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RESEARCH ARTICLE

Effect of Age on Estimated Glomerular Filtration Rate and the Relationship between eGFR and Extubation Time in Patients Undergoing Open Heart Surgery

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ABSTRACT

Objectives: Extracorporeal circulation, while facilitating coronary artery bypass grafting (CABG) surgery, accelerates inflammatory processes and increases morbidity and mortality in elderly patients. The primary aim of this study was to evaluate the effect of aging on postoperative renal function after open heart surgery using an estimated glomerular filtration rate (eGFR) biomarker. The secondary aim was to evaluate the relationship between postoperative extubation times and other laboratory parameters and age and eGFR.

Methods: The data of 90 patients in the American Society of Anesthesiologists score (ASA) I–II groups who underwent CABG with cardiopulmonary bypass under general anesthesia were retrospectively analyzed. Patients were divided into two groups according to age (Group 1 aged ≥65 years and Group 2 aged <65 years). Statistical differences between the groups were evaluated according to the eGFR of the patients (eGFR <60 and >60 mL/min).

Results: The number and percentage of patients with preoperative eGFR <60 mL/min were similar in both groups (p=0.052). However, the number and percentage of patients with eGFR <60 mL/min postoperatively were higher in Group 1 than in Group 2 (p=0.024). Extubation times were found to be higher in Group 1, with 540 and 390 min in Groups 1 and 2, respectively (p=0.002).

Conclusion: The results of this study show that the renal and pulmonary systems of patients aged ≥65 years will be more affected by cardiovascular surgery and anesthesia than those of patients aged <65 years. In CABG surgery, we can obtain an idea about the postoperative extubation time by monitoring preoperative and postoperative eGFR changes.

Keywords: Aging, airway extubation, coronary artery bypass, creatinine, glomerular filtration rate

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Introduction

Cardiopulmonary bypass (CPB) is an extracorporeal circulation technique that offers several advantages in heart and great vessel surgery. It creates a bloodless field for the surgeon, enables temperature control, and provides circulatory and respiratory support.[1] However, despite these benefits, CPB can also lead to systemic complications, such as bleeding problems, neurological damage, atelectasis, and acute kidney injury (AKI).[1]

Ischemia–reperfusion injury, often triggered by CPB-induced hypotension, is a well-established contributor to AKI, with an incidence rate of approximately 18.2%.[2] Studies such as the one by Grams et al.[3] demonstrated that cardiac surgeries carry the highest risk of postoperative AKI compared with other major surgeries.

Age, particularly when accompanied by comorbidities, further elevates the perioperative risk. The inflammatory processes associated with aging can negatively affect organ function, including reduced renal perfusion and glomerular filtration rate (GFR). This highlights the importance of age as a significant morbidity factor in patients undergoing cardiac surgery and anesthesia. Notably, age is also a primary risk factor

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considered in risk classification systems such as European System for Cardiac Operative Risk Evaluation (EuroSCORE) and Parsonnet, which are used for patients undergoing coronary artery bypass grafting (CABG) surgery and anesthesia.[4]

Diagnosing perioperative AKI requires measuring creatinine and urine output. However, creatinine levels only indicate a decline in renal function after a significant decrease in GFR, typically by 50% on the first postoperative day or even later on the second day. This delay renders creatinine a less-than-ideal diagnostic tool.[5] New markers, such as neutrophil gelatinase-associated lipocalin and tissue inhibitor of metalloproteinase-2, can predict AKI before an increase in creatinine levels. Estimated GFR (eGFR) also serves as a potential biomarker of renal injury.[6] Several factors that increase the risk of AKI can be identified during the preoperative period. These factors include female gender; age >70 years; comorbidities such as diabetes, hypertension, congestive heart failure, and renal failure; elevated serum creatinine levels (>2 mg/dL); reduced GFR; use of ACE inhibitors; and left ventricular ejection fraction <35%. Factors such as prolonged CPB and aortic cross-clamp (ACC) durations, the extent of bleeding, and the presence of atrial fibrillation (AF) in the postoperative period are among the determinants of AKI risk.[7–9]

Our primary goal was to evaluate the effect of aging on postoperative renal function after open heart surgery using an eGFR biomarker. Evaluating the correlation of postoperative 24-h cardiac and renal markers and extubation time with aging and postoperative 24-h eGFR was our secondary goal.

Methods

Patients

In this study, the records of patients who underwent cardiac surgery with CPB between November 1, 2019, and 2021, by the Department of Cardiovascular Surgery with the approval of the Kahramanmaras Sutcu Imam University Faculty of Medicine Hospital Clinical Research Ethics Committee (Decision no: 2022/12-05 on 22.06.2022) were examined. Our study was conducted in accordance with the Declaration of Helsinki as a retrospective trial.

The data of 90 patients aged ≥18 years who met the ASA I–II and study criteria and who underwent coronary artery bypass surgery under general anesthesia by the same surgery and anesthesia teams were retrospectively analyzed from hospital information system records and anesthesia follow-up forms. This study excluded patients with the following conditions: congenital heart disease, heart transplant, left ventricular assist device, chronic renal failure, preoperative creatinine levels exceeding 2 mg/dL, and eGFR values <30 mL/min, as well as those undergoing off-pump, emergency, or redo surgeries. Patients were divided into two groups according to age: Group 1 comprised patients aged ≥65 years, and patients <65 years of age were included in Group 2.

Demographic data such as age, gender, comorbidities, medications used, type and amount of cardioplegia administered to the patient, duration of ACC and CPB, and time to extubation were recorded from the anesthesia and intensive care follow-up forms. Preoperative and postoperative 24-h serum creatinine and urea levels and AF rhythm were recorded. The eGFR at the preoperative and postoperative 24^{th} hour was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation, which is a calculation method that includes only the creatinine variable. An eGFR of <60 mL/min/1.73 m^2 was classified as decreased renal function and eGFR, whereas an eGFR of ≥60 mL/min/1.73 m^2 was considered normal eGFR.[10] Additionally, postoperative 24-h CKMB, troponin, lactate, urine, blood loss volume, and length of intensive care unit (ICU) and hospital stay were obtained from the patients' files and recorded. The statistical significance between the preoperative and postoperative cardiorenal variables and extubation times of both groups of patients was investigated.

Statistical Analysis

The recorded data were transferred to the computer environment using a statistical package program and analyzed using SPSS 22.0 (IBM Statistical Package for the Social Sciences; Armonk, NY, USA). Descriptive statistics are expressed as mean±SD, median (lower value-upper value), or percentage (%). The Kolmogorov–Smirnov test was used to determine the variable distribution. The Mann–Whitney U test was used to analyze quantitative data, and the chi-square and Fischer exact tests were used to analyze qualitative data. Factors affecting the length of ICU stay were determined by univariate and multivariate logistic regression analyses.

Results

In this retrospective study, data from 100 patients were initially collected. However, 10 patients (six and four patients from Groups 1 and 2, respectively) did not meet the inclusion criteria and were excluded from the analysis. Consequently, the final study cohort comprised 90 patients, with 44 and 46 patients in Groups 1 and 2, respectively. Among the patients in Group 1, four were excluded because they had preoperative creatinine levels >2 mg/dL. Additionally, two patients were excluded from Group 1 because they required emergency surgery. In Group 2, three patients were excluded because they underwent redo surgery, and one patient was excluded because of the need for postoperative ECMO support. The analysis and interpretation of the study results were based on data collected from the remaining 90 patients who met the inclusion criteria.

Table 1. Comparison of the demographic data of Groups 1 and 2 patients

	Group 1 ≥65 years (n=44)		Group 2 <65 years (n=46)		p
	n	%	n	%	
Diagnosis					
CABG	42	95.45	42	91.30	0.561
CABG+AVR	0	0.0	1	2.17	
CABG+MVR	2	4.55	3	6.52	
Gender					
Female	10	22.73	14	30.43	0.408
Male	34	77.27	32	69.57	
BMI, median (Q1–Q3)	27 (25–30)		27 (25–30)		0.686
EF, median (Q1–Q3)	55 (45–58)		55 (40–60)		0.728
Cardioplegia					
BC	10	22.72	9	19.57	0.873
DN	34	77.28	37	80.43	
The amount of cardioplegia, Median (Q1–Q3)	1.000 (1.000–1.200)		1.000 (1.000–1.000)		0.334
DM					
Yes	18	40.91	26	56.52	0.139
No	26	59.09	20	43.48	
HT					
Yes	30	68.18	27	58.70	0.351
No	14	31.82	19	41.30	

Statistical significance. Mann–Whitney U test; chi-square test; Fisher exact test; a:0.05. CABG: Coronary artery bypass grafting; AVR: Aortic valve replacement; MVR: Mitral valve replacement; BMI: Body mass index; EF: Ejection fraction; BC: Blood cardioplegia; DN: del Nido cardioplegia; DM: Diabetes mellitus; HT: Hypertension.

Demographic data such as gender, body mass index, presence of comorbidities (diabetes mellitus and hypertension), and ejection fraction were similar between the groups. The type of surgery performed and the type and amount of cardioplegia were also similar. In Group 1, two patients underwent coronary artery bypass grafting (CABG)+mitral valve replacement (MVR). In Group 2, one and three patients underwent CABG+aortic valve replacement and CABG+MVR, respectively. In Group 1, blood cardioplegia (BC) and del Nido cardioplegia (DN) were observed in 10 and 34 patients, respectively. In Group 2, BC and DN were used in 9 and 37 patients, respectively (Table 1).

CPB and ACC duration (min) was similar between the groups (p>0.05). Preoperative creatinine values were within the normal ranges as 0.84 (0.76–1.03) and 0.84 (0.65–1.07) mg/dL in Groups 1 and 2, respectively, and there was no significant difference. Preoperative urea values were within the normal ranges but were found to be significantly higher in Group 1 than in Group 2 (20.0 [16.0–25.0] vs. 15.0 [13.0–20.0]; p=0.016). Postoperative 24-h urea (25.5 [23.0–35.0] vs. 21.0 [17.0–28.0]; p=0.003) and creatinine (1.11 [0.78–1.65] vs. 0.91 [0.69–1.12]; p=0.017) values were significantly higher in Group 1 than in Group 2. There was no difference between the two groups in terms of urine, CKMB, troponin, blood loss, and lactate levels at 24 h postoperatively. The presence of preoperative AF was similar between Groups 1 and 2, with 4.5% (two patients) and 2.17% (one patient), respectively. The 24-h postoperative AF rates were similar between Groups 1 and 2, with 20.45% (nine patients) and 15.22% (seven patients), respectively (Table 2). The number and percentage of patients with preoperative eGFR <60 mL/min were similar in both groups (nine patients in Group 1 [20.4%] vs. three patients in Group 2 [6.52%]; p=0.052; Fig. 1). However, the number and percentage of patients with postoperative eGFR <60 mL/min were significantly different, being higher in Group 1 (17 patients in Group 1 [38.6%] vs. 8 patients in Group 2 [17.3%]; p=0.024; Fig. 2). Again, extubation times were significantly different, with 540 and 390 min in Groups 1 and 2, respectively (p=0.002). The total lengths of ICU and hospital stay were found to be similar in both groups (p=0.307 and p=0.689, respectively; Table 2).

A moderate negative correlation was observed between postoperative 24-h eGFR values and postoperative 24-h urea and creatinine values in Group 1 patients aged ≥65 years (r=−0.493, p=0.001; r=−0.788, p<0.001; Table 3). For Group 2 patients <65 years old, a negative correlation

Table 2. Comparison of clinical and laboratory parameters between Groups 1 and 2

	Group 1 ≥65 years (n=44)	Group 2 <65 years (n=46)	p
CPB time (min)			
Median (Q1–Q3)	93.0 (80.0–110.0)	95.5 (80.0–107.0)	0.683
ACC time (min)			
Median (Q1–Q3)	55.0 (41.0–60.0)	54.5 (49.0–63.0)	0.144
Extubation time (min)			
Median (Q1–Q3)	540.0 (360.0–960.0)	390.0 (300.0–450.0)	0.002*
Preoperative urea (mg/dL)			
Median (Q1–Q3)	20.0 (16.0–25.0)	15.0 (13.0–20.0)	0.016*
Postoperative 24-h urea (mg/dL)			
Median (Q1–Q3)	25.5 (23.0–35.0)	21.0 (17.0–28.0)	0.003*
Preoperative creatinine (mg/dL)			
Median (Q1–Q3)	0.84 (0.76–1.03)	0.84 (0.65–1.07)	0.229
Postoperative 24-h creatinine (mg/dL)			
Median (Q1–Q3)	1.11 (0.78–1.65)	0.91 (0.69–1.12)	0.017*
Postoperative 24-h urine (mL)			
Median (Q1–Q3)	3.100.0 (2.400.0–3.575.0)	2.825.0 (2.250.0–3.550.0)	0.619
Postoperative 24-h CKMB (mcg/L)			
Median (Q1–Q3)	7.35 (3.50–12.55)	6.1 (2.2–12.5)	0.538
Postoperative 24-h troponin (mcg/L)			
Median (Q1–Q3)	0.89 (0.26–1.79)	0.94 (0.07–2.0)	0.774
Postoperative 24-h lactate (mmol/L)			
Median (Q1–Q3)	1.80 (1.40–2.60)	1.7 (1.30–2.6)	1.00
Postoperative 24-h blood loss (mL)			
Median (Q1–Q3)	500.0 (375.0–950.0)	500.0 (350.0–750.0)	0.245
Preoperative AF, n (%)			
No	42 (95.5)	45 (97.83)	0.242
Yes	2 (4.5)	1 (2.17)	
Postoperative 24-h AF, n (%)			
No	35.0 (79.55)	39.0 (84.78)	0.370
Yes	9.0 (20.45)	7.0 (15.22)	
Preoperative eGFR (mL/min)			
Mean±SD	77.64±19.55	91.39±19.45	0.01*
Postoperative eGFR (mL/min)			
Mean±SD	67.80±27.54	84.53±24.81	0.419
Preoperative eGFR normality			
<60 mL/min	9 (20.4)	3 (6.52)	0.052
>60 mL/min	35 (79.6)	43 (93.48)	
Postoperative eGFR normality			
<60 mL/min	17 (38.6)	8 (17.3)	0.024*
>60 mL/min	27 (61.4)	38 (82.7)	
Total length of intensive care unit stay (days)			
Median (Q1–Q3)	4.0 (3.0–5.0)	3.0 (2.0–5.0)	0.307
Total length of hospital stay (days)			
Median (Q1–Q3)	14.0 (11.0–18.0)	13.5 (9.0–19.0)	0.689

Mann–Whitney U test; chi-square test; Fisher exact test; a:0.05; *: Statistical significance. CPB: Cardiopulmonary bypass; ACC: Aortic cross-clamp; AF: Atrial fibrillation; eGFR: Estimated glomerular filtration rate; SD: Standard deviation.

of moderate degree was found between postoperative 24-h eGFR values and extubation times, also high degree was found between postoperative 24-h eGFR values and postoperative 24-h urea, creatinine values, respectively (r=–0.307, p=0.038; r=–0.570, p<0.001; and r=–0.732, p<0.001; Table 3).

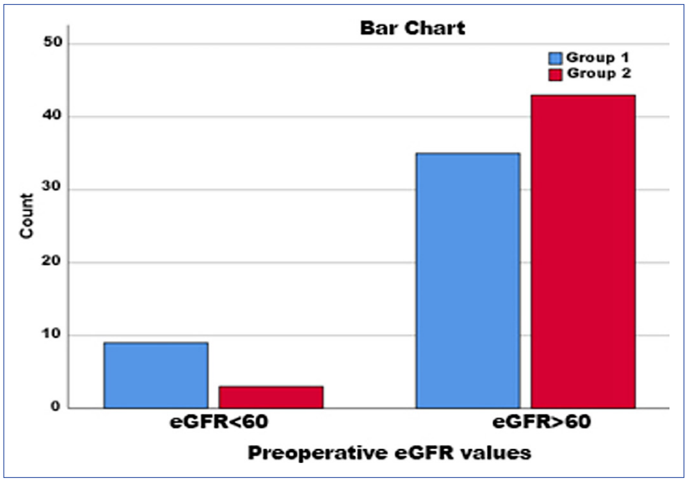

Figure 1. Comparison of the number of patients with eGFR <60 mL/min and >60 mL/min for Groups 1 and 2 in the preoperative period.
eGFR: Estimated glomerular filtration rate (Group 1 age ≥65 years and Group 2 age <65 years).

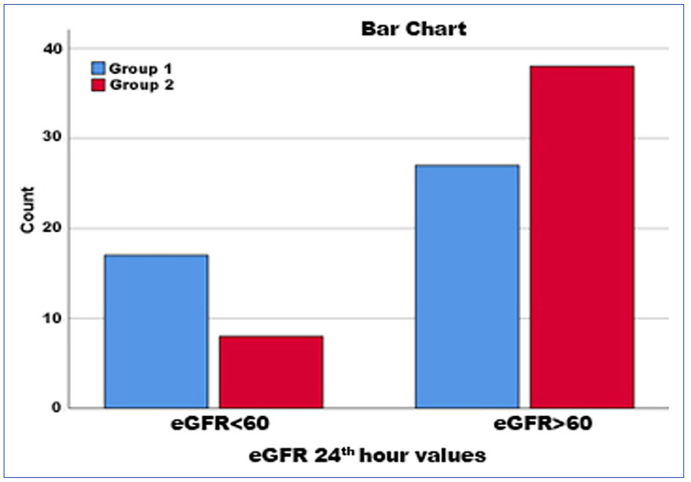

Figure 2. Comparison of the number of patients with eGFR <60 and >60 mL/min in Groups 1 and 2, respectively, at 24 h postoperatively.
Group 1 age ≥65 years and Group 2 age <65 years.

Discussion

This retrospective study investigated the effect of aging on postoperative renal function after open heart surgery using eGFR as a biomarker. Both groups were comparable in terms of demographic and clinical characteristics and comorbidities. During the postoperative period, the number of patients with eGFR values <60 mL/min was higher in the ≥65-year-old group, and in this age group, the time until extubation was longer than that in Group 2.

Surgical techniques, such as thoracotomy and hypothermia, and the release of cytokines (tumor necrosis factor, interleukin 6, and interleukin 8) during CPB can compromise lung and renal function. These effects are often amplified in elderly patients, potentially leading to extended postoperative mechanical ventilation.[11] Our findings support this notion because the elderly group (aged ≥65 years) exhibited a significant postoperative decline in eGFR, indicating decreased renal function and a longer extubation time.

Youssefi et al.[12] investigated the risk factors for unsuccessful fast-track extubation in 451 adult patients undergoing cardiac surgery and found that the strongest predictor was GFR <65 mL/min/body surface area, which indicates low renal function. Hypertension, age, preoperative lactate level, and duration of CPB and ACC were also found to be strong risk factors. In our study, when urea, creatinine, and eGFR were compared between the groups in the evaluation of postoperative renal function, all three variables were significantly different. Although creatinine is widely used because of its practicality and cost-effectiveness, it is not an ideal indicator of renal function. Therefore, alternative markers that better reflect renal function have gained importance. A decrease in eGFR has been reported in the literature even in cases in which increases in urea and creatinine are not noticeable and renal function is not significantly compromised.[13] In other words, eGFR is a more sensitive marker of AKI. For example, eGFR <60 mL/min/1.73 m^2 is now considered an indicator of reduced renal function.[10] Therefore, we focused on eGFR, one of the three markers, in evaluating kidney function related to surgery and age. In our study, the number of patients with decreased postoperative renal function (eGFR <60 mL/min/1.73 m^2) and prolonged extubation time was higher in Group 1 than in Group 2. Additionally, a negative correlation was detected between postoperative eGFR and extubation

Table 3. Correlation of postoperative 24-h eGFR with postoperative 24-h cardiac and renal markers and extubation times for Groups 1 and 2

	Postoperative 24-h eGFR (mL/min)	
	r	p
Group 1 ≥65 years (n=44)		
Extubation time (min)	−0.183	0.234
Postoperative 24-h urea (mg/dL)	−0.493	0.001*
Postoperative 24-h creatinine (mg/dL)	−0.788	<0.001*
Postoperative 24-h urine (mL)	0.238	0.120
Postoperative 24-h troponin (mcg/L)	0.007	0.963
Postoperative 24-h lactate (mmol/L)	0.064	0.680
Group 2 <65 years (n=46)		
Extubation time (min)	−0.307	0.038*
Postoperative 24-h urea (mg/dL)	−0.570	<0.001*
Postoperative 24-h creatinine (mg/dL)	−0.732	<0.001*
Postoperative 24-h urine (mL)	−0.025	0.871
Postoperative 24-h troponin (mcg/L)	0.058	0.711
Postoperative 24-h lactate (mmol/L)	−0.297	0.053

Spearman correlation test; a: 0.05; *Statistical significance.

time in patients <65 years of age. In patients <65 years of age undergoing CABG, low eGFR values in the postoperative period may be associated with prolonged intubation.

Postoperative renal function can be adversely affected by comorbidities, such as hypertension, vasculopathy, and diabetes, along with elevated serum chemokines and cytokines levels during CPB.[14] In our study, the duration of CPB was similar in both groups; therefore, we could not obtain data on the extension of the extubation period by CPB. Among the indicators of renal function, the "calculated GFR (cGFR)" is the most accurate indicator because it eliminates age, gender, and race variables present in the creatinine and eGFR formulas. Decreased cGFR is associated with an increased probability of failure following fast-track extubation [14]. Because age was our criterion for separating our groups, we preferred eGFR when evaluating patients. We also found a negative correlation, such as a decrease in eGFR value and prolongation of extubation time, similar to the relationship between cGFR and extubation time in our patients <65 years of age. The mean extubation times were 540 and 390 min in Groups 1 and 2, respectively. In other words, the elderly group did not have a chance of fast-track extubation, and their eGFR values were higher.

Lemaire et al.[15] compared postoperative complications and mortality rates between two groups of patients who underwent cardiac surgery, consisting of individuals aged 70–79 years and those aged 80–89 years. In other words, both groups were selected from the elderly population >65 years. In the 80- to 89-year-old group, the risk of cardiac, renal, and respiratory complications and postoperative blood loss was higher. In our study, the risk of renal and lung complications was low in the young group. There were similarities between the two groups in terms of the blood loss volume, CKMB, troponin and lactate levels, presence of AF, and length of ICU and hospital stay. Functional reserves of the lungs and kidneys decrease with age. The importance of detailed preoperative examination for elderly patients should be known to reduce postoperative complications in cases that affect circulation and alter organ perfusion, such as cardiac surgery. Additionally, as the patient ages, the CPB duration should be kept as short as possible to preserve cardiac output.

This study has some limitations. First, the number of patients meeting the inclusion criteria was small, and the patients could not be randomized because of the retrospective nature of the study. Second, preoperative EuroSCORE or New York Heart Association (NYHA) scores could not be included. Third, there were situations that could not be equalized one-to-one between the groups. Not only patients who underwent CABG but also those who underwent CABG + valve surgery were included in the study. The cardioplegia given to the patients varied between blood and del Nido.

Conclusion

The results of our study show that the renal and pulmonary systems of patients aged ≥65 years will be more affected by cardiovascular surgery and anesthesia than patients aged <65 years. Postoperative eGFR measurements during cardiac surgeries may provide predictive information regarding postoperative extubation time in relation to age.

Disclosures

Ethics Committee Approval: The study was approved by The Kahramanmaras Sutcu Imam University Faculty of Medicine Hospital Clinical Research Ethics Committee (no: 2022/12-05, date: 22/06/2022).

Authorship Contributions: Concept – F.Ç.; Design – Y.O.; Supervision – Y.O.; Data collection &/or processing – Z.K., S.M.A., A.Ş.K., S.A.K.; Analysis and/or interpretation – A.D.; Literature search – F.Ç.; Writing – F.Ç.; Critical review – Y.O.

Informed Consent: The written consent could not be taken from the patients due to the retrospective design of the study.

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