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Factors associated with acute kidney injury after on-pump coronary artery bypass grafting

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Abstract

Background Acute kidney injury (AKI) frequently occurs as a complication of cardiac surgery and cardiopulmonary bypass (CPB). Its prevalence and severity are determined by various preoperative and intraoperative factors. The aim of this study was to examine the risk factors for AKI following on-pump coronary artery bypass grafting (CABG).

Methods A retrospective analysis of clinical records from a single medical center was performed. The primary determinant for AKI analysis was the creatinine-level changes within the first 48 h after surgery. Records of 120 patients from a prospective cohort study were examined.

Results An AKI incidence of 26% occurred in the study cohort. The univariate analysis revealed that patients who developed AKI had notably higher EuroSCORE II values (2.00 ± 0.98 vs. 1.49 ± 0.74, $p = 0.006$) and higher initial levels of urea (7.62 ± 2.94 vs. 6.12 ± 1.71, $p = 0.002$) and creatinine (0.108 ± 0.039 vs. 0.091 ± 0.016, $p = 0.003$). Additionally, they exhibited a more frequent occurrence of initial albumin levels below 40 g/l (9 (34.6%) vs. 11 (14.9%) cases, $p = 0.030$) and a lower initial hemoglobin level (137.8 ± 13.2 g/l vs. 146.6 ± 13.6 g/l, $p = 0.005$) in comparison to patients without this complication. Moreover, those with AKI had a significantly longer hospital stay duration (14.3 ± 5.45 days vs. 12.6 ± 3.05 days, $p = 0.048$). Logistic regression indicated one risk factor, oxygen delivery during CPB, that correlated with the onset of AKI in the early postoperative period.

Conclusion The prevalence of AKI was higher among patients with a higher EuroSCORE II, lower preoperative hemoglobin, increased preoperative levels of creatinine and urea, infrequent albumin levels below 40 g/L, diminished oxygen delivery during CPB, and greater need for RBC transfusion and furosemide, but it did not correlate with the duration of CPB.

Keywords Coronary artery bypass grafting, Cardiopulmonary bypass, Acute kidney injury

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Introduction

Acute kidney injury (AKI) is one of the most common complications in cardiac surgery and cardiopulmonary bypass (CPB) [1]. Its prevalence varies from 5 to 43%, and up to 7% of patients require renal replacement therapy (RRT) [2]. An increase of 0.3–0.5 mg/dL in serum creatinine (sCr) after cardiac surgery is independently linked to a substantial increase in 30-day mortality [3]. Severe AKI necessitating RRT correlates to 3 to 8-times greater mortality and longer stays in the intensive care unit [4]. The aim of this study was to identify risk factors for AKI in the postoperative period after on-pump coronary artery bypass grafting (CABG).

Materials and methods

This retrospective post-hoc analysis examined data from a prospective cohort study (NCT 05514652), which has been listed at clinicaltrials.gov. The aim of the previous study was to compare the effects of a multimodal low-opioid protocol (MLOP) with a routine-opioid anesthesia protocol (ROP) on early postoperative complications during on-pump CABG. There were 120 consecutive patients who met the inclusion criteria and agreed to participate in the study. These patients were divided into an MLOP group (n=60) and an ROP group (n=60).

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of P.L. Shupyk National Health Care University of Ukraine (Protocol No. 10, November 5, 2018). Each patient signed informed consent forms to participate in the study. The results examined in this study were previously reported by Maruniak et al. in 2023 [5].

This pos-hoc study initially examined data from 120 patients, of which 14 patients were excluded due to the presence of chronic kidney disease (CKD), while 6 patients were excluded due to missing data (Fig. 1). The patients ranged from 18 to 65 years in age and underwent on-pump CABG at the Heart Institute Ministry of Health of Ukraine between 2018 and 2020. The inclusion criteria were ejection fraction above 30% and a EuroSCORE II less than 5% during perioperative risk assessment. The exclusion criteria were missing data, ejection fraction < 30%, a EuroSCORE II > 5%, and chronic renal disease determined by glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2 in accordance with the Kidney Disease Improving Global Outcomes (KDIGO) guidelines.

The glomerular filtration rate (GFR) was calculated using the Cockcroft–Gault formula [6], which takes age, gender, and serum creatinine into account:

$$Glomerular\ filtration\ rate = (((140 - age\,(years)) \times weight\,(kg)/ 72 \times creatinine\,(mg/dL)))) \times 0.85\ (if\ female)$$

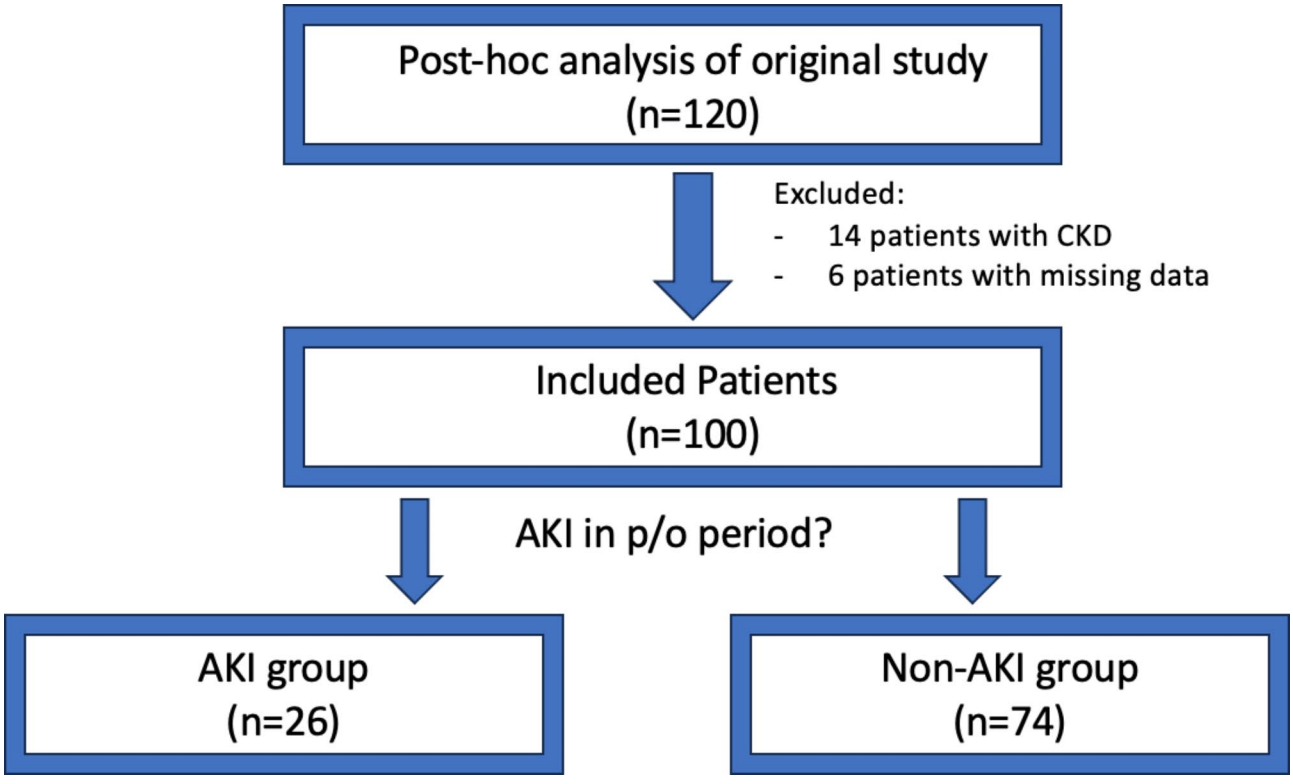

Fig. 1 Flow chart of inclusion criteria

The analyzed data included preoperative data such as demographic values, comorbidities, lab parameters (creatinine, urea, bilirubin, and albumin), and ECHO-CG data (left ventricle ejection fraction (LV EF)). Intraoperative data were also examined, such as fluid balance, intraoperative diuresis, indicators of blood oxygen transport function, need for blood products, duration of anesthesia and CPB, need for diuretics, and inotropic support. Early postoperative data such as biochemical parameters were analyzed as well. The primary outcome was AKI according to the KDIGO criteria, while the secondary outcomes were the lengths of stay in the ICU and overall hospital stay. The key determinant for AKI classification was increases in the creatinine level within the first 48 h postsurgery by more than 1.5-fold or 0.3 mg/dl compared to the initial level.

The data monitored during operations included electrocardiograms, invasive arterial and central venous pressure, oxygen saturation, end-tidal carbon dioxide pressure, end-tidal sevoflurane concentration, nasopharyngeal temperature, and urine output. Furthermore, anesthesia depth was measured using the bispectral index (BIS) in both groups (BIS-Vista monitor, Aspect Medical Systems, Newton, MA). We adjusted the sevoflurane dose to between 1.5 and 2.5 vol% to maintain BIS values within the range of 40–60. The sevoflurane was administered through the oxygenator circuit during CPB via a calibrated vaporizer.

Mechanical ventilation was administered intraoperatively (Dräger Medical Deutschland GmbH, Lübeck, Germany) using a value of FiO_2 of 0.5, and a pCO_2 level of 35–40 mmHg was maintained according to the arterial blood gas analysis. All patients underwent CPB using the System 1 Heart-Lung Machine (HLM) (Terumo, USA), as well as Inspire 6 and Inspire 8 F disposable membrane oxygenators (Sorin Group, Italy) during moderate hypothermia (+32 °C). Before CPB, each patient received heparin intravenously (300 IU/kg body weight) to attain an activated clotting time (ACT) exceeding 480 s. ACT was monitored every 30 min throughout CPB.

After CPB, protamine sulfate was administered to neutralize the anticoagulation effects of heparin. The initial priming volume comprised 500 mL of 4% gelaspan solution (B. Braun Medical SA. Switzerland), 100 mL of 4.2% sodium bicarbonate solution, 300 mL of 0.9% sodium chloride solution, and 100 mL of 15% mannitol solution. If the hemoglobin level fell below 7.0 g/dL, a red blood cell (RBC) transfusion was performed during CPB [7]. Oxygen delivery (DO_2) during CPB was calculated and sustained at more than 272 mL O_2/min/m^2:

$$DO_2 = 1.34 * Hb * BF * SaO_2/BSA$$

where DO_2 is the delivered oxygen, Hb is the hemoglobin level, BF is the blood flow, and BSA is the body surface area. The pump flow was regulated according to the DO_2 calculation.

The intraoperative myocardial protection strategy involved intermittent cross-clamp fibrillation under moderate hypothermia, which is the method accepted by the Heart Institute Ministry of Health of Ukraine. Fibrillation was electrically induced using a fibrillator (Fi 20 M, Stockert GmbH) with a low-voltage generator operating at a frequency of 50 Hz, voltage of 12 volts, and current of 25 mA. Each aorta-clamping session lasted no more than 15 min and was followed by a minimum interval of 5 min before the next session.

Statistical analysis

The results are presented as the mean ± standard deviation. For non-normally distributed results, the data are reported as the median (*Me*) along with the first (*Q25*) and third (*Q75*) quartiles (*Me* (*Q25*; *Q75*)). When data had a normal distribution, their statistical significance was evaluated using Student's *t*-test. When data did not have a normal distribution, the Mann–Whitney U-test was applied.

Univariate analysis was performed using an unpaired *t*-test to compare measurement data, and Pearson's chi-squared test or Fisher's exact test was used to compare enumeration data to assess statistically significant risk factors for AKI. Results with $p<0.05$ were then subjected to a logistic regression analysis to identify independent risk factors for AKI. The occurrence of AKI was the independent variable, while variables with $p<0.05$ in the univariate analysis were dependent variables. A difference was deemed significant in cases of $p<0.05$. The data analysis was conducted using the software SPSS Statistics version 27 (IBM, Armonk, NYC, US).

Results

After the exclusion of 20 patients (Fig. 1), data from 100 patients were analyzed. The most common comorbidities were hypertension (84.0%), a history of myocardial infarction (57%), and diabetes (30.0%). All surgeries (100%) were classified as planned. During the first two postoperative days, AKI occurred in 26 (26%) patients, including first-stage AKI in 15 patients, second-stage AKI in 8 patients, and third-stage AKI in 3 patients.

The univariate analysis revealed that preoperatively, patients who developed post-operative AKI had significantly higher EuroSCORE II values (2.00 ± 0.98% vs. 1.49 ± 0.74%, $p=0.006$) and higher initial levels of urea (7.62 ± 2.94 mmol/l vs. 6.12 ± 1.71 mmol/l, $p=0.002$), creatinine (0.108 ± 0.385 mmol/l vs. 0.091 ± 0.016 mmol/l, $p=0.003$), and GFR (91.5 ± 23.6 vs. 78.3 ± 16.4, $p=0.011$) (Table 1). Initial albumin levels below 40 g/l (9 (34.6%)

Table 1 Univariate analysis of preoperative demographic and clinical characteristics

Variance	AKI group (*n* = 26)	Non-AKI group (*n* = 74)	*p*
Age, years	64 (60.3; 68.5)	63 (58.0; 68.75)	0.279
Male sex, *n* (%)	23 (88.5%)	62 (83.8%)	0.753
Body mass, kg	84.1 ± 14.9	84.5 ± 13.9	0.860
Body mass index, kg/m^2	28.7 ± 4.74	28.8 ± 4.01	0.934
NYHA fc, *n* (%)			
- II	3 (11.5%)	8 (10.8%)	0.901
- III	19 (73.1%)	59 (79.7%)	0.582
- IV	4 (15.4%)	7 (9.50%)	0.469
EuroSCORE II, %	2.00 ± 0.98	1.49 ± 0.74	0.006
MI, *n* (%)	14 (53.8%)	43 (58.1%)	0.705
PCI, *n* (%)	3 (11.5%)	13 (17.6%)	0.552
AH, *n* (%)	24 (92.3%)	60 (81.1%)	0.227
DM, *n* (%)	7 (26.9%)	23 (31.3%)	0.806
LV EF, %	50.3 ± 10.4	53.1 ± 9.04	0.102
LV ESV, ml	76.1 ± 39.5	69.2 ± 27.7	0.138
LV EDV, ml	141.2 ± 49.9	126.8 ± 31.8	0.093
Hemoglobin, g/l	137.8 ± 13.2	146.6 ± 13.6	0.005
Bilirubin, µmol/l	14.7 ± 7.24	13.8 ± 5.59	0.522
Urea, mmol/l	7.62 ± 2.94	6.12 ± 1.71	0.002
Creatinine, mmol/l	0.108 ± 0.039	0.091 ± 0.016	0.003
GFR, mL/min/1.73 m^2	91.5 ± 23.6	78.3 ± 16.4	0.011
Albumin, g/l	41.6 ± 4.00	43.1 ± 3.72	0.084
< 40 g/l, *n* (%)	9 (34.6%)	11 (14.9%)	0.030

Notes. NYHA f.c. – functional class according to the New York Heart Association, MI – myocardial infarction, PCI – percutaneous coronary intervention, AH – arterial hypertension, DM – diabetes mellitus, LV EF – left ventricular ejection fraction, LV EDV – end-diastolic volume of the left ventricle, LV ESV – end-systolic volume of the left ventricle

vs. 11 (14.9%) cases, $p=0.030$) and lower initial hemoglobin levels (137.8±13.2 g/l vs. 146.6±13.6 g/l, $p=0.005$) occurred more often in patients with AKI compared to those without AKI.

During the intraoperative period, patients with AKI had significantly lower hemoglobin levels during CPB compared to those without postoperative AKI (92.0±11.4 g/l vs. 98.5±13.5 g/l, $p=0.030$) (Table 2). Additionally, this group had a lower minimum DO_2 (295.9±36.6 ml O_2/min/m^2 vs. 316.8±43.5 ml O_2/ min/m^2, $p=0.030$). There was also a higher rate of RBC transfusion among patients with AKI (20 (76.8%) vs. 31 (41.9%), $p=0.028$). No significant difference was observed in intraoperative blood gas analysis between patients with and without AKI except for the hemoglobin level throughout all surgical stages (Table 3). The dynamics of the biochemical parameters are shown in Table 4.

There was no significant difference in the ICU stay length between patients with and without AKI (2.80±1.44 days vs. 2.51±0.55 days, $p=0.142$) (Fig. 2). However, the total length of hospital stay for patients with AKI was notably longer (14.3±5.45 days vs. 12.6±3.05 days, $p=0.048$) (Fig. 3). The logistic regression

Table 2 Univariate analysis of intraoperative characteristics

Variance	AKI group (*n* = 26)	Non-AKI group (*n* = 74)	*p*
Duration of CBP, min	87.1 ± 24.2	81.5 ± 19.9	0.251
Aorta XCL, min	24.8 ± 7.14	23.1 ± 9.24	0.415
Duration of surgery, min	182.6 ± 34.9	167.2 ± 42.1	0.054
Duration of anesthesia, min	207.3 ± 33.3	193.3 ± 36.9	0.091
Number of anastomoses, *n* (%)			
- 2	7 (26.9%)	21 (28.4%)	0.983
- 3	19 (73.1%)	53 (71.6%)	
Protocol of anesthesia, *n* (%)			
- MLOP	15 (57.7%)	33 (44.6%)	0.250
- ROP	11 (42.3%)	41 (55.4%)	
Minimum MAP, mmHg	61.5 ± 7.20	61.4 ± 7.28	0.905
MAP < 50 mmHg for > 5 min, *n* (%)	4 (15.4%)	6 (8.10%)	0.208
Minimum DO_2, O_2 /min/m^2	295.9 ± 36.6	316.8 ± 43.5	0.030
< 272 ml O_2 /min/m^2, *n* (%)	7 (26.9%)	8 (10.8%)	0.060
Need of RBC transfusion, *n* of units (%)			
- 0	6 (23.1%)	43 (58.1%)	0.003
- 1	15 (57.7%)	25 (33.8%)	0.946
- 2 or more	5 (19.2%)	6 (8.10%)	
ml	396.3 ± 135.9	393.6 ± 134.8	
Need of FFP, ml	548.1 ± 142.7 (26/26)	525.2 ± 109.9 (73/74)	0.403
Urine output, ml/kg/hour	6.30 ± 1.98	6.60 ± 2.46	0.569
Ultrafiltration, *n* (%)	1 (3.85%)	0 (0.00%)	0.245
Fluid balance during surgery, ml	305 (-115;635)	25.0 (-139;537.5)	0.499
- positive, *n* (%)	40	16	
Diuretic during surgery			
- Furosemide, *n* (%)	22 (84.6%)	4 4 (59.5%)	0.0
- Torasemide, *n* (%)	3 (11.5%)	16 (21.6%)	29
			0.385
Inotropic support			
- Norepinephrine, *n* (%)	23 (88.5%)	55 (74.3%)	0.174
- Dobutamine, *n* (%)	20 (76.9%)	57 (77.0%)	0.974

Notes. CPB – cardiopulmonary bypass, DO_2 – delivery of oxygen, XCL – cross-clamping, MAP – mean arterial pressure, MLOP – multimodal low-opioid protocol, ROP – routine-opioid protocol, RBC – red blood cells, FFP – fresh frozen plasma

revealed that DO_2 during CPB was the only factor associated with developing AKI in the early postoperative phase (Table 5).

Discussion

According to the main findings of this study, patients who develop AKI postoperatively are characterized by an elevated EuroSCORE II, reduced baseline hemoglobin, and increased baseline creatinine and urea levels. Less commonly, albumin levels under 40 g/L also occur. Moreover, patients who develop AKI demonstrated lower DO_2 during CPB and increased requirements for RBC transfusion and furosemide. DO_2 during CPB was identified as the

Table 3 Analysis of indicators of acid-base status and blood gases

Variance		AKI group (*n* = 26)	Non-AKI group (*n* = 74)	*p*
pH	Surgery beginning	7.40 ± 0.06	7.40 ± 0.07	0.861
	CPB	7.36 ± 0.05	7.38 ± 0.06	0.314
	End of CPB	7.39 ± 0.06	7.40 ± 0.06	0.346
pO2, mmHg	Surgery beginning	275.6 ± 88.7	269.9 ± 85.2	0.768
	CPB	227.5 ± 101.4	201.5 ± 63.9	0.164
	End of CPB	236.6 ± 75.1	247.8 ± 69.1	0.486
$pCO_{2,}$ mmHg	Surgery beginning	31.8 ± 4.12	34.0 ± 4.98	0.161
	CPB	37.9 ± 5.34	37.9 ± 5.41	0.949
	End of CPB	33.4 ± 3.92	33.8 ± 5.00	0.684
Hb, g/l	Surgery beginning	118.9 ± 13.6	125.8 ± 14.8	0.040
	CPB	92.0 ± 11.4	98.5 ± 13.5	0.030
	End of CPB	94.7 ± 12.6	103.4 ± 15.4	0.012
Glucose, mmol/l	Surgery beginning	6.44 ± 1.86	6.57 ± 2.05	0.777
	CPB	6.53 ± 1.27	6.72 ± 1.97	0.653
	End of CPB	7.56 ± 2.00	7.76 ± 2.27	0.704
Lactate, mmol/l	Surgery beginning	0.86 ± 0.38	1.12 ± 0.87	0.153
	CPB	1.24 ± 1.14	1.21 ± 0.67	0.868
	End of CPB	1.59 ± 0.68	1.71 ± 1.36	0.673
cBase (Efc), mmol/l	Surgery beginning	-2.80 (-5.68; -0.85)	-2.60 (-4.00; -0.70)	0.283
	CPB	-1.35 (-3, 30; −0.10)	-1.15 (-3, 28; −1.32)	0.651
	End of CPB	-2.40 (-6.15;0.55)	-2.00 (-4.10;1.13)	0.232
$cHCO_3^-$(P, st), mmol/l	Surgery beginning	21.6 ± 2.62	22.6 ± 2.67	0.177
	CPB	22.3 ± 2.66	23.05 ± 2.65	0.235
	End of CPB	22.2 ± 2.78	22.7 ± 2.50	0.358

Notes. CPB – cardiopulmonary bypass

only factor for postoperative AKI in the logistic multivariate analysis.

Table 4 Analysis of dynamics of biochemical indicators

Variance		AKI group (*n* = 26)	Non-AKI group (*n* = 74)	*p*
Bilirubin, μ mol/l	Initial	14.7 ± 7.24	13.8 ± 5.59	0.522
	0 days	19.4 ± 11.3	16.8 ± 8.50	0.223
	1 day	17.6 ± 8.89	17.9 ± 13.5	0.888
	2 days	18.2 ± 6.39	16.1 ± 6.80	0.175
	Discharge	13.3 ± 5.02	11.7 ± 3.96	0.093
Urea, mmol/l	Initial	7.62 ± 2.94	6.12 ± 1.71	0.002
	0 days	8.23 ± 2.50	5.95 ± 1.68	0.0001
	1 day	9.94 ± 3.25	6.13 ± 2.03	0.0001
	2 days	12.4 ± 3.38	7.96 ± 2.71	0.0001
	Discharge	11.9 ± 6.29	7.36 ± 2.49	0.0001
Creatinine, mmol/l	Initial	0.108 ± 0.038	0.091 ± 0.016	0.003
	0 days	0.131 ± 0.041	0.095 ± 0.017	0.0001
	1 day	0.152 ± 0.054	0.092 ± 0.019	0.0001
	2 days	0.154 ± 0.061	0.090 ± 0.020	0.0001
	Discharge	0.135 ± 0.064	0.087 ± 0.017	0.0001
Albumin, g/l	Initial	41.6 ± 4.00	43.1 ± 3.72	0.084
	0 days	34.5 ± 3.79	34.8 ± 4.07	0.736
	1 day	34.1 ± 2.85	33.9 ± 3.62	0.772
	2 days	34.0 ± 4.36	34.1 ± 3.89	0.955
	Discharge	36.6 ± 3.11	36.4 ± 3.70	0.666
Hemoglobin, g/l	Initial	137.8 ± 13.2	146.6 ± 13.6	0.005
	0 days	113.9 ± 12.9	120.9 ± 17.7	0.067
	1 day	114.5 ± 8.49	116.8 ± 13.2	0.410
	2 days	117.0 ± 13.3	117.5 ± 15.7	0.883
	Discharge	124.2 ± 11.8	122.5 ± 15.9	0.818

A large international multicenter study examined patients who underwent major cardiac and non-cardiac surgery and reported that 1 in 10 patients developed acute kidney disease (AKD) by 7 days post-surgery [8]. Furthermore, early postoperative AKI had a strong correlation with subsequent AKD after 7 days, irrespective of

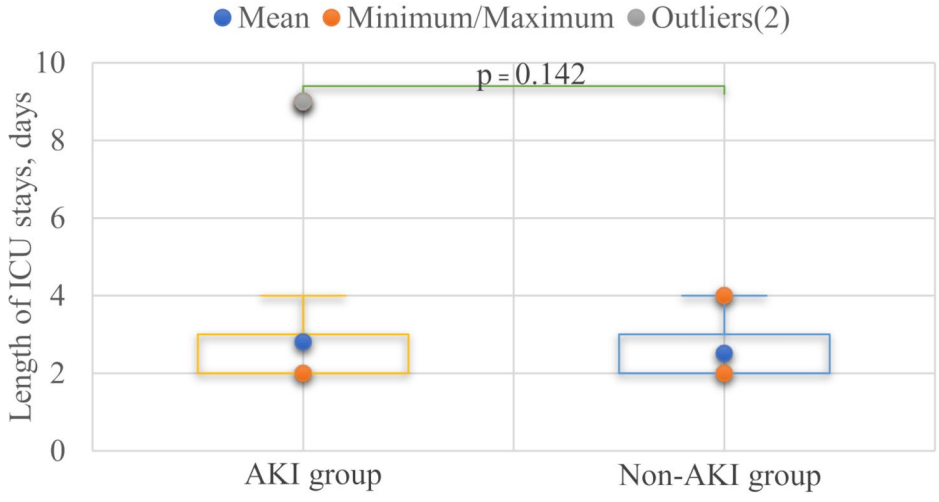

Fig. 2 Length of ICU stay after CABG in days

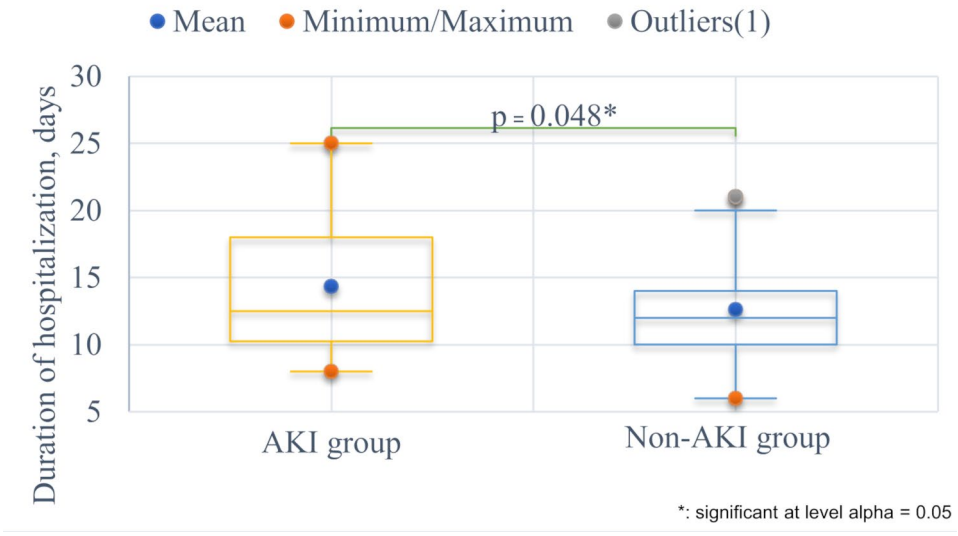

Fig. 3 Duration of hospital stay after CABG in days

Table 5 Logistic analysis of the development of acute kidney injury in the early postoperative period

Variables	Odds ratio	95% CI	*p*-value
EuroSCORE II, %	1.31	0.60–2.89	0.491
Hemoglobin, g/dl	0.97	0.91–1.03	0.334
Urea, mmol/l	1.14	0.81–1.61	0.447
Creatinine, mmol/l	1.02	0.99–1.06	0.128
GFR, mmol/l	1.05	0.97–1.13	0.083
Albumin < 40 g/l, yes/no	1.16	0.22–5.95	0.856
LV EF, %	1.13	0.99–1.30	0.070
LV EDV, ml	0.99	0.94–1.05	0.924
LV ESV, ml	1.04	0.97–1.12	0.276
Minimum DO_2, mlO_2 /m^2 /min	**1.75**	**0.99–3.07**	**0.047**
Need of RBC transfusion, units	0.30	0.06–1.42	0.129
Using Furosemide, yes/no	0.25	0.05–1.30	0.097
Duration of surgery, min	1.06	0.99–1.14	0.079
Duration of anesthesia, min	0.96	0.90–1.01	0.155

Notes. GFR – glomerular filtration rate, LV EF – left ventricular ejection fraction, LV EDV – end-diastolic volume of the left ventricle, LV ESV – end-systolic volume of the left ventricle, DO_2 – delivery of oxygen, RBC – red blood cell, CI – confidence interval

all other potential risk factors. These results are contrary to the present results. In our cohort, 1 in 4 patients suffered from AKI in the postoperative period. In general, our findings are impacted by distinct features of cardiac surgery, such as CPB, aorta cross-clamping, extensive blood product transfusion, and high vasopressor doses, which heighten the risk of AKI relative to non-cardiac surgery. These elements interfere with the renal blood flow, trigger periods of profound ischemia and sudden reperfusion, amplify oxidative harm, elevate renal and systemic inflammation, and thus promote the development of AKI [9].

Palomba et al. [10] developed a predictive score for acute kidney injury following cardiac surgery (AKICS) and reported an AKI incidence of 14%. The used a broad definition of AKI based on oliguria or the need for dialysis. Their morbidity criteria included low cardiac output, prolonged ventilatory support, and neurological complications. Their scoring system considers age greater than 65 years, a pre-operative creatinine level above 1.2 mg/dl, a pre-operative capillary glucose level above 140 mg/dl, heart failure, combined surgeries, CPB duration greater than 2 h, low cardiac output, and low central venous pressure. The AKICS score demonstrated impressive calibration and discrimination in both the initial study group and a subsequent validation dataset.

Yue et al. reported a similar incidence of AKI at 27.9% (151 cases) in another study including 541 patients [11]. Li et al. [12] demonstrated quite similar prevalence of AKI after cardiac surgery of 24.17%, and 0.53% of these patients required dialysis. Factors identified as independent predictors in the derivation cohort by multivariable logistic regression analysis included age ≥ 70 years, body mass index ≥ 25 kg/m^2, estimated GFR ≤ 60 mL/min per 1.73 m^2, ejection fraction ≤ 45%, utilization of adrenaline and statins, implantation of an intra-aortic balloon pump, postoperative low-cardiac-output syndrome, reoperation due to bleeding, and RBC transfusion. Peng et al. [13] developed a predictive model based on an elderly Chinese population of 2,155 patients, which had high prediction accuracy for AKI post-surgery among elderly patients.

Our results indicated an AKI incidence of 26%. We carried out a post-hoc analysis based on a primary study that compared the efficacy of two anesthesia protocols for on-pump CABG: a multimodal low-opioid protocol and a standard anesthesia protocol [5]. The results showed no differences in AKI rates between the two anesthesia

protocols, which differed in the use of the alpha-blocker dexmedetomidine for low-opioid anesthesia. This result is opposite to that of a meta-analysis of 16 studies involving 2148 patients performed by Liu X et al. [14], where intraoperative dexmedetomidine infusion was linked to a significant reduction in AKI incidence (odds ratio (OR) 0.47; 95% confidence interval (CI) 0.36–0.61; $p<0.00001$; I2 = 26%).

A low serum albumin level is a critical factor in AKI development during the early postoperative period. Two meta-analyses of observational studies showed that for each 10-g/l reduction in serum albumin, the likelihood of AKI rises by 134% [15, 16]. Our univariate analysis revealed a significantly higher frequency of albumin levels below 40 g/l in patients with AKI. However, logistic analysis indicated that this parameter is modifiable before elective surgery. Consequently, the albumin level ranged from 32.1 to 53.7 g/l. According to Zamlauski-Tucker and Cohen, the critical serum albumin level that results in a decrease of GFR is less than 30 g/l [17].

Several studies suggest that a low initial hemoglobin level is linked to the development of AKI [18, 19]. Specifically, a multivariate regression analysis by Oprea et al. [20] revealed that for every 1-g/dL increase in preoperative hemoglobin concentration, the risk of postoperative AKI rises by 11% (OR 1.11; 95% CI, 1.08–1.13; $p<0.001$). In our study, patients with AKI had lower preoperative hemoglobin levels. However, this observation was only found in the univariate analysis, and the logistic regression analysis did not indicate a reliable correlation as a modifiable factor before elective surgery.

In the logistic regression, the minimum DO_2 value during CPB (ranging from 263 to 402 ml/min/m^2) significantly affected the onset of AKI. This aligns with the outcomes from many retrospective studies underscoring the relationship between the lowest DO_2 level during CPB and the later occurrence of AKI post-surgery [21–24]. According to these studies, the critical DO_2 threshold for patients subjected to moderate hypothermia (>32 °C) was identified as 260 to 272 ml/min/m^2. Furthermore, a multiple regression analysis performed by Rasmussen et al. confirmed, that a DO_2 level of less than 272 mL/min/m^2 persisting for more than 30 min was independently linked to AKI [25].

Lannemyr et al. showed that renal DO_2 during CBP decreases by 20% due to hemodilution and vasoconstriction. However, the GFR and renal oxygen consumption stay constant, while the renal oxygen extraction climbs to 45%. This suggests an imbalance between the renal oxygen demand and supply [26]. Moreover, due to its distinctive blood supply, the kidney's medulla experiences hypoxia in cases of escalating acute anemia earlier than the heart or gastrointestinal tract. This early onset of hypoxia contributes to the development of acute kidney damage [27].

In our cohort, DO_2 dropping below 272 mL/min/m^2 during CPB persisted no longer than 5 min. This was addressed by enhancing HLM performance when hemoglobin levels were above 70 g/l, performing RBC transfusion when hemoglobin levels were below 70 g/l, or performing ultrafiltration (in one case). Thus, it is important to calculate and maintain DO_2 at a proper level during CPB to prevent AKI development in each case, even for patients with low risk.

Several AKI-predicting scores have not been validated externally and include older AKI definitions or were validated in only specific surgical subspecialties [28]. These include the Cleveland Clinic score (area under the receiver operating characteristics curve (AUC): 0.86), the Mehta score (AUC: 0.81), and the Simplified Renal Index (AUC: 0.89) [29–31]. Despite high AUCs, the scores are not widely used in clinical practice. The main limitation of these models is the use of data obtained at static intervals to predict outcomes affected by multimodal dynamic parameters during the perioperative period [32].

This study has both strengths and limitations. It was a single-center study involving a post-hoc analysis of a small cohort that was biased by various cardiac surgeons performing the CABG surgeries. As the study population was not exceptionally large, many subgroups may not have been sufficient to prove statistical significance. Furthermore, due to our hospital protocol, we were not able to record creatinine levels at day 7 after on-pump CABG. However, the analysis included CABG patients with EuroSCORE risk up to 5% to determine AKI risk factors in a homogeneous population, which should be recognized as a strength compared to other studies. The CPB duration was similar across the cohort and is a well-recognized risk factor in cardiac surgery.

Conclusion

This study has identified risk factors for AKI in a cohort after cardiac surgery and CABG. The identified factors included a higher EuroSCORE II, lower baseline hemoglobin, increased baseline levels of creatinine and urea, infrequent albumin levels below 40 g/L, decreased DO_2 during CPB, and an increased need for RBC transfusion and furosemide. Better understanding of these factors may improve postoperative outcomes of patients undergoing on-pump CABG.

Abbreviations

AH	Arterial hypertension
CPB	Cardiopulmonary bypass
DM	Diabetes mellitus
DO_2	Delivery of oxygen
FFP	Fresh frozen plasma
LV EDV	End-diastolic volume of the left ventricle
LV EF	Left ventricular ejection fraction

LV ESV	End-systolic volume of the left ventricle
MAP	Mean arterial pressure
MI	Myocardial infarction
MLOP	Multimodal low-opioid protocol
NYHA f.c.	Functional class according to the New York Heart Association
PCI	Percutaneous coronary intervention
RBC	Red blood cells
ROP	Routine-opioid protocol
XCL	Cross-clamping

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Author contributions
S.M. collected data, S.M., O.L. and Y.S. wrote the main manuscript text and B.T. made concept and design. All authors reviewed the manuscript.

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Data availability
The data that support the findings of this study are available on request from the corresponding author, Maruniak S.R. upon reasonable request.

Declarations

Ethics approval and consent to participate
This retrospective study was approved by the Ethics Committee of P.L. Shupyk National Health Care University of Ukraine (Protocol No. 10, November 5, 2018). Each patient signed informed consent forms to participate in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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