Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Cardiac Surgery

Pre-Operative Serum Uric Acid Level is a Predictor of Acute Kidney Injury Subsequent off Pump Coronary Artery Bypass Grafting

Tania Nusrat Shanta[1*], Dr. Mirza Md. Nazmus Saquib[2], Dr. CM Mosabber Rahman[3], Muhammad Abul Kalam[4], Md. Hasanuzzaman[5], Karima Binte Kamal[6], Dr. Md. Mostafa Monir[7], Dr. Monoara Begum Probha[8]

[1]Specialist Cardiac Surgeon, Department of Cardiac Surgery, United Hospital Limited, Dhaka, Bangladesh
[2]Director, Nexus Cardiac Hospital & Research Ltd., Mymensingh, Bangladesh
[3]Junior Consultant, Department of Cardiac Surgery, Dhaka Medical College Hospital, Dhaka, Bangladesh
[4]Medical Officer, COVID-19 Emergency Response and Pandemic Preparedness (ERPP) Project, Directorate General of Health Services (DGHS), Mohakhali, Dhaka, Bangladesh
[5]Surveillance Medical Officer, National Tuberculosis Control Program, MBDC, Directorate General of Health Services, Dhaka, Bangladesh
[6]Dental Surgeon, Department of Oral and Maxillofacial Surgery, Rangpur Medical College Hospital, Rangpur, Bangladesh
[7]Resident, Department of Orthopedics, National Institute of Traumatology and Orthopaedic Rehabilitation (NITOR), Dhaka, Bangladesh
[8]Medical Officer, Department of Internal Medicine, Kurmitola General Hospital, Dhaka, Bangladesh

DOI: 10.36347/sjams.2023.v11i11.017 | **Received:** 25.10.2023 | **Accepted:** 21.11.2023 | **Published:** 22.11.2023

***Corresponding author:** Tania Nusrat Shanta
Specialist Cardiac Surgeon, Department of Cardiac Surgery, United Hospital Limited, Dhaka, Bangladesh

Abstract **Original Research Article**

***Introduction*:** Intense kidney harm (AKI) taking after cardiac surgery is one of the common complications and expanding its frequency. AKI is considered as an independent risk factor for morbidity and mortality in hospitalized patients, especially in intensive care unit and in patients undergone major surgery like cardiac surgery. This think about assesses the impact of preoperative expanded serum uric acid (SUA) levels in comparison with other known hazard variables on the pathway of AKI after cardiac surgery. Acute kidney injury after cardiac surgery portends significant morbidity and mortality. ***Aim of the Study*:** The aim of the study was to investigate the determinant factors of acute kidney injury (AKI) after isolated off pump coronary artery bypass grafting (CABG). ***Methods*:** This was a prospective, cross-section, observational study conducted in the Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from July 2021 to June 2022. During 1 year, 140 patients experienced elective coronary artery bypass surgery. ***Result*:** A total of 140 patients group A with uric acid < 5.5 mg/dl (n=70) was 52.82 ± 5.71 years old & group B with uric acid > 5.5 mg/dl (n=70) was 53.56 ± 5.34 years (p = 0.430). We found the BMI Mean ± SD was 28.57 ± 2.29 in the group A versus 29.20 ± 3.31 in the group B (p = 0.193). In our study group A uric acid < 5.5 mg/dl, 10 (14.29%) patients had AKI versus 45 (64.29%) in group B uric acid >5.5 mg/dl. And 60 (85.71%) patients had no AKI in group A versus 25 (35.71%) in group B (p = <0.001). ***Conclusion*:** Elevated preoperative serum uric acid level was associated with higher incidence of AKI, longer mechanical ventilation time, ICU stay, hospital stay and overall postoperative complications following OPCAB surgery.

Keywords: Acute kidney injury, CABG, Serum uric acid, Bypass, Renal impairment.

INTRODUCTION

Acute kidney injury (AKI) occurs frequently after coronary artery bypass surgery (CABG), worsening short-term and long-term clinical outcomes, morbidity and mortality, survival and increasing patient costs [1-3]. Acute kidney injury (AKI) following cardiac surgery is a frequent complication and has a significant impact on postoperative mortality [5-7]. Risk factors increasing the incidence of AKI after cardiac surgery imply age [8], female gender [9] and several comorbidities as hypertension [10], peripheral vascular disease [5], diabetes mellitus [5, 10], congestive heart failure [5, 8], chronic obstructive pulmonary disease [5, 6, 8], prior heart surgery, recent myocardial infraction (< 7–30 days) [6], preoperative creatinine concentrations and current diuretic use [11]. Ejaz *et al.*, [12] have examined the role of serum uric acid (SUA) as a potential risk factor for AKI after cardiac valve and aneurysm surgery. Preoperative SUA higher than an arbitrary level of 6.1 mg/dl conferred a 4-fold risk for postoperative acute kidney injury. Acute kidney injury induced by increased uric acid levels commonly occurs in patients with tumor lysis syndrome (TLS). In this context uric acid impairs

renal function by intratubular crystal precipitation as well as by inducing oxidative stress and renal inflammation [13]. Kuwabara *et al.,* [14] as well as Feig *et al.,* [15] hypothesized that elevated uric acid levels have a role in kidney disease: they impair endothelial function and cause subtle renal damage. The effect of CPB on renal function is among the causes of renal failure caused by on-pump coronary artery bypass grafting (CABG). Renal dysfunction after CPB may be related to renal hypoperfusion, non-pulsatile flow, hypothermia, and stimulation of the inflammatory response during the procedure [16-18]. The performance of off-pump CABG (without cardiopulmonary bypass) requires manipulation of the heart while maintaining hemodynamic stability [19]. Although less than one-third of all CABG operations worldwide are performed off-pump, many investigators have attempted to compare this surgical technique with on-pump CABG. Comparing off-pump coronary artery bypass grafting (CABG) to on-pump CABG through retrospective review is less valuable due to its inherent selection bias. However, when nonrandomized retrospective reviews and propensity-matched comparisons were conducted, they indicated that off-pump CABG was associated with several benefits. These benefits included reduced mortality, decreased morbidity (including factors like blood transfusion, stroke, pulmonary complications, renal failure, and reoperation, use of intra-aortic balloon-pump, gastrointestinal complications, major adverse cardiac events, and atrial fibrillation), reduced release of cardiac enzymes, shorter hospital stays, and decreased duration of mechanical ventilation for patients undergoing off-pump CABG [20-22]. In addition, the performance of off-pump CABG is technically challenging and has a definite learning curve [23-24]. The true advantage of off-pump coronary artery bypass grafting (CABG) becomes apparent when applied to high-risk patients, which includes women. Operative mortality in women undergoing on-pump CABG may be as high as twice that of men [25], whereas the operative mortality in women undergoing off-pump CABG is equivalent to that of men. Furthermore, patients with a background of cerebrovascular issues, kidney problems, or bleeding disorders may also experience advantages from employing off-pump surgical techniques. In contrast, patients with diffusely diseased, calcified, small, or intracoronary vessels may not be suitable for off-pump techniques [26].

OBJECTIVE OF THE STUDY

The aim of the present study was to investigate the determinant factors of acute kidney injury (AKI) after isolated off pump coronary artery bypass grafting (CABG).

METHODOLOGY & MATERIALS

This was a prospective, cross-section, observational study conducted in the Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from July 2021 to June 2022. During 1 year, 140 patients who fulfilled the inclusion criteria, experienced elective off pump coronary artery bypass surgery. We analyzed 140 patients divided into two groups: Group A (n = 70): uric acid < 5.5 mg/dl and Group B (n=70): uric acid > 5.5 mg/dl. The essential endpoint was the rate of AKI as characterized by the AKI criteria comparing patients with preoperative serum uric acid (SUA) levels with postoperative serum creatinine level. Multivariate calculated relapse examination was utilized to recognize autonomous indicators of postoperative AKI. When severe ascending aortic atherosclerosis was present, medical professionals used echocardiography and manual palpation (often with inflow occlusion) to assess possible locations for arterial cannulation and cross-clamp placement. In such cases, proximal anastomoses were completed using a single clamp application. To minimize the impact of patient selection on the outcome comparison, we employed propensity score-based matching. This involved pairing patients who underwent off-pump surgery with serum uric acid level< 5.5mg/dl from the pool of patients following a previously described method. The propensity score-matched analysis is a technique designed to address any bias in patient selection by creating comparable risk groups for analysis. The propensity score represents the likelihood that patients received a specific-criteria, such as preoperative serum uric acid level in this case. Patients from both normal or increased serum uric acid level groups were paired based on their propensity score to enable a comparison about outcomes. We utilized a multivariable logistic regression analysis to identify the independent factors associated with preoperative SUA and AKI for the patients undergoing OPCAB. we excluded variables like ejection fraction below 25%, the necessity for an urgent or emergency operation, a history of stroke or cerebrovascular disease, previous cardiac surgeries. Once we established a concise model based on these factors, we expanded it to include other significant clinical variables, such as renal insufficiency, age, obesity, gender, hypertension, diabetes, peripheral vascular disease, calcified ascending aorta, and chronic obstructive pulmonary disease. To complete the analysis, patient preoperative serum uric acid level is compared with post-operative serum creatinine level in case of off-pump coronary artery bypass surgery thorough matching strategy.

Statistical Analysis:

All data were recorded systematically in preformed data collection form quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed using SPSS 21 (Statistical Package for Social Sciences) for windows 10.

RESULT

Table 1: Distribution of patients by age (n=140)

Age (years)	Group A (Uric acid < 5.5 mg/dl) (n=70)	Group B (Uric acid > 5.5 mg/dl) (n=70)	P value
41-50	22 (31.43%)	16 (22.86%)	0.430^{ns}
51-60	36 (51.43%)	46 (65.71%)	
61-70	12 (17.14%)	8 (11.43%)	
Mean ± SD	52.82 ± 5.71	53.56 ± 5.34	

Table 1 shows the mean age of group A patients was 52.82 ± 5.71 years & group B was 53.56 ± 5.34 years (p = 0.430). In the age group 41-50 years 22 (31.43%) patients were in the group A versus 16 (22.86%) in the group B, then 51-60 years was 36 (51.43%) versus 46 (65.71%) and 61-70 years was 12 (17.14%) versus 8 (11.43%) respectively.

Table 2: Distribution of patients by BMI & Comorbidities (n=140)

	Group A (Uric acid < 5.5 mg/dl) (n=70)	Group B (Uric acid > 5.5 mg/dl) (n=70)	P value
BMI (kg/m^2)	28.57 ± 2.29	29.20 ± 3.31	0.193^{ns}
HTN	46 (65.71%)	55 (78.57%)	0.090^{ns}
DM	25 (35.71%)	30 (42.86%)	0.388^{ns}
PVD	5 (7.14%)	3 (4.2%)	0.467^{ns}
COPD	12 (17.14%)	8 (11.43%)	0.333^{ns}
Serum creatinine (mmol/L)	1.02 ± 0.14	1.04 ± 0.13	0.383^{ns}

In table 2 we found the distribution of patients by BMI and comorbidities. BMI Mean ± SD was 28.57 ± 2.29 in the group A versus 29.20 ± 3.31 in the group B (p = 0.193). In the group A, 46 (65.71%) patients had HTN versus 55 (78.57%) in the group B (p = 0.090). 25 (35.71%) patients had DM in the group A versus 30 (42.86%) in the group B (p = 0.388). In the group A, 5 (7.14%) patients had PVD versus 3 (4.2%) in the group B (p = 0.457). 12 (17.14%) patients had COPD in the group A versus 8 (11.43%) in the group B (p = 0.333). And S creatinine Mean ± SD was 1.02 ± 0.14 in group A versus 1.04 ± 0.13 in group B (p = 0.383) respectively.

Table 3: Distribution of patients by surgical duration & perioperative outcome (n=140)

	Group A (Uric acid < 5.5 mg/dl) (n=70)	Group B (Uric acid > 5.5 mg/dl) (n=70)	P value
Surgery (mins)	304.43 ± 26.06	308.89 ± 24.37	0.298^{ns}
Perioperative MI	6 (8.57%)	8 (11.43%)	0.574^{ns}
Arrhythmia	13 (18.57%)	18 (25.71%)	0.311^{ns}

Table 3 shows the distribution of patients by surgical duration & perioperative outcome. Surgery duration was 304.43 ± 26.06 minutes in the group A and 308.89 ± 24.37 in the group B (p = 0.298). 6 (8.57%) patients had Perioperative MI in group A versus 8 (11.43%) in group B (p = 0.574). And 13 (18.57%) had Arrhythmia in group A versus 18 (25.71%) in group B (p = 0.311) respectively.

Table 4: Relationship of preoperative uric acid with postoperative AKI (n=140)

	Group A (Uric acid < 5.5 mg/dl) (n=70)	Group B (Uric acid > 5.5 mg/dl) (n=70)	P value
AKI	10 (14.29%)	25 (35.71%)	<0.003^{s}
No AKI	60 (85.71%)	45 (64.29%)	

Table 4 shows the relationship of preoperative uric acid with postoperative AKI. In group A, 10 (14.29%) patients had AKI versus 25 (35.71%) in group B. And 60 (85.71%) patients had no AKI in group A versus 45 (64.29%) in group B (p = <0.003) respectively.

Table 5: Comparison of mechanical ventilation time, ICU stay, and hospital stay after surgery (n=140)

	Group A (Uric acid < 5.5 mg/dl) (n=70)	Group B (Uric acid > 5.5 mg/dl) (n=70)	P value
Mechanical ventilation time (hrs)	9.72 ± 2.63	10.54 ± 3.22	0.101^{ns}
ICU stay (days)	5.92 ± 2.32	6.39 ± 4.51	0.440^{ns}
Hospital stay after surgery (days)	8.77 ± 2.18	12.27 ± 3.71	<0.001^{s}

In table 5 we found the comparison of mechanical ventilation time, ICU stay, and hospital stay after surgery between the two groups. In group A mechanical ventilation time was 9.72 ± 2.63 hours versus 10.54 ± 3.22 hours in group B (p = 0.101), then ICU stay was 5.92 ± 2.32 days in group A versus 6.39 ± 4.51 days in group B (p = 0.440) and hospital stay after surgery was 8.77 ± 2.18 days in group A versus 12.27 ± 3.71 days in group B (p = <0.001) respectively.

Table 6: Comparison of postoperative creatinine at 2nd hour, 12th hour, 24th hour & 48th hour (n=140)

Serum creatinine (mmol/L)	Group A (Uric acid < 5.5 gm/dl) (n=70)	Group B (Uric acid > 5.5 gm/dl) (n=70)	P value
At 2nd hour	1.14 ± 0.17	1.16 ± 0.23	0.560^{ns}
At 12th hour	1.25 ± 0.22	1.43 ± 0.45	0.003^{s}
At 24th hour	1.18 ± 0.17	1.27 ± 0.24	0.012^{s}
At 48th hour	1.11 ± 0.16	1.15 ± 0.25	0.262^{ns}

Table 6 shows the comparison of postoperative creatinine at the 2nd hour, 12th hour, 24th hour & 48th hour between the two groups. At the 2nd hour we found S creatinine Mean SD label was 1.14 ± 0.17 in group A versus 1.16 ± 0.23 in group B (p=0.560), then at the 12th hour 1.25 ± 0.22 was in group A versus 1.43 ± 0.45 in group B (p=0.003), at the 24th hour 1.18 ± 0.17 was in group A versus 1.27 ± 0.24 in group B (p=0.012) and at the 48th hour 1.11 ± 0.16 was in group A versus 1.15 ± 0.25 in group B (p=0.262) respectively.

DISCUSSION

Serum uric acid levels have been studied as a potential predictor of acute kidney injury (AKI) in various clinical settings, including cardiac surgery. AKI is a common complication after cardiac surgeries like off-pump coronary artery bypass grafting, and identifying predictors of AKI can help with risk assessment and patient management. Our study has shown that elevated pre-operative serum uric acid levels may be associated with an increased risk of developing AKI after off pump coronary artery bypass grafting. High levels of uric acid can indicate various factors that may contribute to kidney injury, such as inflammation, oxidative stress, and impaired renal function. However, it's important to note that while there is evidence to suggest a correlation, uric acid levels alone are not a definitive predictor of AKI. They are typically considered as one of many risk factors that should be evaluated in combination with other clinical and demographic factors.

To assess the risk of AKI in the context of off pump coronary artery bypass grafting or any other surgical procedure, healthcare providers usually consider a range of risk factors, including patient age, pre-existing kidney function, comorbidities (e.g., diabetes, hypertension), the complexity of the surgery, and other clinical parameters. The combination of these factors can provide a more comprehensive assessment of the patient's risk for developing AKI. Ultimately, the decision to use pre-operative serum uric acid levels as a predictor of AKI in the context of OPCABG or any other surgery should be made based on the most current evidence and in consultation with a healthcare provider. It's also important to keep in mind that medical research is an ongoing field, and new findings may continue to refine our understanding of risk factors for AKI in the future.

In our study, we found the mean age of group A patients was 52.82 ± 5.71 years versus group B was 53.56 ± 5.34 years (p = 0.430). In a similar study Kaufeld T *et al.,* [27] found 67.40 ± 12.22 versus 68.26 ± 10.85 years (p=0.557). We found BMI Mean ± SD was 28.57 ± 2.29 in the group A versus 29.20 ± 3.31 in the group B (p = 0.193) respectively. Aksoy *et al.,* [28] showed that preoperative low serum album level, high BMI, and preoperative severe HT are related to enhanced risk of AKI development.

In patients having tumor lysis syndrome (TLS) increased uric acid induces AKI by intratubular crystal precipitation as well as on a crystal-independent pathway [13]. By stimulating the renin-angiotensin system, reducing nitric oxide NO releases from endothelial cells and inhibiting NO synthase 1 uric acid causes renal vasoconstriction & leads to renal ischemia and hypertension [29]. Uric acid is also considered to have proinflammatory properties: in-vitro it induced the expression of C-reactive protein (CRP) by human endothelial & vascular smooth muscle cells and the production of the monocyte chemoattractant protein-1 (MCP-1) [30, 31].

We found serum creatinine Mean ± SD was 1.02 ± 0.14 in the group A versus 1.04 ± 0.13 in the group B (p = 0.383). In our study group A uric acid < 5.5 mg/dl, 10 (14.29%) patients had AKI versus 25 (35.71%) in group B uric acid >5.5 mg/dl & an odd ratio was 3.3. And 60 (85.71%) patients had no AKI in group A versus 45 (64.29%) in group B with a 95% CI 1.45-7.63 (p = <0.004). Hyperuricemia had been strongly linked to renal disease in various clinical conditions [15], and recent experimental and clinical studies suggested that

hyperuricemia may be an independent risk factor for AKI and chronic kidney disease [32-33]. In a similar study, Ejaz *et al.,* [12] found 58 patients undergoing complicated cardiac surgery; found that preoperative uric acid > 6.0 mg/dl was associated with a nearly 4-fold increased risk of AKI and a longer hospital stay than preoperative uric acid ≤ 6.0 mg/dl.

At the 2nd hour we found S creatinine Mean SD label was 1.14 ± 0.17 in group A versus 1.16 ± 0.23 in group B (p=0.560), then at 12th hour 1.25 ± 0.22 was in group A versus 1.43 ± 0.45 in group B (p=0.003), at 24th hour 1.18 ± 0.17 was in group A versus 1.27 ± 0.24 in group B (p=0.012) and at 48th hour 1.11 ± 0.16 was in group A versus 1.15 ± 0.25 in group B (p=0.262).

Limitations of the Study

We took a small sample size due to our short study period. A higher number of sample size could give better information. Data was collected from patients of Bangabandhu Sheikh Mujib Medical University (BSMMU). If samples were collected from the patients of different hospitals that may give more precise information. Therefore, in future further study may be undertaken with a large sample size.

CONCLUSION AND RECOMMENDATIONS

In conclusion, we accept that hyperuricemia may lead to AKI by two distinctive pathways: chronically it may have actuated unobtrusive renal harm that inclines to AKI which may not be preoperatively recognized by serum creatinine. Intensely the impact of intraoperative renal hypoperfusion may be exasperated by the proinflammatory and prooxidative properties of SUA. At long last, our information demonstrates that measuring of SUA levels may contribute to evaluate renal function preoperatively for exploring a management plan to prevent postoperative renal injury.

REFERENCES

1. Dasta, J. F., Kane-Gill, S. L., Durtschi, A. J., Pathak, D. S., & Kellum, J. A. (2008). Costs and outcomes of acute kidney injury (AKI) following cardiac surgery. *Nephrol Dial Transplant*, *23*, 1970-4.
2. Hobson, C. E., Yavas, S., Segal, M. S., Schold, J. D., Tribble, C. G., Layon, A. J., & Bihorac, A. (2009). Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. *Circulation*, *119*, 2444-53.
3. Lee, E. H., Baek, S. H., Chin, J. H., Choi, D. K., Son, H. J., Kim, W. J., Hahm, K. D., Sim, J. Y., & Choi, I. C. (2012). Preoperative hypoalbuminemia is a major risk factor for acute kidney injury following off-pump coronary artery bypass surgery. *Intensive Care Med*, *38*, 1478-86.
4. Loef, B. G., Epema, A. H., Smilde, T. D., Henning, R. H., Ebels, T., Navis, G., & Stegeman, C. A. (2005). Immediate postoperative renal function deterioration in cardiac surgical patients predicts in-hospital mortality and long-term survival. *Journal of the American Society of Nephrology*, *16*(1), 195-200.
5. Rosner, M. H., & Okusa, M. D. (2006). Acute kidney injury associated with cardiac surgery. *Clin J Am Soc Nephrol*, *1*, 19–32.
6. Chertow, G. M., Lazarus, J. M., Christiansen, C. L., Cook, E. F., Hammermeister, K. E., Grover, F., & Daley, J. (1997). Preoperative renal risk stratification. *Circulation*, *95*, 878–84.
7. Martinelli, S. M., Patel, U. D., Phillips-Bute, B. G., Milano, C. A., Archer, L. E., Stafford-Smith, M., ... & Swaminathan, M. (2009). Trends in cardiac surgery-associated acute renal failure in the United States: A disproportionate increase after heart transplantation. *Renal failure*, *31*(8), 633-640.
8. Rodrigues, A. J., Evora, P. R. B., Bassetto, S., Alves Júnior, L., Scorzoni Filho, A., Araújo, W. F., & Vicente, W. V. A. (2009). Risk factors for acute renal failure after heart surgery. *Brazilian Journal of Cardiovascular Surgery*, *24*(4), 441-446.
9. Ahmadi, H., Karimi, A., Davoodi, S., Movahedi, N., Marzban, M., Abbasi, K., ... & Tazik, M. (2009). Determinant factors of renal failure after coronary artery bypass grafting with on-pump technique. *Medical Principles and Practice*, *18*(4), 300-304.
10. Metz, L. I., LeBeau, M. E., Zlabek, J. A., & Mathiason, M. A. (2009). Acute renal failure in patients undergoing cardiothoracic surgery in a community hospital. *Wmj*, *108*(2), 109-114.
11. Perez-Valdivieso, J. R., Monedero, P., Vives, M., Garcia-Fernandez, N., Bes-Rastrollo, M., & GEDRCC (Grupo Español de Disfunción Renal en Cirugía Cardiaca) jrpvaldi@ unav. es. (2009). Cardiac-surgery associated acute kidney injury requiring renal replacement therapy. A Spanish retrospective case-cohort study. *BMC nephrology*, *10*, 1-10.
12. Ejaz, A. A., Beaver, T. M., Shimada, M., Sood, P., Lingegowda, V., Schold, J. D., ... & Johnson, R. J. (2009). Uric acid: a novel risk factor for acute kidney injury in high-risk cardiac surgery patients?. *American journal of nephrology*, *30*(5), 425-429.
13. Shimada, M., Johnson, R. J., May Jr, W. S., Lingegowda, V., Sood, P., Nakagawa, T., ... & Ejaz, A. A. (2009). A novel role for uric acid in acute kidney injury associated with tumour lysis syndrome. *Nephrology Dialysis Transplantation*, *24*(10), 2960-2964.
14. Kuwabara, M., Bjornstad, P., Hisatome, I., Niwa, K., Roncal-Jimenez, C. A., Andres-Hernando, A., ... & Johnson, R. J. (2017). Elevated serum uric acid level predicts rapid decline in kidney function. *American journal of nephrology*, *45*(4), 330-337.

15. Feig, D. I., Kang, D.-H., & Johnson, R. J. (2008). Uric acid and cardiovascular risk. *N Engl J Med.*, *359*(17), 1811–21.
16. Gamoso, M. G., Phillips-Bute, B., Landolfo, K. P., Newman, M. F., & Stafford-Smith, M. (2000). Off-pump versus on-pump coronary artery bypass surgery and postoperative renal dysfunction. *Anesth Analg*, *91*, 1080–1084.
17. Suen, W. S., Mok, C. K., Chiu, S. W., Cheung, K. L., Lee, W. T., Cheung, D., ... & He, G. W. (1998). Risk factors for development of acute renal failure (ARF) requiring dialysis in patients undergoing cardiac surgery. *Angiology*, *49*(9), 789-800.
18. Hall, R. I., Smith, M. S., & Rocker, G. (1997). The systemic inflammatory response to cardiopulmonary bypass: pathophysiological, therapeutic, and pharmacological considerations. *Anesthesia & Analgesia*, *85*(4), 766-782.
19. Lawton, J. S. (2012). Off-pump coronary artery bypass grafting. *Mo Med*, *109*(4), 277-80.
20. Mack, M. J., Pfister, A., Bachand, D., Emery, R., Magee, M. J., Connolly, M., & Subramanian, V. (2004). Comparison of coronary bypass surgery with and without cardiopulmonary bypass in patients with multivessel disease. *The Journal of thoracic and cardiovascular surgery*, *127*(1), 167-173.
21. Sharony, R., Grossi, E. A., Saunders, P. C., Galloway, A. C., Applebaum, R., Ribakove, G. H., ... & Colvin, S. B. (2004). Propensity case-matched analysis of off-pump coronary artery bypass grafting in patients with atheromatous aortic disease. *The Journal of thoracic and cardiovascular surgery*, *127*(2), 406-413.
22. Stamou, S. C., Hill, P. C., Haile, E., Prince, S., Mack, M. J., & Corso, P. J. (2006). Clinical outcomes of nonelective coronary revascularization with and without cardiopulmonary bypass. *The Journal of thoracic and cardiovascular surgery*, *131*(1), 28-33.
23. Chen, Y., & Wan, F. (2009). Off-pump coronary artery bypass graft surgery: a training course for novices and its learning curve. *The Thoracic and Cardiovascular Surgeon*, *57*(03), 141-147.
24. Song, H. K., Petersen, R. J., Sharoni, E., Guyton, R. A., & Puskas, J. D. (2003). Safe evolution towards routine off-pump coronary artery bypass: negotiating the learning curve. *European journal of cardio-thoracic surgery*, *24*(6), 947-952.
25. Vaccarino, V., Abramson, J. L., Veledar, E., & Weintraub, W. S. (2002). Sex differences in hospital mortality after coronary artery bypass surgery: evidence for a higher mortality in younger women. *Circulation*, *105*(10), 1176-1181.
26. Mack, M. J., Brown, P., Houser, F., Katz, M., Kugelmass, A., Simon, A., ... & Becker, E. (2004). On-pump versus off-pump coronary artery bypass surgery in a matched sample of women: a comparison of outcomes. *Circulation*, *110*(11_suppl_1), II-1.
27. Kaufeld, T., Foerster, K. A., Schilling, T., Kielstein, J. T., Kaufeld, J., Shrestha, M., ... & Schmidt, B. M. W. (2018). Preoperative serum uric acid predicts incident acute kidney injury following cardiac surgery. *BMC nephrology*, *19*, 1-6.
28. Aksoy, R., Adademir, T., Yilmaz, E., Cevirme, D., Sengor, M., Koksal, C., & Rabus, M. B. (2019). Is hypoalbuminemia a predictor for acute kidney injury after coronary bypass grafting in diabetes mellitus patients?. *Brazilian Journal of Cardiovascular Surgery*, *34*(5), 565-571.
29. Ejaz, A. A., Mu, W., Kang, D. H., Roncal, C., Sautin, Y. Y., Henderson, G., ... & Johnson, R. J. (2007). Could uric acid have a role in acute renal failure?. *Clinical Journal of the American Society of Nephrology*, *2*(1), 16-21.
30. Kang, D. H., Park, S. K., Lee, I. K., & Johnson, R. J. (2005). Uric acid–induced C-reactive protein expression: implication on cell proliferation and nitric oxide production of human vascular cells. *Journal of the American Society of Nephrology*, *16*(12), 3553-3562.
31. Kanellis, J., Watanabe, S., Li, J. H., Kang, D. H., Li, P., Nakagawa, T., ... & Johnson, R. J. (2003). Uric acid stimulates monocyte chemoattractant protein-1 production in vascular smooth muscle cells via mitogen-activated protein kinase and cyclooxygenase-2. *Hypertension*, *41*(6), 1287-1293.
32. Shimada, M., Dass, B., & Ejaz, A. A. (2011, September). Paradigm shift in the role of uric acid in acute kidney injury. In *Seminars in Nephrology* (Vol. 31, No. 5, pp. 453-458). WB Saunders.
33. Filiopoulos, V., Hadjiyannakos, D., & Vlassopoulos, D. (2012). New insights into uric acid effects on the progression and prognosis of chronic kidney disease. *Renal failure*, *34*(4), 510-520.