Original Article

Albumin and Urine Albumin–Creatinine Ratio as Acute Kidney Injury Predictors in Patients Undergoing Cardiac Surgery

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Abstract

Context: Postoperative acute kidney injury (AKI) is associated with increased morbidity and mortality in patients undergoing cardiac surgery. **Aim:** The aim of the present study is to compare preoperative and postoperative serum albumin levels, urine albumin–creatinine ratio (UACR), and estimated glomerular filtration rate (eGFR) in patients undergoing cardiac surgery as a predictor of AKI. **Settings and Design:** The prospective study was conducted at cardiothoracic unit in the individuals of age 40–70 years admitted for coronary artery bypass grafting. **Materials and Methods:** The study participants admitted for cardiac surgery with normal serum creatinine value of 0.3–1.3 mg/dl were included. Preoperative and postoperatively (days 1 and 3 after cardiac surgery) parameters such as serum albumin, creatinine, and UACR were analyzed. Baseline serum creatinine >1.6 mg/dl was excluded. eGFR was calculated with Cockcroft's formula and categorized as Group A with eGFR <60 ml/min and Group B with eGFR ≥60 ml/min. **Results:** Mean UACR compared to baseline was found to be increased progressively on day 1 and day 3 postoperative period after cardiac surgery. Compared with baseline data, albumin levels were found to be decreased during postoperative phase. eGFR reflected the risk of kidney damage as it gets decreased by 15% on day 1 after cardiac surgery. Receiver operating characteristic curve analysis of albumin and UACR revealed sensitivity and specificity that predicts lowered eGFR. **Conclusion:** Decreased serum albumin and increased UACR after cardiac surgery reflected with lowered eGFR indicate the renal injury after cardiac surgery. Serum hypoalbuminemia and UACR are predictors of AKI in the postoperative phase.

Keywords: Albumin–creatinine ratio, estimated glomerular filtration rate, hypoalbuminemia

Introduction

Microalbuminuria is defined as a urinary albumin excretion (UAE), and it is the strong predictor for diabetic nephropathy and the main cause of morbidity and mortality in patients with diabetes mellitus (DM).[1] It appears as a low amount of protein (albumin) in urine (30–300 mg/day in 24-h collection or 30–300 μg/mg creatinine in a spot collection). It presents before the diagnosis of DM, mainly in type 2 DM.[2] Many studies demonstrated the risk of microalbuminuria and nephropathy in nondiabetics and nonhypertensive obese individuals.[3] Glomerular hyperfiltration causes a high glomerular filtration rate that is a sign of renal damage.[4] Microalbuminuria arises with significant glomerular pathology with renal microvascular damage which, in turn, results in increased renal and cardiovascular risks.[5]

As per Steno hypothesis, albuminuria reflects general vascular dysfunction which indicates leakage of albumin leading to inflammatory response and progression to atherosclerotic process.[6] The increased systemic arterial blood pressure in patients impacts the glomerular and peritubular capillaries and promotes abnormal glomerular filtration eventually leading to albuminuria. In fact, a meta-analysis of albumin–creatinine ratio (ACR) data of general population had revealed albuminuria and concluded the association with cardiovascular morbidity.[6]

Following increased UAE, there is more risk to progress to overt proteinuria and result in end-stage renal disease. Thus,

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albuminuria is considered as a marker of diffuse endothelial dysfunction and microvascular damage, which might indicate the coincidental risk of acute kidney injury (AKI).[7] The aim of the present study is to compare preoperative and postoperative serum albumin levels, urine ACR (UACR), and estimated glomerular filtration rate (eGFR) in patients undergoing cardiac surgery as a predictor of AKI and to determine the effectiveness of albumin and ACR as a predictor tool with better diagnostic performance to predict the risk of AKI.

Materials and Methods

This prospective study was conducted at cardiothoracic unit. The study protocol was followed in accordance with the approval of the institutional ethics committee (IEC no. 1884/IEC/2019), and informed written consent was taken from all the participants. The sample size was calculated based on the mean albumin levels in non-AKI and AKI patients after cardiac surgery.[8] By purposive sampling method, the patients who attended cardiothoracic unit were recruited for the study.

Inclusion criteria for the study included cardiac patients in the age group of 40–70 years of both sexes with DM or hypertension or both admitted for cardiac surgery and also with normal serum creatinine concentration. Exclusion criteria include patients with chronic renal failure or serum creatinine >1.6 mg/dl and liver diseases.

Patients' medical history and general examination details were documented in the pro forma sheet on the day of admission. Anthropometric measurements such as height and weight were recorded. Body weight was measured using digital weighing scale with no shoes to the nearest 0.1 kg. Height was measured to the nearest 0.1 cm. Body mass index was calculated with Wt kg/Ht m^2. The routine biochemical investigations were done preoperatively followed by cardiac surgery and then postoperative day 1 and day 3 biochemical investigations were reanalyzed to monitor the patients. The biochemical parameters analyzed were blood urea, serum creatinine, total protein, serum albumin, globulin, and A/G ratio in the autoanalyzer Beckman Coulter AU 480. UACR was measured in the spot urine sample by pyrogallol red method for urine albumin and modified Jaffe's method for estimating urine creatinine. Furthermore, eGFR was calculated with Cockcroft's formula: CrCl: (140 − age) × weight (kg) ×0.85 (if females)/(serum creatinine × 72).

Statistical analysis was performed with SPSS software version 25.0 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Student's "*t*" test was used to compare the biochemical parameters between the groups. The data were expressed in mean and standard error of mean. ANOVA was utilized for comparison of the data between preoperative and postoperative data. Receiver's operating curve analysis was utilized to assess the diagnostic performance of the analyte of interest.

Results

The study was conducted in 30 patients admitted for coronary artery bypass grafting (CABG) with normal creatinine values. As per the preoperative data of the cardiac patients, the participants had presented with a mean age of 56.30 ± 0.89 years. In this study 72.27% of the participants were in the age category of 51–60 years. From analysis of the available data, about 80% of the participants had a history of diabetes, 7% were hypertensive, and 13% were both DM and hypertensive. The average systolic and diastolic blood pressure was found to be 120.46 mmHg and 74 mmHg, respectively. Tables 1 and 2 represent the comparison of biochemical parameters of the participants of preoperative and day 1/3 postoperative phase. The mean baseline creatinine was 0.83 mg/dl. Subsequently, no significant difference was found with serum creatinine postoperatively on day 1 and day 3 as compared with baseline data preoperatively. Total protein and serum albumin levels were reduced postoperatively, and a significant difference of $P = 0.000$ was observed in comparison with baseline data. As shown in Table 3, a statistically significant increased value of UACR was observed on day 1 (35.7 ± 4.04 µg/mg) of creatinine and day 3 (30.9 ± 4.25 µg/mg) of creatinine as compared with preoperative baseline data. Excretion of urine albumin and urine creatinine was increased on day 1 as compared with postoperative day 3 data. eGFR was 15% decreased on day 1 (81 ± 4.78 ml/min) as compared to day 3 postoperative period (89.9 ± 6.95 ml/min) and preoperative data. Table 4 further adds to the subcategory of the participants based on eGFR <60 ml/min (Group A) and more than 60 ml/min (Group B). Based on the data, there observed a significant decrease in albumin and increase in UACR on day 1 as well as on day 3. The diagnostic performance of postoperative albumin and UACR revealed diagnostic sensitivity and specificity as shown in Table 5 with Receiver's operative curve analysis. As per the scatter plot in Figure 1, UACR revealed a statistically significant negative correlation with eGFR in day 1 postoperative day. Figure 2 depicts the scatter plot analysis of UACR with biochemical parameters that highlighted with statistically significant R^2

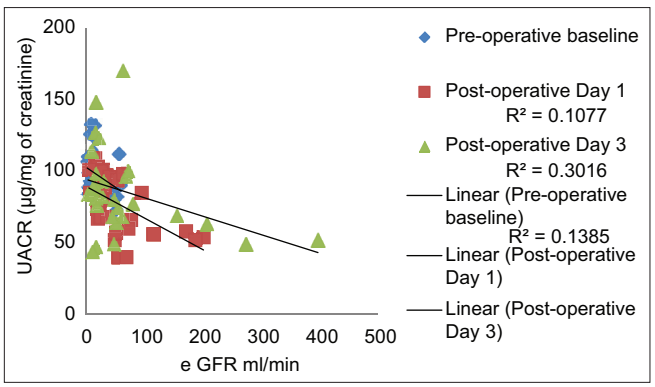

Figure 1: Correlation of urine albumin–creatinine ratio and estimated glomerular filtration rate in preoperative and postoperative cardiac patients

Table 1: The paired *t*-test analysis: Comparison of biochemical parameters between (baseline) preoperative and day 1 postoperative periods

Parameters	Preoperative (*n*=30)	Postoperative day 1 (*n*=30)	*t*	*P*
Total protein g/dL	6.8±0.14	5.85±0.14	−0 4.626	0.0001***
Albumin g/dL	3.65±0.1	3.07±0.05	−5.061	0.0001***
Globulin g/dL	3.11±0.07	2.64±0.06	−4.764	0.0001***
A/G ratio	1.12±0.01	1.32±0.01	15.191	0.0001***
Urea mg/dl	25.3±1.67	30.7±2.05	2.046	0.045*
Creatinine mg/dl	0.84±0.03	0.90±0.04	1.047	0.299 (NS)
UACR (µg/mg of creatinine)	17.5±3.03	35.7±4.04	3.965	0.0002**
eGFR (ml/min)	95.8±5.24	81.0±4.78	−0 0.677	0.5

*P<0.05 is considered significant, **Highly significant, ***Very highly significant. Values are expressed in mean±SEM. NS: Not significant, SEM: Standard error of mean, UACR: Urine albumin–creatinine ratio, eGFR: Estimated glomerular filtration rate, A/G ratio: Albumin: Globulin ratio

Table 2: The paired *t*-test analysis: Comparison of biochemical parameters between (baseline) preoperative and day 3 postoperative periods

Parameters	Preoperative (*n*=30)	Postoperative day 1 (*n*=30)	*t*	*P*
Total protein g/dL	6.8±0.14	5.81±0.08	−6.114	0.0001***
Albumin g/dL	3.65±0.1	2.98±0.05	−5.451	0.0001***
Globulin g/dL	3.11±0.07	2.6±0.04	−4.990	0.0001***
A/G ratio	1.12±0.01	1.10±0.01	−1.29	0.208
Urea mg/dl	25.3±1.67	29.1±2.18	1.387	0.17
Creatinine mg/dl	0.84±0.03	0.83±0.04	−0.184	0.899 (NS)
UACR (µg/mg of creatinine)	17.5±3.03	30.9±4.25	2.82	0.006**
eGFR (ml/min)	95.8±5.24	89.8±6.95	0.465	0.64 (NS)

*P<0.05 is considered significant, **Highly significant, ***Very highly significant. Values are expressed in mean±SEM. NS: Not significant, SEM: Standard error of mean, UACR: Urine albumin–creatinine ratio, eGFR: Estimated glomerular filtration rate, A/G ratio: Albumin: Globulin ratio

Table 3: The one-way ANOVA analysis: Comparison of total protein, albumin, and urine albumin–creatinine ratio between preoperative and day 1 and day 3 postoperative periods

Parameters	Baseline (*n*=30)	Postoperative day 1 (*n*=30)	Postoperative day 3 (*n*=30)	*F*	*P*
Total protein g/dL	6.8±0.14	5.85±0.14	5.81±0.08	19.28	0.0001***
Albumin g/dL	3.65±0.1	3.07±0.05	2.98±0.05	25.18	0.0001***
UACR (µg/mg of creatinine)	17.5±3.03	35.7±4.04	30.9±4.25	8.78	0.005**

*P<0.05 is considered significant, **Highly significant, ***Very highly significant. Values are expressed in mean±SEM. NS: Not significant, SEM: Standard error of mean, UACR: Urine albumin–creatinine ratio

Table 4: The independent *t*-test analysis: Comparison of albumin and urine albumin–creatinine ratio on day 1 and day 3 postoperative phase with<and>60 ml/min of estimated glomerular filtration rate

Parameters	Group A eGFR<60 ml/min (*n*=6)	Group B eGFR>60 ml/min (*n*=24)	*t*	*P*
Day 1 postoperative phase				
Albumin g/dL	2.76±0.05	3.17±0.09	5.01	0.0001***
UACR (µg/mg of creatinine)	47.33±4.04	17.5±3.03	−3.61	0.0001***
eGFR (ml/min)	51.2±3.11	93.7±4.1	5.03	0.0001***
Day 3 postoperative phase				
Albumin g/dL	2.6±0.08	3.07±0.06	3.61	0.0012***
UACR (µg/mg of creatinine)	69.28±9.34	18.84±4.25	−3.86	0.0006***
eGFR (ml/min)	50.72±4.14	15.84±3.2	6.68	0.0001***

UACR: Urine albumin–creatinine ratio, eGFR: Estimated glomerular filtration rate, *P<0.05 is considered significant, **Highly significant, ***Very highly significant.

value eGFR (R^2 = 0.3016), blood urea nitrogen (R^2 = 0.3783), creatinine (R^2 = 0.6552), total protein (R^2 = 0.6645), albumin (R^2 = 0.6348), globulin (R^2 = 0.2792), and AGR (R^2 = 0.6348).

Discussion

Postoperative AKI is an underrecognized perioperative complication as the consequence of intraoperative risk factors

Table 5: Receiver's operating curve analysis of serum albumin and urine albumin–creatinine ratio in cardiac patients during postoperative period

Markers	Cutoff value	Sensitivity (%)	Specificity (%)	AUC	Significance
Serum albumin g/dL	2.85	85.7	66.7	0.82	0.006**
UACR (µg/mg of creatinine)	46.5	87.5	59.1	0.821	0.008**

AUC (0.5) - no discrimination (0.7–0.8): Considered acceptable (0.8–0.9): Considered excellent (more than 0.9): Outstanding. UACR: Urine albumin–creatinine ratio, AUC: Area under curve, *P<0.05 is considered significant, **Highly significant, ***Very highly significant

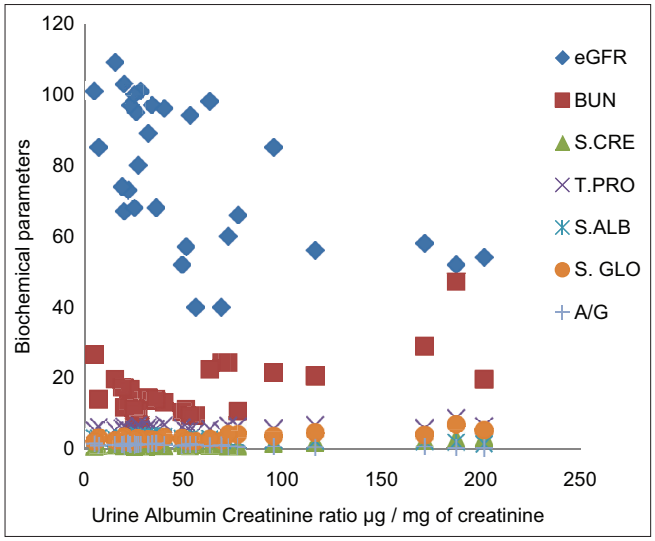

Figure 2: Correlation of urine albumin–creatinine ratio and biochemical parameters (estimated glomerular filtration rate, blood urea nitrogen, creatinine, total protein, albumin, globulin, and albumin–globulin ratio in preoperative and postoperative cardiac patients. Estimated glomerular filtration rate (R^2 = 0.3016), blood urea nitrogen (R^2 = 0.3783), creatinine (R^2 = 0.6552), total protein (R^2 = 0.6645), albumin (R^2 = 0.6348), globulin (R^2 = 0.2792), and AGR (R^2 = 0.6348)

associated with cardiac surgery.[9] The impact of postoperative outcome after cardiac surgery determines the morbidity status of an individual. Chronic kidney disease (CKD) is a very common long-term adverse outcome after CABG surgery.[10] The present prospective study evaluated serum albumin, UACR, and eGFR (based on Cockcroft's formula) preoperatively and postoperatively in patients undergoing cardiac surgery. About 81% of the cardiac patients were male in the age group between 51 and 60 years as that of 19% were female. The preoperative biochemical variables revealed normal liver function test and renal function test. In the current study, simple biochemical parameters such as serum albumin, UACR, and eGFR were identified as predictors of AKI.

Serum albumin was observed to be lowered on day 1 and day 3 postoperative period. Serum albumin is the primary protein involved in maintenance of plasma oncotic pressure. It plays a pivotal role that protects renal function by increasing oncotic pressure, especially in patients with coronary artery disease.[8] It favors the continuation of renal perfusion and facilitates maintaining the glomerular filtration. Our work is supported by researchers' studies that resulted in low serum albumin levels which enhance the incidence of AKI in patients who underwent CABG surgical procedure.[11] Individuals with low albumin were found to be associated with AKI which is in concordance with the work done by Findik *et al*.[12] Researchers have stated the effect of proteinuria in postoperative period which is related to reduce coronary flow reserve and also elevated microvascular resistance.[13] The current study revealed that drop in the albumin levels is observed in the early postoperative period, possibly on account of blood loss, capillary leakage leading to distribution of fluid to extracellular space. This may be further triggered by the associated systemic inflammatory process.

We observed increased excretion of urine albumin and urine creatinine on the 1st postoperative day that supports the fact that there exists subtle renal injury during cardiac surgery as reflected by lowered eGFR (15%) on the 1st postoperative day which would make the patient more vulnerable to AKI. Furthermore, it is evident that serum albumin levels are decreased with increased UACR in the patients who had eGFR <60 ml/min on day 1 and as monitored on day 3 postoperative period.[13] Patients with albuminuria and lowered eGFR had poor outcomes, hence these patients should be prioritized for early therapeutic intervention to reduce the risk of CKD and mortality during post-operative period.[14]

The diagnostic performance of UACR was well appreciated with receiver operating characteristic analysis between albumin versus eGFR had sensitivity of 85.7% and specificity of 67% at a cutoff value of 2.85 g/dl. Whereas, UACR had better diagnostic performance with 87.5% sensitivity and 59.1% specificity at a cutoff value of 46.5 µg/mg of creatinine.

Thus, the present study highlights the importance of estimating postoperative albumin, and UACR reflects the individuals at risk for AKI and considered as predictors of AKI in patients undergoing cardiac surgery.

Conclusion

AKI is a critical condition that has poor outcome in patients undergoing cardiac surgery. Hypoalbuminemia and increased UACR within 24 h after cardiac surgery are predictors of AKI. Thus, the platform helps to devise treatment strategies that can prevent AKI in the postoperative phase in patients undergoing cardiac surgery.

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Conflicts of interest
There are no conflicts of interest.

References
1. Chowta NK, Pant P, Chowta MN. Microalbuminuria in diabetes mellitus: Association with age, sex, weight, and creatinine clearance. Indian journal of nephrology. 2009;19(2):53-56.
2. Pathania M, Rathaur VK, Yadav B, Jayara A, Chaturvedi A. Quantiative micro- albuminuria assessment from 'random voided urinary albumin: Creatinine ratio' versus '24 hours urinary albumin concentration' for screening of diabetic nephropathy. J Clin Diagn Res 2013;7:2828-31.
3. Basi S. Microalbuminuria in type 2 diabetes and hypertension: A marker, treatment target, or innocent bystander? Diabetes Care 2008:31 Suppl 2:S194-201.
4. Bhatt VR, Khese VB, Jadhav SL, Kakrani AL. Urinary albumin excretion, estimated glomerular filtration rate, and prevalence of microalbuminuria in obese non-diabetic and nonhypertensive adults: A cross-sectional study. Indian J Nephrol 2019;29:166-71.
5. Ramidha VP, Sebastián NC, Bhavani N. Micro albuminuria in type 2 DMprevalence and its association with microvascular complications. Indian J Clin Anat Physiol 2019;6:93-97.
6. de Zeeuw D, Parving HH, Henning RH. Microalbuminuria as an early marker for cardiovascular disease. J Am Soc Nephrol 2006;17:2100-5.
7. Sung KC, Ryu S, Lee JY, Lee SH, Cheong E, Hyun YY, *et al*. Urine albumin/creatinine ratio below 30 mg/g is a predictor of incident hypertension and cardiovascular mortality. J Am Heart Assoc 2016;5:e003245.
8. Sato Y, Kato TS, Oishi A, Yamamoto T, Kuwaki K, Inaba H, *et al*. Preoperative factors associated with postoperative requirements of renal replacement therapy following cardiac surgery. Am J Cardiol 2015;116:294-300.
9. Aksoy R, Ademir T, Yilmaz E, Cevirme D, Sengor M, Koksal C, *et al.* Is Hypoalbuminemia a predictor for acute kidney injury after coronary bypass grafting in diabetes mellitus patients? Braz J Cardiovasc Surg 2019;34:565-71.
10. Findik O, Aydin U, Baris O, Parlar H, Alagoz GA, Ata Y, *et al.* Preoperative low serum albumin levels increase the requirement of renal replacement therapy after cardiac surgery. Heart Surg Forum 2016;19:E123-7.
11. Lee EH, Kim WJ, Kim JY, Chin JH, Choi DK, Sim JY, *et al.* Effect of exogenous albumin on the incidence of postoperative acute kidney injury in patients undergoing off-pump coronary artery bypass surgery with a preoperative albumin level of less than 4.0 g/dl. Anesthesiology 2016;124:1001-11.
12. Findik O, Aydin U, Baris O, Parlar H, Alagoz GA, Ata Y, *et al.* preoperative low serum albumin levels increase the requirement of renal replacement therapy after cardiac surgery. Heart Surg Forum 2016;19:E123-7.
13. Kramer RS, Herron CR, Groom RC, Brown JR. Acute kidney injury subsequent to cardiac surgery. J Extra Corpor Technol 2015;47:16-28.
14. Lee EH, Baek SH, Chin JH, Choi DK, Son HJ, Kim WJ, *et al.* Preoperative hypoalbuminemia is a major risk factor for acute kidney injury following off-pump coronary artery bypass surgery. Intensive Care Med 2012;38:1478-86.