The Effect of Comorbid Illness on Mortality Outcomes in Cardiac Surgery

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Hypothesis: Comorbid conditions are associated with the risk of death from coronary artery bypass graft surgery.

Design: Prospective cohort study data were collected on patient and disease characteristics and comorbid conditions including hypertension, diabetes, obesity, vascular disease, chronic obstructive pulmonary disease, cancer (excluding nonmelanoma skin cancer), dialysis-dependent renal failure, liver disease, and dementia. Statistical analysis used logistic regression for the calculation of adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

Setting: Regional cardiac surgery database.

Patients: A total of 27,239 consecutive patients undergoing isolated coronary artery bypass graft surgery.

Main Outcome Measure: In-hospital mortality rate.

Results: The prevalence of comorbid conditions was as follows: hypertension, 64.3%; diabetes, 30.1%; obesity, 24.6%; severe obesity, 7.2%; vascular disease, 18.3%; chronic obstructive pulmonary disease, 10.9%; peptic ulcer, 7.5%; cancer, 3.8%; renal failure, 1.5%; liver disease, 0.6%; and dementia, 0.1%. After adjustment for patient and disease characteristics, including age, sex, previous cardiac surgery, priority of surgery, degree of left main coronary stenosis, number of diseased coronary arteries, and left ventricular ejection fraction, the following comorbid conditions were significant predictors of in-hospital mortality: diabetes (OR, 1.19; 95% CI, 1.01-1.40; P = .03), vascular disease (OR, 1.67; 95% CI, 1.41-1.97; P < .001), chronic obstructive pulmonary disease (OR, 1.57; 95% CI, 1.29-1.91; P < .001), peptic ulcer (OR, 1.34; 95% CI, 1.05-1.71; P = .02), and dialysis-dependent renal failure (OR, 3.68; 95% CI, 2.65-5.13; P < .001). There was no significant association between in-hospital mortality and hypertension, obesity or severe obesity, cancer, liver disease, or dementia.

Conclusion: Even after adjustment for other patient and disease characteristics, comorbid conditions (especially diabetes, vascular disease, chronic obstructive pulmonary disease, peptic ulcer disease, and dialysis-dependent renal failure) are associated with significantly increased risk of death after coronary artery bypass graft surgery.

Arch Surg. 2002;137:428-433
PATIENTS AND METHODS

DATA COLLECTION

This was a multicenter study of 27,239 consecutive patients undergoing isolated CABG surgery in northern New England between January 2, 1992, and December 31, 1999. There were 813 in-hospital deaths (2.98%). Data for all patients had been prospectively entered in a data registry, which records patient and disease characteristics, processes of care, and outcomes. From the registry, the following data were available: patient age, sex, height, and weight; baseline laboratory studies, including blood chemical and hematological findings; degree of left main coronary artery stenosis; total number of significantly diseased vessels; left ventricular ejection fraction; recent myocardial infarction; previous CABG or percutaneous transluminal coronary angioplasty; and priority of surgery (elective or urgent/emergent). Complete definitions of these variables have been previously published. The dependent variable in these analyses was in-hospital mortality.

COMORBID CONDITIONS

Data were collected on the following comorbid conditions: hypertension (documented in medical record or patient history); diabetes (documented in medical record or patient history); vascular disease (including cerebrovascular disease [previous cerebrovascular accident or transient ischemic attack, previous carotid surgery, carotid stenosis by history, imaging studies, or presence of carotid bruit] and/or lower extremity disease [claudication, amputation, previous lower extremity bypass, absent pedal pulses, or lower extremity ulcers]); COPD or asthma requiring treatment with inhalers, theophyllines or aminophyllines, or corticosteroids); cancer (physician’s statement in the medical record indicating leukemia, lymphoma, or solid cancer but excluding nonmelanoma skin cancer); renal failure (patient currently receiving peritoneal dialysis or hemodialysis); liver disease (cirrhosis, chronic active hepatitis, or primary biliary cirrhosis); dementia (documented in medical record or patient history); obesity or severe obesity (body mass index [weight in kilograms divided by the square of height in meters] of ≥30 indicates nonobese; 31-36, obese; and >36, severely obese); and peptic ulcer (known current problem requiring treatment).

STATISTICAL METHODS

Usual statistical methods were used for the calculation of the odds ratio (OR) and its 95% confidence interval (CI), the χ² test, Pearson product moment correlation coefficient, and P values for tests of significance. Baseline patient and disease characteristics were summarized by means for the continuous variables and by percentages for the discrete variables. To adjust for confounding variables, we used multivariate logistic regression and direct standardization techniques. Variables that differed significantly among groups, as well as common known risk factors for morbidity and mortality after CABG, were selected for the multivariate analysis. All statistical analyses were conducted with the STATA 6.0 statistical program.

RESULTS

The relative frequencies of the comorbid conditions are shown in the Figure. Hypertension (64.3%) was the most frequent, followed by diabetes (30.1%), obesity (24.6%), vascular disease (18.3%), COPD, cancer (excluding nonmelanoma skin cancer), dialysis-dependent renal failure, liver disease, peptic ulcer, and dementia. The goal of this study was to determine the necessary set of comorbid conditions that would significantly predict mortality in this study of consecutive patients undergoing isolated CABG surgery.
Cancer (3.8%), renal failure (1.5%), liver disease (0.6%), and dementia (0.1%) were substantially less frequent. There were statistically significant (all P<.001), but relatively weak (r=0.07-0.12), positive correlations between diabetes and hypertension, diabetes and vascular disease, diabetes and renal failure, and diabetes and obesity, and a positive correlation between vascular disease and COPD. Table 1 shows the overall prevalence rates of the comorbid conditions by medical center. The rank order of the comorbid conditions was virtually identical by medical center. However, there were some differences in the reported frequencies. For example, the mean frequency of hypertension was 64.3% and the range was 59.8% to 71.6%. In this large dataset, all of the differences across medical centers were statistically significant (P<.001) but were of rather small magnitude. Some of the differences in reported prevalence of specific comorbid conditions can be explained by local circumstances. The highest rates of cancer and renal failure were from a medical center with a large cancer center and a renal dialysis program.

Table 2 shows the univariate associations between the specific comorbid conditions and the rates of in-hospital mortality. The percentage mortality with and without the specific comorbidity is shown along with the P value from the χ² test. There were statistically significant differences in the in-hospital mortality rate for patients with and without hypertension, diabetes, obesity, vascular disease, peptic ulcer, and renal failure. Some of these were small, eg, hypertension (2.96% vs 2.21%) and diabetes (3.52% vs 2.76%), while others were large, eg, renal failure (12.59% vs 2.84%). No statistically significant differences in mortality rates were seen for severe obesity, cancer, liver disease, or dementia.

Table 3 shows the results of the multivariate analyses. These analyses show the independent effect of each of the comorbid conditions after adjustment for a variety of patient and disease characteristics. These variables used in the logistic regression model include age, sex, previous cardiac surgery, priority at surgery (elective, urgent, or emergency), left main coronary disease (<50%, 50%-89%, or ≥90%), number of diseased coronary arteries (1, 2, or 3), and left ventricular ejection fraction. BMI indicates body mass index.

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or 3), and left ventricular ejection fraction. In these analyses, we present the adjusted ORs, their 95% CIs, and P values. The following comorbid conditions were significant predictors of in-hospital mortality: diabetes (OR, 1.19; 95% CI, 1.01-1.40; P = .03); vascular disease (OR, 1.67; 95% CI, 1.41-1.97; P < .001), COPD (OR, 1.57; 95% CI, 1.29-1.91; P < .001), peptic ulcer (OR, 1.34; 95% CI, 1.05-1.71; P = .02), and dialysis-dependent renal failure (OR, 3.68; 95% CI, 2.65-5.13; P < .001). There was no significant association between in-hospital mortality and hypertension, obesity or severe obesity, cancer, liver disease, or dementia.

## COMMENT

This regional study of the association between comorbid conditions and the rate of in-hospital mortality associated with CABG surgery showed that, even after adjustment for a variety of patient and disease characteristics, COPD, vascular disease, dialysis-dependent renal failure, peptic ulcer, and diabetes were associated with a significant increase in CABG mortality rates. There was no significant association between in-hospital mortality and hypertension, obesity, cancer, liver disease, or dementia.

There are some limitations to this study. It was regional and used data from only 6 medical centers. However, the patients were consecutive and represent the entire experience of those 6 medical centers. In addition, the group has collaborated on data collection projects for more than 14 years and has adopted uniform definitions for patient and disease characteristics. Northern New England is racially homogeneous, and factors associated with race or ethnicity cannot be effectively studied. Also, even in a dataset of more than 27,000 patients, there is limited statistical power for studying interactions between infrequently occurring conditions.

Cardiac surgery is certainly the most carefully studied surgical procedure in history. Other investigators have examined the role of comorbid conditions in mortality associated with CABG procedures. On the basis of analyses from 3500 patients undergoing cardiac surgery, Parsons et al2 devised a method for incorporating risk factors into the interpretation of results of cardiac surgical procedures. Comorbid conditions retained in the multivariate model included morbid obesity, diabetes, hypertension, and dialysis-dependent renal failure. The Veterans Administration Preoperative Risk Assessment Study3 evaluated data from 8136 patients undergoing CABG surgery, and the only comorbid conditions retained in their multivariate model were COPD and peripheral vascular disease. A major determinant of high risk was “poor general medical condition,” which was not more clearly defined but increased mortality from 3.8% to 18.8%.4 Hannan et al5 conducted a multivariate analysis of risk factors and hospital mortality among 7596 patients undergoing cardiac surgery in New York State. It showed that both diabetes and renal failure were significantly associated with the risk of hospital death. Higgins et al6 at the Cleveland Clinic (Cleveland, Ohio) developed a clinical severity score based on data from 5051 patients who underwent CABG surgery in 1986 to 1990. The comorbid conditions included in their regression model were serum creatinine level, COPD, and previous vascular surgery.13

The Cooperative CABG Database Project14 performed parallel analyses on 7 cardiac surgery databases with a total of more than 170,000 patients. The investigators did not include any comorbid conditions in their “core” variables. On the basis of their findings, they recommended that data be collected on the following comorbid conditions: level 1 (likely important) comorbidity variables included height and weight, diabetes, peripheral vascular disease and cerebrovascular disease, COPD, and creatinine level; level 2 (requiring further study) comorbidity variables included hypertension, diabetic sequelae, and liver disease.14 In Ontario, Tu et al7 identified a small number of core variables that could be used to compare risk-adjusted mortality rates for CABG. They noted that comorbid conditions did little to alter the predictive value of these core variables (age, sex, emergency, previous CABG, left ventricular function, and left main coronary artery disease) when mortality rates were compared in 9 hospitals in Ontario. Peripheral vascular disease was the only comorbidity condition that was statistically significant in their multivariate model.7 The Society of Thoracic Surgeons cardiac surgery database has been used to assess risk factors associated with mortality in coronary artery bypass surgery.2 The 1997 multivariate model, based on approximately 117,000 patients, retained the following comorbidity variables: diabetes, renal failure, hypertension, COPD, peripheral vascular disease, and cerebrovascular disease.5 In 2001, Holman et al8 reported the results of the Alabama Coronary Artery Bypass Grafting Project. Their multivariate model included 3 comorbid conditions: peripheral vascular disease, cerebrovascular disease, and COPD.15

These previous studies are in general agreement on the adverse effects of diabetes, vascular disease, COPD, and dialysis-dependent renal failure on CABG mortality rates. There is no consistency in the findings for hypertension, obesity, liver disease, or dementia. The current data are in agreement with the findings of previous studies on the pernicious effects of diabetes, vascular disease, COPD, and renal failure. Our adjusted ORs are similar to those that have been obtained in other studies. We set out to look closely at other comorbid conditions, including obesity, peptic ulcer disease, liver disease, and dementia. All of these have been found to be important predictors of adverse outcomes in other patient populations.8,9,10,17 We did not find any statistically significant association between obesity and mortality, either in this study or in a previously published study from our group.18

Neither liver disease nor dementia was significantly associated with CABG mortality. However, both conditions were rare (<1%) in our database. In fact, in more than 27,000 cases, there was not one death among a patient diagnosed as having dementia and only a few among patients with liver disease. These disorders are undoubtedly serious for individual patients, but we have little to say about their quantitative effect on risk of death after CABG surgery.

The association between peptic ulcer and death after CABG surgery is puzzling. To our knowledge, this finding has not been reported previously. We are sure that...
these data counted only patients with preexisting peptic ulcer—not stress ulcers occurring during the postoperative period. The cause of the association between peptic ulcer and death is not clear. It may be a chance association and should be confirmed in other datasets. We plan to look at the mode of death of these patients with preexisting peptic ulcer disease to see whether that shows any pattern suggesting an etiologic association.

The topic of comorbidity among patients undergoing CABG surgery will undoubtedly continue to be important. The aging of the patient population will be accompanied by an increased prevalence of comorbid conditions. An increase in mortality rates for patients undergoing CABG surgery in the decade of the 1980s has been attributed to an increase in preoperative risk factors, specifically a higher incidence of diabetes, chronic lung disease, hypertension, renal disease, and peripheral vascular disease.\(^{3,19}\) Cardiac surgical outcomes will continue to be of interest to the profession and to the public as specific states, health plans, and Web sites continue to publish outcomes.

Our regional cardiac surgical database is now in its 14th year and has allowed us to evaluate the prevalence and significance of various comorbid conditions as well as processes of clinical care. As the patient population becomes even more complex, this information should be useful to surgeons and their patients as they try to accurately determine operative risk and to assess clinical outcomes.

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This study was supported by grant 9970047N from the American Heart Association, Dallas, TX.

This paper was presented at the 82nd Annual Meeting of the New England Surgical Society, Providence, RI, September 22, 2001.

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DISCUSSION

Richard Shemin, MD, Boston, Mass: First, I would like to make a few comments about the large databases that exist in cardiac surgery. Coronary bypass surgery has become not only the most widely performed major operation throughout the world but the most studied in history. Millions of dollars have been spent studying the appropriateness, efficacy, risk factors, as well as the mortality rates, complication rates, and the need for repeat procedures. Since the 1970s, multicenter randomized trials have been performed on both sides of the Atlantic, and they have studied comparisons to medical therapy and, most recently, to interventional procedures such as PTCA [percutaneous transluminal coronary angioplasty] and stents. During the 1980s and 1990s, increasing concern about the appropriate application of this costly procedure performed in over 300,000 Americans annually led to a serious scrutiny by payers, especially HCFA [Health Care Financing Administration].

Public consumerism, desire for accountability by the medical profession, found that coronary artery bypass operation was a very easy and convenient target to be tracked. The cardiac surgical community really responded with the development of these outcomes databases in self-defense, either large hospital-based databases such as at Duke and the Cleveland Clinic, professional society–based databases such as the Society of Thoracic Surgeons national database, and the regional multi-
The public reporting of coronary bypass surgery data was initiated by HCFA and later abandoned due to inadequate risk adjustment. New York followed by Pennsylvania were the first states where the legislature enacted law requiring annual hospital reports of audited data including data on individual surgeons. With the expansion of cardiac surgery to community hospitals in Massachusetts, which will occur this year, public disclosure of risk-adjusted data will become a reality.

To date, the Northern New England Cardiovascular Study Group has been a model of risk-adjusted reporting of outcomes. The member hospitals have joined together in the spirit of cooperation instead of competition to share best practices, thereby improving clinical results and pursuing continuous quality improvement. In addition, the database has been a valuable resource for outcomes research, an example of which we have heard presented this morning.

The impact of tracking outcomes has indeed led to reductions in hospital mortality for coronary bypass surgery even in the contemporary setting of older and sicker patient populations. Risk factors for coronary bypass surgery have been studied in all the databases previously mentioned. Cardiac factors such as a recent myocardial infarction, emergency surgery, reoperations, and low ejection fractions are intuitive. Through the database they are quantifiable and can be measured over time. Improvements in preoperative and intraoperative care have reduced the impact of these factors on mortality.

The present study focuses on quantifying the impact of comorbidity, such as pulmonary disease, renal failure, diabetes, obesity, and vascular disease, upon the author's major end point of in-hospital mortality. The data the authors have presented are consistent in magnitude with the relative risks published from other databases, such as the STS [Society of Thoracic Surgeons], which have been tracking data for 10 years with over 1.5 million patients entered into their database.

In the current study, peptic ulcer disease is a surprisingly significant comorbid risk factor for in-hospital mortality. My major concern and criticism of the current paper is the choice of in-hospital mortality as the primary end point. Truly, it is convenient and easy to obtain. Far more important is the impact these comorbidities may have on 30-day or even 6-month mortality, not a commonly or easily collected data point. With the radical changes in length of stay and the widespread use of rehab settings after coronary bypass surgery, a significant number of in-hospital survivors die within 30 days while being cared for at other medical settings. This fact has been clearly documented in the HCFA database. These deaths are often attributable to the comorbid conditions. Most importantly, comorbid conditions significantly impact ICU length of stay, hospital length of stay, stroke, and sternal wound and other postoperative complications. Database studies on comorbid conditions should study these end points quantitatively. Comorbid conditions significantly impact the overall procedural costs, disability, and human suffering.

I would like to compliment the authors and the members of the Northern New England Cardiovascular Study Group for their multiple contributions to our understanding of risk factors and outcomes in coronary bypass surgery. They have established a regional model of continuous quality improvement and fostered the ability of the cardiac surgical centers to work cooperatively, seeking quality for all. It has always been somewhat perverse for hospitals to compete on quality and not service. I would appreciate the authors' comments on: (1) changing their database from in-hospital to a 30-day mortality end point; (2) give us some explanation why you think peptic ulcer disease was a significant risk factor for in-hospital mortality; (3) what is the overall and institutional cost to maintain the Northern New England Cardiovascular Study Group; and, (4) comment on the proposition that studying comorbidities' impact on complication rates and procedural costs would yield important new data to improve cardiac surgical care.

Dr Clough: As you rightly point out, in-hospital mortality is something that we can easily measure and we can validate through all of our datasets at all of our member institutions. That is the reason we chose it. I agree with you completely that when we are talking about comorbid conditions and complications, longer-term follow-up would be valuable. It is difficult for us to accomplish, given the geography in which we work, however.

Why do we have ulcer disease as a marker for poor outcome? We do not know, but one of the things we have reviewed in the past is modes of death. We know that most of our patients, for instance, who do die, die in low-output failure from some cardiac cause. Why should ulcer be a marker for this? We do not know, but what we plan to do as a next step is go back and review why these people with the preoperative diagnosis of ulcer did die. Hopefully, there will be more information on that.

The cost to maintain the institution is not insignificant. We do receive grant aid from the American Heart Association, and all of the member institutions are assessed a fee annually to participate. Much of this goes to support the data collection and analysis that we have at Dartmouth.

Comorbid conditions and their cost was your final comment. Clearly our prediction card does take this into consideration. Comorbidities and the risk of complications such as mediastinitis, which is probably the costliest complication we face in cardiac surgery, as well as stroke, another long-term event, are predicted, but we have not attached a dollar amount to that.