Early Evaluation of Renal Function in High-Risk Patients after Off-Pump Coronary Artery Bypass Grafting

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Key Words : *Ischaemic heart disease, Renal failure, Coronary artery bypass surgery.*

Abstract :

Background: *Cardiopulmonary bypass (CPB) is an unphysiological state and widely regarded as an important contributor to renal failure. Despite improvement in cardiopulmonary bypass technique, anesthesia and intensive care, perioperative renal dysfunction still represents a significant and potentially lethal complication after coronary artery bypass graft surgery (CABG). Renal dysfunction is a serious complication of coronary revascularization with CPB and results in increased morbidity, mortality and prolonged hospital stay. We compared the incidence of perioperative renal dysfunction in patients who underwent CABG, on-pump and off-pump (OPCAB).*

Methods: *A total of 60 high -risk patients with ischaemic heart diseases were included in the study who underwent CABG. Out of the total 60 patients, 30 were in the Off-pump group (Group A) and the rest 30 were in the On-pump group (Group B). They were diagnosed as high-risk patients considering serum creatinine level>1.7mg/dl with age ≥60 years, ejection fraction 30-40%. Renal function was evaluated in both groups preoperatively and postoperatively (on 1st, 2nd and 7th postoperative day) and compared between two groups.*

Results: *One patient in the On-pump group died on 6th postoperative day. Preoperative renal parameters were also similar and showed no statistically significant difference. So both groups were comparable. Comparison of renal parameter in OPCAB and on-pump CABG between preoperative and 7th day postoperatively found in this study were blood urea 50.33±6.29, 39.87±4.8 vs 52.67±9.05 , 66.21±6.91 ; S. Creatinine (mg/dl) 1.94±0.19 , 1.28±0.19 vs 2.07±0.31 , 2.82±0.47; Creatinine Clearance Rate(ml/min) 46.61±4.1, 71.51±12.3 vs 46.53±4.6, 34.02±4.49 ; Urine output (ml/24 hrs)1692.7±71.53, 1755.7±82.91 vs 1591.2±78.76, 1492.1±196.29 all are statistically significant(p<0.05). Mean period of mechanical ventilation, ICU stay and total postoperative hospital stay were significantly greater in On-pump group. One patient of Group –B died due to multi organ failure including acute renal failure on 6th postoperative day (3.3%) (p>0.05). Statistically significant difference of renal parameters in different postoperative days showed evidence of well preservation of renal function in OPCAB.*

Conclusion: *Adaptation of OPCAB offers better preservation of renal function as well as better early postoperative outcome specially in high-risk CABG patients.*

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Introduction:

Coronary artery bypass grafting is one of the procedures with the highest impact in the history of medicine. No other operation has led to more lives prolonged and been better characterized with respect to its short and long term outcomes. CABG constitutes the keystone of adult cardiac surgery.[1]Cardiopulmonary bypass is an unphysiological state and widely regarded as an important contributor to renal failure.[2] Despite improvement in CPB technique, anesthesia and intensive care, preoperative renal dysfunction still represents a significant and potentially lethal complication after cardiac operations.[3] Renal dysfunction is a serious complication of coronary revascularization with CPB and results in increased morbidity, mortality and prolonged hospital stay.[4]

Off-pump coronary artery bypass grafting operation on a beating heart significantly reduces oxidative stress and suppresses the inflammatory reaction associated with the use of CPB.[5] OPCAB is considered renoprotective.[6] It is associated with lower in- hospital mortality and complication rates than On-pump CABG and also reduces length of hospital stay, incidence of atrial fibrillation and wound infections.[7,8]

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OPCAB has been proposed as a means of minimizing many of the alterations caused by CPB to reduce the risk of postoperative renal insufficiency. Avoidance of the pump may result in better preservation of glomerular and tubular function with less evidence of damage. The population of patients referred for CABG has substantially changed in the last years. The progress in medical therapy and interventional cardiology coupled with the increase in life expectancy and the widespread availability of cardiac surgery facilities have shifted toward the high risk profile of patients proposed for surgical myocardial revascularization and there is clear evidence that the cardiac and the systemic preoperative status of CABG patient have become progressively more complex, and that high risk patients represent now a substantial proportion of surgical candidates.[9]

Any patient with one or more of the following characteristics was considered to be at high-risk for early mortality and morbidity. Age of 75 years or more, ejection fraction lower than 40%, serum creatinine level of 150 μmol/l or higher.[10] Incidence of postoperative renal dysfunction in CABG patients is about 10% and renal complication in high-risk subgroup of patients underwent bypass surgery was 3.3% in off-pump and 5.4% in on-pump.[11,12] Though the incidence of acute renal failure(ARF) requiring dialysis after open heart operation is relatively low (1% to 5%) but it is associated with a mortality rate up to 60%.[13] Elevation in serum creatinine (Cr) has been a commonly used marker of ARF in hospitalized patients.[14]

Postoperative renal dysfunction markedly affects the surgical outcome of these high-risk patients in terms of increase the length of ICU stay, hospital stay and cost of surgery, last but not least the rate of mortality. To improve the clinical outcome of these high-risk patients for renal impairment now off-pump coronary artery bypass grafting is being performed frequently.

Methods:

This prospective clinical study was performed in the department of Cardiac surgery, National Institute of Cardiovascular Diseases (NICVD) from July 2006 to June 2008. A total of sixty high-risk patients aged from 45 to 68 years undergoing coronary artery bypass grafting were enrolled in the study. Study population was divided in two groups- Group A- undergoing off pump CABG and Group B undergoing on pump CABG. In each group thirty patients were included consecutively. They were diagnosed as high risk patients considering serum creatinine ≥1.7 with age ≥60 years, ejection fraction 30-40%. Patients with coexisting valve disease and congenital heart disease were excluded from the study. The aims and objectives of this study were to evaluate the renal function in high-risk patients after off-pump coronary artery bypass grafting, to compare preoperative renal function between off-pump and on-pump CABG patients, to compare renal function in different postoperative days (POD1, POD2 and POD7) between off-pump and on-pump CABG and to observe changes of renal function from preoperative period to postoperative periods in each group.

The objective of the study was discussed in details with the patients before their decision to enroll themselves into the study. A detailed clinical history was taken from the patient regarding smoking, diabetes, hypertension, dyslipidemia. Relevant physical examination was also done in all the cases. All the patients were categorized according to NYHA classification preoperatively. Ultimately all the sixty patients, thirty in each group underwent CABG. Their renal functions were evaluated preoperatively as well as postoperatively on 1st POD, 2nd POD and 7th POD. Blood urea, serum creatinine, creatinine clearance rate and urine output were considered as parameters for evaluation of renal function. During observation, total operating time was also recorded in each patient. Regarding post operative events, total ICU stay, period of mechanical ventilation and total hospital stay were recorded. Major post operative complications like acute renal failure, need for dialysis, prolonged ventilation >48hrs, deep sternal would infection, respiratory infection & number of death were also recorded. Each patient was followed-up up to 3 months. All the relevant collected data were collected from each participant using predesigned data collection sheets (proforma). All the collected data were compiled on a master chart first and then organized by using scientific calculator and standard statistical formulas. Statistical analyses of the results were done by computer software device as statistical

packages for social scientist (SPSS). The results were presented in tables. For comparison between two groups, the study outcomes were evaluated regarding unpaired 't' test and chi-square test. A "p" value<0.05 was considered as significant.

Results:

The mean age was 57.03±4.35 vs. 54.47±4.47, most of the patients belong to 50-59 years (p>0.05). Most of the patients were in NYHA class-II 53.3% vs. 46.7% in both groups. Regarding risk factors hypertension was on the top (60% vs. 70%), among others smoking (56.7% vs. 63.3%), diabetes mellitus (70% vs. 30%), angina (26.7% vs. 36,7%) and dyslipidaemia (60% vs. 63.3%) all were insignificant statistically (p>0.05) except diabetes mellitus. Comparison of high-risk indicators between off- pump and on- pump CABG patients was: age ≥60 yrs (33.3% vs. 16.7%), EF 30-40% (26.7% vs. 33.3%), renal dysfunction (S. creatinine ≥1.7 mg/dl) (100% vs. 100%).

Mean ± SD of total operative time in minute between groups were 222.67 ± 21.88 vs. 317.67 ± 48.69 statistically found highly significant (p=0.001). Comparison of postoperative events between off-pump and on pump CABG patients Mean ± SD of period of mechanical ventilation in hours (9.87±1.68 vs. 17.57±6.34, p=0.001). ICU stay in days (3.17 ± 0.83 vs. 4.47 ± 1.17, p=0.001), total hospital stay in days (9.27±1.28 vs 11.43±2.49, p=0.001)^{S} between group –A & group-B. Regarding postoperative complications acute renal failure (3.3% vs. 13.3%, p=0.176) , dialysis was needed (0% vs. 6.7% p=0.245), deep sternal wound infection (3.3% vs. 13.3%, p=0.176), respiratory infection (3.3% vs. 16.7%, p=0.097), death only 1 in group-B (3.3%, p=0.5).

No significant difference regarding baseline values of all renal parameters (pre-operative values) between two groups. But statistically significant difference were observed regarding blood urea , serum creatinine, creatinine clearance rate and urine output in POD1, POD2 and POD7 between two groups.

Table-I

Comparison of blood urea (mg/dl) in two groups of study population (n=60).

Blood UreaMg/dl	Group A(n=30) Mean±SD	Group B(n=30) Mean±SD	p- value
Preoperative	50.33±6.29	52.67±9.05	0.251
POD1	60.33±6.42	73.9±12.22	0.001
POD2	60.43±6.5	75.3±16.61	0.001
POD7	39.87±4.8	66.21±6.91	0.001

p value reached from paired-t test, POD- Post operative day.

Table-II

Comparison of serum creatinine (mg/dl) in two groups of study population (n=60).

Serum creatinine	Group A(n=30) Mean±SD	Group B(n=30) Mean±SD	p- value
Preoperative	1.94±0.19	2.07±0.31	0.053
POD1	2.31±0.37	3.49±0.8	0.001
POD2	2.27±0.43	3.57±0.93	0.001
POD7	1.28±0.19	2.82±0.47	0.001

p value reached from paired-t test, POD- Post operative day.

Table-III

Comparison of creatinine clearance rate (ml/min) in two groups of study population (n=60).

Creatinine Clearance Rate	Group A(n=30) Mean±SD	Group B (n=30) Mean±SD	p- value
Preoperative	46.61±4.1	46.53±4.6	0.947
POD1	39.7±6.01	28.17±5.36	0.001
POD2	40.67±7.21	27.74±5.27	0.001
POD7	71.51±12.3	34.02±4.49	0.001

p value reached from paired-t test, POD- Post operative day.

Table-IV

Comparison of urine output (ml/24 hours) in two groups of study population (n=60).

URINE output	Group A(n=30) Mean±SD	Group B(n=30) Mean±SD	p- value
Preoperative	1692.7±71.53	1591.2± 78.76	0.001
POD1	1619.3±181.18	1480.7±170.68	0.003
POD2	1631±90.91	1383.7±319.21	0.001
POD7	1755.7±82.91	1492.1±196.29	0.001

p value reached from paired-t test, POD- Post operative day.

Discussion:

The population of patients referred for coronary artery bypass grafting (CABG) has substantially changed world-wide as wells in our country in the last years. The progress in medical therapy and intervention cardiology coupled with the increase in life expectancy and the widespread availability of cardiac surgery facilities have shifted towards the high-risk profile patients for surgical revascularisation.[9]

National Institute of Cardiovascular diseases, Dhaka, Bangladesh has been performing the central role in the field of cardiac surgery countrywide. CABG has been performing from 1985 and off pump coronary artery bypass grafting (OPCAB) is being performed since 1997 in NICVD. In 2007 a total of 186 CABG were performed in NICVD, among them OPCAB 105(56%) and on-pump 81(44%).

The present study was elicited by the need to improve the clinical outcome of high-risk coronary artery bypass patients by applying different surgical approaches to different patients. The aim of this clinical prospective study was to compare the postoperative renal function in high-risk patients undergoing on-pump & off-pump CABG. Maximum number was found in the age group of 50-59 years in both the off-pump and on-pump groups. On the contrary a study done by Calafiore et al. had mean age 64.4±9.6 years for OPCAB and 63.3±9.7 years for on-pump CABG patients.[15] These higher mean ages of patients undergoing bypass surgery in developed country may explain the improved & sophisticated surgical technique & ICU support as well as increase in life expectancy which has enabled them to choose more & more elderly patients for bypass grafting. In our study risk factors were compared between off-pump & on-pump CABG groups . In this study 17 (56.7%) patients in group A & 19 (63.3%) patients in group B were smoker. No significant difference exists in between two groups. Arom *et al*. found 22% & 18.8% smoker in off-pump & on- pump group respectively.[16] This incidence is much higher in our study. This may explain the lack of awareness about the hazards of smoking in our country. In the present study 21 (70%) patients in OPCAB group & 9 (30%) patients in on- pump group had diabetes mellitus. The difference was statistically significant. On the other hand, Arom *et al*. found diabetes in 33.3% & 33.8% patients in OPCAB & on-pump group respectively.[16] A study on 1570 high-risk patients by chamberlain *et al*. reported hypertension was 60.7% and 61.9% in off-pump and on- pump CABG group respectively and

hyperlipidemia was found 75.2% & 68.3% in off-pump and on-pump group respectively.[10] On the other hand, in this study, hypertension was found in 18(60%) & 21(70%) patients in off-pump and on-pump CABG groups respectively and hyperlipidemia was found in 18 (60%) patients and 19 (63.3%) in off-pump and on-pump group respectively. In the present study, among the common risk factors significant difference exists between the two groups regarding diabetes mellitus. In both groups predominant risk factors were smoking, diabetes mellitus, hypertension and hyperlipidemia .

High-risk patients in the study were found elderly ≥60 years (33.3% vs. 16.7%), ejection fraction between 30-40% (26.7%vs 33.3%), renal dysfunction (S.creatinine ≥1.7 mg/dl) (100% vs 100%) in off-pump vs on-pump group respectively. The high-risk indicators between off-pump and on-pump CABG were almost comparable. The above findings showed that the preoperative patient characteristics regarding age, NYHA functional class, risk factors of CAD and cardiopulmonary functional status were almost similar to the studies conducted by other authors.[10,12] These features have no significant influence on peroperative and postoperative clinical outcome. Comparison of peroperative variables between groups demonstrate that total operation time in off-pump group was significantly less than that of on-pump group in this study. The difference was statistically significant. Arom *et al*. reported that total operation time was 175(36) min and 235(65) min in off-pump & on-pump group respectively, which corresponds with our study.[16]

Several postoperative variables have been compared between the two groups. In this study mean ventilation period in off-pump group was 9.87±1.68 hrs and in on-pump group was 17.57±6.34 hrs. The difference was statistically significant. That is OPCAB procedures to be better tolerated by the patients; ventilation time was significantly higher in on-pump group. According to Ascione *et al.* ventilation time was12.5±7.1 hours and 11.8±9.6 hours in on-pump and off-pump group respectively.[13] But Arom *et al*. reported significantly higher ventilation time in on-pump group.[16] Ventilation time was 19 hours in on-pump vs 9 hours in off-pump group (p<0.001). Cleveland et al. and Plomondon et al. also showed significantly higher ventilation tine in on-pump group.[18,19] This finding is similar to our study. On the other hand, mean period of total ICU stay in OPCAB and on-pump CABG groups were 3.17±0.83 days and 4.47±1.17 days respectively. The difference in two groups was statistically significant. Calafiore *et al*. showed in a study that ICU stay was 13.5±16.6 hrs in off-pump and 16.2±15.3 hrs in on-pump group, whereas Boyd *et al.* reported ICU stay (hrs) 24±10.9 hrs in off-pump and 36.6±33.5 hrs in on-pump group.[15,20] These findings were similar to our study because in all these study on-pump group required more ICU stay. Total postoperative hospital stay 9.27±1.28 days and 11.43±2.49 days in off-pump and on-pump group respectively. The difference is statistically significant (p<0.001). Ascione *et al.* reported length of hospital stay 5.84±1.5 days and 7.36±3 days in off-pump vs on-pump group respectively.[21] It was statistically significant (p<0.03). This finding corresponds to our study. Thus the mean period of mechanical ventilation, ICU stay and total postoperative hospital stay were significantly greater in on-pump group than off-pump group. All these reflect definite clinical advantage as well as favorable economic outcome associated with off-pump group of patients. In this prospective clinical study, the patients had been followed up to 3 months. Among the total sixty patients, one patient in on-pump group died on 6th POD due to multiorgan failure. Mortality rate was 0% versus 3.3% in off-pump and on-pump group respectively and that was not statistically significant. Arom *et al*. reported operative mortality in high-risk patient was 28.5% in on-pump versus 7.7% in off-pump group (p=0.008).[16] This finding did not correspond to our study.

In the present study, postoperative morbidities were acute renal failure (3.3% vs13.3%), need for dialysis (0% vs 6.7%), deep sternal wound infection (3.3% vs 13.3%), respiratory tract infection (3.3% vs 16.7%) in off-pump group and on-pump group respectively. None of them required prolonged ventilation (>48hours) in either group. In comparison of major postoperative complications statistically significant difference was not observed in between two groups. Yokoyama *et al.* in a study on off-pump vs on-pump coronary artery bypass in high-risk group showed renal complication was 3.3% vs 5.4%, prolonged ventilation was 3.7% vs

6.6% in off-pump vs on-pump CABG groups respectively.[12] In a study by Ascione *et at*. reported acute renal failure (5.9% vs 15.8%), infective complication (5.9% vs 7.42%) in off-pump and on-pump group respectively.[13]

Renal function was compared between OPCAB and on-pump groups both preoperatively and postoperatively. Preoperative mean blood urea values showed no statistically significant difference in between two groups. But the mean blood urea values on the 1st, 2nd and 7th POD showed significantly higher level in on-pump group. Mean preoperative serum creatinine level was 1.94±0.19 mg/dl and 2.07±0.31 mg/dl in group A and group B respectively. The difference in preoperative values in two groups was not statistically significant. Mean serum creatinine level in the 1st POD, 2nd POD and 7th POD showed significantly higher level in on-pump group than off-pump group. Here the difference in the postoperative values in two groups was statistically significant. Promodh *et al*. found that serum creatinine levels increased progressively in both groups from preoperatively to 24 hrs postoperatively and thereafter decreased by 48 hrs postoperatively.[22] This finding was similar to our observation. But Tang *et al.* reported in their study that no significant difference in serum creatinine or blood urea was detected between the two groups during the study period with both parameters staying within the normal range throughout.[6] Comparison of creatinine clearance rate (ml/min) in two groups was also evaluated preoperatively and of different postoperative days. No significant difference was found in preoperative values between group A and group B patients. But significant differences were found in values on 1st, 2nd and 7th POD. Tang *et al.* advocated in their study that there was no significant difference in OPCAB and on-pump group regarding creatinine clearance.[6] Loef *et al.* also found no significant difference in creatinine clearance rate throughout the entire observation period.[4] Promodh *et al*. found statistically significant decrease in creatinine clearance in both groups from preoperatively to 24 hrs postoperatively.[22] In case of off-pump group creatinine clearance rate (CcR) increase and reached to preoperative level by 48 hrs but in on-pump group gradual increase of CcR but not reach up to preoperative level.

Comparison of 24 hours urine output (ml) in two groups were done preoperatively as well as on different postoperative days. Here it was observed that in all the periods 24 hours urine output was lower significantly in on-pump group than off-pump group. Loef *et al.* suggesting that renal perfusion was equally adequate in the postoperative periods as urine output did not differ between groups in his study.[4] Gerritsen *et al*. reported that mean preoperative urine output was significantly lower than the mean urine output during and after the surgery in both groups.[23] Besides comparing renal parameters in between OPCAB and on-pump CABG groups, time course of renal variables were also observed. Regarding blood urea levels, OPCAB and on-pump groups had almost similar baseline values (preoperative value) and in course of time values increased on 1st POD and 2nd POD in both groups and blood urea level declines on consecutive POD in OPCAB group but remained elevated in on-pump group. But statistically significant difference remained between preoperative blood urea level and value on 7th POD in both groups. Tang *et al.* stated that no significant difference in blood urea was detected between the groups during the study period (preoperative to 5th POD).[6] Trend of change in serum creatinine level was observed in both OPCAB and on-pump group. Comparison over time between groups showed no significant difference in baseline values between two groups. Serum creatinine was increased in two groups on 1st POD. Thereafter creatinine value declined in group A over time and reached lower than preoperative value but at each time point (2nd and 7th POD) creatinine value remained elevated in group B. There was highly significant difference between preoperative and 7th POD serum creatinine value in group B. Ascione *et al.* reported similar initial changes as in our study regarding serum creatinine but they followed each patient for only 60 hrs postoperatively.[13] Change of CcR over each point of time was observed in both groups. Preoperative CcR in both group showed no statistically significant difference. During the postoperative period CcR reduced in both groups significantly on 1st and 2nd POD. Thereafter CcR gradually increased over time. In OPCAB group CcR reached a level higher than preoperative level which was statistically highly significant. In on-pump group CcR was also elevated from 1st POD to 7th POD,

but reached a level below the preoperative level. Promodh *et al*. reported similar initial changes as in our study, regarding CcR but they followed for only 48 hrs postoperatively.[22] Ascione *et al*. also reported that at 24 and 48 hrs postoperatively the creatinine clearance values decreased significantly in the on-pump group, reaching levels markedly lower than preoperative levels.[21] Conversely, in the off-pump group the values returned to preoperative levels at both 24 and 48 hrs postoperatively. Their findings were almost similar to our study is case of on-pump group but differ is case of off-pump group. They reported that CcR returned to preoperative level at both 24 and 48 hrs but in our study level decreased in POD1 then slightly increase in 48 hrs and returned to preoperative level by 7th POD.

From the above discussion it is conceived that patients in both groups were similarly distributed in regards of age, risk factors, NYHA class, risk indicators. Preoperative renal parameters were also similar and showed no statistically significant difference. So both groups were comparable. But the renal parameters showed significant difference in different postoperative periods in two groups with evidence of well preservation of renal function in off-pump group that showed significant impact on postoperative outcome. So our data furnish substantial evidence that the adaptation of OPCAB confer significant clinical advantages in high-risk CABG patients.

Conclusion:

This prospective clinical study on high-risk patients undergoing on-pump and off-pump CABG revealed significant difference in renal parameters on different postoperative days. The trend of changes in renal parameters on different postoperative days also showed significant preservation of renal function in OPCAB group. On the other hand, cardiopulmonary bypass has detrimental effect on renal function and required longer duration of mechanical ventilation, ICU stay and hospital stay. So it can be concluded that OPCAB offers better preservation of renal function as well as better early postoperative outcome specially in renal high-risk CABG patients.

Limitation of the Study:

We had some limitations in the study like- Period of study was short; Sample size was small; Lack of proper investigation facilities (like microalbumin-to-creatinine ratio, *N*-acetyl-β-D-glucosaminidase (NAG), α_1 –macroglobulin, glutathione transferase-α, fractional excretion of sodium (EF_{Na}), retinol-binding protein).

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