# Impact of Renal Dysfunction on Outcomes of Coronary Artery Bypass Surgery

## Results From the Society of Thoracic Surgeons National Adult Cardiac Database

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***Background*****—**Although patients with end-stage renal disease are known to be at high risk for mortality after coronary artery bypass graft (CABG) surgery, the impact of lesser degrees of renal impairment has not been well studied. The purpose of this study was to compare outcomes in patients undergoing CABG with a range from normal renal function to dependence on dialysis.

***Methods and Results*****—**We reviewed 483 914 patients receiving isolated CABG from July 2000 to December 2003, using the Society of Thoracic Surgeons National Adult Cardiac Database. Glomerular filtration rate (GFR) was estimated for patients with the use of the Modification of Diet in Renal Disease study formula. Multivariable logistic regression was used to determine the association of GFR with operative mortality and morbidities (stroke, reoperation, deep sternal infection, ventilation >48 hours, postoperative stay >2 weeks) after adjustment for 27 other known clinical risk factors. Preoperative renal dysfunction (RD) was common among CABG patients, with 51% having mild RD (GFR 60 to 90 mL/min per 1.73 $m^2$, excludes dialysis), 24% moderate RD (GFR 30 to 59 mL/min per 1.73 $m^2$, excludes dialysis), 2% severe RD (GFR <30 mL/min per 1.73 $m^2$, excludes dialysis), and 1.5% requiring dialysis. Operative mortality rose inversely with declining renal function, from 1.3% for those with normal renal function to 9.3% for patients with severe RD not on dialysis and 9.0% for those who were dialysis dependent. After adjustment for other covariates, preoperative GFR was one of the most powerful predictors of operative mortality and morbidities.

***Conclusions*****—**Preoperative RD is common in the CABG population and carries important prognostic importance. Assessment of preoperative renal function should be incorporated into clinical risk assessment and prediction models. **(*Circulation*. 2006;113:1063-1070.)**

**Key Words:** bypass ■ kidney ■ renal insufficiency ■ risk assessment ■ surgery



Patients with renal dysfunction (RD) requiring coronary artery bypass graft (CABG) surgery represent a complex group of patients with an accelerated process of atherosclerosis and advanced cardiovascular disease. Both RD and end-stage renal disease (ESRD) are important risk factors for patients undergoing cardiopulmonary bypass.[1–3] Despite this risk, increasing numbers of patients with RD and ESRD are being referred for coronary revascularization[4] and CABG in particular.[4–7]

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Patients with chronic RD have a high prevalence of known atherosclerotic risk factors (such as hypertension, diabetes mellitus, smoking, dyslipidemia, and advanced age). These patients also have unique risk factors more directly associated with the uremic state (such as dyslipoproteinemia, hyperfibrinogenemia, and hyperhomocysteinemia).[8] The increased prevalence of disease in these patients has led to higher cardiovascular complications (up to 3 times the rate of the general population) and is a major cause of death in patients with ESRD.[9,10]

Although more severe RD and ESRD are understood to be risk factors for operative outcomes, limited information exists on risks associated with lesser degrees of RD in patients undergoing CABG. Much of the previous research relates to serum creatinine level,[11–14] which can be an imprecise measure of renal function.[15] Furthermore, although renal function is measured on a continuous scale, published CABG mortal-

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**The online-only Data Supplement, which contains an Appendix, can be found at http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.580084/DC1.**

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ity models have treated nondialysis RD as a dichotomous variable.[16,17]

Having access to the clinically rich data available from the Society of Thoracic Surgeons (STS) National Adult Cardiac Database (NCD), our goal was to examine the degree to which RD affects postoperative morbidity and mortality among patients undergoing isolated bypass surgery. Measurement of renal function was based on the estimated glomerular filtration rate (GFR), which is the most reliable index of renal function according to National Kidney Foundation (NKF) guidelines.[18,19] GFR was analyzed as a continuous variable and was also categorized with the use of NKF-suggested cutpoints.

## Methods

### Society of Thoracic Surgeons National Adult Cardiac Database

Patient data are harvested semiannually from individual participant site providers contributing to the STS NCD. The data are uploaded to a central facility, the Duke Clinical Research Institute, where biannual aggregate data analysis is performed. An executive summary of the semiannual report is posted at http://www.sts.org/database. A series of standard data quality analyses and checks are implemented before a site's data are aggregated into the national sample. Prior publications have summarized more complete descriptions of the database and data quality activities.[20–22]

### Study Population

We reviewed 520 270 patients receiving isolated coronary artery bypass from July 1, 2000, to December 31, 2003, from the STS NCD. We excluded from our analysis 7 STS sites (1%) at which serum creatinine (SCr) measurements were not routinely collected, resulting in 515 763 patients. Finally, patients for whom renal function could not be estimated (because of missing data) and who were not on dialysis were excluded, leaving a final population of 483 914 patients. We subsequently compared characteristics of these excluded patients with our final inclusion population to determine any potential sampling bias.

### Data Definitions

The primary outcome for this analysis was operative mortality (death during the same hospitalization as surgery, or after discharge, but within 30 days of surgery). As secondary analyses, we also examined permanent stroke (new-onset cerebrovascular accident persisting >72 hours); reoperation for any reason; deep sternal infection (involving muscle, bone, and/or mediastinum and including 1 of the following: wound opened with excision of tissue, positive culture, or treatment with antibiotics); prolonged ventilation (pulmonary insufficiency requiring ventilatory support for 48 hours); and prolonged postoperative stay (discharge >14 days after surgery). Additional outcomes include cross-clamp and perfusion time; intraoperative and postoperative intra-aortic balloon pump (IABP) usage; reoperation for bleeding; septicemia; and dialysis as a complication of surgery. Dialysis as a postoperative complication is only available for years 2002 and 2003. Remaining definitions are available at http://www.sts.org/database.

### Measurement of Renal Function

The STS NCD collects preoperative SCr, defined as the last single SCr measurement before surgery. Preoperative renal dialysis dependence was also available. For those not on dialysis, we estimated GFR on the basis of the Modification of Diet in Renal Disease (MDRD) study formula as suggested by the NKF guidelines.[18] The MDRD formula is as follows[15]:

$$GFR=186.3\times SCr^{-1.154}\times age^{-0.203}$$
$$\times 1.212\text{ (if black)}\times 0.742\text{ (if female)}$$

In addition, an estimate of creatinine clearance ($CrCl_1$) was obtained by applying the Cockcroft-Gault formula,[23] as follows:

$$CrCl_{male}=(140-age)\times LBW_{male}/(SCr\times 140)$$

$$CrCl_{female}=0.85\times(140-age)\times LBW_{female}/(Scr\times 140)$$

where LBW denotes an estimate of lean body weight: $LBW_{male}=50+2.3\times$(height in inches$-60$) and $LBW_{female}=45.5\times$(height in inches$-60$). Finally, a modified estimate of creatinine clearance, denoted $CrCl_2$, was obtained by substituting measured body weight (in kilograms) in place of LBW in the Cockcroft-Gault formula.

### Statistical Analysis

Our initial analyses investigated the relative prognostic importance of alternative measures that reflect renal function including SCr, GFR, $CrCl_1$, and $CrCl_2$. Identical analyses (described subsequently) were performed with each variable used as the measure of renal function. Because results were generally similar regardless of metric selected, we summarize our findings using estimated GFR to be consistent with national guideline recommendations.[18]

For descriptive purposes, renal function was labeled as normal (GFR ≥90 mL/min per 1.73 $m^2$, excludes dialysis), mild dysfunction (GFR 60 to 90 mL/min per 1.73 $m^2$), moderate dysfunction (GFR 30 to 59 mL/min per 1.73 $m^2$, excludes dialysis), severe dysfunction (GFR <30 mL/min per 1.73 $m^2$, excludes dialysis), or dialysis dependence (regardless of GFR). These cutpoints were selected on the basis of published guidelines.[18] Baseline clinical and demographic variables were compared across RD categories with the Kruskal-Wallis test for continuous variables and the $\chi^2$ test of general association for categorical variables.

Multivariable logistic regression models were used to assess the effect of GFR on outcomes after adjustment for important risk factors (listed in the Appendix in the online Data Supplement.) These were selected on the basis of results of the STS CABG mortality and morbidity models.[17] All models were adjusted for diabetes, which was a variable of interest in previous investigations.[2,24] For presentation purposes, we first analyzed the main effects of GFR, and then we investigated models with interactions between GFR and other key risk factors. A significance level of $P<0.01$ was used as a criterion for reporting interactions. For all logistic regression models, missing data values were imputed by assigning the median or modal value, except for body surface area, which was assigned the sex-specific median value.

In addition to categorizing GFR, we also performed univariate and multivariable analyses in which GFR was treated as a continuous variable. Data were initially smoothed by grouping GFR into 30 equally sized categories. Adjusted and unadjusted within-category mortality rates were then plotted against the within-category averages of GFR after applying a nonparametric smoothing function (lowess). For plotting purposes, adjusted mortality was defined as the ratio of within-category observed mortality compared with within-category average predicted mortality, multiplied by the overall observed mortality rate for the entire sample. Predicted mortality estimates for this analysis were obtained by fitting a logistic regression model that included all of the selected clinical variables (listed in the Appendix in the online Data Supplement) except for renal function. Patients on dialysis were excluded from these analyses.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

## Results

In the study population of 483 914, 104 880 patients (22%) were classified as having normal renal function (GFR ≥90 mL/min per 1.73 $m^2$), 247 535 patients (51%) were classified having mild RD (GFR 60 to 89 mL/min per 1.73 $m^2$), 114 661 (24%) were classified

**TABLE 1. Overall Preoperative Patient Descriptive Statistics**

| | GFR Level, mL/min per 1.73 m² | | | | |
|---|---|---|---|---|---|
| Variable | Normal (≥90) (n=104 880) | Mild (90–60) (n=247 535) | Moderate (59–30) (n=114 661) | Severe (<30 ) (n=9686) | Dialysis (n=7152) |
| Age, mean, y | 58.9 | 65.2 | 70.6 | 69.3 | 63.0 |
| BSA, m², mean | 2.0 | 2.0 | 1.9 | 1.9 | 1.9 |
| Female, % | 20.7 | 24.4 | 42.0 | 51.3 | 35.7 |
| Race, % | | | | | |
| White | 83.6 | 88.9 | 89.5 | 83.4 | 64.2 |
| Black | 7.7 | 4.0 | 3.7 | 6.3 | 19.8 |
| Hispanic | 3.5 | 2.5 | 2.4 | 4.4 | 8.4 |
| Other | 5.3 | 4.6 | 4.4 | 5.9 | 7.7 |
| Ejection fraction, mean | 51.2 | 51.3 | 49.4 | 45.9 | 45.5 |
| Diabetes, % | | | | | |
| Oral | 20.7 | 17.8 | 21.0 | 23.7 | 16.8 |
| Insulin | 8.8 | 8.0 | 14.3 | 28.9 | 44.2 |
| MI within 3 weeks, % | 27.7 | 24.8 | 27.6 | 35.4 | 32.0 |
| CVA, % | 4.9 | 6.2 | 10.4 | 14.6 | 15.7 |
| Chronic lung disease, % | 18.2 | 17.4 | 21.0 | 25.0 | 21.9 |
| PVD, % | 11.5 | 13.8 | 22.1 | 34.4 | 38.3 |
| CVD, % | 8.9 | 11.7 | 19.2 | 25.2 | 22.3 |
| Shock, % | 1.5 | 1.5 | 2.5 | 4.2 | 2.9 |
| NYHA class IV, % | 21.1 | 19.4 | 22.6 | 29.7 | 27.6 |
| Reoperation, % | 6.2 | 7.6 | 8.5 | 8.1 | 6.0 |
| Preoperative status, % | | | | | |
| Elective/urgent | 95.7 | 96.0 | 95.3 | 94.0 | 96.5 |
| Emergent | 4.2 | 3.9 | 4.3 | 5.4 | 3.2 |
| Salvage | 0.2 | 0.2 | 0.4 | 0.6 | 0.3 |
| Triple-vessel disease, % | 73.2 | 74.8 | 77.4 | 79.9 | 78.5 |
| Left main disease 50, % | 23.2 | 24.5 | 26.0 | 26.1 | 25.2 |
| Preoperative IABP, % | 7.4 | 6.4 | 7.4 | 8.7 | 6.1 |
| PTCA within 6 h, % | 0.9 | 0.8 | 0.8 | 0.6 | 0.7 |
| Hypercholesterolemia, % | 68.5 | 69.0 | 68.2 | 66.8 | 60.2 |
| Hypertension, % | 69.0 | 72.8 | 82.7 | 89.8 | 92.2 |
| Immunosuppressive treatment, % | 1.6 | 1.7 | 2.6 | 4.2 | 5.15 |
| Aortic stenosis, % | 1.0 | 1.3 | 2.0 | 2.6 | 3.0 |
| Mitral insufficiency, % | | | | | |
| Mild | 4.6 | 5.7 | 8.4 | 10.6 | 10.5 |
| Moderate/severe | 1.3 | 1.7 | 3.2 | 5.0 | 4.8 |
| Current smoker, % | 33.6 | 21.3 | 14.7 | 15.4 | 15.3 |

BSA indicates body surface area; MI, myocardial infarction; PVD, peripheral vascular disease; and CVD, cerebrovascular disease.

as having moderate RD (30 to 59 mL/min per 1.73 m²), 9686 (2%) were classified as having severe RD without dialysis (<30 mL/min per 1.73 m²), and 7152 (1.5%) required dialysis.

Characteristics among the 31 849 nondialysis patients who were excluded because of missing creatinine levels were generally similar to our study population, although they experienced slightly fewer comorbidities and had fewer complications (any major morbidity 11.7% versus 14.0%). Rates of operative mortality were similar for those who were excluded (2.58%) and those who were included (2.52%).

Across worsening RD categories, patients were older, more often female, and more likely to have comorbidities such as hypertension and diabetes mellitus (Table 1). There was a marked increase in the frequency of black race among dialysis patients compared with proportion of black race in other RD categories. Extensive atherosclerosis as evidenced by the increasing percentage of patients with concomitant peripheral vascular disease was also noted as a function of worsening RD. Many risk factors such as recent myocardial infarction, chronic lung disease, shock, NYHA class IV, and

**TABLE 2. Unadjusted Operative Characteristics and Outcomes**

| | GFR Level, mL/min per 1.73 m$^2$ | | | | |
|---|---|---|---|---|---|
| | Normal (≥90) (n=104 880) | Mild (89–60) (n=247 535) | Moderate (59–30) (n=114 661) | Severe (<30) (n=9686) | Dialysis (n=7152) |
| Operative characteristics | | | | | |
| Mean cross-clamp time | 67.0 | 67.0 | 67.2 | 68.8 | 67.6 |
| Mean perfusion time | 98.2 | 98.3 | 99.8 | 102.7 | 101.5 |
| IABP, % | | | | | |
| Intraoperative | 1.3 | 1.6 | 2.5 | 3.1 | 2.8 |
| Postoperative | 0.3 | 0.4 | 0.6 | 0.7 | 0.5 |
| Outcomes, % | | | | | |
| Operative mortality | 1.3 | 1.8 | 4.3 | 9.3 | 9.0 |
| Stroke | 0.9 | 1.3 | 2.4 | 3.5 | 3.3 |
| Reoperation | | | | | |
| For bleeding | 2.1 | 2.4 | 3.1 | 4.4 | 3.4 |
| For any reason | 4.2 | 4.8 | 7.1 | 10.6 | 11.0 |
| Infection | | | | | |
| Deep sternal infection | 0.4 | 0.4 | 0.6 | 0.9 | 1.5 |
| Septicemia | 0.7 | 0.8 | 1.6 | 3.0 | 3.9 |
| Prolonged ventilation | 5.3 | 6.1 | 11.1 | 19.7 | 19.0 |
| Postoperative stay >14 d | 3.2 | 4.1 | 8.5 | 17.3 | 16.6 |
| New requirement for dialysis* | 0.2 | 0.5 | 1.8 | 10.9 | NA |

Results are for years 2002 and 2003 only.
*New variable.



reoperation were more prevalent among nondialysis patients with severe RD compared with those on dialysis.

## Association With Outcomes

In univariate analysis, worsening renal function was associated with increasing operative mortality as well as postoperative complications including stroke, reoperation, infection, prolonged ventilation, prolonged postoperative stay, and a new requirement for dialysis (Table 2; each $P<0.0001$). Rates of adverse outcomes were slightly higher for nondialysis patients with severe RD compared with patients on dialysis. Severe RD or dialysis carried a >6-fold increase in operative mortality and a >3-fold increase in the frequency of stroke, septicemia, prolonged ventilation, and prolonged postoperative stay compared with normal GFR. Severe RD was also associated with longer pump times (cross-clamp and perfusion times) and more frequent balloon pump usage compared with normal GFR.

After we accounted for 27 other clinical risk factors, RD category remained a strong predictor of mortality and major morbidities (Table 3). Compared with patients with normal renal function, those with moderate RD (GFR 30 to 59 mL/min per 1.73 m$^2$) had 55% higher odds for operative mortality (adjusted odds ratio [OR], 1.55; 95% CI, 1.45 to 1.65). This rose to >3.8 times higher mortality risks among those on dialysis (adjusted OR, 3.82; 95% CI, 3.44 to 4.25).

**TABLE 3. Relationship of Renal Function and Major Postoperative Complications (Risk-Adjusted ORs and 95% CIs for Events)**

| Variable (Renal Function) | Normal (≥90) (n=104 880) | Mild RD (89–60) (n=247 535) | Moderate RD (59–30) (n=114 661) | Severe RD (<30) (n=9686) | Dialysis Dependent (n=7152) |
|---|---|---|---|---|---|
| Operative mortality | 1.00 | 1.02 (0.96–1.09) | 1.55 (1.45–1.65) | 2.87 (2.61–3.16) | 3.82 (3.45–4.25) |
| Stroke | 1.00 | 1.17 (1.08–1.26) | 1.47 (1.36–1.60) | 1.76 (1.55–2.01) | 2.00 (1.72–2.32) |
| Prolonged ventilation | 1.00 | 1.04 (1.01–1.08) | 1.49 (1.44–1.54) | 2.43 (2.28–2.59) | 2.77 (2.59–2.98) |
| Deep sternal wound infection | 1.00 | 0.99 (0.88–1.11) | 1.25 (1.10,1.43) | 1.35 (1.06–1.73) | 2.44 (1.96–3.05) |
| Any reoperation | 1.00 | 1.03 (0.99–1.07) | 1.30 (1.25–1.36) | 1.79 (1.66–1.93) | 2.05 (1.88–2.22) |
| Prolonged length of stay (>14 d) | 1.00 | 1.05 (1.01–1.10) | 1.54 (1.47–1.61) | 2.82 (2.64–3.02) | 3.25 (3.01–3.51) |
| New dialysis requirement* | 1.00 | 1.70 (1.42–2.04) | 4.65 (3.87–5.60) | 20.37 (16.68–24.87) | NA |

Results are for years 2002 and 2003 only.
*New variable.

**TABLE 4. Adjusted ORs for Effect of RD on Operative Mortality in Specific Populations**

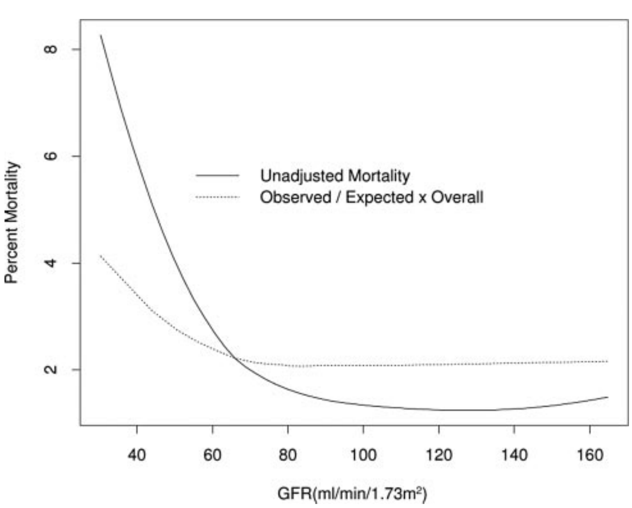
| | OR vs Normal Renal Function | | | |
|---|---|---|---|---|
| | Mild (89–60) (n=247 535) | Moderate (59–30) (n=114 661) | Severe (<30) (n=9686) | Dialysis (n=7152) |
| Gender | | | | |
| Male | 1.0 (0.9–1.1) | 1.7 (1.5–1.8) | 3.2 (2.8–3.7) | 3.6 (3.2–4.2) |
| Female | 1.0 (0.9–1.1) | 1.4 (1.2–1.5) | 2.5 (2.2–2.9) | 4.0 (3.4–4.7) |
| Ejection fraction | | | | |
| ≥40 | 1.0 (0.9–1.1) | 1.6 (1.5–1.8) | 3.1 (2.8–3.5) | 4.6 (4.0–5.3) |
| <40 | 1.1 (1.0–1.2) | 1.5 (1.3–1.7) | 2.6 (2.2–3.1) | 3.1 (2.6–3.8) |
| Insulin-dependent diabetes | | | | |
| Yes | 0.9 (0.8–1.0) | 1.2 (1.0–1.4) | 1.8 (1.5–2.3) | 3.0 (2.4–3.7) |
| PVD/CVD | | | | |
| None | 1.0 (1.0–1.1) | 1.6 (1.5–1.8) | 3.3 (2.9–3.7) | 4.0 (3.4–4.7) |
| 1 | 1.0 (1.0–1.2) | 1.4 (1.4–1.6) | 2.7 (2.3–3.1) | 3.8 (3.3–4.4) |
| Both | 0.9 (0.7–1.0) | 1.2 (1.0–2.5) | 2.1 (1.7–2.7) | 2.9 (2.3–3.8) |
| Reoperation | | | | |
| No | 1.1 (1.0–1.1) | 1.6 (1.5–1.7) | 3.1 (2.8–3.4) | 4.2 (3.8–4.7) |
| Yes | 0.8 (0.7–1.0) | 1.1 (1.0–1.3) | 1.7 (1.3–2.2) | 1.7 (1.2–2.4) |
| Hypertension | | | | |
| No | 1.1 (1.0–1.2) | 1.8 (1.5–2.0) | 4.3 (3.4–5.4) | 4.5 (3.2–6.2) |
| Yes | 1.0 (0.9–1.2) | 1.5 (1.4–1.6) | 2.7 (2.4–3.0) | 3.7 (3.3–4.1) |
| IMA used | | | | |
| No | 1.1 (1.0–1.2) | 1.7 (1.5–2.0) | 4.2 (3.3–5.3) | 4.3 (3.1–6.1) |
| Yes | 1.0 (0.9–1.1) | 1.5 (1.4–1.6) | 2.7 (2.4–3.0) | 3.6 (3.2–4.4) |

PVD indicates peripheral vascular disease; CVD, cerebrovascular disease; and IMA, internal mammary artery.

The increase in risk associated with dialysis dependence was >2-fold for stroke, prolonged ventilation, deep sternal wound infection, and reoperation and was >3-fold for prolonged length of stay >14 days. Even mild RD (60 to 90 mL/min per 1.73 $m^2$) was significantly associated with an increased risk of stroke, prolonged ventilation, and prolonged length of stay. Finally, GFR among nondialysis patients was a strong predictor of postoperative renal failure requiring dialysis. Although risk of acute renal failure was greatest among patients in the severe RD category (OR, 20.4; 95% CI, 16.7 to 24.9), even mild RD was associated with increased risk (OR, 1.70; 95% CI, 1.4 to 2.0).

When we allowed for interaction between GFR and other risk factors, the effect of RD was generally attenuated in higher-risk patients (Table 4). Significant interactions were found between GFR and gender, ejection fraction, insulin-dependent diabetes, peripheral vascular disease, cerebrovascular disease, hypertension, reoperation, and left internal mammary artery usage (each $P<0.01$). As shown in Table 4, the odds ratios (ORs) for comparing patients with RD with those with normal renal function were smaller for patients in the higher-risk categories. For patients receiving a left internal mammary artery graft, the ORs for renal function were smaller than for those not receiving a left internal mammary artery graft ($P=0.0009$).

The estimated probability of operative mortality as a function of continuous GFR among nondialysis patients is displayed in the Figure. The estimated probability falls sharply with increasing GFR in the 0 to 60 mL/min per 1.73 $m^2$ range and is relatively flat in patients with GFR ≥90 mL/min per 1.73 $m^2$. The relationship between GFR and mortality is similar after adjustment for other covariates,




Operative mortality vs GFR.

although the effect of GFR on mortality is attenuated after controlling for these covariates.

As a sensitivity analysis, we repeated all analyses using various alternative definitions of renal function including SCr, $CrCl_1$, and $CrCl_2$ (see Methods). In univariate analyses, SCr alone was slightly inferior to composite measures of renal function (GFR, $CrCl_1$, $CrCl_2$) that incorporated other risk factors such as patient age and gender. In multivariable analysis, all measures of renal function performed similarly well in models predicting operative mortality as measured by the C statistic (C=0.79 for each model). Model calibration was also not affected by the form of the renal function variable included.

## Discussion

This study adds to a growing body of literature documenting the effects of mild to moderate RD on mortality and morbidity after CABG surgery.[2,11,12,22,25,26] The present study builds on these findings by employing a more reliable estimate of renal function (GFR) and by examining a variety of outcomes in addition to operative mortality.

The association between RD and worse outcomes after CABG surgery for patients not on dialysis has multiple possible explanations. First, the greater frequency of triple-vessel disease and left main involvement among renal disease patients indicates that these patients may have more extensive coronary disease preoperatively than patients with normal renal function (Table 1). The deleterious consequences of renal failure led to a global reduction of oxygen supply to the myocardium due to severe damage to epicardial coronary macrovessels but also depressed coronary reserve secondary to microvessel disease.[27] Although the exact mechanisms for these deleterious effects are not clear, autopsies on ESRD patients have revealed a higher myocardial calcium content and calcium deposits in large and small coronary vessels.[28]

Second, increased risk may also be attributed to a multitude of concomitant factors seen in RD patients, including older age, poor left ventricular function, diabetes, hypertension, and peripheral vascular disease (Table 1). However, GFR remained an important risk factor beyond these traditionally assessed predictors (Table 3). Third, and perhaps most probable, renal function is likely a direct risk factor for intraoperative and postoperative adverse events and complications that lead to longer ventilator and operative times. We found evidence for both of these. Specifically, patients with RD had longer cross-clamp times and were more likely to require a balloon pump for cardiopulmonary bypass weaning (Table 2). We also found that nonfatal postoperative complications were more common in patients with RD (Table 3). For example, reoperation was twice as common among nondialysis patients with severe RD as among patients with normal GFR. It is conceivable that more frequent reoperation was a causal factor for higher rates of infection, including deep sternal wound infection and septicemia. Additionally, RD contributes to impaired platelet function, increasing patients' risk for perioperative bleeding complications. The increased frequency of certain complications, such as bleeding, may further be related to complications from renally cleared therapeutic agents such as non–antibody glycoprotein IIb/IIIa inhibitors and low-molecular-weight heparin, which can increase bleeding risks in patients with RD if not appropriately dose adjusted. Finally, patients with RD before surgery were much more likely to have acute renal failure postoperatively. Among patients not on dialysis preoperatively, a new requirement for dialysis postoperatively occurred in ≈0.5% of cases and was associated with a subsequent operative mortality rate of 43%. As a result, patients with a new requirement for dialysis after surgery accounted for 9% of the observed operative mortalities.

McCullough (2002)[29] has proposed 4 basic explanations for the association between chronic kidney disease and poor prognosis after coronary revascularization procedures: (1) excess comorbidities in patients with chronic kidney disease; (2) lesser use of beneficial therapies in patients with chronic kidney disease (therapeutic nihilism); (3) excess toxicities in those with chronic kidney disease; and (4) a special adverse pathobiological state in which there is acceleration of atherosclerotic, myocardial, and valvular disease. In this study it appears that explanations 1, 3, and 4 are operative.

Because our study consists entirely of a surgery population, we are unable to fully assess the role of therapeutic nihilism in contributing to worse outcomes for patients with chronic kidney disease. It is notable that the proportion of patients undergoing surgery electively was roughly constant across categories of chronic kidney disease. As such, there is no direct evidence that patients with chronic kidney disease were referred for surgery later than patients without chronic kidney disease. On the other hand, we do not have information about possibly sicker patients who were not referred for surgery. In addition, among patients who did receive surgery, it is conceivable that the chronic effects of underutilization of appropriate therapies, such as blood pressure control, may have contributed to their risk for adverse outcomes at the time of surgery.

The acute risks of performing CABG in those with RD must be carefully weighed against those procedural risks associated with alternative forms of coronary revascularization, namely, percutaneous transluminal coronary intervention (PCI). Specifically, multiple prior PCI studies have found that although procedural success rates tend to be high in those with RD, these patients face higher risks for mortality, morbidity, and restenosis.[5,6,30,31] Additionally, procedural risks of revascularization by either form have to be weighed against the long-term hazards associated with not performing revascularization in those with severe obstructive coronary disease. In this regard, Keeley et al[32] (2003) have previously demonstrated poor long-term outcomes (mean survival, 44.3±1.5 months) among acute coronary syndrome patients with severe chronic kidney disease who were treated with conservative medical care. This finding was confirmed by Hemmelgarn et al[13] (2004), who reported worse 8-year adjusted survival rates for kidney disease patients not on dialysis who were medically managed after catheterization compared with those who underwent revascularization (45.9% for CABG, 32.7% for PCI, versus 29.7% for no revascularization).

This study provides valuable data on the frequency of adverse outcomes among patients with RD undergoing

CABG surgery. Overall mortality in the study sample was 2.5% and ranged from 1.3% among patients with normal renal function to 9.3% for patients with GFR $<$30 mL/min per 1.73 $m^2$ and 9.0% for patients on dialysis before surgery. The estimated operative mortality rate among patients on dialysis in this study agrees closely with the in-hospital mortality rate of 8.6% observed in a sample of dialysis patients captured in the United States Renal Data System who underwent CABG during 1995–1998.[33]

Our results based on nonparametric smoothing suggest a nonlinear relationship between GFR and the risk-adjusted probability of operative mortality. The Figure reveals that the effect of renal function is essentially flat for patients with GFR $\geq$90 mL/min per 1.73 $m^2$, that risk-adjusted mortality begins to increase in the interval between 60 and 90 mL/min per 1.73 $m^2$, and that the effect of low GFR is most pronounced below a threshold of $\approx$60 mL/min per 1.73 $m^2$. These results are consistent with those of Reddan et al[2] (2003), who identified a threshold of 85 mL/min for the effect of creatinine clearance on mortality risk after CABG surgery. These results are also consistent with those of Manjunath et al[34] (2003), who identified 78 mL/min per 1.73 $m^2$ as the best change point for a 2-slope model predicting future atherosclerotic disease as a function of GFR in a longitudinal study of coronary heart disease.

All models reported in this article were adjusted for diabetes, which was a variable of interest based on previous investigations.[2,24] Szczech et al[24] (2002) reported that diabetes and chronic kidney disease work synergistically to increase risk of adverse outcomes after PCI and CABG. In contrast, Reddan et al[2] (2003) reported that the association between renal function and mortality was more pronounced among patients without diabetes. In our study, both orally treated and insulin-dependent diabetes were strong predictors of operative mortality ($P=0.0023$ for oral, $P<0.0001$ for insulin; data not shown), and the interaction between GFR category and insulin-dependent diabetes is statistically significant ($P<0.0001$; data not shown). Consistent with Reddan et al[2] (2003), the association between renal status and operative mortality was more pronounced for patients without insulin-treated diabetes (Table 4).

There were several limitations of the present study. First, although our study population includes the majority of isolated CABG procedures performed in the United States annually, patients predisposed to worse outcomes may be underrepresented in this analysis because the most severe cases are often medically managed.[32] Second, although the present study was able to identify the increasing risks of renal insufficiency, we did not interrogate the mechanisms associated with increased morbidity and mortality in patients with renal failure. Similarly, we do not have information of the detailed intraoperative and postoperative management of these patients. Thus, we cannot determine whether the surgical risks can be altered by optimal anesthetic and postoperative care strategies. Third, because renal function measurements were based on a single serum creatinine value, we were unable to examine the effect of a rising or falling creatinine trajectory. Fourth, we examined multiple mortality and morbidity outcomes, and therefore we acknowledge the possibility for chance findings to be significant. However, the impact of moderate to severe RD on outcomes was quite consistent and highly significant across all outcomes assessed. Finally, the current database evaluated short-term risks to patients but did not have information on their long-term survival.



## Conclusions

With continuing advances in the fields of nephrology, cardiology, and cardiac surgery, more patients with RD are being offered revascularization. This study has demonstrated that preoperative GFR is a powerful multivariable predictor of CABG operative mortality. Given these and other study findings, assessment of preoperative GFR as a continuous variable should be incorporated into clinical risk prediction models for mortality after bypass surgery. With careful consideration of all the important risk factors, cardiologists, nephrologists, and cardiac surgeons can convey to patients and their families accurate risk-based assessments of operative mortality after CABG.

## Disclosures

None.

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## CLINICAL PERSPECTIVE

Patients referred for coronary artery bypass graft (CABG) surgery are progressively older and have advanced atherosclerosis and comorbid illness. Our study of 483 914 CABG patients in the Society of Thoracic Surgeons National Adult Cardiac Database found that renal impairment was quite common. Fifty-one percent had mild renal dysfunction (RD) (glomerular filtration rate [GFR] 60 to 90 mL/min per 1.73 $m^2$), 24% had moderate RD (GFR 30 to 59 mL/min per 1.73 $m^2$), and 3.5% had severe RD (GFR $<$30 mL/min per 1.73 $m^2$) or were dialysis dependent. Operative mortality rose inversely with declining renal function, from 1.3% for those with normal renal function to 9.3% for patients with severe RD not on dialysis and 9.0% for those who were dialysis dependent. After adjustment, renal function was one of the most powerful predictors of operative mortality and morbidities. These data confirm that preoperative renal dysfunction is common in the CABG population and carries important prognostic importance. Thus, clinicians need to consider preoperative renal function when assessing patients' clinical risk for CABG.