Original paper

What is the optimal time interval between heart catheterization and surgery to prevent acute kidney injury in patients with isolated coronary artery bypass?

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A b s t r a c t

Aim: The aim of the article was to study the role of the time between cardiac catheterization and cardiac surgery in the development of early postoperative acute kidney injury in patients who underwent isolated coronary artery bypass grafting was investigated.

Material and methods: A total of 1196 patients (832 males, 364 females; mean age 60.8 ±8.2 years; range: 32–74 years) operated between November 2006 and June 2014 at the same centre and by the same team for isolated coronary artery bypass grafting with cardiopulmonary bypass, whose preoperative serum creatinine level was < 1.5 mg/dl, were enrolled in the study. Patients were divided into group 1 – with acute kidney injury in the early postoperative period (n = 207) and group 2 – without (n = 989). Univariate analyses were done to determine significant clinical factors, and subsequent multiple logistic regression analysis was performed to determine independent predictors of acute kidney injury.

Results: A total of 207 (17.3%) patients developed acute kidney injury during 72 h postoperatively. Regarding the time interval between coronary angiography and coronary artery bypass grafting, there was a statistically highly significant difference between the patients with and without acute kidney injury (7.8 and 11.9 days, respectively; p = 0.0001). Postoperative C-reactive protein (p = 0.0001) and erythrocyte sedimentation rate (p = 0.0001) were significantly increased in group 1. Multivariate logistic regression analysis revealed the time between cardiac catheterization and surgery (p = 0.0001), increased postoperative C-reactive protein (p = 0.007 and p = 0.0001, respectively), and erythrocyte sedimentation rate (p = 0.0001) as independent predictors of early postoperative acute kidney injury in patients undergone isolated coronary artery bypass grafting.

Conclusions: If patients to be operated on are stable from a cardiac aspect, limitation of surgery in the early period following catheterization results in reduction of the incidence of postoperative acute kidney injury.

Key words: coronary artery bypass grafting, coronary angiography, acute kidney injury.

S u m m a r y

Coronary angiography using contrast agents is the gold standard method in the diagnosis and estimation of the prevalence of coronary artery disease. Patients who need coronary artery bypass grafting surgery after coronary angiography have a higher risk of postoperative acute kidney injury. The main purpose of this study was to investigate the relationship between the timing of coronary artery bypass grafting after coronary angiography and the incidence of acute kidney injury developing in the early postoperative period. According to our results, as the time interval between coronary angiography and isolated coronary artery bypass grafting surgery becomes shorter, the risk of early postoperative acute kidney injury increases significantly in these patients.

Introduction

Coronary artery bypass grafting (CABG) operations for the surgical treatment of coronary artery disease are performed successfully in our country as well as elsewhere in the world [1]. Patients undergoing major surgery such as CABG are at risk of acute kidney injury (AKI) [2].

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AKI is a complex pathology with a broad spectrum ranging from minimal increase in serum creatinine levels to anuric status [3]. AKI, seen as a minor or major problem following cardiac surgery, is a very important pathology leading to increased duration of stay in the intensive care unit and hospital, increased health costs, and high mortality rates [4]. The incidence of AKI after cardiac surgery is reported as 5–30%, and 1–2% of these patients require renal replacement therapy [5].

Coronary angiography (CAG) using contrast agents is the gold standard method in the diagnosis and estimation of the prevalence of coronary artery disease (CAD) [6]. Contrast-induced nephropathy (CIN) is seen in up to 10% of patients with normal renal function, but this rate rises to 25% in patients with underlying renal dysfunction [7]. The novel concern about AKI following cardiac surgery is the time from diagnostic CAG to subsequent cardiac surgery [8]. Patients who need CABG surgery after CAG have a higher risk of postoperative AKI because renal tubules do not have enough time to recover from the toxic effects of the contrast agent [9]. Studies have shown that cardiac surgery performed 1 day after CAG is associated with an increased risk of postoperative AKI [10, 11]. Ranucci *et al.* showed in another study that AKI following cardiac surgery was multifactorial; also, cardiac surgery performed on the same day as cardiac catheterization significantly increased the risk of AKI, and limiting this practice results in a significantly reduced incidence of postoperative AKI [12]. Nevertheless, Kim *et al.* showed that postoperative renal function was not affected in patients who underwent off-pump CABG surgery within 2 days after CAG [13].

Aim

The main purpose of this study was to investigate the relationship between the timing of CABG after CAG and the incidence of AKI developing in the early postoperative period.

Material and methods

The medical records of 1446 patients who underwent isolated CABG between November 2006 and June 2014 were reviewed retrospectively. The operations were performed at the same centre by the same surgery team. In total, 1196 (82.7%) patients who had serum creatinine (sCr) levels < 1.5 mg/dl, who underwent isolated CABG with cardiopulmonary bypass (CPB), were included in the study. The diagnosis of AKI was based on the highest sCr concentration measured during the first 7 days after surgery compared with the baseline sCr concentration, defined as the last concentration measured before surgery. Urine output was not used to define AKI because it might have been be altered by diuretics administered during anaesthesia and CPB. Patients who developed AKI in the early postoperative period were classified as group 1 (n = 207), and the patients with normal postoperative renal functions were classified as group 2 (n = 989). The diagnosis of AKI was made by comparing the baseline and post-operative sCr to determine the predefined significant change based on the Kidney Disease Improving Global Outcomes (KDIGO) definition (increase in sCrby ≥ 0.3 mg/dl within 48 h of surgery or increase in sCr to ≥ 1.5 times baseline within 3 days of cardiac surgery) [14].

We excluded patients previously diagnosed with end-stage renal disease who were on dialysis. The patients who had peripheral and carotid arterial disease, valvular heart disease, chronic obstructive pulmonary disease, malignancy, autoimmune diseases, endocrinological disorders, advanced age (> 75 years), systemic inflammatory diseases, left ventricular systolic function disorder (left ventricular ejection fraction ≤ 30%), decompensated congestive heart failure, congenital cardiac disease, patients who are severely overweight (body mass index > 30 kg/m^2), renal impairment (sCr > 1.5 mg/dl), haematological proliferative diseases, patients with low preoperative haemoglobin levels (≤ 10 g/dl), the use of steroids or nonsteroidal anti-inflammatory drugs, immunosuppressive drug treatment during the 2 weeks before surgery, the presence of the clinical infection signs (fever 37.5°C, C-reactive protein (CRP) ≥ 5 mg/dl, erythrocyte sedimentation rate (ESR) > 20 mm/h, or leukocyte count > 11000/µl) before surgery, application of femoral artery cannulation due to the ascending aorta calcification, patients who had an acute myocardial infarction and percutaneous coronary intervention in the 30 days prior to operation, emergency operations, patients who were reoperated due to haemodynamic instability or bleeding, patients who required intra-aortic balloon pump, and patients who were operated on beating heart or redo CABG were also excluded from the study. In patients who were ineligible for side clamping, proximal anastomoses were performed under a single aortic cross-clamping (ACC). These patients were excluded from the study. Additionally, patients for whom data such as serum creatinine levels or urine output were missing were excluded. Patients whose cardiac catheterization was done more than 30 days prior to surgery were also excluded from the study.

The demographic and clinical data of the patients were obtained by using the software system of the hospital for records and archives to investigate the patient files, epicrisis, operation notes, and laboratory results. We also cross-checked the coronary angiography database to identify patients who underwent cardiac catheterization at our institution prior to cardiac surgery. The demographic and clinical characteristics of the patients, complete blood counts routinely studied preoperatively and postoperatively, serum creatinine, urea and uric acid, estimated glomerular filtration rate (eGFR), ESR, and CRP levels were recorded. Operation information, the number of grafts used, duration of CPB and aortic cross clamping, amount of blood products used, and length of stay in the intensive care unit and hospital were recorded.

Coronary angiography was performed after the cessation of nephrotoxic medications and following hydration with 0.9% saline infusion. During CAG, 6 images for the left coronary artery system and 2 images for the right coronary artery system were obtained, and similar amounts of contrast agents were used. The time of surgery was decided depending on the clinical status of the patient and the availability of the operating room.

This study complied with the Declaration of Helsinki and was carried out following approval of the Ethics Committee for Clinical Trials of Kocaeli Derince Training and Research Hospital of Health Sciences University Ethics Committee (approval number: 2021/13).

Operative technique

All patients were operated with median sternotomy under general anaesthesia. Standard CPB was established with aortic and venous cannulations, systemic heparin (300 IU/kg), with maintenance of activated clotting time (ACT) > 450 s. Hyperkalemic cold blood cardioplegia was applied for cardiac arrest. Surgery was performed under moderate hypothermia (28–30°C). CPB flow was maintained at 2.2–2.5 l/min/m^2, mean perfusion pressure between 50 and 80 mm Hg, and haematocrit level between 20% and 25%. All distal anastomoses were done during ACC period and proximal anastomoses onto the ascending aorta on beating heart. All patients were extubated following onset of spontaneous breathing, normalized cooperation, and appropriate haemodynamic and respiratory functions.

All patients were transferred to an intensive care unit and intubated postoperatively. They were extubated following onset of spontaneous breathing and normalization of orientation and cooperation if the haemodynamic and respiratory functions were appropriate.

Statistical analysis

Statistical analysis was performed using SPSS software version 22.0 (SPSS Inc., Chicago, IL, USA). Among the data measured, those showing normal distribution were expressed as mean ± standard deviation; those not showing normal distribution were expressed as median (minimum–maximum). The data obtained by counting were given as percentages (%). Among the data measured, the normality of distribution was evaluated by histogram or Kolmogorov-Smirnov test, and the homogeneity of distribution was evaluated by Levene's test for equality of variance. Among the data measured, the difference between the groups was evaluated by Student's *t*-test in normal and homogenous distribution and by Mann-Whitney *U* test in non-normal and homogenous distribution. Among the data obtained by counting, the differences between the groups were evaluated by parametric or non-parametric Pearson χ^2 test or Fisher's exact test according to the distribution being parametric or not. The effects of the risk factors suggested to be influential on the early postoperative AKI were studies through the univariate logistic regression analysis. The multiple effects of the risk factors that are influential, or are suggested to be influential, in predicting the early postoperative AKI as a result of the univariate statistical analysis were studied through the retrospective selective multivariate logistic regression analysis. The odds ratio, the 95%-confidence interval, and the significant level for each of the risk factors were found to be statistically significant for $p < 0.05$.

Results

The demographic characteristics and clinical data of the patients are summarized in Table I. There were no differences between the 2 groups in terms of demographic or clinical data. The median time interval between CAG

Table I. Demographic and clinical properties of the patients

Patient characteristics	Group I AKI (*n* = 207)	Group II Non-AKI (*n* = 989)	*P*-value
Age (mean ± SD)	60.2 ±8.1	61.0 ±8.2	0.18**
Male	138 (66.7%)	694 (70.2%)	0.32*
Female	69 (33.3%)	295 (29.8%)	0.32*
Hypertension	86 (41.5%)	357 (36.1%)	0.14*
Diabetes mellitus	66 (31.9%)	321 (32.5%)	0.87*
Smoking	92 (44.4%)	385 (38.9%)	0.14*
Hyperlipidaemia	88 (42.5%)	471 (47.6%)	0.18*
BMI [kg/m^2] (mean ± SD)	25.8 ±2.9	25.5 ±2.7	0.22**
Ejection fraction (mean ± SD)	54.3 ±8.7	55.2 ±8.9	0.18**
Euro SCORE (mean ± SD)	2.02 ±1.7	2.09 ±1.5	0.59**
Basal heart rate (mean ± SD)	65.7 ±7.5	66.4 ±7.4	0.24**
Time interval between coronary angiography and on-pump cardiac surgery [day] (mean ± SD)	7.9 ±2.6	12.2 ±3.7	0.0001**

*AKI – acute kidney injury, BMI – body mass index, Euro SCORE – European System for Cardiac Operative Risk Evaluation. *Pearson χ^2 test, **Student's t-test.*

and CABG was significantly different between the patients with and without AKI (7.8 (range: 3 to 19) days and 11.9 (range: 3 to 28) days, respectively; $p = 0.0001$).

According to the KDIGO classification, 64.7% ($n = 134$) of the patients were stage I, 31.9% ($n = 66$) were stage II, and 3.4% ($n = 7$) were stage III. Renal failure requiring dialysis developed in 3 of 7 patients with stage III acute kidney injury. The preoperative blood analysis and haematological parameters of the patients are summarized in Table II. There were no statistically significant differences between the 2 groups in terms of preoperative blood analysis and haematological parameters.

The early postoperative blood analysis and haematological parameters of the patients are summarized in Table III. CRP levels ($p = 0.0001$) in the first, third, and seventh postoperative days and ESR ($p = 0.0001$) in the first, third, and seventh postoperative days were significantly different between the groups.

The intraoperative and postoperative data of the patients are shown in Table IV. The length of stay in the intensive care unit ($p = 0.0001$) and total length of stay in the hospital $p = 0.0001$) were significantly different between the groups. The neurological event rate (transient ischaemic event, speech disorder, hemiplegia, or hemiparesis) within the first 72 h postoperatively was significantly higher in group 1 compared to group 2 (9 (4.3%) patients vs. 15 (1.5%) patients; $p = 0.008$). Likewise, in-hospital mortality following the first 72 postoperative hours occurred in 6 (2.9%) patients in group 1 and in 8 (0.8%) patients in group 2, which showed a sta-

Table II. Preoperative blood results and haematological parameters of patients

Preoperative blood results and haematological parameters	Group I AKI (n = 207) Mean ± SD	Group II Non-AKI (n = 989) Mean ± SD	*P*-value
Haemoglobin [mg/dl]	13.5 ±1.5	13.4 ±1.4	0.22*
Creatinine [mg/dl]	0.76 ±0.3	0.74 ±0.3	0.40*
Urea [mg/dl]	41.0 ±4.6	40.9 ±4.5	0.72*
HbA_1c	6.2 ±1.4	6.3 ±1.5	0.58*
Uric acid [mg/dl]	5.3 ±1.5	5.4 ±1.6	0.78*
eGFR [ml/min/1.73 m^2]	96.2 ±31.4	95.4 ±30.6	0.69*
Leucocyte counts [× 10^3/µl]	8.0 ±1.7	8.1 ±1.7	0.89*
Thrombocyte counts [× 10^3/µl]	261 ±61	264 ±62	0.58*
CRP [mg/l]	0.64 ±0.40	0.69 ±0.56	0.17*
ESR [mm/h]	2.02 ±1.7	2.09 ±1.5	0.32*
CK-MB levels [U/l]	11.01 ±5.01	10.79 ±4.91	0.77*
Troponin I levels [ng/ml]	0.051 ±0.006	0.052 ±0.003	0.56*

*AKI – acute kidney injury, eGFR – estimated glomerular filtration rate, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, HbA_{1c} – glycated haemoglobin. *Student's t-test.*

Table III. Early postoperative blood results and haematological parameters of patients

Early postoperative period blood results and haematological parameters		Group I AKI (n = 207) Mean ± SD	Group II Non-AKI (n = 989) Mean ± SD	*P*-value
Haemoglobin [mg/dl]	1 day	9.16 ±1.13	9.11 ±1.09	0.53*
Haematocrit (%)	1 day	29.02 ±3.10	28.89 ±3.09	0.51*
Uric acid [mg/dl]	1 day	5.99 ±1.36	6.03 ±1.27	0.48*
CK-MB levels [U/l]	1 day	34.80 ±9.72	34.71 ±8.68	0.52*
Troponin I levels [ng/ml]	1 day	1.87 ± 0.18	1.84 ±0.20	0.43*
Leukocyte count [× 10^3/µl]	1 day	13.22 ±3.40	13.28 ±3.22	0.82*
	3 days	11.40 ±3.09	11.64 ±3.13	0.32*
	7 days	10.54 ±2.87	10.16 ±2.61	0.08*
CRP [mg/l]	1 day	29.48 ±5.86	27.31 ±4.54	0.0001*
	3 days	35.12 ±8.14	29.19 ±6.56	0.0001*
	7 days	15.59 ±4.51	11.23 ±3.94	0.0001*
ESR [mm/h]	1 day	38.18 ±12.10	32.13 ±11.06	0.0001*
	3 days	47.89 ±10.42	43.90 ±8.42	0.0001*
	7 days	33.23 ±8.61	27.33 ±6.06	0.0001*

*AKI – acute kidney injury, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, *Student's t-test.*

tistically highly significant difference between the groups (p = 0.02).

The results of univariate and multivariate regression analyses of patients who developed AKI in the early postoperative period are shown in Tables V and VI. In the multivariate analysis of the variables that were found to be statistically significant in univariate analysis associated with postoperative AKI, the time interval between CAG and CABG (p = 0.0001), increased CRP levels on the first (p = 0.002), third (p = 0.007), and seventh (p = 0.0001) postoperative day, and increased ESR levels on the first (p = 0.04), third (p = 0.001), and seventh (p = 0.0001) postoperative day were found to be independent predictors of early postoperative AKI.

The result of the analyses showed not only that the regression model was significant (F(7, 1188) = 83.069, p < 0.0001) but also that 32.5% (R^2 adjusted = 0.325) of the variance of postoperative acute kidney injury, as the dependent variable, was expressed by the independent variables.

Table IV. Intraoperative and postoperative data of the patients

Characteristics	Group I AKI (n = 207) Mean ± SD	Group II Non-AKI (n = 989) Mean ± SD	*P*-value
Aortic cross clamp time [min]	52.4 ±12.3	52.2 ±13.0	0.88*
Cardiopulmonary bypass time [min]	82.6 ±15.9	83.2 ±16.4	0.61*
Number of anastomoses	3.32 ±0.96	3.33 ±0.97	0.90*
Amount of Drainage [ml]	360 ±139	348 ±128	0.26*
Intubation time [h]	5.73 ±1.43	5.64 ±1.49	0.40*
Stay in the intensive care unit [h]	22.45 ±3.52	21.00 ±2.20	0.0001*
Total duration of hospital stay [days]	8.5 ±3.1	6.0 ±1.6	0.0001*
Use of blood products (%)	83 (40.1%)	365 (36.9%)	0.39**
Use of inotropic support (%)	15 (7.2%)	65 (6.6%)	0.72**

**Student's t-test, **Pearson χ^2 test.*

Table V. Univariate and multivariate regression analysis of preoperative risk factors for postoperative acute kidney injury

Variables	Postoperative AKI				
	Unadjusted OR (95% CI)	*P*-value	R^2	Adjusted OR (95% CI)	*P*-value
Male gender	1.18 (0.86–1.62)	0.32	–	1.04 (0.97–1.11)	0.30
Age	1.01 (0.99–1.03)	0.18	–	1.35 (0.80–2.29)	0.46
Ejection fraction	0.99 (0.97–1.01)	0.18	–	0.98 (.83–1.16)	0.51
Diabetes mellitus	0.97 (0.71–1.34)	0.87	–	1.01 (0.99–1.02)	0.42
Hypertension	1.26 (0.93–1.71)	0.14	–	0.83 (0.59–1.05)	0.83
Hyperlipidaemia	0.81 (0.60–1.10)	0.18	–	0.96 (0.88–1.02)	0.39
Smoking	1.25 (0.93–1.70)	0.14	–	1.01 (0.98–1.03)	0.43
Euro SCORE	0.96 (0.68–1.36)	0.84	–	0.98 (0.88–1.08)	0.64
Basal heart rate	1.01 (0.99–1.03)	0.24	–	–	–
Preoperative creatinine	0.80 (0.48–1.34)	0.40	–	–	–
Preoperative platelet	0.99 (0.98–1.00)	0.58	–	–	–
Preoperative CRP	1.26 (0.91–1.74)	0.17	–	–	–
Preoperative haemoglobin	0.94 (0.84–1.04)	0.22	–	–	–
Preoperative leucocyte	0.99 (0.98–1.00)	0.89	–	–	–
Preoperative ESR	0.96 (0.91–1.01)	0.74	–	–	–
Preoperative urea	0.99 (0.95–1.03)	0.72	–	–	–
Preoperative HbA_{1c}	1.03 (0.93–1.15)	0.58	–	–	–
Preoperative uric acid	0.98 (0.95–1.01)	0.81	–	–	–
Preoperative eGFR	1.02 (0.98–1.06)	0.37	–	–	–
Time interval between coronary angiography and on-pump cardiac surgery	1.62 (1.51–1.74)	0.0001	0.27	0.61 (0.55–0.67)	0.0001

CPB – cardiopulmonary bypass, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, AKI – acute kidney injury, eGFR – estimated glomerular filtration rate.

Table VI. Univariate and multivariate regression analysis of perioperative and postoperative risk factors for postoperative acute kidney injury

Variables	Postoperative AKI				
	Unadjusted OR (95% CI)	*P*-value	R^2	Adjusted OR (95% CI)	*P*-value
Postoperative first day haemoglobin	0.96 (0.84–1.10)	0.53	–	–	–
Postoperative first day CK-MB	1.18 (0.94–1.46)	0.45	–	–	–
Postoperative first day troponin I	1.39 (0.48–4.02	0.54	–	–	–
Postoperative first day CRP	0.92(0.89–0.95)	0.0001	0.18	0.91 (0.84–0.98)	0.002
Postoperative third day CRP	0.91 (0.89–0.93)	0.0001	0.10	0.94 (0.90–0.98)	0.007
Postoperative seventh day CRP	0.81 (0.78–0.84)	0.0001	0.14	1.17 (1.11–1.24)	0.0001
Postoperative first day ESR	0.96 (0.95–0.97)	0.0001	0.11	1.03 (0.99–1.06)	0.04
Postoperative third day ESR	1.04 (1.02–1.06)	0.0001	0.18	0.98 (0.94–1.02)	0.001
Postoperative seventh day ESR	0.89 (0.87–0.91)	0.0001	0.12	1.09 (1.06–1.12)	0.0001
Aortic cross clamp time	1.00 (0.99–1.01)	0.88	–	–	–
Number of anastomoses	0.99 (0.85–1.16)	0.90	–	–	–
CPB time	1.00 (0.99–1.01)	0.61	–	–	–
Intubation time	0.96 (0.87–1.06)	0.40	–	–	–
Use of blood products	1.15 (0.85–1.56)	0.39	–	–	–
Use of inotropic support	1.11 (0.62–1.99)	0.73	–	–	–
Amount of drainage	1.00 (0.99–1.01)	0.23	–	–	–

CPB – cardiopulmonary bypass, CRP – C-reactive protein, ESR – erythrocyte sedimentation rate, AKI – acute kidney injury.

The risk of developing early postoperative AKI was detected as 7.84 (95% confidence interval, OR = 7.84 (5.65–10.87) p = 0.0001) times higher in patients who underwent cardiac surgery 7 days or less after coronary angiography compared to patients who underwent cardiac surgery after 7 days.

Discussion

Previous studies have focused on evaluating the effect of the time interval between CAG and cardiac surgery, over postoperative renal function [10]. In our study, we examined the contribution of the time interval between CAG and surgery to the development of early postoperative AKI in patients who underwent isolated CABG using CPB. We found that the time interval between CAG and isolated CABG was a strong independent predictor of early postoperative AKI. In addition, we found that preoperative and early postoperative increased CRP and ESR values were associated with AKI occurring in the early postoperative period. As a result, the decreased time interval between coronary angiography and on-pump cardiac surgery was found to be associated with early postoperative AKI following isolated CABG.

Despite advances in surgical techniques, anaesthesia, and adjunctive medical treatments, major adverse renal and cardiac events remain dangers after cardiac surgery [15]. One of the most serious complications for patients undergoing CABG is postoperative AKI [16]. Depending on the decrease in renal functions, AKI is defined as an increase in sCr, a decrease in GFR, and a decrease in urine output [17]. Acute kidney injury development subsequent to cardiac surgery is related with increased morbidity and mortality, and prolonged hospital stay [18]. After cardiac surgery, AKI is a complication seen at a rate of 5–48% associated with a 50% increase in early postoperative mortality [19]. In our study, we identified the rate of occurrence of AKI after CABG as 20.9%.

The AKI incidence following cardiac surgery depends on its definition. The risk, injury, failure, loss of kidney function, and end-stage kidney disease (RIFLE) classification, Acute Kidney Injury Network (AKIN) criteria, and KDIGO stages are all practical predictors of AKI after CABG and/or heart valve operations [1, 14]. In our study, AKI was defined according to the KDIGO criteria.

The pathophysiology of AKI occurring after cardiac surgery is complex and multifactorial; many factors such as renal ischaemia-reperfusion injury, exogenous and endogenous toxins, use of radiocontrast agents, neurohormonal activation, metabolic factors, hypoproteinaemia, inflammation, and oxidative stress are involved in its aetiopathogenesis [20]. Another cause of AKI following cardiac surgery could be a pro-inflammatory event such as operative trauma, blood exposed to the artificial surface of the CPB circuit, or ischaemia-reperfusion injury [21]. C-reactive protein is a marker of inflammation that is used extensively in clinical practice. Recently, several prospective clinical studies have shown that modest elevations in baseline CRP levels predict future cardiovascular events [22]. Parlar *et al.* reported that early postoperative increased CRP level is an independent risk factor for the development of AKI in the early postoperative period [5]. Şahin *et al.* reported in their study involving 546 patients that preoperative CRP levels were not associated with complications such as early-stage renal dysfunction after cardiac surgery [23]. Han *et al.* reported that an elevated preoperative CRP level predicts AKI after CABG [24]. In our study, however, no relationship was found between preoperative CRP levels and postoperative AKI, but increased CRP levels on the third and seventh postoperative day were found to be an independent risk factor for the development of postoperative AKI.

The erythrocyte sedimentation rate is an inexpensive, routine, and easy-to-apply preoperative test that is routinely used in patients in many health centres [25]. ESR often reflects the inflammatory status of patients, and owing to the recently defined inflammatory processes involved in the development of cardiac disease, certain studies have reported its predictive value and association with postprocedural complications [26]. Togan *et al.* reported that preoperative high ESR levels cause adverse events such as postoperative mid-term morbidity and mortality in male patients undergoing CABG [27]. There are many studies in the literature showing the relationship between ESR levels and postoperative AKI after cardiac surgery; however, ESR levels were found to be statistically significantly higher on the first, third, and seventh postoperative days in the group developing AKI, in our study. However, we found that high ESR levels on the seventh postoperative day are an independent risk factor for the development of postoperative AKI.

Medical imaging has become an important diagnostic and therapeutic tool in clinical medicine in the era of great technological advances. Contrast media (CM) are increasingly used for better imaging in a broad spectrum of areas such as diagnostic computed tomography and magnetic resonance imaging, procedures of interventional radiology, cardiac catheterization, and percutaneous transluminal coronary angioplasty [28]. Cardiac catheterization is a procedure performed to help diagnose and treat heart problems; CAG is usually done as part of cardiac catheterization to help find blockages in the arteries that supply blood to the heart muscle [29]. Diagnostic invasive CAG using iodinated CM is an important tool for identifying patients with obstructive coronary disease who may benefit from coronary revascularization [30].

Acute kidney injury is reported to occur in up to 30% of patients after cardiac surgery with CPB, whereas CIN after CAG has been reported to occur in 10% of patients with normal renal function but in 25% of patients with pre-existing renal failure [31]. Contrast-induced AKI is defined as the onset of acute renal failure within 2–7 days after administration of iodinated CM (most commonly after CAG and percutaneous coronary intervention), and it is one of the leading causes of acute renal failure during hospital stay [32]. The mechanism of CIN includes the direct toxic effect of contrast agents as well as contrast-induced vasospasm leading to decreased renal medullary blood flow; thus, this causes medullary ischaemia, increased reactive oxygen substrate formation, and oxidative stress [6]. Contrast agent-related risk factors for CIN include a high volume of contrast agents, the use of hyperosmolar contrast agents, repeated exposure to contrast agents within a short period, and intra-arterial administration of contrast agents [33]. Contrast-induced nephropathy is generally regarded as a transient and reversible form of kidney injury, and the mean incidence of CIN in the general population is 2%, but it may be as high as 20–30% in the presence of pre-existing risk factors such as older age or chronic renal impairment [34]. Multiple factors have been implicated as contributors to postoperative AKI, including advanced age, diabetes, obesity, female gender, albuminuria, hypertension, chronic kidney disease, time delay between heart catheterization and surgery, ACC time, duration of CPB time, differences in the preoperative and intraoperative mean arterial pressure, and blood transfusion following surgery [3]. Because we excluded patients aged 75 years and over, obesity (body mass index > 30 kg/m^2), and chronic renal failure in our study, the relationship between postoperative AKI after CABG and the time between CAG and surgery is more prominent.

Among the criteria that can be modified for the development of AKI, the time elapsed between CAG and CABG is an important risk factor [31]. The reason for this is that the contrast agents used in CAG and stress of CABG (double hit) may cause postoperative AKI in these patients [28]. Therefore, it has been suggested that it might be necessary to optimize the time interval between CAG and CABG to reduce the additive effect of contrast agents and surgery in patients undergoing CABG [6]. CI-AKI has been defined as the acute deterioration of renal function after contrast media administration in the absence of other causes [16]. Previous studies have also focused on the relationship between the time interval after CAG to CABG and postoperative AKI [11]. Ji *et al.* followed up patients who underwent off-pump CABG surgery 5 days or less after CAG and patients who underwent off-pump CABG surgery more than 5 days after CAG, for the development of postoperative AKI, and they found that the incidence of postoperative AKI development was higher in patients with 5 days or less between CAG and off-pump CABG surgery [8]. Andersen *et al.* reported in their study that the postoperative AKI risk was low in patients who underwent elective proximal aortic surgery, and surgery could be performed safely within one to 3 days after cardiac catheterization [35]. Mehta *et al.* in their study, in which they performed elective CABG surgery, classified the time intervals between cardiac catheterization and CABG surgery as ≤ 1 day, 2 days, 3 days, 4 days, and ≥ 5 days and examined its relationship with the development of postoperative AKI; they reported that the shorter the time between CABG and cardiac catheterization, the higher the risk of postoperative AKI [11]. Del Duca *et al.* reported that the risk of developing AKI increased significantly after cardiac surgery performed within the first 5 days after CAG. However, this study included patients who underwent different surgeries such as isolated heart valve surgery, heart valve surgery with CABG, other complex surgeries, and emergency surgeries [36]. Kramer *et al.* reported the rate of postoperative AKI as 50.2% in patients who underwent CABG surgery before being discharged from the hospital after cardiac catheterization [37]. Mariscalco *et al.* reported that valve surgery and CABG increased the risk of AKI in the first 5 days after cardiac catheterization, but this increase was not seen in patients who underwent isolated CABG [38]. In their study, Doğan *et al.* reported that CABG can be performed without any delay, without an increase in the risk of AKI, after CAG, in patients with diabetes mellitus [6].

In light of these studies, there are no clear data on the optimal time interval between CAG and isolated CABG surgery. In this study, unlike the others, we did not categorize the patients according to the time interval between CAG and cardiac surgery but classified them as patients with postoperative AKI and normal follow-up. The reason for this was to determine the relationship between the time interval between CAG and cardiac surgery and the development of AKI, to establish whether it is an independent risk factor. In our study, the time between CAG and cardiac surgery for the development of postoperative AKI was an independent risk factor in univariant and multivariate analysis. We found that this time interval predicted postoperative AKI.

Our study has some limitations. This was a retrospective single-centre observational study with inherent limitations and possible selection biases. Due to the observational nature of this study, our findings should be considered hypothesis-generating. Implications for causality should be considered. The retrospective nature of the research based on the institutional database limits the possibility of addressing possible risk factors for AKI that were not included in our data collection. In addition, prospective randomized studies should be conducted to determine the effect of the time interval between CAG and CABG surgery on the incidence of postoperative AKI. Again, our study population was small. In particular, the absence of reliable data on the contrast media volume used for the angiography represents a major limitation. Another limitation of our study is the lack of specific biomarkers for AKI and the direct measurement of creatinine clearance. Also, the availability of relevant data on a hydration protocol during and after CAG using contrast media could provide a preliminary insight into postoperative AKI; however, this information was not available in this study.

Although adjustments for many variables were collected in our database, the effects of occult or uncollectible factors such as preoperative volume status, data of preoperative amounts of infused fluid, intraoperative haemodynamic status, and strategies used could not be excluded to prevent postoperative AKI.

Conclusions

We can say that there are conflicting results in the literature about the optimum time interval between CAG, which is the most widely used method to diagnose occlusion in CAD all over the world, and CABG surgery using CPB. There are many reasons for this, such as inclusion of different types of surgery in the studies (i.e. isolated CABG, CABG plus valve surgery, and other complex surgeries) and some studies not differentiating between primary and emergency surgeries. Keeping wide exclusion criteria, we included patients with normal preoperative renal function, less than 75 years of age, and who had elective isolated CABG surgery. According to our results, as the time interval between CAG and isolated CABG surgery gets shorter, the risk of early postoperative AKI increases significantly. Therefore, our results show that if patients scheduled for surgery by council decision after CAG are cardiac stable regarding symptoms or haemodynamically, there is an opportunity to reduce the incidence of postoperative AKI by separating genuine emergency patients from elective or non-emergency patients. Considering these findings, by increasing the time interval between CAG and CABG surgery, we can resolve some predisposing factors contributing to postoperative AKI and reduce overall morbidity and mortality for patients undergoing cardiac surgery. We hope that the present study will provide more evidence about the effectiveness and applicability of this policy.

Conflict of interest

The authors declare no conflict of interest.

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