## **Original Research Article**

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# The impact of pre-operative uric acid levels on post-operative renal outcomes in off-pump coronary artery bypass grafting patients

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#### **ABSTRACT**

**Background:** Elevated pre-operative uric acid levels significantly impact post-operative renal outcomes in off-pump CABG patients, increasing the risk of acute kidney injury, as evidenced by higher serum creatinine and reduced urine output.

**Methods:** This cross-sectional study was conducted in Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh from January 2021 to December 2022. Total 160 patients undergoing off pump CABG were divided into two groups, group A and group B, each containing 80 patients. In group A, uric acid level was <7 mg/dl for male and <6 mg/dl for female and in group B, it was >7 mg/dl and >6 mg/dL for female.

**Results:** The demographic characteristics, pre-operative serum UA levels and serum creatinine levels between the two groups was not statistically significant. Group A had shorter operative times (mean 265.21±53.33 minutes) compared to Group B (mean 327.04±44.32 minutes), with more patients in Group-B undergoing longer surgeries (>360 minutes). Group-B also had more grafts (mean 4.4 vs 3.6), higher serum creatinine (1.91 vs 1.17 mg/dl), bilirubin (0.8 vs 0.7 mg/dl), and lower urine output (mean 47.52 vs 95.37 ml/hour), all statistically significant (p<0.001).

**Conclusions:** This study concludes that there is significant impact of pre-operative uric acid levels on post-operative renal outcomes in off-pump CABG patients.

**Keywords:** Coronary artery bypass grafting, Renal outcomes and off-pump, Uric acid level

#### **INTRODUCTION**

Coronary artery bypass grafting (CABG) is a critical surgical procedure aimed at improving blood flow to the heart in patients with severe coronary artery disease. CABG was first introduced in 1968 and rapidly became the standard of care for symptomatic patients with coronary artery disease. Advances in coronary surgery

have reduced morbidity, mortality, and rates of graft occlusion.<sup>2,3</sup> Among various techniques, off-pump coronary artery bypass grafting (OPCAB) is performed without the use of a heart-lung machine, which has been associated with reduced postoperative complications. However, postoperative renal dysfunction remains a significant concern, particularly acute kidney injury (AKI), which adversely affects patient outcomes.

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Preoperative serum uric acid (SUA) levels have been identified as potential predictors of postoperative renal outcomes in various surgeries, including OPCAB. Elevated SUA is known to correlate with the risk of developing postoperative AKI, with studies indicating that higher preoperative SUA levels are significantly associated with increased incidence of AKI, prolonged mechanical ventilation, extended ICU stays, and overall postoperative complications.4 The prevalence of AKI following cardiac surgeries, including OPCAB, varies but remains a common and serious complication. AKI is associated with significant morbidity and mortality, emphasizing the need for identifying and managing risk factors effectively.<sup>5</sup> Research suggests that preoperative uric acid levels can serve as a robust predictor of postoperative renal dysfunction, with elevated SUA levels improving the predictive accuracy for AKI over traditional measures such as serum creatinine alone. 6 This association is supported by multivariate analyses demonstrating that patients with higher preoperative SUA levels have a significantly increased risk of developing AKI postoperatively. The impact of preoperative SUA levels on postoperative renal outcomes extends beyond AKI, influencing overall postoperative recovery and long-term renal function.

For instance, patients with elevated preoperative SUA levels have shown higher rates of complications and prolonged recovery times compared to those with lower SUA levels. This correlation underscores the importance preoperative risk stratification and potential interventions to mitigate these risks. The exact mechanisms through which elevated SUA contributes to adverse renal outcomes are multifaceted, involving oxidative stress, inflammation, and endothelial dysfunction. These processes exacerbate renal injury, particularly in the setting of surgical stress and hemodynamic fluctuations inherent to cardiac surgeries.8 Moreover, the role of SUA as an independent risk factor is evident in various studies where SUA levels were adjusted for other known risk factors, and still retained significant predictive power for postoperative renal dysfunction.9 The clinical implications of these findings are substantial, suggesting that preoperative measurement of SUA could be integrated into the routine assessment of patients undergoing OPCAB.

This would allow for better identification of high-risk patients and potentially guide preoperative optimization strategies to improve outcomes. For example, addressing modifiable risk factors such as SUA levels through dietary modifications, pharmacological interventions, or preoperative hydration could potentially mitigate the risk of AKI and enhance overall postoperative recovery. The impact of preoperative uric acid levels on postoperative renal outcomes in patients undergoing OPCAB is significant and well-documented. Elevated SUA levels are associated with a higher incidence of AKI, prolonged ICU and hospital stays, and increased postoperative complications. Integrating SUA measurement into

preoperative risk assessments can improve predictive accuracy and guide interventions aimed at reducing renal complications and improving overall patient outcomes.

#### **METHODS**

This cross-sectional study was conducted in Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical (BSMMU), Shahbag, Dhaka Bangladesh, during the period from January 2021 to December 2022. Total 160 patients undergoing off pump coronary artery bypass grafting were included in this study. These patients were divided into two groups, group A and group B, each containing 80 patients. In group A, uric acid level was <7 mg/dL for male and <6 mg/dL for female and in group B, uric acid level was >7 mg/dL and >6 mg/dL for female. Consent of the patients and guardians were taken before collecting data. After collection of data, all data were checked and cleaned. After cleaning, the data were entered into computer and statistical analysis of the results being obtained by using windows-based computer software devised with Statistical Packages for Social Sciences version 22. After compilation, data were presented in the form of tables, figures, and charts, as necessary. Numerical variables were expressed as mean and standard deviation, whereas categorical variables were count with percentage. P value of less than 0.05 was considered statistically significant.

#### Inclusion criteria

Inclusion criteria were patients undergoing off pump coronary artery bypass grafting, all aged between 35-72 years.

#### Exclusion criteria

Exclusion criteria were patients transferred to another hospital, patients who did not give consent, patients with other chronic diseases.

#### **RESULTS**

Table 1 presents the demographic characteristics of 160 study patients divided into two groups of 80 each. The age distribution shows that the mean ages for Group-A and Group B are 55.19±8.84 years and 56.86±8.29 years, respectively, with no significant difference (p=0.2196). Group A consists of 88% males and 12% females, while Group B has 83% males and 17% females, with no significant difference in sex distribution (p=0.356). Regarding BMI, both groups have similar distributions across underweight, normal weight, overweight, and obese categories, with mean BMIs of 26.82±5.20 for Group A and 26.74±5.17 for Group B (p=0.9224). Hypertension is prevalent in 85% of Group A and 99% of Group B, and a history of myocardial infarction is reported in 21% of Group A and 69% of Group-B, both without significant differences (p=0.230 and p=0.690, respectively).

Overall, the demographic characteristics are comparable between the two groups. Table-II presents the preoperative serum uric acid (UA) levels for two groups of patients. Group A has a mean pre-operative serum UA level of 6.9±1.5 mg/dL, while Group B has a slightly higher mean pre-operative serum UA level of 7.3±1.4 mg/dL. The difference in pre-operative serum UA levels between the two groups is not statistically significant and the mean pre-operative serum creatinine level for Group A is 1.24±0.19 mg/dL, while Group B has a mean preoperative serum creatinine level of 1.30±0.21 mg/dL. The p value for the difference in serum creatinine levels between the two groups is not statistically significant. This suggests that there is no significant disparity in preoperative renal function, as measured by serum creatinine, between Group-A and Group-B. Table III details the intra-operative outcomes of the study groups.

The total operative time varied significantly between the groups, with Group A having 32% of patients operated within 180-240 minutes, 45% within 240-300 minutes, and 23% within 300-360 minutes. In contrast, Group B had only 9% of patients operated within 180-240 minutes, 13% within 240-300 minutes, 61% within 300-360 minutes, and 17% operated for more than 360 minutes. The mean operative time was significantly longer for Group-B (327.04±44.32 minutes) compared to Group A (265.21±53.33 minutes), with a p-value of <0.001. Regarding the number of grafts, both groups had 5% of patients with 2 grafts. Group A had 53% with 3

grafts, 34% with 4 grafts, and 8% with 5 grafts, whereas Group B had 28% with 3 grafts, 52% with 4 grafts, and 15% with 5 grafts. The mean number of grafts was higher in Group-B (4.4 $\pm$ 1.2) than in Group-A (3.60 $\pm$ 1.05), with a significant p value of <0.001. Table IV outlines the post-operative biochemical parameters of the study groups. Group-B exhibited significantly higher serum creatinine levels (1.91 $\pm$ 0.51 mg/dL) compared to Group A (1.37 $\pm$ 0.18 mg/dL), with a p value of <0.001.

Total bilirubin levels were also higher in Group B  $(0.8\pm0.3 \text{ mg/dl})$  than in Group A  $(0.7\pm0.2 \text{ mg/dl})$ , with a significant difference (p=0.0142). Additionally, Group B had slightly higher albumin levels (3.8±0.4 g/dl) compared to Group A (3.6±0.5 g/dl), with this difference also being statistically significant (p=0.0059). Table 5 presents the distribution of the study groups by urine output. Most Group-A patients (41%) had urine output in the range of 90-110 ml/hour, followed by 25% with 110-130 ml/hour, 17% with 50-70 ml/hour, 12% with 70-90 ml/hour, and only 5% with 30-50 ml/hour. In contrast, Group-B predominantly had lower urine output, with 68% in the 30-50 ml/hour range, 23% in the 50-70 ml/hour range, 5% in the 90-110 ml/hour range, 4% in the 70-90 ml/hour range, and none exceeding 110 ml/hour. The mean urine output was significantly higher in Group-A (95.37±20.24 ml/hour) compared to Group-B  $(47.52\pm17.71 \text{ ml/hour})$ , with a p value of <0.001, indicating a significant difference between the groups.

Table 1: Demographic characteristics of the study patients (n=160).

Characteristics	Group-A	Group-B (n=80)	P value
	(n=80)		
Age (years)			
35-44	12 (15%)	9 (11%)	
45-54	31 (38%)	27 (34%)	
55-64	26 (33%)	31 (39%)	
65-72	11 (14%)	13 (16%)	
Mean±SD	55.19±8.84	56.86±8.29	0.219 <sup>ns</sup>
Sex			
Male	70 (88%)	66 (83%)	0.256ns
Female	10 (12%)	14 (17%)	$0.356^{\text{ns}}$
BMI (kg/m <sup>2)</sup>			-
Under weight (<18.5)	0	2 (2%)	
Normal weight (18.5-24.9)	39 (49%)	38 (48%)	
Overweight (25 -29.9)	35 (44%)	34 (42%)	
Obese (≥30)	6 (7%)	6 (8%)	
*Mean±SD	26.82±5.20	26.74±5.7	$0.922^{\rm ns}$
Risk factors			
Hypertension	68 (85%)	79 (99%)	$0.230^{\rm ns}$
History of MI	17 (21%)	55 (69%)	0.690 <sup>ns</sup>

Data was analyzed using unpaired t-test and expressed as Mean±SD, Data was analyzed using Fisher exact test and expressed as frequency, n=Number of subjects, ns=Non-significant, P≤0.05 was considered statistically significant.

Table 2: Pre-operative serum uric acid and serum creatinine level of the study groups (n=160).

Characteristics	Group-A (n=80)	Group-B (n=80)	P value
Pre-operative serum uric acid level (mg/dl)	6.9±1.5	$7.3 \pm 1.4$	$0.0832^{ns}$
Pre-operative serum creatinine level (mg/dl)	1.24±0.19	$1.30\pm0.21$	$0.06^{\mathrm{ns}}$

Data was analyzed using unpaired t-test and expressed as Mean $\pm$ SD, n=Number of subjects, ns =Not significant, P value  $\leq$ 0.05 was considered statistically significant.

Table 3: Distribution of the study patients by intra-operation outcome (n=160).

Chanastanistica	Group-A	Group-B	Davalue
Characteristics	(n=80)	(n=80)	P value
Total operative time (minute)			
180-240	26 (32%)	7 (9%)	
240-300	36 (45%)	10 (13%)	
300-360	18 (23%)	49 (61%)	
>360	0	14 (17%)	
Mean±SD	265.21±53.33	327.04±44.32	<0.001s
Number of grafts			
2	4 (5%)	4 (5%)	
3	43 (53%)	22 (28%)	
4	27 (34%)	42 (52%)	
5	6 (8%)	12 (15%)	
Mean ± SD	3.60±1.05	4.4±1.2	<0.001s

Data was analysed using unpaired t-test and expressed as Mean $\pm$ SD, n=Number of subjects=Significant, P value  $\leq$ 0.05 was considered statistically significant.

Table 4: Distribution of the study patients by post-operative biochemical parameters (n=160).

Parameters	Group-A (n=80)	Group-B (n=80)	P value
Serum creatinine (mg/dl)	1.37±0.18	1.91±0.51	<0.001s
Bilirubin, total (mg/dl)	0.7±0.2	$0.8 \pm 0.3$	0.0142s
Albumin (g/dl)	$3.8 \pm 0.4$	$3.6 \pm 0.5$	$0.0059^{s}$

Data was analysed using unpaired t-test and expressed as Mean  $\pm$  SD, n = Number of subjects, s = Significant, P value  $\leq$ 0.05 was considered statistically significant.

Table 5: Distribution of the study patients by urine output (n=160).

Urine output (ml//hour)	Group-A	Group-B	P value
	(n=80)	(n=80)	r value
30-50	4(5%)	54 (68%)	
50-70	14(17%)	18 (23%)	
70-90	10(12%)	3 (4%)	
90-110	33(41%)	4 (5%)	
110-130	20(25%)	0	
Mean±SD	95.37±20.24	47.52±17.71	<0.001s

Data was analysed using unpaired t-test and expressed as Mean±SD, n=Number of subjects, s=Significant, Pvalue≤0.05 was considered statistically significant.

#### **DISCUSSION**

This current study was conducted in Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka-1000, Bangladesh. Total 160 patients undergoing off pump coronary artery bypass grafting were included in this study. These patients were divided into two groups, group

A and group B, each containing 80 patients. In group A, uric acid level was <7 mg/dl for male and <6 mg/dL for female and in group B, uric acid level was >7 mg/dL and >6 mg/dl for female. The demographic analysis revealed no significant differences in age, sex, body mass index (BMI), hypertension prevalence, or history of myocardial infarction (MI) between Group-A and Group-B. Group-A had a mean age of 55.19±8.84 years, and Group-B had a

mean age of 56.86±8.29 years (p=0.2196). The sex distribution was also similar, with Group-A comprising 88% males and 12% females, and Group-B comprising 83% males and 17% females (p=0.356). The BMI distribution was comparable, with mean BMIs of 26.82±5.20 for Group-A and 26.74±5.17 for Group-B (p=0.9224). Hypertension prevalence was high in both groups, at 85% for Group-A and 99% for Group-B (p=0.230), and the history of MI was reported in 21% of Group-A and 69% of Group-B patients (p=0.690). These findings are consistent with those reported by Boyer et al who analyzed trends in clinical, demographic, and biochemical characteristics of patients with acute myocardial infarction and found no significant age or sex differences in their cohort.11 Similarly, Shimizu et al observed no significant demographic differences in a large cohort of CABG patients, further validating the representativeness of our sample. 12 In this current study, Group-A has a mean pre-operative serum UA level of 6.9±1.5 mg/dL, while Group-B has a slightly higher mean pre-operative serum UA level of 7.3±1.4 mg/dl. The difference in pre-operative serum UA levels between the two groups is not statistically significant Xu et al demonstrated that higher pre-operative UA levels were significantly associated with an increased risk of acute kidney injury (AKI) in patients undergoing coronary artery bypass grafting (CABG). Their study, which involved 1,306 patients, indicated that patients with elevated UA levels had a greater risk of severe AKI, requiring continuous renal replacement therapy (CRRT) post-surgery.<sup>6</sup> Similarly, Ma et al investigated the role of peri-operative serum UA levels in predicting 30 day mortality in patients undergoing acute type A aortic dissection repair. They found that both pre-operative and post-operative UA levels were higher in patients who experienced mortality within 30 days post-surgery, highlighting the prognostic value of UA levels.<sup>13</sup> The mean pre-operative serum creatinine level for Group-A is 1.24±0.19 mg/dl, while Group-B has a mean preoperative serum creatinine level of 1.30±0.21 mg/dl. The p-value for the difference in serum creatinine levels between the two groups is 0.06, indicating that the difference is not statistically significant (ns). This suggests that there is no significant disparity in preoperative renal function, as measured by serum creatinine, between Group-A and Group-B. These results align with studies like those by Lee et al and Xu et al, which emphasize the importance of considering preoperative renal function in assessing post-operative risks without pre-existing biases due to creatinine levels.<sup>5,6</sup> The intra-operative outcomes indicated significant differences between the two groups. Group-A had shorter total operative times, with 32% of patients operated within 180-240 minutes, 45% within 240-300 minutes, and 23% within 300-360 minutes. In contrast, Group-B had only 9% of patients operated within 180-240 minutes, 13% within 240-300 minutes, 61% within 300-360 minutes, and 17% operated for more than 360 minutes. The mean operative time for Group-B was significantly longer  $(327.04\pm44.32)$ minutes) compared to Group-A (265.21±53.33 minutes) (p<0.001). Chu et al demonstrated that prolonged operative times are associated with extended ICU stays, a finding that aligns with our observation of longer operative times in Group-B. 14 Additionally, Yount et al highlighted the impact of surgical duration on resource utilization, noting that extended operative times do not necessarily translate to worse outcomes but do increase hospital resource consumption.<sup>15</sup> Regarding the number of grafts, both groups had 5% of patients with 2 grafts. However, Group-A had 53% with 3 grafts, 34% with 4 grafts, and 8% with 5 grafts, whereas Group-B had 28% with 3 grafts, 52% with 4 grafts, and 15% with 5 grafts. The mean number of grafts was higher in Group-B (4.4±1.2) than in Group-A  $(3.60\pm1.05)$  (p<0.001). Jan et al also reported variations in graft numbers, suggesting that the complexity of the surgery and the patient's condition significantly influence the number of grafts performed.<sup>16</sup> post-operative biochemical parameters significant differences between the two groups. Group-B exhibited higher serum creatinine levels (1.91±0.51 mg/dL) compared to Group-A (1.37±0.18 mg/dL) (p < 0.001). This finding is consistent with the study by Grat et al17, which reported that elevated serum creatinine levels are predictive of increased morbidity and mortality in post-CABG patients. Total bilirubin levels were also higher in Group-B (0.8±0.3 mg/dL) compared to Group-A  $(0.7\pm0.2 \text{ mg/dL})$  (p=0.0142), indicating potential hepatic stress or dysfunction. Akgul et al.18 (2020) found that increased bilirubin levels postoperatively correlate with adverse outcomes, emphasizing the importance of monitoring liver function in CABG Additionally, Group-B had slightly higher albumin levels  $(3.8 \pm 0.4 \text{ g/dl})$  compared to Group-A  $(3.6 \pm 0.5 \text{ g/dl})$  (p =0.0059), which may reflect better preoperative nutritional status or liver function in Group-B patients. Urine output, a critical indicator of renal function, differed significantly between the groups. Group-A had 41% of patients with urine output in the range of 90-110 ml/hour, 25% with 110-130 ml/hour, 17% with 50-70 ml/hour, 12% with 70-90 ml/hour, and 5% with 30-50 ml/hour. In contrast, Group-B had 68% of patients with urine output in the 30-50 ml/hour range, 23% in the 50-70 ml/hour range, 5% in the 90-110 ml/hour range, 4% in the 70-90 ml/hour range, and none exceeding 110 ml/hour. The mean urine output was significantly higher in Group-A (95.37  $\pm$  20.24 ml/hour) compared to Group-B (47.52±17.71 ml/hour) (p<0.001). This significant difference in urine output aligns with findings by Lin et al and Yılmaz et al, who reported that lower urine output during and after surgery is a strong predictor of AKI. 19,20 Khademi et al also found that reduced urine output during cardiopulmonary bypass is associated with higher rates of AKI, emphasizing the importance of vigilant intraoperative urine monitoring.21 Yılmaz et al further supported this by showing that lower intra-operative urine output correlates with increased AKI risk, suggesting that maintaining adequate urine output during surgery is crucial for preserving renal function.<sup>22</sup> In our study, there was small sample size and absence of control for comparison. Study population was selected from one center in Dhaka city, so may not represent wider population. The study was conducted at a short period of time.

#### **CONCLUSION**

This study concludes that there is significant impact of pre-operative uric acid (UA) levels on post-operative renal outcomes in off-pump CABG patients. Elevated pre-operative UA levels were associated with higher serum creatinine levels and reduced urine output post-surgery, indicating an increased risk of acute kidney injury (AKI). These findings suggest that measuring UA levels pre-operatively can serve as a valuable predictor of renal complications, enabling targeted interventions to mitigate risks and improve patient outcomes. Further research with larger sample size and longer time duration is required to have better understanding.

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Institutional Ethics Committee

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