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Research article

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Age, body mass index, and diabetes mellitus are associated with an increased risk of acute kidney injury after coronary surgery: Retrospective cohort study

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Ethics Committee Approval
The study was approved by the Ankara City Hospital 1° Ethics Committee (E1-22-2572, 20.04.2022).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Cardiac surgery-associated acute kidney injury (CSA-AKI) is a significant complication of cardiac surgery and is associated with increased morbidity and mortality. Identifying risk factors can help clinicians alleviate the risk of developing CSA-AKI and associated complications. Therefore, this study aimed to identify pre-operative patient-related risk factors of CSA-AKI in patients undergoing coronary surgery.

Methods: The current study was a single-center retrospective cohort study of adult patients undergoing coronary surgery with cardiopulmonary bypass (CPB) over an 8-month period. AKI was scored according to The Kidney Disease Improving Global Outcomes (KDIGO) scoring system. Patients' age, gender, body mass index (BMI), comorbidities, KDIGO staging in AKI patients, and 30-day mortality rates were recorded. These variables were compared between AKI(−) and AKI (+) groups. Univariate binary regression analysis was performed between the variables that had statistically significant differences and AKI.

Results: A total of 248 coronary surgery patients were analyzed. The overall incidence of CSA-AKI was 16.5%. Age, BMI, and the proportion of diabetic patients were significantly higher in the AKI (+) group ($P = 0.04$, $P < 0.001$, and $P = 0.022$, respectively). The proportion of gender, chronic obstructive pulmonary disease (COPD), hypertension (HT), baseline creatinine levels, aortic cross-clamping, cardiopulmonary bypass (CPB), total operation duration, and 30-day mortality were similar between the groups. Univariate analysis demonstrated that CSA-AKI was significantly associated with age ≥ 65 years (odds ratio [OR] = 2.506; confidence interval [CI]: 1.265–4.967; $P = 0.008$), BMI of ≥ 25 kg m^{-2} (OR = 8.994; CI: 1.199–67.980; $P = 0.033$), and diabetes mellitus (OR = 2.171; CI: 1.103–4.273; $P = 0.025$).

Conclusion: The current study revealed that patients with increased age, BMI, and DM had a higher incidence of CSA-AKI. Therefore, even though these patient-related variables are known as non-modifiable parameters, more attention should be paid to preventing CSA-AKI during peri-operative management of these patients.

Keywords: Cardiac surgery, Acute kidney injury, BMI, Obesity, Diabetes mellitus, Age

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Introduction

Cardiac surgery-associated acute kidney injury (CSA-AKI) is the most common major complication of cardiac surgery and has an incidence ranging from 7% to 40% [1]. The severity of CSA-AKI varies from asymptomatic increases in creatinine levels to the requirement for renal replacement therapies, which significantly affect intensive care unit (ICU) and hospital lengths of stay and mortality. Severe CSA-AKI causes a 3–8‐ fold higher peri-operative mortality and prolonged length of stay in the ICU and hospital [2]. Furthermore, the risk of mortality remains high for years regardless of other risk factors even in patients with complete renal recovery.

Identifying risk factors could help clinicians alleviate the risk of CSA-AKI and CSA-AKI-associated complications [3]. Current research has found many components related to CSA-AKI, and these factors are multifactorial, interrelated, and mostly synergistic. The development of CSA-AKI mainly occurs in older, sicker patients who undergo more complex surgeries. However, patients without these risk factors can still develop CSA-AKI [4].

This study focuses on patient-related factors affecting AKI in coronary surgery patients. In line with this objective, AKI was evaluated in patients who had undergone coronary surgery, and the relationship between AKI and pre-operative variables was compared.

Materials and methods

The current study was a retrospective cohort study of patients who underwent coronary surgery with cardiopulmonary bypass (CPB) between June 2021 and April 2022. It was approved by the Ankara City Hospital 1° Ethics Committee (E1-22-2572, 20.04.22). A total of 248 eligible adult patients were included in the final analysis. The number of coronary surgery cases in our hospital during the study period determined the sample size. The exclusion criteria included patients under 18 years of age, pre-operative kidney injury, emergency cases, repeat surgeries, and/or a lack of clinical data. The pre- and post-operative patient data were obtained from the electronic database of the hospital, intra- and post-operative anesthesia records, and ICU follow-charts.

AKI was divided into three stages: (1) Stage I, an increase in serum creatinine by ≥ 0.3 mg/dL within 48 h or an increase in serum creatinine of 1.5–1.9 times the value at baseline; (2) Stage II, an increase in serum creatinine levels 2.0-2.0 times the value at baseline; and (3) Stage III, an increase in serum creatinine levels of 3.0 times the value at baseline, an increase in serum creatinine to ≥ 4 mg/dL, and/or initiation of renal replacement therapy as defined by The Kidney Disease Improving Global Outcomes (KDIGO) [5].

All patients received balanced anesthesia using our routine clinical protocols. Standard CPB was established, and antegrade cold blood cardioplegia was used for myocardial protection. Hemoglobin concentrations were kept above 7.5 g dl^{-1} during CPB and above 8.5 g dl^{-1} after CPB. All patients were transferred to the ICU after surgery.

Patients' ages, genders, body mass index (BMI) values, comorbidities, such as diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD) and/or hypertension (HT), total operation, CPB, and aortic cross-clamping duration, pre- and post-operative creatinine levels, KDIGO staging in AKI patients, and 30-day mortality rates were recorded. According to AKI development, patients were divided into AKI (−) and AKI (+) groups.

Statistical analysis

Statistical analyses were performed using IBM SPSS for Windows (IBM Corp., version 22.0, Armonk, NY, USA). Kolmogorov-Smirnov test was utilized to determine the distribution of data. Baseline data were expressed as mean (standard deviation), median (IQR 25-75), or number (percentage) as appropriate. The chi-squared test was used for the independent samples with categorical variable. An independent t-test was used for normally distributed variables, and Mann–Whitney U test was used for variables that were not normally distributed. Univariate binary regression analysis was performed to determine the relationship between the variables that had statistically significant differences and CSA-AKI. Univariate regression analysis was performed by categorizing the numerical data that were not normally distributed and statistically different between the groups. A *P*-value < 0.05 based on two-sided tests was considered statistically significant.

Results

A total of 248 patients were enrolled, of which 200 (80.6%) were male. The median age was 60 (55–66) years. Ninety-four (37.9%) patients had DM, 15(6%) had COPD) and 170 (68.5%) of them had HT. The median BMI was 27 (25–30). The overall incidence of CSA-AKI was 16.5% (41/248). The incidence of AKI stage I was 14.5%, stage II 2%, and stage III 0% according to the AKI diagnosis criteria of KDIGO (Table 1).

Table 1: Peri-operative variables of all study population

	Value
Age (years)	60 (55–66) *
Male sex	200 (80.6%) †
Diabetes mellitus	94 (37.9%) †
Chronic obstructive pulmonary disease	15 (6%) †
Hypertension	170 (68.5%) †
BMI (kg/m^2)	27 (25–30) *
Total operation duration (min)	270 (240–313) *
CPB duration (min)	100 (84-124) *
CC duration (min)	69 (25) Ψ
Preoperative creatinine	0.86 (0.77–1.01) *
Postoperative acute kidney injury	41 (16.5%) †
• KDIGO stage I	36 (14.5%) †
• KDIGO stage II	5 (2%) †
• KDIGO stage III	0 †
30-days mortality	4 (1.6%) †

* Median (interquartile range [IQR] 25%–75%); †: n (%); Ψ: Mean (standard deviation [SD]); BMI: Body Mass Index; CPB: Cardiopulmonary Bypass; CC: Cross-clamping; KDIGO: Kidney Disease Improving Global Outcome.

The proportion of gender, COPD, HT, baseline creatinine, aortic cross-clamping, CPB, and total operation duration, postoperative drainage, and 30-day mortality rates were similar between the groups. Age, BMI, and the proportion of diabetic patients were significantly higher in the AKI (+) group (*P* = 0.04, *P* < 0.001, and *P* = 0.022, respectively) as shown in Table 2.

Since they were not distributed normally, age was categorized as < 65 and ≥ 65, and BMI was categorized as < 25 and ≥ 25 to use these parameters in the univariate binary logistic regression analysis. Univariate analysis demonstrated that CSA-AKI was significantly associated with age ≥ 65 years (odds ratio [OR] = 2.506; confidence interval [CI]: 1.265–4.967; *P* = 0.008), BMI ≥ 25 kg m^{-2} (OR = 8.994; CI: 1.199–67.980; *P* = 0.033), and DM (OR = 2.171; CI: 1.103–4.273; *P* = 0.025) as shown in Table 3.

Table 2: Peri-operative variables of two groups

Variables	AKI (–) group n = 207	AKI (+) group n = 41	*P*-value
Age (years)	59 (54–65)	64 (58–72)	0.004*
Age ≥ 65	57 (27.5%)	20 (48.8%)	0.007Ψ
Male Gender	165 (79%)	35 (87%)	0.686Ψ
BMI (kg/m^2)	27 (25–27)	30 (28–32)	< 0.001*
BMI ≥ 25	169 (81.6%)	40 (97.6%)	0.011Ψ
Diabetes Mellitus	72 (34%)	22 (53%)	0.022Ψ
Hypertension	31 (14%)	9 (21%)	0.152Ψ
Chronic Obstructive Pulmonary Disease	13 (6%)	2 (5%)	0.731Ψ
Total Operation Duration (min)	270 (240–310)	278 (240–310)	0.468*
Cardiopulmonary Bypass Duration (min)	98 (83–121)	101 (88–128)	0.379*
Aortic Cross-Clamping Duration (min)	67 (25)	71 (24)	0.382†
Postoperative Drainage (ml)	650 (500–850)	600 (450–750)	0.324*
Preoperative Creatinine (mg/dl)	0.86 (0.77–1)	0.86 (0.78–1.06)	0.878*
30-day Mortality	2 (0.9%)	2 (4%)	0.069Ψ

BMI: Body Mass Index; *: Mann–Whitney U Test, Ψ: Chi-Squared Test, †: Independent Samples T-Test

Table 3: Univariate predictors of CSA-AKI

Variables	*P*-value	OR	95% CI
Age ≥ 65 (years)	0.008	2.506	1.265–4.967
BMI ≥ 25 (kg/m^2)	0.033	8.994	1.199–67.480
Diabetes Mellitus	0.025	2.171	1.103–4.273

OR: Odds Ratio, CI: Confidence Interval, BMI: Body Mass Index

Discussion

In this study, the overall incidence of CSA-AKI was 16.5%, which is in accordance with previous studies in the literature [2, 4]. Older age, DMI , and higher BMI were associated with an increased risk of developing CSA-AKI.

Standardizing the definition of AKI has advantages for diagnosing and staging. Although many novel biomarkers have been shown to be effective in detecting AKI, creatinine is nonetheless still the gold standard. The KDIGO consensus definition of AKI describes stage 1 AKI as an increase of 0.3 mg/dL creatinine within 48 h or an increase of 1.5 times the baseline value over seven days with the subsequent stages representing more severe kidney injury [5]. Patients who have had cardiac surgery in the past seven days and meet the KDIGO criteria for AKI can be said to have CSA-AKI.

Many studies have revealed several components of injury related to CSA-AKI. These components can be active at various stages of surgery with different intensities. The primary injury factors are hemodynamic and metabolic, ischemia–reperfusion injury, oxidative stress, inflammation, toxins, microembolization, and/or neurohormonal activation [6]. Risk factors can be classified as patient-related, operation-related, and physiological. It is generally suggested that operative risk factors (surgical complexity, CPB, aortic cross-clamping, operation duration, and low hematocrit during CPB) and physiological risk factors (hypotension, hypovolemia, blood transfusion) are commonly modifiable, procedure-related, and potentially preventable. It has been shown that shortening the duration of CPB and aortic cross-clamping, preventing hypotension, low hematocrit levels, and also blood transfusions are cornerstones for preventing CSA-AKI [1]. In contrast, patient-related factors (age, gender, smoking, obesity, and/or comorbidities) are considered non-modifiable factors. However, some patient-related factors, such as cessation of smoking, lowering one's BMI, and well controlled blood glucose and blood pressure levels may be modifiable in the long-term in cardiac patients. As Kunt et al. [7] reported, metabolic syndrome, which is defined as the coexistence of hyperglycemia, dyslipidemia, abdominal obesity, and HT, seems to be associated with an increased incidence of AKI after cardiac surgery. Moreover, it is suggested that it can be modifiable risk factor if its components are well-controlled.

Normal renal function decreases after the mid-30s. Consequently, the incidence of AKI increases with increasing age. However, patients over the age of 65 are more susceptible to AKI development. It is suggested that creatinine clearance and glomerular filtration rates decrease with increasing age [8]. Four main reasons for renal deterioration in elderly patients have been defined: (1) structural and functional deterioration of the kidneys associated with the aging process, (2) decreased renal reserve, (3) the presence of comorbidities, and (4) decreased ability to recover from surgery or injuries [9]. In our study population, AKI (+) patients were older than AKI (-) patients as found in other studies [10–12].

DM is another well-known risk factor for developing diabetic nephropathy and kidney injury. Several interrelated mechanisms have been suggested for how hyperglycemia exacerbates kidney injury [11]. Hyperglycemia can increase oxidative stress, augment ischemia-reperfusion injury, and induce endothelial dysfunction [13, 14]. Hyperglycemia can also cause cellular glucose overload (which generates mitochondrial dysfunction) and also increase inflammatory cytokines, thereby aggravating kidney injury [15, 16]. In the present study, diabetic patients had higher AKI incidences than non-diabetic patients. In a similar study, Wang et al. [11] investigated the association between DM and AKI in coronary surgery patients and found that diabetic patients were associated with an increased risk of AKI, which was independent of baseline renal and cardiac function. Another study reported by Hertzberg et al. [17] also reported the same results in which diabetic patients had a higher incidence of AKI after coronary surgery.

It is generally suggested that obesity causes an increase in oxidative stress, endothelial dysfunction, and inflammation. The markers of these pathological processes, including F_2-isoprostanes, interleukin 6 (IL-6), and plasminogen activator inhibitor-1, were shown to be associated with obesity [18, 19]. Moreover, their increases have also been shown in cardiac surgery [20]. Billings et al. [21] reported that BMI is an independent risk factor for CSA-AKI. Furthermore, these authors suggested that the relationship between obesity and CSA-AKI can partially be attributed to the effect of obesity on oxidative stress. Kumar et al. [22] also showed that obese patients (BMI > 40) had a higher risk of CSA-AKI than patients with lower BMI. They suggested that through secreted hormones and cytokines, visceral adipose tissue can cause inappropriate activation of the renin–angiotensin–aldosterone system and an increase in oxidative stress. Likewise, obese patients demonstrate an increase in renal plasma flow and glomerular filtration rate, thereby facilitating glomerular capillary hypertension [23]. The current study revealed that patients who developed CSA-AKI, even though they were not morbidly obese, still had a high BMI.

Limitations

This study has some limitations. First, this retrospective, non-randomized register study with a relatively small study population over eight months on patients undergoing coronary surgery was subject to selection bias. Studies on AKI usually compare surgical techniques, anesthesia, and/or CPB management techniques. However, this study population underwent the same coronary surgery technique, anesthesia, fluid, and CPB management and had similar durations of CPB and aortic cross-clamping, which may have affected CSA-AKI incidence. Therefore, this study provided a more comparable population to determine patient-related factors in terms of CSA-AKI development.

Second, the authors did not perform long-term follow-up; only hospital stay complications were analyzed. Therefore, the long-term risk of CSA-AKI could not be discussed. In addition, serum creatinine was the only parameters used to classify CSA-AKI (rather than urine output). Because urine output is affected by several factors and is usually inadequately recorded, for these reasons, several authors only use serum creatinine to diagnose AKI [10, 24].

Conclusions

The pathophysiology of CSA-AKI seems to be intricate and associated with several risk factors, presenting notable heterogeneity in cardiac surgery patients, especially surgeries performed with CPB. The current study revealed that patients with increased age, increased BMI, and DM had higher incidences of CSA-AKI. Even though these patient- related variables are counted as non-modifiable parameters of CSA-AKI, cardiac patients should be encouraged to lower BMI and regulate blood sugar levels for the long-term duration. Besides, considering that these patients may have a higher risk of CSA-AKI, more attention should be paid to peri-operative modifiable risk factors during cardiac surgery management. These results may encourage further studies for insight into the role of patient-related risk factors in AKI in cardiac surgery patients.

References

1. Gaffney AM, Sladen RN. Acute kidney injury in cardiac surgery. Curr Opin Anaesthesiol. 2015;28:50-9. doi: 10.1097/ACO.0000000000000154.
2. Wang Y, Bellomo R. Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol. 2017;13:697-711. doi: 10.1038/nrneph.2017.119.
3. Husain-Syed F, Quattrone MG, Ferrari F, et al. Clinical and Operative Determinants of Acute Kidney Injury after Cardiac Surgery. Cardiorenal Med. 2020;10:340-52. doi: 10.1159/000507777.
4. Schurle A, Koyner JL. CSA-AKI: Incidence, Epidemiology, Clinical Outcomes, and Economic Impact. J Clin Med. 202;10:5746. doi: 10.3390/jcm10245746.
5. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120:c179-84. doi: 10.1159/000339789.
6. Vives M, Wijeysundera D, Marczin N, Monedero P, Rao V. Cardiac surgery-associated acute kidney injury. Interact Cardiovasc Thorac Surg. 2014;18:637-45. doi: 10.1093/icvts/ivu014.
7. Tekeli Kunt A, Parlar H, Findik O, Duzyol C, Baris O, Balci C. The Influence of Metabolic Syndrome on Acute Kidney Injury Occurrence after Coronary Artery Bypass Grafting. Heart Surg Forum. 2016;19:E099-103. doi: 10.1532/hsf.1400.
8. Martin JE, Sheaff MT. Renal ageing. J Pathol. 2007;211:198-205. doi: 10.1002/path.2111.
9. Chao CT, Tsai HB, Lin YF, Ko WJ. Acute kidney injury in the lederly: Only the tip of the iceberg. J Clin Gerontol Geriatr. 2014;5:7-12. doi: 10.1016/j.jcgg.2013.04.022.
10. Mokhtar AT, Tennankore K, Doucette S, Herman CR. Predicting acute kidney injury following nonemergent cardiac surgery: A preoperative scorecard. J Card Surg. 2021;36:2204-12. doi: 10.1111/jocs.15503.
11. Wang R, Zhang H, Zhu Y, Chen W, Chen X. The impact of diabetes mellitus on acute kidney injury after coronary artery bypass grafting. J Cardiothorac Surg. 2020;15:289. doi: 10.1186/s13019-020-01312-x.
12. Zou Z, Zhuang Y, Liu L, et al. Role of Body Mass Index in Acute Kidney Injury Patients after Cardiac Surgery. Cardiorenal Med. 2017;8:9-17. doi: 10.1159/000477824.
13. Hirose R, Xu F, Dang K, et al. Transient hyperglycemia affects the extent of ischemia-reperfusion-induced renal injury in rats. Anesthesiology. 2008;108:402-14. doi: 10.1097/ALN.0b013e318164cff8.
14. Ellger B, Debaveye Y, Vanhorebeek I, et al. Survival benefits of intensive insulin therapy in critical illness: impact of maintaining normoglycemia versus glycemia-independent actions of insulin. Diabetes. 2006;55:1096-105. doi: 10.2337/diabetes.55.04.06.db05-1434.
15. Vanhorebeek I, Gunst J, Ellger B, et al. Hyperglycemic kidney damage in an animal model of prolonged critical illness. Kidney Int. 2009;76:512-20. doi: 10.1038/ki.2009.217.
16. Esposito K, Nappo F, Marfella R, et al. Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress. Circulation. 2002;106:2067-72. doi: 10.1161/01.cir.0000034509.14906.ae.
17. Hertzberg D, Sartipy U, Holzmann MJ. Type 1 and type 2 diabetes mellitus and risk of acute kidney injury after coronary artery bypass grafting. Am Heart J. 2015;170:895-902. doi: 10.1016/j.ahj.2015.08.013.
18. Pou KM, Massaro JM, Hoffmann U, et al. Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress: the Framingham Heart Study. Circulation. 2007;116:1234-41. doi: 10.1161/CIRCULATIONAHA.107.710509.
19. Skurk T, Hauner H. Obesity and impaired fibrinolysis: role of adipose production of plasminogen activator inhibitor-1. Int J Obes Relat Metab Disord. 2004;28:1357-64. doi: 10.1038/sj.ijo.0802778.
20. Czerny M, Baumer H, Kilo J, et al. Inflammatory response and myocardial injury following coronary artery bypass grafting with or without cardiopulmonary bypass. Eur J Cardiothorac Surg. 2000;17:737-42. doi: 10.1016/s1010-7940(00)00420-6.
21. Billings FT 4th, Pretorius M, Schildcrout JS, Mercaldo ND, Byrne JG, Ikizler TA, Brown NJ. Obesity and oxidative stress predict AKI after cardiac surgery. J Am Soc Nephrol. 2012;23:1221-8. doi: 10.1681/ASN.2011090940.
22. Kumar AB, Bridget Zimmerman M, Suneja M. Obesity and post-cardiopulmonary bypass-associated acute kidney injury: a single-center retrospective analysis. J Cardiothorac Vasc Anesth. 2014;28:551-6. doi: 10.1053/j.jvca.2013.05.037.
23. Chagnac A, Weinstein T, Korzets A, Ramadan E, Hirsch J, Gafter U. Glomerular hemodynamics in severe obesity. Am J Physiol Renal Physiol. 2000;278:F817-22. doi: 10.1152/ajprenal.2000.278.5.F817.
24. Hu P, Chen Y, Wu Y, Song L, Zhang L, Li Z, Fu L, Liu S, Ye Z, Shi W, Liang X. Development and validation of a model for predicting acute kidney injury after cardiac surgery in patients of advanced age. J Card Surg. 2021;36:806-814. doi: 10.1111/jocs.15249.

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