Risks of Morbidity and Mortality in Dialysis Patients Undergoing Coronary Artery Bypass Surgery

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Background—Although dialysis patients are undergoing CABG with increasing frequency, large studies specifically comparing patient characteristics and procedure-related risks in this population have not been performed.

Methods and Results—We conducted a regional prospective cohort study of 15,500 consecutive patients undergoing CABG in northern New England from 1992 to 1997. We used multiple logistic regression analysis to examine associations between preoperative dialysis-dependent renal failure and postoperative events and to adjust for potentially confounding variables. The 279 dialysis-dependent renal failure patients (1.8%) were 4.4 times more likely to experience in-hospital mortality than were other CABG patients (12.2% versus 3.0%, respectively; \( P<0.001 \)). Dialysis-dependent renal failure patients were older and had more comorbidities and more severe cardiac disease than did other CABG patients. After adjusting for these factors in multivariate analysis, however, dialysis-dependent renal failure patients remained 3.1 times more likely to die after CABG (adjusted odds ratio [OR] 3.1, 95% CI 2.1 to 4.7; \( P<0.001 \)). Dialysis-dependent renal failure patients compared with other CABG patients also had a substantially increased risk of postoperative mediastinitis (3.6% versus 1.2%, respectively; adjusted OR 2.4, 95% CI 1.2 to 4.7; \( P=0.011 \)) and postoperative stroke (4.3% versus 1.7%, respectively; adjusted OR 2.1, 95% CI 1.1 to 3.9; \( P=0.016 \)), even after controlling for potentially confounding variables. Risks of reexploration for bleeding were similar for patients with and without dialysis-dependent renal failure.

Conclusions—Preoperative dialysis-dependent renal failure is a strong independent risk factor for in-hospital mortality and mediastinitis after CABG. (Circulation. 2000;102:2973-2977.)

Key Words: kidney □ mortality □ morbidity □ bypass

Patients with chronic renal failure have a high prevalence of coronary artery disease and cardiovascular death. Cardiac risks are particularly high in dialysis-dependent renal failure patients. Published reports indicate a 30% to 53% increase in death due to coronary artery disease in dialysis-dependent renal failure patients, which is unchanged over the past 10 years.1 With the increasing use of renal replacement therapy (transplant, hemodialysis, and peritoneal dialysis), especially in the older populations, efforts are being made to improve long-term survival.2,3 For these reasons, dialysis-dependent renal failure patients are considered for myocardial revascularization procedures. Because the results of PTCA have been shown to be relatively poor for this population,4 patients are recommended for CABG with increasing frequency.5-7

Despite the increasing use of CABG among dialysis-dependent renal failure patients, procedure-related risks in this population are not well understood. A number of studies have identified indicators of preoperative impaired renal function as risk factors for mortality8-12 and morbidity11-15 with CABG. However, prior studies specifically assessing patient characteristics and perioperative risks among patients with dialysis-dependent renal failure have been small single-institution case series.2,3,16-31

We conducted a regional cohort study of 15,550 patients undergoing CABG in northern New England from 1992 to 1997 to clarify the association between dialysis-dependent renal failure and in-hospital morbidity and mortality with CABG.

Methods

Subjects
The Northern New England Cardiovascular Disease Study Group is a voluntary research consortium representing all 5 medical centers in Maine, New Hampshire, and Vermont and 1 center in Massachusetts.
where CABG surgery is performed. Since 1987, the Northern New England Cardiovascular Disease Study Group has maintained a prospective registry of all patients undergoing CABG surgery in the region. For this analysis, we excluded patients undergoing CABG surgery incidental to heart valve repair, resection of ventricular aneurysm, or another surgical procedure.

Data Collection
The following data were recorded prospectively for all patients: age, sex, height, weight, cardiac catheterization results (degree of left main coronary artery stenosis, total number of significantly diseased coronary arteries, left ventricular end-diastolic pressure, and ejection fraction), prior cardiac surgery (CABG, PTCA, or valve procedure), PTCA during the current admission, unstable angina during the current admission, prior myocardial infarction, comorbidities (diabetes, peripheral vascular disease, renal failure, chronic obstructive pulmonary disease, congestive heart failure, cancers, and liver disease), ischemia treatment factors (preoperative intra-aortic balloon pump, preoperative intravenous nitroglycerin therapy, and preoperative thrombolytic therapy), priority of surgery (emergency, urgent, or elective), and in-hospital outcomes (status at hospital discharge [dead or alive], intraoperative or postoperative stroke [yes or no], reoperation for bleeding [yes or no], and sternal wound infection [yes or no]).

Cardiac catheterizations were performed by use of 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.23 Priority of surgery was assessed by the cardiothoracic surgeons and is defined as follows: "emergency" means that medical factors relating to the patient’s cardiac disease dictate that surgery should be performed within hours to prevent morbidity or death, "urgent" means that medical factors require that the patient remain in the hospital before surgery, and "elective" means that medical factors indicate the need for operation, but the clinical situation allows discharge from the hospital with readmission for surgery at a later date.

Dialysis-dependent renal failure, defined by the preoperative use of hemodialysis or peritoneal dialysis, was determined prospectively. Patients in whom dialysis was initiated after surgery were included in the other CABG population, not in the dialysis-dependent renal failure group.

Postoperative bleeding was defined as bleeding that required surgical reexploration after initial departure from the operating room. Postoperative stroke was defined as a new neurological event occurring postoperatively that persisted for >24 hours after its onset and was noted before discharge. Mediastinitis was defined as a sternal infection requiring antibiotics and return to the operating room for sternal debridement.

Analysis
Candidate predictor variables were selected from the core variables (age, sex, previous heart operation, left ventricular ejection fraction, percent stenosis of the left main coronary artery, number of major coronary arteries with stenosis >70%, and priority of surgery), level I variables (height, weight, PTCA on current admission, date of most recent myocardial infarction, angina history [including use of preoperative intra-aortic balloon pump, nitroglycerin, and thrombolytics], congestive heart failure, and chronic obstructive pulmonary disease), and available level II variables (left ventricular end-diastolic pressure, liver disease, and malignancy), which are suggested for risk adjustment of in-hospital CABG outcomes by Jones et al33 and the American College of Cardiology/American Heart Association practice guidelines.34 Core variables have been shown to be unequivocally related to operative mortality. Level I variables are likely related to short-term CABG mortality, and level II variables are not clearly shown to relate to short-term CABG mortality but are thought to be of research interest. In our multivariate analyses, we did not include the level I variables that are potentially in the causal pathway between renal failure and adverse outcomes of CABG, including diabetes, peripheral vascular disease, and creatinine. In addition, serious ventricular arrhythmias and mitral regurgitation are level I variables that were not included in our analysis because they are not available in our CABG data registry.

Univariate analyses involving χ2 tests for categorical variables and t tests for continuous variables were performed to assess the statistical significance of observed differences in patient characteristics between patients with and without dialysis-dependent renal failure.35 We used logistic regression analysis to assess the effect of dialysis-dependent renal failure on each outcome (expressed in terms of odds ratios [ORs], which approximate relative risk) after adjustment for potentially confounding variables.36 The C statistic (equivalent to the area under the receiver operating characteristic curve) and the Lemeshow-Hosmer goodness of fit statistic36 were calculated to assess the performance and calibration of each model, respectively. Analysis was performed by use of Stata release 5.0 software.37

## Results

Patient Characteristics
Table 1 lists patient clinical and treatment factors based on the presence or absence of dialysis-dependent renal failure. Overall, 279 of the 15 500 patients (1.8%) had dialysis-dependent renal failure before surgery. Dialysis-dependent renal failure patients versus other CABG patients were older (66.7 versus 64.8 years, P=0.005) and had a slightly lower

| TABLE 1. Patient Characteristics According to Presence or Absence of Preoperative Dialysis-Dependent Renal Failure |
|---------------------------------------------------------------|------------|-----------------|---|
| Patient Characteristics                                      | Preoperative Dialysis |               |  |
| Overall, n                                                   | 15 271     | 279             |  |
| Mean age, y                                                  | 64.8       | 66.7            | 0.005 |
| Male, %                                                      | 72.0       | 66.3            | 0.035 |
| Mean body surface area, m²                                    | 2.0        | 1.9             | <0.001 |
| Preoperative comorbidities                                    |            |                 |     |
| Chronic obstructive pulmonary disease, %                     | 11.8       | 27.2            | <0.001 |
| Diabetes mellitus, %                                         | 28.2       | 48.0            | <0.001 |
| Peripheral vascular disease, %                               | 12.5       | 40.9            | <0.001 |
| Liver disease, %                                             | 0.4        | 1.1             | 0.086  |
| Malignancy, %                                                | 3.6        | 3.9             | 0.743  |
| Cardiac profile                                              |            |                 |     |
| Ejection fraction, %                                         | 53.5       | 47.6            | <0.001 |
| Left ventricular end-diastolic pressure, mm Hg               | 16.9       | 20.0            | 0.001  |
| Congestive heart failure, %                                   | 12.4       | 37.3            | <0.001 |
| History of myocardial infarction, %                          | 50.8       | 65.5            | <0.001 |
| Unstable angina this admission, %                            | 48.1       | 57.7            | 0.002  |
| Preoperative intra-aortic nitroglycerin, %                    | 20.1       | 28.7            | <0.001 |
| Preoperative thrombolytic use, %                             | 3.6        | 6.8             | 0.004  |
| Preoperative intra-aortic balloon pump, %                    | 5.1        | 7.5             | 0.063  |
| Angioplasty this admission, %                                 | 4.2        | 6.1             | 0.120  |
| No. of major coronary arteries >70% stenosis (mean)           | 2.4        | 2.6             | <0.001 |
| Prior cardiac surgery, %                                     | 22.6       | 17.6            | 0.046  |
| Left main coronary artery stenosis, %                        | 24.3       | 26.5            | 0.303  |
| Surgical priority                                            |            |                 |     |
| Urgent/emergent, %                                           | 63.8       | 70.6            | 0.018  |
body surface area (1.9 versus 2.0 m², P<0.001). Males made up 66.3% of the dialysis-dependent renal failure patients compared with 72.0% of the other CABG patients. Dialysis-dependent renal failure patients versus other CABG patients had more comorbid conditions including the following: diabetes (48.0% versus 28.2%, P<0.001), peripheral vascular disease (40.9% versus 12.5%, P<0.001), and chronic obstructive pulmonary disease (27.2% versus 11.8%, P<0.001). There were no statistically significant differences between the 2 groups with regard to liver disease or malignancy. On average, dialysis-dependent renal failure patients versus other CABG patients had lower ejection fractions (47.6% versus 53.5%, P<0.001) and higher left ventricular end-diastolic pressure (20.0 versus 16.9 mm Hg, P=0.001). In addition, dialysis-dependent renal failure patients versus other CABG patients were more likely to have a history of congestive heart failure (37.3% versus 12.4%, P<0.001), a prior history of a myocardial infarction (65.5% versus 50.8%, P<0.001), and unstable angina (57.7% versus 48.1%, P=0.002) and were more likely to receive treatment with preoperative intravenous nitroglycerin (28.7% versus 20.1%, P<0.001) and thrombolytics (6.8% versus 3.6%, P=0.004). There was not a statistically significant difference between dialysis patients and other CABG patients in rates of use of preoperative intra-aortic balloon pump or PTCA during the current admission. Dialysis patients versus nondialysis patients had a higher number of diseased coronary vessels (2.6 versus 2.4, P<0.001), and more dialysis patients underwent an urgent/emergent surgical procedure (70.6% versus 63.8%, P=0.018). However, nondialysis patients were slightly more likely to have had a prior CABG (22.6% versus 17.6%, P=0.046), and there was no difference in left main coronary artery disease between the 2 groups.

**Patient Outcomes**

The incidence of in-hospital mortality after CABG surgery was 12.2% in the dialysis-dependent renal failure population and 3.0% in the other CABG patients (P<0.001). Mediastinitis developed in 3.6% of the dialysis-dependent renal failure patients versus 1.2% of the other CABG patients (P<0.001). Stroke was observed in 4.3% of the dialysis-dependent renal failure patients and 1.7% of the other CABG patients (P=0.001). Dialysis-dependent renal failure patients had higher rates of return to the operating room for bleeding than did other CABG patients (3.6% versus 2.9%), but this difference was not statistically significant (P=0.478).

The results from both univariate and multivariate logistic models are presented in Table 2. Dialysis-dependent renal failure patients were 4.4 times more likely to experience in-hospital mortality than were the other CABG patients (OR 4.4, 95% CI 3.0 to 6.4; P<0.001). After adjusting for confounding variables, dialysis remained an important predictor of in-hospital mortality with an OR of 3.1 (95% CI 2.1 to 4.7, P<0.001). After adjustment was made for confounding variables, dialysis-dependent renal failure patients still had a 2.4 times higher rate of mediastinitis compared with the nondialysis CABG population (OR 2.4, 95% CI 1.2 to 4.7; P=0.011). Similarly, dialysis patients compared with nondialysis CABG patients were 2.1 times more likely to suffer a stroke after adjustment was made for confounding variables (OR 2.1, 95% CI 1.1 to 3.9; P=0.016) Dialysis-dependent renal failure was not significantly associated with increased risk of reexploration for bleeding in either univariate analysis (OR 1.3, 95% CI 0.67 to 2.4; P=0.478) or multivariate analysis (OR 1.3, 95% CI 0.69 to 2.5; P=0.41).

Adjusted outcome rates are compared for dialysis and nondialysis patients in the Figure. The adjusted in-hospital mortality rate is 9.6% for dialysis-dependent renal failure patients versus 3.1% for other CABG patients (P<0.001). With regard to mediastinitis, the dialysis-dependent renal

### TABLE 2. Observed and Adjusted ORs of Postoperative Adverse Outcomes After CABG, According to Presence or Absence of Preoperative Dialysis-Dependent Renal Failure

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Crude (95% CI)</th>
<th>Adjusted (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4.4 (3.0-6.4)</td>
<td>3.1 (2.1-4.7)†</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.6 (1.5-4.8)</td>
<td>2.1 (1.1-3.9)§</td>
</tr>
<tr>
<td>Mediastinitis</td>
<td>3.1 (1.6-5.9)</td>
<td>2.4 (1.2-4.7)‡</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1.3 (0.67-2.4)</td>
<td>1.3 (0.69-2.5)∥</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, body surface area, preoperative congestive heart failure, priority of surgery (elective, urgent, or emergent), prior cardiac surgical procedures (none, CABG, valve surgery, or PTCA), PTCA during current admission, preoperative unstable angina, preoperative intravenous nitroglycerin, preoperative thrombolytic therapy, preoperative intra-aortic balloon pump, left ventricular end-diastolic pressure >22 mm Hg, ejection fraction <40%, left main coronary stenosis (%), history of myocardial infarction (none, within 1 week of CABG, or >1 week before CABG), number of coronary arteries with >70% stenosis, chronic obstructive pulmonary disease, liver disease, or malignancy.33

†C=0.77, Lemeshow-Hosmer goodness of fit P=0.502; ‡C=0.70, Lemeshow-Hosmer goodness of fit P=0.637; §C=0.71, Lemeshow-Hosmer goodness of fit P=0.632; and ∥C=0.64, Lemeshow-Hosmer goodness of fit P=0.309.
failure patients had an adjusted rate of 3.1% compared with 1.2% for nondialysis CABG patients \( (P=0.011) \). The difference in adjusted stroke rate between dialysis and nondialysis patients was significant (3.7% versus 1.7%, \( P=0.016 \)). Adjusted rates for bleeding were similar for dialysis-dependent renal failure patients and nondialysis patients (3.8% versus 2.9%, \( P=0.401 \)).

Discussion

Preoperative dialysis dependence is an important independent predictor of in-hospital mortality, mediastinitis, and stroke for patients undergoing CABG. In this region, 279 dialysis-dependent renal failure patients underwent CABG between 1992 and 1996 (1.8% of CABG patients). In univariate analysis, the risk of death was 4.4 times higher (12.2% versus 3.0%), the risk of mediastinitis was 3.1 times higher (3.6% versus 1.2%), and the risk of stroke was 2.6 times higher (4.3% versus 1.7%) for the dialysis patients versus the nondialysis patients. However, dialysis patients were older, had a higher prevalence of comorbid conditions, and had more severe cardiac disease before surgery than did nondialysis CABG patients. After adjustment for these factors, risks of mortality, mediastinitis, and stroke remained 3.1, 2.4, and 2.1 times higher, respectively, among dialysis patients. We observed no significant relationship between dialysis-dependent renal failure and the risk of postoperative bleeding in either univariate or multivariate analysis.

A number of studies have identified indicators of preoperative impaired renal function as risk factors for mortality\(^8\)–\(^12\) and morbidity\(^11\)–\(^15\) with CABG. In a prior study from this group, preexisting renal failure was present in 1.2% of patients undergoing CABG and was associated with 5.2 times greater risk of in-hospital mortality.\(^5\) In the Veterans Administration Risk Assessment Study for Cardiac Surgery, preoperative creatinine levels were positively associated with risks of mortality in univariate analysis\(^10\) and with complications in multivariate analysis.\(^13\) A more recent study in the VA population found that mild renal failure (serum creatinine \( \geq 1.5 \) mg/dL) was associated with 30-day mortality, postoperative bleeding, and ventilatory complications in multivariate analyses.\(^15\) A retrospective analysis of patients undergoing CABG at the Cleveland Clinic found that patients with preoperative serum creatinine levels \( \geq 168 \) \( \mu \)mol/L had higher perioperative morbidity (OR 2.8) and mortality (OR 3.7) in multivariate analysis.\(^11\) Similar to the results of the present study, preoperative dialysis dependence was independently associated with an increased risk of in-hospital mortality (OR 3.2) among CABG patients in New York State.\(^9\) Another study from the state of New York identified renal failure (creatinine \( \geq 2.5 \) mg/dL or on dialysis) as an independent risk factor for postoperative stroke (OR 2.0).\(^15\) Chronic renal failure has also been linked to higher rates of morbidity and mortality in numerous case series.\(^2,3,16–31\)

A number of theories about the mechanisms for increased morbidity and mortality among renal failure patients undergoing surgery have been proposed. Dialysis-dependent renal failure patients are an immune compromised population, and this may contribute to their increased risk of postoperative infection. For example, dialysis-dependent renal failure patients have a higher wound infection rate after lower extremity bypass.\(^38\) Whether increased infection rates are due to uremia, diabetes, steroid use secondary to autoimmune causes of renal failure, and other variables that are known to increase the risk of infection is unknown. Dialysis patients are also chronically anemic from the loss of erythropoietin production by the kidneys,\(^39,40\) and anemia has been shown to be associated with increased risks of mortality among CABG patients.\(^31\) Platelet dysfunction and coagulation defects from uremia are cited as mechanisms for increased bleeding among patients on dialysis,\(^23\) and renal failure may serve as a marker for generalized arteriosclerosis predisposing to thromboembolic events and stroke,\(^15\) as well as to less adequate revascularization and the development of postoperative low-output syndrome.\(^3\)

It is important to consider both the strengths and limitations of the present study. The strengths of our study include prospective data collection on a regional level such that biases in the collection of data or selection of study participants should not be limitations. Random misclassification of the primary exposure variable (dialysis dependence) is unlikely but would only result in an underestimate of the true relationship between dialysis-dependent renal failure and adverse outcomes if it occurred. The present study had adequate power to detect the differences between dialysis and nondialysis patients in the occurrence of adverse events while controlling for confounding variables due to the large size of the study population. In addition, our data registry contained detailed information from which to base risk-adjustment models. These models were well calibrated and had reasonable performance characteristics, so confounding by patient case mix should also not be a serious concern. Although some residual confounding from unmeasured or inaccurately recorded variables is likely, it is implausible that differences of the magnitude noted herein are completely explained by this cause. For this to be responsible for the entire effect observed, the confounder(s) would have to be a strong predictor(s) of outcome, substantially uncorrelated with known predictors that were considered, and unequally distributed among dialysis and nondialysis patients.

Dialysis-dependent renal failure patients are in general older and burdened with more comorbidities than are other patients undergoing CABG. They are at an increased risk for mortality, mediastinitis, and stroke. However, we have found no significant increase in rates of return to the operating room for bleeding among dialysis-dependent renal failure patients after adjustment for potentially confounding variables. These results should be considered when discussing surgical risks with dialysis-dependent renal failure patients.

References

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