Coronary artery bypass grafting with or without cardiopulmonary bypass in patients with preoperative non–dialysis dependent renal insufficiency: A randomized study

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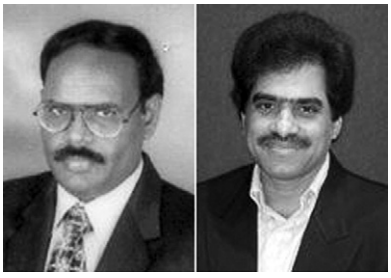

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Supplemental material is available online.

Objective: Preoperative renal insufficiency is a predictor of acute renal failure in patients undergoing coronary artery revascularization with cardiopulmonary bypass. Off-pump coronary artery bypass grafting has been shown to be less deleterious than on-pump bypass in patients with normal renal function, but the effect of this technique in patients with non–dialysis dependent renal insufficiency in a randomized study is unknown.

Methods: From August 2004 through October 2005, 116 consecutive patients with preoperative non–dialysis-dependent renal insufficiency (glomerular filtration rate measured using the Modification of Diet in Renal Disease equation [MDRD GFR] ≤ 60 mL $\cdot$ min^{-1} $\cdot$ 1.73 m^{-2}) undergoing primary coronary artery bypass grafting were randomized to on-pump (n = 60) and off-pump (n = 56) groups. MDRD GFR and serum creatinine levels were measured preoperatively and postoperatively at days 1 and 5. The changes in renal function and clinical outcomes were compared between the two groups.

Results: Preoperative characteristics were comparable between the two groups. The repeated-measures analysis of variance was performed on the data that showed worsening of renal function in the on-pump group compared with the off-pump group (serum creatinine, $P < .000$; glomerular filtration rate, $P < .000$). Further analysis of subgroups of patients with diabetes alone, hypertension alone, and combined hypertension and diabetes also showed significant deterioration renal function in the on-pump group compared with the off-pump group. In covariate analysis, diabetes has emerged as a significant covariate by serum creatinine criteria while compromised left ventricular function has emerged as a significant covariate by glomerular filtration rate criteria. These analyses showed that the use of cardiopulmonary bypass is significantly associated with adverse renal outcome ($P < .000$). Three patents required hemodialysis in the on-pump group and none in the off-pump group. The mean number of grafts per patient was 3.85 $\pm$ 0.86 and 3.11 $\pm$ 0.89 in the on-pump and off-pump groups, respectively ($P < .001$), but the indices of completeness of revascularization, 1.00 $\pm$ 0.08 for off-pump coronary bypass and 1.01 $\pm$ 0.08 for on-pump coronary bypass, were similar ($P = .60$).

Conclusions: This study suggests that on-pump as compared with off-pump coronary artery bypass grafting is more deleterious to renal function in diabetic patients with non–dialysis dependent renal insufficiency. MDRD GFR is a more sensitive investigation than serum creatinine levels to assess renal insufficiency in patients undergoing coronary bypass.

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Cardiac operations with cardiopulmonary bypass (CPB) adversely affect renal function, causing varying degrees of postoperative renal impairment. Postoperative renal failure remains a serious complication of cardiac surgery, although the incidence of acute renal failure (ARF) necessitating dialysis after cardiac operations is relatively low (1%-5%).[1-4] It is associated with increased

Abbreviations and Acronyms

ARF = acute renal failure
CABG = coronary artery bypass grafting
CPB = cardiopulmonary bypass
GFR = glomerular filtration rate
K/DOQI CKD = Kidney Disease Outcomes Quality Initiative Chronic Kidney Disease guidelines
LV = left ventricular
LVEF = left ventricular ejection fraction
MDRD = Modification of Diet in Renal Disease
OPCAB = off-pump coronary artery bypass grafting

mortality, morbidity, and intensive care unit stay, particularly if there is a requirement for hemodialysis.[5-8] The precise level at which renal dysfunction begins is unknown. Clinical impression suggests that even mild or moderate elevation of serum creatinine levels has an adverse effect on outcome.[9] The results of the study by Durmaz and colleagues[10] suggest that even those patients with relatively mild renal insufficiency remain at risk for a poor outcome. In patients with creatinine levels higher than 2.5 mg/dL, there is a strong likelihood of needing postoperative dialysis besides increased risks of mortality and morbidity. Several studies have assessed the risk associated with mild to moderate renal insufficiency in patients undergoing coronary artery bypass grafting (CABG).[10-12] However, in these studies renal function has been defined according to the levels of serum creatinine and not by calculated creatinine clearance or glomerular filtration rate (GFR). Because serum creatinine concentration is affected by several factors other than the filtration of creatinine, calculated creatinine clearance or GFR provides a more accurate estimate of renal function.[13] The effect of off-pump CABG (OPCAB) on postoperative renal impairment has also been controversial. Although it has been reported that OPCAB may minimize renal injury in elective patients with normal and impaired preoperative renal function and in high-risk patients,[14-18] other studies have failed to show such benefit.[19-22] However, there had been no published data from randomized studies of patients with non–dialysis-dependent renal insufficiency undergoing CABG with or without CPB. In this randomized study, we evaluated the effect of off-pump and on-pump techniques on renal function assessed by serum creatinine and GFR in patients with preoperative non–dialysis-dependent renal insufficiency undergoing primary CABG.

Patients and Methods

Patient Enrollment and Random Assignment

This study was designed to compare the effect of off-pump and on-pump techniques on renal function in patients with non–dialysis-dependent renal insufficiency with a GFR of 60 mL · min^{-1} · 1.73 m^{-2} or less undergoing primary, elective CABG. In an effort to minimize variability, all the procedures were performed by two surgeons (G.M., L.R.S.) experienced in OPCAB surgery and all patient management was conducted by a single team according to strict, unbiased, criteria-driven protocols. After approval by the institutional review board and informed consent, a total of 120 patients requiring primary CABG at CARE Hospital, Banjara Hills, Hyderabad, India, were enrolled to the study between August 3, 2004 (first patient) and September 26, 2005 (116th patient) and were randomized, 60 patients each, to with-CPB or without-CPB groups by a computer-generated random number table. This was done for each patient after the operating surgeon had documented the intended revascularization to be performed, which was based on review of the preoperative coronary angiogram. Random assignment was not stratified by diabetic status, hypertension, or compromised left ventricular (LV) function. Four of these patients (2 were found to require mitral valve repair, 1 patient needed emergency CABG because of unstable angina, and 1 patient did not report for surgery) dropped out after random assignment and were subsequently excluded from the study. All 4 of these patients belonged to the off-pump group. Hence, the total number of intent-to-treat population was 116 patients (on-pump group, n = 60; off-pump group, n = 56.).

Methods

A standard set of perioperative data were collected prospectively for all patients: age, sex, height, weight, diabetes mellitus, hypertension, peripheral vascular disease, LV ejection fraction (LVEF), number of significantly stenosed coronary arteries, prior myocardial infarction, angina class, serum creatinine, and GFR measured using the equation of the Modification of Diet in Renal Disease (MDRD) study. All patients in both groups received 600 mg of *N*-acetylcysteine orally once daily immediately before revascularization and for the first 5 postoperative days. None of the patients received aminoglycosides or nonsteroidal anti-inflammatory agents perioperatively. Two patients in the on-pump group received aprotinin 500,000 KIU in the postoperative period because of excessive mediastinal bleeding due to generalized oozing; the other patients in the study did not receive any antifibrinolytics. Postoperatively, whole blood or packed red blood cells were transfused for all patients whose hemoglobin value was less than 9 gm/dL.

Renal Function

Serum creatinine levels and GFRs were measured at the time of hospitalization and postoperatively on day 1 and day 5. The GFR was measured with the MDRD equation. Renal insufficiency was defined according to the guidelines from the National Kidney Foundation.[23] The Kidney Disease Outcomes Quality Initiative Chronic Kidney Disease (K/DOQI CKD) guidelines have established a 5-stage classification of patients with chronic kidney disease that is based solely on kidney function. These stages are defined by a GFR greater than or equal to 90 mL · min^{-1} · 1.73 m^{-2} (stage 1), 60 to 89 mL · min^{-1} · 1.73 m^{-2} (stage 2), 30 to 59 mL · min^{-1} · 1.73 m^{-2} (stage 3), 15 to 29 mL · min^{-1} · 1.73 m^{-2} (stage 4), and less than 15 mL · min^{-1} · 1.73 m^{-2}