surgeons are often asked to provide short-term and long-term mortality rates for possible CABG surgery to patients and families. Often, a surgeon bases the estimation of the morbidity and mortality of an operation on personal experience or the “last case” situation. This study will provide the surgical clinician with documented and accurate determination of annual mortality rates and long-term survival for these critically ill patients.

**Conclusions**

This study involved 36,641 consecutive patients undergoing CABG in northern New England. Diabetes was present in 30% of the population studied. The annual incidence rate of mortality for nondiabetic subjects was 3.1 deaths per 100 person-years compared with 4.4 deaths per 100 person-years to patients with diabetes alone. The presence of RF and PVD significantly reduced long-term survival among diabetic patients. In diabetic patients with RF, PVD, or both, the 10-year survival rate was 40% and there was an annual incidence rate of death of 9.4 deaths per 100 person-years.

**References**


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