Original Article

Is Hypoalbuminemia a Predictor for Acute Kidney Injury after Coronary Bypass Grafting in Diabetes Mellitus Patients?

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Abstract

Objective: Acute kidney injury (AKI) is one of the most important complications after coronary artery bypass grafting (CABG) procedure. Serum albumin, which is an acute phase reactant, is suggested to be associated with AKI development subsequent to various surgical procedures. In this study, we research the relation between preoperative serum albumin levels and postoperative AKI development in diabetes mellitus (DM) patients undergoing isolated CABG.

Methods: We included a total of 634 diabetic patients undergoing CABG (60.5±9.1 years, 65.1% male) into this study, which was performed between September 2009 and January 2014 in a single center. The relation between preoperative serum albumin levels and postoperative AKI development was observed. AKI was evaluated and diagnosed using the Kidney Disease: Improving Global Outcomes (KDIGO) classification.

Results: AKI was diagnosed in 230 (36.3%) patients. Multiple logistic regression analysis was performed to determine the independent predictors of AKI development. Proteinuria (odds ratio [OR] and 95% confidence interval [CI], 1.066 [1.002-1.135]; \(P=0.043\)) and low preoperative serum albumin levels (OR and 95% CI, 0.453 [0.216-0.947]; \(P=0.035\)) were found to be independent predictors of AKI. According to the receiver operating characteristic curve analysis, albumin level <3mg/dL (area under the curve: 0.621 [0.572-0.669], \(P<0.001\)) had 83% sensitivity and 10% specificity on predicting the development of AKI.

Conclusion: We observed that a preoperative low serum albumin level was associated with postoperative AKI development in patients with DM who underwent isolated CABG procedure. We emphasize that this adjustable albumin level should be considered before the operation since it is an easy and clinically implementable management for the prevention of AKI development.

Keywords: Coronary Bypass. Diabetes Mellitus. Hypoalbuminemia.

Abbreviations, acronyms & symbols

| ACC | = Aortic cross-clamping |
| AKI | = Acute kidney injury |
| ANOVA | = Analysis of variance |
| AUC | = Area under the curve |
| BMI | = Body mass index |
| CABG | = Coronary artery bypass grafting |
| CI | = Confidence interval |
| CPB | = Cardiopulmonary bypass |
| CRP | = C-reactive protein |
| DM | = Diabetic mellitus |
| EDTA | = Ethylenediaminetetraacetic acid |
| EF | = Ejection fraction |
| GFR | = Glomerular filtration rate |
| Hgb | = Hemoglobin |
| HT | = Hypertension |
| ICU | = Intensive care unit |
| IQR | = Interquartile range |
| KDIGO | = Kidney Disease: Improving Global Outcomes |
| LVEF | = Left ventricular ejection fraction |
| MI | = Myocardial infarction |
| OR | = Odds ratio |
| RDW | = Red cell distribution width |
| ROC | = Receiver operating characteristic |
| SD | = Standard deviation |
| Scr | = Serum creatinine |
| SPSS | = Statistical Package for Social Sciences |

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INTRODUCTION

Twenty to 30% of all patients undergoing coronary artery bypass grafting (CABG) are diabetic[1]. Patients with type 2 diabetes mellitus (DM) have been reported to show high morbidity and mortality rates following CABG operations[11]. Type 2 DM is reported to increase postoperative acute kidney injury (AKI) development rates in patients undergoing CABG surgery[2,3]. AKI, which is not rarely seen after cardiac surgery, is associated with increased morbidity and mortality rates. AKI subsequent to cardiac surgery is diagnosed in 5-30% of the patients and renal replacement therapy is required in 1-2% of them[4]. And AKI subsequent to CABG is also associated with longer intensive care unit (ICU) and in-hospital stays and increased rates of hemodialysis requirement and chronic renal failure[5]. Serum albumin, which is a plasma protein that has an important role on the regulation of plasma oncotic pressure, is also an acute-phase reactant. The normal range of albumin in serum is 3.5-5 g/dL[6]. In many studies, hypoalbuminemia subsequent to cardiac surgical procedures was found to be associated with increased rates of mortality and morbidity[7,8]. There are also studies showing that hypoalbuminemia is associated with AKI development after various surgical procedures[9]. In this study, we aimed to research the relation between preoperative serum albumin levels and postoperative AKI development in selected patients with DM undergoing isolated CABG surgery.

METHODS

This study was performed retrospectively on the perioperative data of 634 diabetic patients undergoing isolated CABG surgery in a single-center between September 2009 and January 2014. Of the patients, 65.1% (n=413) were male and 34.9% (n=221) were female. The average age was 60.5±9.1 years. After the local ethical committee approval, the data of the patients were collected from the archive records, hospital data recording program, patients’ discharge summaries, operative reports, laboratory results, and radiological images. In this study, the relation between preoperative serum albumin levels and postoperative AKI development was observed. The AKI developing and non-AKI groups were compared.

AKI was diagnosed and evaluated according to the Kidney Disease: Improving Global Outcomes (KDIGO) classification[9]. The stages of AKI based on KDIGO classification are:

Stage 1: Increase in serum creatinine (Scr) ≥ 0.3 mg/dL (in 48 hours) or 1.5 to 1.9 mg/dL multiplied by baseline Scr (in seven days);

Stage 2: Between 2.0 to 2.9 mg/dL multiplied by baseline Scr;

Stage 3: 3.0 mg/dL or more multiplied by baseline Scr; increase in Scr ≥ 4.0 mg/dL; or beginning of renal replacement therapy regardless of a previous KDIGO stage.

Preoperative serum albumin levels were measured by the bromocresol green dye-binding method. The groups were not identified due to reference ranges but AKI development of patients regarding to serum albumin levels was observed. Patients with chronic renal failure requiring hemodialysis or with Scr >1.6 mg/dL were excluded from this study[9]. And patients excluded from this study had systemic disorders associated with hypoalbuminemia, which were liver dysfunction, malnourishment, congestive heart failure, active malignancy, endocrinologic disorders (hypothyroidism, hyperthyroidism, etc.), lymphoproliferative disease, low hemoglobin (Hgb) levels (≤10 g/dL), active infection, and active or chronic autoimmune disease; patients taking steroids or chemotherapeutic drugs were also excluded.

Demographic characteristics and preoperative clinical conditions, like age, sex, body surface area, hypertension (HT) incidence, DM incidence previous myocardial infarction (MI), and preoperative ejection fraction (EF), were noted. Preoperative and postoperative laboratory results of creatinine, C-reactive protein (CRP), and Hgb were also noted. Perioperative data of cardiopulmonary bypass (CPB) and aortic cross-clamping (ACC) duration, postoperative drainage level, intubation duration, and ICU and in-hospital stays duration were measured for every individual patient. Proteinuria was measured by calorimetry.

In this study, HT was defined as a history of antihypertensive drug intake or blood pressure measurement ≥140/90 mmHg. In addition, DM was defined as history of antidiabetic drug intake or a measured fasting blood glucose level >126 mg/dL[10]. Peripheric venous blood of 5 to 7 cc was drawn to ethylenediaminetetraacetic acid (EDTA) vacutainers to prevent clotting from all the patients prior to surgery. All the hemogram parameters were measured in automatic Abbott CELL-DYN 3700 (Abbott Laboratory, Abbott Park, Illinois, USA) analyzers.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software (SPSS version 21.0, IBM, Armonk, New York). Continuous variables with normal distribution were presented as mean (standard deviation [SD]), non-normal variables were reported as median (interquartile range [IQR]), and categorical variables were reported as percentage. Univariate comparisons between groups were performed using the chi-square test for categorical variables and the Student’s t-test or Mann-Whitney
rank sum test for continuous variables, as appropriate. Variables with a P-value <0.05 in univariate analysis were assessed in the multiple logistic regression model to determine the independent predictors of postoperative AKI. Receiver operating characteristic (ROC) curves were plotted to determine the optimal cut-off values for individual parameters in order to predict AKI and to establish the optimal cut-off points for use in clinical decision making. One-way repeated measure analysis of variance (ANOVA) was used to determine the change for creatinine over the first three postoperative days. A P-value <0.05 was considered to be significant.

RESULTS

We included a total of 634 diabetic patients (60.59.1 years, 65.1% male) into this study. Eighty-three of them required coronary endarterectomy procedures with CABG and 13 underwent cardiac reoperation. The median ACC time was 51 (33-74) minutes. Mean baseline creatinine level was 1.05±0.60 (ranged from 0.4 to 6.6) mg/dL and creatinine level at the 48th hour was 1.17±0.76 (ranged from 0.3 to 6.6) mg/dL. Two hundred and thirty (36.3%) patients developed AKI according to KDIGO classification. The preoperative mean blood urea level of the non-AKI group was 21.4±9.9 mg/dL and of the AKI group was 25.1±12.6 mg/dL (P<0.05). The postoperative mean blood urea level of the non-AKI group was 20.9±7.9 mg/dL and of the AKI group was 30.2±13.7 mg/dL (P<0.05). Preoperative, intraoperative, and postoperative clinical characteristics of AKI and non-AKI patients were summarized in Table 1.

Female gender, older age, high body mass index (BMI) level, existence of HT, preoperative proteinuria, high baseline creatinine level, low Hgb, low albumin level, high uric acid level, and long ACC time were found to be related with high AKI development risk in univariate analysis. Multiple logistic regression analysis was used to determine the independent predictors of postoperative

| Table 1. Baseline characteristics of the study subjects. |
|---------------------------------------------------------|
| AKI (n=230) | Non-AKI (n=404) | P-value |
| Male % (N) | 58.6 (135) | 68.8 (278) | 0.010 |
| Age (years) | 61.8±9.1 | 59.7±9 | 0.005 |
| BMI | 30.5±5.7 | 29.2±4.8 | 0.007 |
| Hypertension | 51.7 (209) | 41.8 (138) | <0.001 |
| Previous MI | 7.4 (17) | 7.6 (31) | 0.495 |
| Previous cardiac surgery | 1.3 (3) | 2.5 (10) | 0.379 |
| Fasting blood glucose (mg/dl) | 182±59 | 171±54 | 0.023 |
| Proteinuria (mg) | 15.2 (35) | 12.5 (38) | 0.004 |
| Creatinine (mg/dL) | 1.2±0.89 | 0.95±0.33 | <0.001 |
| Hemoglobin (g/dL) | 12.2±1.7 | 13.0±1.7 | <0.001 |
| RDW (%) | 15.1±1.7 | 14.5±1.7 | <0.001 |
| Albumin (g/dL) | 3.96±0.47 | 4.1±0.48 | <0.001 |
| Uric acid (mg/dL) | 5.9±2 | 5.3±1.7 | 0.002 |
| C-reactive protein (mg/L) | 1.54±2 | 1.6±1.2 | 0.742 |
| LVEF (%) | 52.6±12.3 | 53.9±11.6 | 0.267 |
| Drainage (mL) | 550 (350-800) | 600 (450-800) | 0.317 |
| Intubation time (hour) | 13 (10-19) | 10 (8-13) | <0.001 |
| ACC time (minutes) | 54 (32-82) | 48.5 (33-70) | 0.024 |
| CPB | 89.5 | 87.3 | 0.412 |
| ICU stay (days) | 70 (39-121) | 55 (24-71) | <0.001 |
| Creatinine, first day (mg/dL) | 1.6±1 | 0.95±0.31 | <0.001 |
| Creatinine, second day (mg/dL) | 1.67±1 | 0.88±0.30 | <0.001 |
| Creatinine, third day (mg/dL) | 1.71±1.2 | 0.90±0.34 | <0.001 |

ACC=aortic cross-clamping; AKI=acute kidney injury; BMI=body mass index; CPB=cardiopulmonary bypass; ICU=intensive care unit; LVEF=left ventricular ejection fraction; MI=myocardial infarction; RDW=red cell distribution width
AKI development. High BMI levels (odds ratio [OR] and 95% confidence interval [CI], 1.066 [1.002-1.135]; \( P = 0.043 \)), existence of HT (OR and 95% CI, 2.153 [1.023-4.531]; \( P = 0.043 \)), existence of preoperative proteinuria (OR and 95% CI, 2.454 [1.007-5.984]; \( P = 0.048 \)), and low preoperative albumin levels (OR and 95% CI, 0.453 [0.216-0.947]; \( P = 0.035 \)) were found to be independent predictors for postoperative AKI development (Table 2).

AKI developed patients had statistically significant lower serum albumin levels but higher rates of HT existence, proteinuria, and higher BMI levels than non-AKI patients (Table 1, Figure 1).

The diagnostic performance analysis made for each independent predictor showed that HT existence results in AKI development with a sensitivity of 78.8% and a specificity of 37% as proteinuria leads to AKI development with a sensitivity of 23% and a specificity of 88.3%. ROC curve analyses showed that albumin levels <3 mg/dL have 83% sensitivity and 10% specificity for predicting AKI development while BMI >29 has a 57% sensitivity and 53% specificity (Figure 2).

A one way-repeated measures ANOVA was conducted to determine the SCr level over the first three postoperative days in AKI and non-AKI groups. The assumption of sphericity was violated (Mauchly’s test \( P \)-value <0.001). There was a statistically significant change in creatinine level over three days in both groups. A significant increase in creatinine levels on postoperative first, second, and third days was observed in the AKI group (Figure 3).

In the overall population, the incidence of all-cause mortality was 8.2% (n=52) and of postoperative infection was 11% (n=70). Non-AKI patients were associated with less all-cause mortality (17.4% vs 3.0%, \( P < 0.001 \)) and postoperative infection (16.5% vs 7.9%, \( P = 0.001 \)).

**DISCUSSION**

AKI following CPB is an important cause of morbidity and mortality[12]. In this study, our aim was to research the effect of preoperative low serum albumin levels on postoperative AKI development in diabetic patients undergoing isolated CABG operation.

AKI development subsequent to cardiac surgery is related with increased morbidity, mortality, and prolonged in-hospital stay. The incidence of AKI is 5%-30% after cardiac surgical procedures. Renal replacement therapy due to AKI development is the independent risk factor of mortality[4,13]. AKI following cardiac surgery is multi-factorial. The known risk factors are old age, diabetes, low preoperative glomerular filtration rate (GFR) (<60 mL/min/m²), low EF (<35%), and administration of nephrotoxic agents. The incidence of AKI was found to be high in patients with DM[14-16]. Our results showed that preoperative low serum albumin level,

**Table 2. Multivariate predictors for acute kidney injury after coronary artery bypass grafting.**

| Predictor                  | Univariate OR, 95% CI | P-value | Multivariate OR, 95% CI | P-value |
|---------------------------|-----------------------|---------|-------------------------|--------|
| Male (N)                  | 0.644 (0.460-0.902)   | 0.010   | 0.572 (0.288-1.137)     | 0.111  |
| Age (years)               | 1.026 (1.008-1.045)   | 0.005   | 1.006 (0.971-1.043)     | 0.725  |
| BMI                       | 1.046 (1.012-1.082)   | 0.007   | 1.066 (1.002-1.135)     | 0.043  |
| Hypertension              | 2.195 (1.434-3.360)   | <0.001  | 2.153 (1.023-4.531)     | 0.043  |
| Proteinuria (mg)          | 2.094 (1.260-3.480)   | 0.004   | 2.454 (1.007-5.984)     | 0.048  |
| Preoperative Hgb (g/dL)   | 0.760 (0.687-0.841)   | <0.001  | 1.111 (0.882-1.400)     | 0.370  |
| Preoperative RDW (%)      | 1.218 (1.106-1.342)   | <0.001  | 1.045 (0.862-1.266)     | 0.657  |
| Baseline creatinine (mg/dL)| 2.260 (1.560-3.273)  | <0.001  | 1.150 (0.609-2.172)     | 0.665  |
| Preop uric acid (mg/dL)   | 1.189 (1.065-1.328)   | 0.002   | 1.086 (0.918-1.284)     | 0.336  |
| Preoperative albumin (g/dL)| 0.426 (0.292-0.620)  | <0.001  | 0.453 (0.216-0.947)     | 0.035  |
| ACC time (minutes)        | 1.006 (1.001-1.012)   | 0.024   | 1.001 (0.993-1.009)     | 0.847  |

ACC=aortic cross-clamping; BMI=body mass index; CI=confidence interval; Hgb=hemoglobin; OR=odds ratio; RDW=red cell distribution width
high BMI, and preoperative severe HT are related with enhanced risk of AKI development defined by KDIGO criteria.

Albumin is the primary protein to maintain the plasma oncotic pressure as it obtains 70% of the oncotic pressure. It's an anti-inflammatory, antioxidant, and anticoagulant protein. Hypoalbuminemia is an indicator for liver and renal insufficiency. And hypoalbuminemia was found to be associated with increased mortality and morbidity subsequent to various surgical procedures in many studies. Many studies have shown albumin not only to be an inflammatory marker but also an AKI predictor. Also, hypoalbuminemia is a strong predictor for end-stage renal failure. Albumin protects renal function by increasing the oncotic pressure in coronary artery disease patients, it provides the continuation of renal perfusion and improves the glomerular filtration, and it protects the kidneys from toxic agents. The effect of hypoalbuminemia on postoperative renal failure was shown in many studies. Foley et al. showed that there is a strong correlation between hypoalbuminemia and ischemic heart disease. The same study revealed the need for hemodialysis in patients with low albumin levels in the same group of patients. Wiedermann et al. showed hypoalbuminemia as an independent risk factor for AKI.

In the presented studies, it is shown that low serum albumin levels enhance the incidence of AKI development in patients who underwent CABG surgical procedure. Lee et al. performed a single-center, randomized, double blind trial with patients whose preoperative albumin level was <4mg/dL. They found out that a decreasing in serum albumin levels was associated with AKI. Fındık et al. have searched the relation between AKI and CABG procedure and have shown that patients with albumin levels <3.5 g/dL are tend to develop AKI more often. Patients with diabetes who underwent CABG procedure in our centre were isolatelly-maintained and had their details observed in this study. Serum albumin levels <3 g/dL are the independent risk factor for AKI development in diabetic patients who underwent CABG surgical procedure.

Engelman et al. found low BMI and low serum albumin levels associated with high postoperative mortality and morbidity in a study with 5168 CABG patients. The same study revealed that a low serum albumin level (<2.5g/dL) is an independent risk factor for postoperative bleeding, prolonged ICU stay, prolonged mechanical ventilation, and renal failure. This study also showed that a high BMI is related with increased sternum and saphenous vein wound infection risk. However, our study found out that a high BMI is an independent risk factor of postoperative AKI development.
Wu et al. found preoperative proteinuria related with AKI development and as an independent risk factor for end-stage renal failure after CABG surgery. Hsu et al. evaluated the data of 600,000 patients and revealed that proteinuria and decrease in GFR are the independent risk factors for AKI development. Similarly, our study also found proteinuria as an independent risk factor for postoperative AKI development. In our study, high BMI, history of HT, and proteinuria were not found associated with AKI stage, except for the relation between presence of proteinuria and stage-3 AKI.

CONCLUSION

We showed that preoperative low serum albumin level, high BMI, preoperative HT, and proteinuria are associated with AKI development, defined by the KDIGO classification, in the diabetic patients who underwent CABG surgical procedure postoperatively.

Serum albumin level <3 g/dL is an independent risk factor for AKI development in the isolated diabetic patients who underwent CABG surgical procedure. We emphasize that this adjustable albumin level should be considered before the operation since it is an easy and clinically implementable management for the prevention of AKI development.

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Authors’ roles & responsibilities

RA Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published

TA Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published

EY Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published

DC Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published

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CK Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published

MBR Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; final approval of the version to be published

REFERENCES

1. Szabo Z, Hakansson E, Svedjeholm E. Early postoperative outcome and medium-term survival in 540 diabetic and 2239 non-diabetic patients undergoing coronary artery bypass grafting. Ann Thorac Surg. 2002;74(3):712-9. doi:10.1016/S0002-9475(02)03778-5.

2. Cohen Y, Raz I, Merin G, Mozes B. Comparison of factors associated with 30-day mortality after coronary artery bypass grafting in patients with versus without diabetes mellitus. Israeli Coronary Artery Bypass (ISCAB) Study Consortium. Am J Cardiol. 1998;81(1):7-11. doi:10.1016/S0002-9149(97)00797-2.

3. Kulab C, Srinivasan AK, Grayson AD, Fabri BM, Chalmers JA. Effect of risk-adjusted diabetes on mortality and morbidity after coronary artery bypass surgery. Ann Thorac Surg. 2005;79(5):1570-6. doi:10.1016/j.athoracsur.2004.10.035.

4. Takaki S, Shehabi Y, Pickering JW, Endre Z, Miyashita T, Goto T. Perioperative change in creatinine following cardiac surgery with cardiopulmonary bypass is useful in predicting acute kidney injury: a single-centre retrospective cohort study. Interact Cardiovasc Thorac Surg. 2015;21(4):465-9. doi:10.1093/icc/vtuv184.

5. Yousefshahi F, Yasseri AMF, Barkhordari K, Amini M, Omran AS, Hemami MR, Asadi M. Incidence and complications of acute kidney injury following coronary artery bypass graft: a retrospective cohort study. Iran J Kidney Dis [Internet]. 2015 [cited 2019 Apr 27];9(2):113-8. Available from: https://pdfs.semanticscholar.org/f2bb/9892be330dd1ae6245caef5f2ed2b0c08acafad.pdf.

6. Yu MW, Lee SW, Baek SH, Na KY, Chae DW, Chin HJ et al. Hypoalbuminemia at admission predicts the development of acute kidney injury in hospitalized patients: a retrospective cohort study. PLoS One. 2017 Jul 19;12(7):e0180750. doi:10.1371/journal.pone.0180750.

7. Engelmann OT, Adams DH, Byrne JG, Aranki SF, Collins Jr JJ, Couper GS, et al. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. J Thorac Cardiovasc Surg. 1999;118(5):866-73. doi:10.1016/S0022-5223(99)70056-5.

8. Delgado-Rodríguez M, Medina-Cuadros M, Gómez-Ortega A, Martínez-Gallego G, Mariscal-Ortiz M, et al. Cholesterol and serum albumin levels as predictors of cross infection, death, and length of hospital stay. Arch Surg. 2002;137(7):805-12. doi:10.1001/archsurg.137.7.805.

9. Kellum JA, Lameire N, Aspelin P, Burdmann EA, Goldstein SL, et al. Kidney disease: improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. Kidney International Supplements. 2012;2(1):1-138. doi:10.1038/ksup.2012.1.

10. Gernuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2003;26(1):3160.

11. Furnary AP, Wu Y, Bookin SO. Effect of hyperglycaemia and continuous intravenous insulin infusions on outcomes of cardiac surgical procedures: the Portland diabetic project. Endocr Pract. 2004;10 Suppl 2:21-33. doi:10.4158/EP.10.52.21.

12. Freeland K, Hamidian Jahromi A, Duvall LM, Mancini MC. Postoperative blood transfusion is an independent predictor of acute kidney injury in cardiac surgery patients. J Nephropathol. 2015;4(4):121-6. doi:10.12860/jnp.2015.23.

13. Cruz KL, Bakaeen FG, Wang XL, Huh J, LeMaire S, Coselli JS et al. Hypoalbuminemia and long-term survival after coronary artery bypass: a propensity score analysis. Ann Thorac Surg. 2011;91(3):671-6. doi:10.1093/athoracsur.2010.09.004.

14. Bove T, Calabro MG, Landoni G, Aletti G, Marino G, Crescenzi G et al. The incidence and risk of acute renal failure after cardiac surgery. J Cardiothorac Vasc Anesth. 2004;18(4):442-5. doi:10.1053/j.jvca.2004.05.021.
15. Maitra G, Ahmed A, Rudra A, Wankhede R, Sengupta S, Das T. Renal dysfunction after off-pump coronary artery bypass surgery-risk factors and preventive strategies. Indian J Anaesth [Internet]. 2009 [cited 2019 Apr 27];53(4):401-7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2894497/.

16. Karkouti K, Beattie WS, Wijeysundera DN, et al. Hemodilution during cardiopulmonary bypass is an independent risk factor for acute renal failure in adult cardiac surgery. J Thorac Cardiovasc Surg. 2005;129(2):391-400. doi:10.1016/j.jtcvs.2004.06.028.

17. Fanali G, di Masi A, Trezza V, Marino M, Fasano M, Ascenzi P. Human serum albumin: from bench to bedside. Mol Aspects Med. 2012;33(3):209-90. doi:10.1016/j.mam.2011.12.002.

18. Contreras A, Ramirez M, Cueva L, Alvarez S, de Loza R, Gamba G. Low serum albumin and the increased risk of amikacin nephrotoxicity. Rev Invest Clin [Internet]. 1993 [cited 2019 Apr 27]; 46(1):37-43. Available from: https://www.ncbi.nlm.nih.gov/pubmed/8079062.

19. Zamlauski-Tucker M, Cohen JJ. Effect of substrate-free albumin on perfused rat kidney function. Ren Physiol. 1988;10(6):352-60. doi:10.1159/000173144.

20. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE. Hypoalbuminemia, cardiac morbidity and mortality in end-stage renal disease. J Am Soc Nephrol [Internet]. 1996 [cited 2019 Apr 27];7(5):728-36. Available from: https://jasn.asnjournals.org/content/7/5/728.

21. Wedermann CI, Wedermann W, Joannidis M. 2010. Hypoalbuminemia and acute kidney injury: a meta-analysis of observational clinical studies. Intensive Care Med. 36(10):1657-65. doi:10.1007/s00134-010-1928-z.

22. 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(5):1001-11. doi:10.1097/ALN.0000000000001051.

23. 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(3):E123-7. doi:10.1532/hsf.1577.

24. Wu V-C, Huang T-M, Wu P-C, Wang W-J, Chao C-T, Yang SY et al. (2012) Preoperative proteinuria is associated with long-term progression to chronic dialysis and mortality after coronary artery bypass grafting surgery. PLoS One. 7(1):e27687. doi:10.1371/journal.pone.0027687.

25. Hsu RK, Hsu C. Proteinuria and reduced glomerular filtration rate as risk factors for acute kidney injury. Curr Opin Nephrol Hypertens. 2011;20(3):211-7. doi:10.1097/MNH.0b013e328345f8bd.