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Primary Coronary Artery Bypass Surgery in the Presence of Decreasing Preoperative Renal Function: Effect on Short-term Outcomes

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ABSTRACT

Background: This study evaluated the impact of decreasing renal function on short-term outcomes in patients undergoing primary coronary artery bypass grafting (CABG).

Methods: The study period was from February 1999 to February 2009. Data on 4050 patients undergoing primary CABG were prospectively collected and analyzed retrospectively. The study population was divided into 3 groups: the CABG:N group, patients with preoperative serum creatinine levels <2 mg/dL (n = 3947); the CABG:RF group, patients with preoperative creatinine levels >2 mg/dL (n = 87); and the CABG:D group, patients on dialysis (n = 16).

Results: The significant differences between the groups (CABG:D > CABG:RF > CABG:N) in short-term outcomes were with respect to blood product use ($P < .001$), postoperative acute myocardial infarction ($P < .001$), pulmonary complications (P .001), infection ($P < .001$), and death ($P < .001$). The risk of short-term death (30 days) in the CABG:D group (4/16, 25%) was 25 times greater than that in the CABG:N group (38/3947, 0.96%).

Conclusion: CABG in the presence of renal failure is associated with significant morbidity and mortality.

INTRODUCTION

The decision to offer coronary artery bypass grafting (CABG) surgery is based on careful consideration of the risks and the benefits of the intervention offered. Patients with chronic renal dysfunction (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). 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 end-stage renal disease (ESRD) [Liu 2000; Cooper 2006; Yeo 2008; Lin 2009].

The outcomes after CABG, and in fact all cardiac surgical procedures associated with RD, are poor [Cooper 2006]. Patients with dialysis-dependent renal failure remained 3.1 times more likely to die after CABG [Liu 2000]. Operative mortality rises inversely with declining renal function, from 1.3% for those with a normal renal function to 9.3% for patients with severe RD not on dialysis, and to 9.0% for those who are dialysis dependent [Cooper 2006].

Although more severe RD and ESRD are understood to be risk factors for operative outcomes, limited information exists on the risks associated with lesser degrees of RD in patients undergoing CABG. We studied the impact of increasing RD on short-term outcomes after primary CABG in relation to 3 groups of patients from our study population—ie, patients with no significant renal impairment (CABG:N), patients with significant renal impairment but not on dialysis (CABG:RF), and patients on dialysis (CABG:D).

MATERIALS AND METHODS

The study period was from February 1999 to February 2009. Data on 4050 patients undergoing primary CABG were prospectively collected and analyzed retrospectively.

The study population was stratified into 3 groups. The CABG:N group had preoperative serum creatinine levels <2 mg/dL (3947/4050), the CABG:RF group had creatinine levels >2 mg/dL (87/4050) but were not on dialysis, and the patients in the CABG:D group were on dialysis (16/4050). Dialysis-dependent status was based on patients receiving intermittent venovenous, continuous venovenous, or peritoneal dialysis for chronic renal failure >1 week prior to their CABG operation. Patients who were not on routine dialysis but were undergoing dialysis preoperatively to reduce the risk of renal failure were not included in the study. Patients on preoperative dialysis underwent dialysis a day before CABG, while on cardiopulmonary bypass, and as needed in

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the intensive care unit, depending on the acid-base balance. These patients were returned to their preoperative dialysis regimen once they were back on the ward. Patients with preoperative RD were hemofiltered on cardiopulmonary bypass.

All definitions of complications were based on the Society of Cardiothoracic Surgeons Audit Database.

The data were categorized into 11 preoperative variables, 7 intraoperative variables, and 17 variables concerning postoperative intervention, complications, and morbidity. Paired Student t tests were conducted to identify statistically significant variables within the 3 arms of the study population.

The majority of the procedures were carried out with the patient on cardiopulmonary bypass; <1% of surgeries were performed off pump. Conduits for CABG were predominantly internal thoracic artery and saphenous vein grafts. Every effort was made to use the left internal thoracic artery in all patients. All 16 patients on dialysis received the left internal thoracic artery.

RESULTS

The preoperative and intraoperative characteristics for the 3 groups are summarized in Tables 1 and 2. Hypertension and unstable angina was significantly more common in the dialysis group, and patients with insulin-dependent diabetes mellitus and previous acute myocardial infarction (AMI) were significantly more prevalent in the CABG:RF group. There were no differences between the 3 groups in smoking history, left ventricular ejection fraction, body mass index, and urgency of operation. The mean cross-clamp and bypass times for the 3 groups were similar.

Table 1. Perioperative Variables in Renal Failure Patients*

Variables	CABG:N (n = 3947)	CABG:RF (n = 87)	CABG:D (n = 16)	*P*
Preoperative, n (%)				
Smoking history	2770 (70.17)	55 (63.22)	8 (50.00)	.10
IDDM	40 (1.01)	13 (14.94)	1 (6.25)	**<.001**
NIDDM	848 (21.48)	22 (24.29)	2 (12.50)	
Hypertension	3086 (78.18)	73 (83.91)	16 (100.00)	.05
Dyslipidemia	3356 (85.03)	72 (82.76)	14 (87.50)	.56
AMI < 6 d	244 (6.18)	14 (16.09)	0 (0.00)	**<.001**
Previous AMI	2011 (50.95)	56 (64.37)	9 (56.25)	**<.001**
Unstable angina	1281 (32.46)	41 (47.13)	9 (56.25)	**<.001**
BMI (mean), kg/m^2	28.37	28.18	26.09	>.05
LVEF (mean)	54.53%	53.96%	50.875%	>.05
30%, n (%)	189 (4.66)	7 (8.05)	2 (12.5)	.45
30%-45%, n (%)	682 (16.83)	16 (18.39)	4 (25)	
45-60%, n (%)	973 (24.02)	16 (18.39)	2 (12.5)	
60%, n (%)	2206 (54.49)	48 (55.17)	8 (50)	

**P* values in boldface are statistically significant (*P* < .05). CABG indicates coronary artery bypass grafting (surgery); CABG:N, CABG patients with no significant renal impairment (preoperative serum creatinine <2 mg/dL); CABG:RF, CABG patients with significant renal impairment but not on dialysis (preoperative serum creatinine >2 mg/dL); CABG:D, CABG patients on dialysis; IDDM, insulin-dependent diabetes mellitus; NIDDM, non–insulin-dependent diabetes mellitus; AMI, acute myocardial infarction; BMI, body mass index; LVEF, left ventricular ejection fraction.

Table 2. Intraoperative Variables in Renal Failure Patients*

Intraoperative Variables	CABG:N	CABG:RF	CABG:D	*P*
Surgery, n (%)				
Elective	2648 (67.09)	48 (55.17)	9 (56.25)	.51
Urgent	1324 (33.54)	36 (41.38)	7 (43.75)	
Emergent	78 (1.98)	3 (3.45)	0 (0.00)	
Off-pump CABG, n (%)	33 (0.84)	2 (2.30)	0 (0.00)	.21
Cross-clamp time (mean), min	51.45	51.27	46.56	>.05
Bypass time (mean), min	77.61	79.09	89.06	>.05
LITA used, n (%)	3797 (96.20)	74 (85.06)	16 (100.00)	**<.01**

**P* values in boldface are statistically significant (*P* < .05). LITA indicates left internal thoracic artery. Other abbreviations are expanded in the footnote to Table 1.

Table 3. Short-term Outcomes in Renal Failure Patients*

Postoperative Variables	CABG:N	CABG:RF	CABG:D	*P*
Postoperative management, n (%)				
Blood used	418 (10.59)	17 (19.54)	4 (25.00)	.14
Blood products	631 (15.99)	20 (22.99)	7 (43.75)	**<.001**
Ventilation > 24 h	103 (2.61)	3 (3.00)	2 (12.50)	**<.001**
Return to theater	152 (3.85)	3 (3.45)	2 (12.50)	.19
Bleeding/tamponade	102 (2.58)	2 (2.30)	2 (12.50)	.16
Cardiogenic shock	50 (1.27)	1 (1.15)	0 (0.00)	
Complications, n (%)				
New arrhythmia	1034 (26.20)	21 (24.14)	4 (25.00)	.96
Postoperative AMI	22 (0.56)	2 (2.30)	1 (6.25)	**<.001**
Pulmonary	252 (6.38)	9 (10.34)	6 (37.50)	**<.001**
Neurologic	28 (0.71)	1 (1.15)	0 (0.00)	.76
Infection	69 (1.75)	4 (4.60)	3 (18.75)	**<.001**
GI complications	20 (0.05)	1 (1.15)	1 (6.25)	**<.001**
Multiorgan failure	21 (0.53)	2 (2.30)	3 (18.75)	**<.001**
30-Day mortality, n (%)	38 (0.96)	1 (1.15)	4 (25.00)	**<.001**
Lenght of stay (median), d	6	8	10.5	

**P* values in boldface are statistically significant (*P* < .05). GI indicates gastrointestinal. Other abbreviations are expanded in the footnote to Table 1.

The results are summarized in Table 3. The significant differences between the groups (CABG:D > CABG:RF > CABG:N) in short-term outcomes were in blood product use ($P < .001$), ventilation >24 hours ($P < .001$), postoperative AMI ($P < .001$), pulmonary complications (P .001), infection ($P < .001$), and death ($P < .001$). Of the 3947 patients in the CABG:N group, 252 (6.4%) experienced pulmonary complications, compared with 10 (11.5%) of the 87 patients in the CABG:RF group and 6 (37.5%) of the 16 patients in the CABG:D group. The short-term mortality rate was 0.96% (38/3947) in the CABG:N group, compared with 2.3% (2/87) in the CABG:RF group and 25% (4/16) in the CABG:D group. In relative terms, the risks of pulmonary complications and death are 6 times greater and 25 times greater, respectively in dialysis patients than in patients with a near-normal renal function. The length of stay was longer in the dialysis group. Surprisingly, the 3 groups showed no differences in the frequencies of returning to the operating theater and of neurologic complications.

DISCUSSION

Patients with RD requiring CABG surgery are a complex group of patients with an accelerated process of atherosclerosis and advanced cardiovascular disease. Both RD and ESRD are important risk factors for patients undergoing cardiopulmonary bypass. Despite this risk, increasing numbers of patients with RD and ESRD are being referred for coronary revascularization and CABG in particular [Cooper 2006].

Renal disease tends to be a progressive disease that imparts a great burden on the physiological mechanisms of homeostasis. The causes of renal failure are many but can be divided into extrarenal and intrarenal causes [Cheung 2009]. Systolic hypertension and atherosclerotic disease leads to luminal narrowing of vessels and a decreased blood supply to the glomeruli, an age-related extrarenal cause of renal disease. Poorly controlled diabetes mellitus can greatly increase the pathophysiological progression of renal insufficiency from both macro- and microvascular causes. Disease progression is increased compared with the general population [Akman 2007; Cheung 2009; McCullough 2009]. Dialysis patients tend to have a poorer long-term survival rate than patients with no renal impairment. Patients receiving dialysis therapy have a transient correction of their metabolic derangement; however, they experience a slow, continuous decline in their end-organ function and, subsequently, in their physical capacity. These patients are at higher risk of adverse events during major surgical interventions compared with the general population. The glomerular filtration rate (GFR) has been used in prior studies as a prognostic indicator of long-term clinical outcome in CABG surgery. The validity of creatinine levels as a classification tool (versus the GFR) for RD has been challenged in some studies [van de Wal 2005; Mageed 2007; Brown 2008]. The variability in predicting the GFR depends on a number of factors, including the formula used. The Cockroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) formula are commonly used. The MDRD formula tends to be more reliable for patients older than 65 years, whereas the Cockroft-Gault formula better estimates renal function in patients younger than 65 years [Verhave 2005]. The margin of error appears to increase with increasing body mass index [Verhave 2005]. Lin et al [2009] found that the estimated GFR (eGFR) calculated by the Cockroft-Gault formula was a more accurate predictor than the eGFR calculated by the MDRD formula, whereas both are more clinically relevant than the serum creatinine concentration. Lin et al found in a multivariate analysis that the eGFR was an independent predictor of in-hospital mortality (odds ratio, 4.51; $P < .001$) and long-term mortality (hazard ratio, 1.54; P = .003). Najafi et al [2009] recommend preoperative calculation of creatinine clearance as well as the serum creatinine concentration for estimating renal function, especially in older women with a lower body mass index. We used serum creatinine as a marker of renal function because it remains the basis of the 2 most important risk-stratification scoring systems, ie, the Society of Thoracic Surgeons scoring system and the EuroSCORE.

We found that greater impairment of renal function carried a higher risk of morbidity and mortality, in the order CABG:N > CABG:RF > CABG:D. The risk of pulmonary complications increased 2-fold in the CABG:RF group and 6-fold in the CABG:D group, compared with the CABG:N group. The risk of death following surgery was increased by greater than 2-fold in the CABG:RF group and by greater than 25-fold in the CABG:D group, compared with the CABG:N group (relative risks of 1.47 and 25.88, respectively). Similar results were seen in another study, in which dialysis-dependent patients with renal failure also had substantially increased risks, compared with other CABG patients, of postoperative mediastinitis (3.6% versus 1.2%, respectively; P = .011) and postoperative stroke (4.3% versus 1.7%, respectively; $P = .016$), although there was no significant difference in bleeding rates [Liu 2000]. Najafi et al [2009] used both creatinine clearance and the serum creatinine concentration as a tool for predicting surgical outcome in patients undergoing CABG. The findings of our study are consistent with these investigators' conclusions. The study of Najafi et al was carried out with 11,884 patients who underwent primary CABG, of whom 706 (5.6%) had occult renal failure (serum creatinine <1.1 mg/dL). Their multivariate analysis found that occult renal insufficiency was associated with significantly higher risks of mortality ($P = .022$) and a prolonged hospital stay ($P = .22$). Lin et al [2009] also found that a decreasing eGFR was an independent predictor of increasing in-hospital and long-term mortality among 5559 patients who underwent primary CABG. Howell et al [2008] studied 7621 patients who underwent cardiac surgical procedures and were not on preoperative renal-replacement therapy. They found that chronic kidney disease stage as classified according to the eGFR was an independent predictor of in-hospital and long-term mortality. The data were obtained from the UK Central Cardiac Audit Database. Similar results were found in 2 other studies carried out with patients undergoing primary CABG. van der Wal et al [2005] studied 358 patients at a median follow-up of 18.2 years and found that a lower eGFR was an independent predictor of cardiac mortality (hazard ratio, 1.51;

P = .032). They found no significant differences between the groups with respect to myocardial infarction and reintervention. Chonchol et al [2007] studied 931 patients and found that a lower eGFR was an independent predictor of the composite outcome of death, need for reintervention, stroke, and acute coronary syndrome (*P* = .047) at a mean follow-up of 3.3 years. Increasing renal impairment in our study was associated with higher rates of blood product use, pulmonary complications, infection, and AMI. One of the major studies published was a multicenter investigation by Cooper et al [2006]. They accessed the Society of Thoracic Surgeons National Adult Cardiac Database and reviewed 483,914 patients who underwent isolated CABG from July 2000 to December 2003. The GFR was estimated for patients with the MDRD 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 RD was common among CABG patients, with 51% having mild RD (GFR, 60-90 mL/min per 1.73 m2; dialysis cases excluded), 24% having moderate RD (GFR, 30-59 mL/min per 1.73 m2; dialysis cases excluded), 2% having severe RD (GFR <30 mL/min per 1.73 m2; dialysis cases excluded), and 1.5% requiring dialysis. Operative mortality increased 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 to 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.

The present study is retrospective. The number of patients who underwent CABG over the 10-year study period was 4050. The number of these patients who were on dialysis patients was only 16, however, so the statistical significance of such a small group within the larger population has limited power. The patients were classified according to their preoperative creatinine levels, compared with the eGFR. Transient fluctuations in patients' hydration levels may have led to some patients being grouped inappropriately.

CONCLUSION

Cardiac surgery in the presence of renal failure is associated with significant morbidity and mortality, the magnitude of which is directly proportional to the degree of dysfunction.

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