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Original Article

Does Mild to Moderate Renal Dysfunction in Non-Dialysis Dependent Patients Affects the Outcomes after On-Pump Coronary Artery Bypass Grafting?

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Abstract:

Objectives: Algorithms of risk stratification for coronary artery bypass grafting (CABG) do not include a weighting for preoperative mild to moderate renal impairment defined as a serum creatinine 130 to 199μmol/L, which may impact mortality and morbidity after CABG. Hence our first objective was to ascertain the effect of a mild-to-moderate elevation in the preoperative serum creatinine level on post-operative outcomes. Our second objective was to ascertain which patient variables contributed to an increase in the serum creatinine level in association with coronary artery bypass grafting.

Materials and methods: We reviewed the prospectively collected data from the cardiac surgical database, which holds clinical information on all the patients undergoing cardiac surgery at our department since July 2014 to June 2017. A total of 101 patients who had known pre-existing mild to moderate renal disease and who were undergoing first-time coronary artery bypass grafting with cardiopulmonary bypass were recruited for the study. Patients were divided, based on preoperative serum creatinine level, into 3 groups as follows: Group A: creatinine level of less than 130μmol/L; Group B: creatinine level of 130 to 159μmol/L; and Group C: creatinine level of 160μmol/L or greater.

Result: Multivariate logistic regression showed that elevation of the preoperative serum creatinine level to 130μmol/L or greater increased the likelihood of hemodialysis postoperatively (P<0.001), as well as the need for postoperative ICU stay (P<0.001). Other factors contributing to a prolonged ICU stay were being 60 years of age or older (P=0.007), having a preoperative left ventricular ejection fraction of less than 40% (P=0.001), and having a prolonged cardiopulmonary bypass time (P< 0.001). In-hospital mortality was also significantly elevated in Group B and Group C; P=0.045 and <0.001 respectively with a few factors contributing to an increase in mortality on multivariable analysis were being female (P<0.001), being 60 years of age or older (P=0.004), having a preoperative left ventricular ejection fraction of less than 40% (P=0.006), and having a prolonged cardiopulmonary bypass time (P<0.001). Of particular note, the method of myocardial protection (cardioplegia with or without topical cooling) did not significantly influence in-hospital mortality, need for mechanical renal support, or ICU stay.

Conclusions: Mild to moderate renal dysfunction is an important predictor of outcome in terms of in-hospital mortality, morbidity, and midterm survival in patients undergoing CABG. As the preoperative serum creatinine level increases further (≥160 μmol/L), this effect is more pronounced.

Key Words: Coronary artery bypass surgery, Renal dysfunction

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Introduction:

Renal dysfunction (RD) is an adverse prognostic indicator in patients with coronary artery disease[1]. In patients undergoing coronary artery bypass grafting (CABG), moderate or end-stage renal dysfunction (ESRD) are recognized risk factors for increased perioperative mortality and are accounted for in the commonly used cardiac risk stratification scoring systems[2,3]. Despite this risk, increasing numbers of patients with RD and ESRD are being referred for coronary revascularization[4] and particularly in CABG[4–7].

Although severe preoperative renal disease is associated with a higher incidence of morbidity, need for dialysis, and length of hospital stay after CABG[8,9]; the precise level at which renal dysfunction begins to adversely affect outcome is unknown. Limited information exists on the influence of mild to moderate non-dialysis-dependent renal disease on the immediate postoperative mortality and long-term survival of patients undergoing isolated first time CABG.

The aim of this study was to investigate the impact of mild to moderate renal dysfunction on the outcome of patients undergoing isolated first-time on-pump CABG at our institution.

Materials and methods:

Patient selection: We reviewed the prospectively collected data from the cardiac surgical and perfusion database at Ibrahim Cardiac Hospital (Dhaka), which holds clinical information on all the patients undergoing cardiac surgery at our unit since July 2014 to June 2017. We recruited 101 patients who had known pre-existing mild to moderate renal disease for the study. Criteria for selection were that patients were having first-time coronary artery bypass grafting with cardiopulmonary bypass. The highest preoperative serum creatinine level within 7 days preceding the operation was taken as the preoperative creatinine level. Patients were grouped based on preoperative creatinine level into 1 of 3 groups. The postoperative creatinine level was taken as the highest value in the first 28 days after the operation. A baseline creatinine of 130μmol/L or 1.47 mg/dL was used as the threshold to define renal dysfunction[10].

Surgical technique: All patients underwent standard CABG surgery with the use of cardio-pulmonary bypass. The method of myocardial protection used was antegrade cold blood cardioplegia without topical cooling in 34 (33.6%) patients and with topical cooling in 67 (66.4%) patients. Cardiopulmonary bypass was performed by means of aortocaval cannulation, a Stockert roller pump (Stockert Instrumente, Munich, Germany) and a Skipper microporous hollow-fiber membrane oxygenator (Eurosets s.r.l. Italy). The mean blood pressure on cardiopulmonary bypass was maintained at 60 to 70 mm Hg. The lowest core temperature in degrees Celsius was noted as the core temperature of the body during the operation.

Statistical analysis: Analysis of the data was performed with SPSS 16.0. Univariate analysis was initially performed to ascertain associations between explanatory variables and outcome, χ^2 tests were used for categoric variables, and 2-sample-t-tests were used for the continuous variables. Stepwise logistic multivariate regression analysis was used with both forward and backward variable selection. Variables significant at the 5% level were retained in the final multivariable models. In-hospital mortality is used for the mortality analysis. Variables considered for inclusion in the multivariate models were as follows: sex, age, diabetes mellitus, hypertension, hypercholesterolemia, New York Heart Association (NYHA) grade of angina, previous myocardial infarction, smoking, ejection fraction, cardiogenic shock, number of diseased coronary arteries, left main stem coronary stenosis of greater than 50%, preoperative urea, surgical priority, type of myocardial protection, core temperature during the operation, and cardiopulmonary bypass time. Table 1 shows the distribution of these variables in the preoperative creatinine groups.

Table 1. *Preoperative and intraoperative variables used in developing all multivariable models presented in the study*

Variable	Group A Creatinine level <130µmol/L	Group B Creatinine level 130-159µmol/L	Group C Creatinine level ≥160µmol/L
Sex			
Male	56 (83.6%)	19 (90.4%)	11 (84.6%)
Female	11 (16.4%)	2 (9.6%)	2 (15.4%)
Age (y)			
<60	55 (82.1%)	14 (66.7%)	8 (61.5%)
≥60	12 (17.9%)	7 (33.3%)	5 (38.5%)
Diabetes mellitus	15 (22.4%)	7 (33.3%)	4 (30.8%)
Hypertension	28 (41.8%)	9 (42.9%)	9 (69.2%)
Hypercholesterolemia	29 (43.3%)	8 (38.1%)	3 (23.1%)
Angina			
≤NYHA II	41 (61.2%)	12 (57.1%)	5 (38.5%)
≥NYHA III	26 (38.3%)	9 (42.9%)	8 (61.5%)
Past MI	38 (56.7%)	12 (57.1%)	8 (61.5%)
Smoking	46 (68.7%)	16 (76.2%)	9 (69.2%)
Ejection fraction			
≥30%	61 (91.1%)	13 (61.9%)	10 (76.9%)
<30%	6 (8.9%)	8 (38.1%)	3 (23.1%)
Cardiogenic shock	1 (1.5%)	1 (4.8%)	0 (0%)
Diseased coronaries			
≤3	14 (20.9%)	5 (23.8%)	1 (7.8%)
>3	53 (79.1%)	16 (76.2%)	12 (92.3%)
Left main stem stenosis >50%	3 (4.5%)	3 (14.3%)	2 (15.4%)
Preoperative urea			
<7.5 mmol/L	55 (82.1%)	8 (38.1)	1 (7.8%)
≥7.5 mmol/L	12 (17.9%)	13 (61.9%)	12 (92.3%)
Surgical priority			
Elective	51 (76.1%)	8 (38.1%)	8 (61.5%)
Non-elective	16 (23.9%)	13 (61.9%)	5 (38.5%)
Myocardial protection with topical cooling	45 (67.2%)	14 (66.7%)	7 (53.8%)
Core temperature (°C) Mean ± SD	32.7 ± 2.2	33.1 ± 2.2	32.6 ± 2
Cardiopulmonary bypass time (min) Mean ± SD	77 ± 24.3	71.8 ± 24.5	85.5 ± 23

The number and percentage of patients within each preoperative creatinine group for the variable under consideration is shown unless otherwise indicated. NYHA=New York Heart Association.

Results:

Morbidity Analysis:

The effect of the preoperative serum creatinine groups on the need for hemodialysis, the need for intensive care and total postoperative stay, and the occurrence of pulmonary, neurologic, and infective complications in the hospital were analyzed. Of the 101 patients in the study, 8 (7.92%) required hemodialysis. Multivariate analysis with all variables in Table-1 showed a preoperative creatinine level of 130µmol/L or greater (P<0001), non-elective operation (P=0.01), and female sex (P=0.02) to increase the likelihood of hemodialysis (Table-2).

Table 2. *Factors contributing significantly toward the need for postoperative hemodialysis*

Covariate	Odds ratio	P value	95% CI
Preoperative creatinine level			
<130µmol/L	1		
≥130µmol/L	24.43	<0.001	10.31-55.45
Sex			
Male	1		
Female	2.93	0.02	1.17-7.31
Surgical priority			
Elective	1		
Non-elective	3.11	0.01	1.39-7.20

Multivariate regression analysis was done with all variables included in Table-1.

The median (interquartile range) for Intensive Care Unit (ICU) stay was 2 (2-3) days. A stay greater than the 90th percentile was defined as prolonged. This equated to a ICU stay of greater than 3 days in 15 patients. On multivariate analysis, patients with a preoperative creatinine level of 130 to 159µmol/L were 3 times as likely (P<0.001) and patients with a preoperative creatinine level of 160µmol/L or greater were 3.9 times as likely (P<0.001) to have a prolonged ICU stay than those with a creatinine level of less than 130µmol/L. Other factors contributing to a prolonged ICU stay were being 60 years of age or older (P=0.007), having a preoperative left ventricular ejection fraction of less than 40% (P=0.001), and having a prolonged cardiopulmonary bypass time (P<0.001; Table-3).

Table 3. *Factors affecting prolonged ICU stay more than 3 days*

Co-variate	Odds ratio	P value	95% CI
Preoperative creatinine level			
<130µmol/L	1		
130-159µmol/L	3.08	<0.001	1.63-5.70
≥160µmol/L	3.89	<0.001	2.02-7.59
Age (y)			
<60	1		
≥60	1.73	0.007	1.16-2.57
Left ventricular function			
EF ≥40%	1		
EF <40%	2.14	0.001	1.39-3.37
Cardiopulmonary bypass time (*For increments of 10 min)*	1.18	<0.001	1.10-1.25

EF=Ejection Fraction

Mortality analysis:

In-hospital intraoperative or postoperative death was defined as mortality for the purposes of the study. There were 6 (5.94%) deaths. The mortality for the 3 preoperative creatinine groups is shown in Fig-1. The odds ratio for mortality on multivariable analysis was 3 times (P=0.045) higher if the preoperative creatinine level rose from less than 130µmol/L to 130 to 159µmol/L. As the preoperative creatinine level rose further to 160µmol/L or higher, the odds ratio for mortality increased to 7 times (P<0.001) that of patients with a preoperative serum creatinine level of less than 130µmol/L. Other factors contributing to an increase in mortality on multivariable analysis were being female (P<0.001), being 60 years of age or older (P=0.004), having a preoperative left ventricular ejection fraction of less than 40% (P=0.006), and having a prolonged cardiopulmonary bypass time (P<0.001). In contrast, no significant difference was present between the use of cardioplegia with or without topical cooling on mortality (P=0.21) in the multivariate analysis.

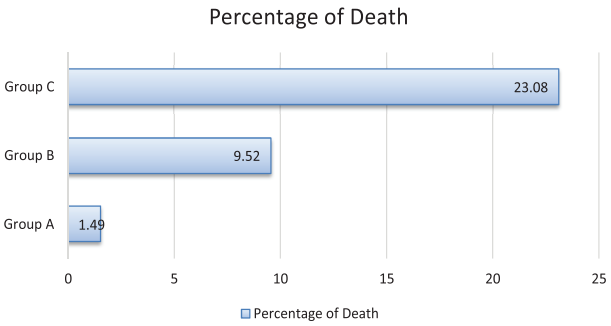

Figure 1. *In-hospital mortality by preoperative creatinine group. The mortality within each creatinine group is given as a percentage of the total patients within that group.*

Discussion:

Although serum creatinine level is not the most accurate tool, it is still the most readily available clinical tool to assess renal function. The increase in morbidity and mortality associated with dialysis-dependent renal disease is widely recognized[4]. An increased morbidity has also been shown in association with moderately elevated serum creatinine levels in patients with non–dialysis-dependent renal insufficiency[9,10].

We performed the multivariate analysis in this study that showed a few preoperative factors are associated with renal dysfunction and poor outcome. Despite including these risk factors in the multivariate analysis, even a mild increase in the preoperative serum creatinine level over the normal range significantly increased the risk of the need for hemodialysis, as well as prolonging the ICU stay. One of the most important observations from the study was the pronounced effect a mild-to-moderate elevation in the preoperative serum creatinine level had on the mortality from coronary artery bypass grafting.

These results are important because they identify the effect of the preoperative serum creatinine level has on morbidity and mortality independent of the presence of other risk factors, such as sex, age, left ventricular function, and cardiopulmonary bypass time. Patients with higher preoperative serum creatinine levels are likely to have a higher proportion of functionally borderline glomeruli, which potentially are more susceptible to deterioration of their function when exposed to the insults of an on-pump CABG.

On performing multivariate analysis to include all the risk factors outlined in Table 1, it was seen that the type of myocardial protection used did not influence mortality significantly. Similarly, there was no difference on multivariate analysis of cardioplegia with or without topical cooling on the need for hemodialysis or on the ICU stay. Moreover, the lowest core body temperature achieved during the operation also had no independent effect on morbidity or mortality.

This study confirms clinical observations that the morbidity and mortality from coronary artery bypass grafting increase with even mild-to-moderate elevation of the preoperative serum creatinine level. The factors that contribute significantly to renal dysfunction because of coronary surgery are also outlined. We hope the result of this study will help in a more rigorous design and assessment of strategies aimed at reducing the increased morbidity and mortality from on-pump coronary artery bypass grafting seen in patients with non–dialysis-dependent renal dysfunction.

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