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Is cystatin C a good predictor of acute kidney injury after elective aortic surgery?

Da li je cistatin C dobar prediktor akutne bubrežne slabosti nastale posle elektivne operacije aorte?

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Abstract

Background/Aim. Acute kidney injury (AKI) is a frequent and serious complication after aortic surgery, which increases the length of hospital stay, costs, morbidity, and mortality. The aim of the study was to investigate the incidence of AKI and the most important preoperative and intraoperative predictive factors for AKI 72 hrs after elective infrarenal aortic surgery (IAS). **Methods.** This prospective observational study was performed at the Clinic of Anesthesia, Intensive Care and Pain Therapy, University Clinical Center of Vojvodina (UCCV), from October 2017 to April 2019. It included 140 adult patients who underwent an elective IAS. The occurrence of AKI was noted according to the Acute Kidney Injury Network (AKIN) criteria. A multivariate logistic regression model was used for potential predictive factors. **Results.** The incidence of AKI after the elective IAS at the Clinic of Anesthesia, Intensive Care and Pain Therapy, UCCV, was 28.56%. According to the receiver operating characteristic (ROC) curve analysis, the cut-off value of cystatin C serum concentration of 1.14 mg/L had the highest sensitivity (82.5%) and specificity (76%) in the differentiation of patients who will develop AKI. The final model contained the following variables: the presence of chronic kidney disease, the preoperative serum concentration of cystatin C > 1.14 mg/L, the application of colloid solutions in volume > 500 mL during the operation, and the total intravascular fluid replacement volume > 59 mL/kg in the intraoperative period. **Conclusion.** The incidence of AKI at the Clinic of Anesthesia, Intensive Care and Pain Therapy, UCCV, is somewhat higher compared to the literature data. A presurgical value of cystatin C above 1.14 mg/L is a good predictor of AKI after the elective IAS.

Key words:
aorta; cystatin c; elective surgical procedures; kidney failure, acute; prognosis; sensitivity and specificity.

Apstrakt

Uvod/Cilj. Akutno bubrežno oštećenje (ABO) je česta i ozbiljna komplikacija koja produžava i poskupljuje bolničko lečenje i povećava morbiditet i mortalitet bolesnika nakon hirurške rekonstrukcije abdominalne aorte. Cilj rada bio je da se utvrde incidenca ABO i najznačajniji preoperativni i intraoperativni prediktivni faktori od nastanka ABO 72 sata nakon elektivnih operacija na infrarenalnom segmentu aorte (ISA). **Metode.** Na Klinici za anesteziju, intenzivnu terapiju i terapiju bola Kliničkog centra Vojvodine (KCV) sprovedeno je prospektivno opservaciono istraživanje od oktobra 2017. do aprila 2019. godine. U istraživanje je bilo uključeno 140 bolesnika koji su bili podvrgnuti elektivnom operativnom zahvatu na ISA. Nastanak ABO je potvrđivan na osnovu kriterijuma *Acute Kidney Injury Network* (AKIN) klasifikacionog sistema. Za dobijanje modela predikcije primenjena je multivarijantna logistička regresija. **Rezultati.** Incidenca ABO nakon elektivnih operacija na ISA na Klinici za anesteziju, intenzivnu terapiju i terapiju bola KCV iznosila je 28,56%. Prema analizi *receiver operating characteristic* (ROC) krive, granična vrednost koncentracije cistatina C od 1,14 mg/L imala je najvišu senzitivnost (82,5%) i specifičnost (76%) u diferenciranju bolesnika koji će razviti ABO. Finalni model predikcije ABO nakon elektivnih operacija na ISA sadržao je sledeće faktore: prisustvo hronične bubrežne slabosti, preoperativnu koncentraciju cistatina u serumu C > 1,14 mg/L, primenu koloida u volumenu > 500 mL u toku operacije i ukupni volumen nadoknade u intraoperativnom periodu > 59 mL/kg. **Zaključak.** Incidenca ABO nakon elektivnih operacija na ISA na Klinici za anesteziju, intenzivnu terapiju i terapiju bola KCV je nešto viša u odnosu na podatke iz literature. Preoperativna vrednost cistatina C iznad 1,14 mg/L je dobar prediktor ABO nakon elektivnih operacija na ISA.

Ključne reči:
aorta; cistatin c; hirurgija, elektivna, procedure; bubreg, akutna insuficijencija; prognoza; senzitivnost i specifičnost.

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Introduction

Acute kidney injury (AKI) is a common and severe complication after surgical reconstruction of the abdominal aorta. It prolongs and increases the cost of hospital stay and increases the morbidity and mortality of patients [1, 2]. Earlier diagnosis, monitoring, and earlier initiation of renal replacement therapy (RRT) significantly reduces patient mortality [3, 4].

Due to many AKI definitions, comparing the results of different studies is difficult. The incidence of AKI after elective abdominal aortic aneurysm (AAA) surgery varies from 1–28% depending on the study and the criteria used. AKI is an independent predictor of mortality [5].

Many preoperative and intraoperative factors can influence AKI's occurrence after abdominal aortic surgery. Therefore, it is crucial to understand AKI's risk and the tendency to alter perioperative approaches to prevent or minimize AKI [6].

One of the most important factors for the onset and outcomes of AKI is the patient's renal reserve prior to surgery. Preoperative chronic kidney disease (CKD), measured using serum creatinine (SCr), is associated with a higher risk of AKI following aortic surgery [7, 8].

Cystatin C (CyC) is a 13-kD cysteine protease inhibitor synthesized in all nucleated cells at a steady state. It is freely filtered by the glomerulus, not secreted by renal tubules, and completely metabolized at the level of the renal tubules. These properties have made it an attractive marker of the glomerular filtration rate (GFR) in CKD [9–11].

Factors such as surgical trauma and hemodynamic and humoral changes during and after aortic cross-clamping have been shown to induce ischemia-reperfusion changes and systemic inflammatory response syndrome (SIRS) after aortic surgery [5, 12–13].

Fewer studies about AKI after elective surgery on the infrarenal segment of the aorta have been conducted worldwide.

The aim of this study was to investigate the incidence of AKI and the most essential preoperative and intraoperative predictive factors for AKI.

Methods

This prospective observational study was performed at the Clinic of Anesthesia, Intensive Care and Pain Therapy, University Clinical Center of Vojvodina (UCCV), for 18 months, from October 2017 to April 2019. The study was approved by the Ethics Committee of the UCCV (00-15/34, from February 02, 2017), and all the subjects signed informed consent. The study sample included 140 adult patients who underwent elective infrarenal aortic surgery, with the American Society of Anesthesiologists (ASA) physical status scores of I-III, without CKD or with CKD stage 1 or stage 2. Patients who had to be reoperated and who developed sepsis in the postoperative period of 72 hrs were excluded from the study.

Potential predictive factors, such as patient history, anesthesia lists, daily therapeutic lists, vital parameters, and laboratory values lists, were identified from the medical records. The occurrence of AKI was noted according to the Acute Kidney Injury Network (AKIN) criteria.

During the postoperative 72-hour treatment period, attention was paid to the time and degree of AKI onset and many other significant parameters during the treatment of the patient.

Preoperative period

During the preanesthetic visit, the patients recruited to the study signed informed consent. Relevant anamnestic data were taken, along with necessary medical history and laboratory data obtained by standard measurements and recorded in the research protocol. The following data were obtained: age, gender, diagnosis, body mass, body height, body mass index (BMI), ASA patient status, chronic diseases [the presence of CKD and its stage; cardiovascular diseases (CVD): documented hypertension, ischemic heart disease, myocardial infarction or valvular heart disease; documented diabetes mellitus, type 1 or 2 (fasting plasma glucose $\geq$ 7.0 mmol/L or venous plasma glucose 2 hrs after ingestion of 75 g oral glucose load $\geq$ 11.1 mmol/L); documented chronic obstructive pulmonary diseases (COPD): chronic bronchitis or emphysema (abnormalities in the small airways of the lung lead to limitation of airflow in and out of the lungs); documented previous cerebrovascular stroke, ischemic or hemorrhagic (a focal or global disorder of brain function that occurs suddenly, and is a consequence of cerebral circulation disorder or a condition in which blood flow is insufficient to meet the metabolic needs of neurons for oxygen and glucose); documented hypothyroidism (which is proven by low level of serum thyroxine and high level of thyroid-stimulating hormone); chronic drug therapy (with emphasis on nephrotoxic drugs: nonsteroidal anti-inflammatory drugs, angiotensin converting enzyme inhibitors, angiotensin receptor inhibitors, diuretics, proton pump inhibitors, H2 inhibitors); pernicious habits (smoking, alcoholism); information on common values of arterial blood pressure; laboratory values of blood urea nitrogen (BUN), creatinine, CyC, glucose in blood].

Creatinine clearance (ClCr) was calculated using the Cockcroft-Gault formula: ClCr, mL/min = [(140 – age, years) × body weight, kg] / 0.814 × SCr, μmol/L × 0.85 (for female) and GFR by plasma concentration of CyC, GFR CyC, mL/min (CKD-EPI CyC Equation-2012).

Intraoperative period

All patients received general balanced endotracheal anesthesia, with standard monitoring for these types of operations: continuous electrocardiography, noninvasive measurement of arterial blood pressure, invasive measurement of arterial blood pressure (arterial cannula placed in the radial artery), measurement of central venous pressure (central venous catheter placed via internal jugular or subclavian vein), pulse oximetry, capnometry, and measurement of urine output. During the surgery, controlled mechanical ventilation with positive end-expiratory pressure (PEEP) of 3–5 mmHg

was performed with FiO_2 50% to achieve normocapnia. The patients were actively warmed during the surgery. The main aim was to maintain hemodynamic parameters within 20% of their basal values.

The following parameters were recorded in the research protocol: the duration of operation, the duration of aortic cross-clamping, blood loss volume, hourly and total diuresis, the amount and type of intravenous fluid given, the amount of autologous blood volume given, the amount and type of heterologous blood products given, the duration of episodes of hypotension when median arterial pressure (MAP) < 65 mmHg, use of vasopressors, diuretics, the minimal value of central venous pressure, PEEP value, the laboratory data from gas analysis of arterial and central vein blood [blood lactate level, acid-base status: pH, base excess (BE), blood glucose concentration, the saturation of central venous blood].

Postoperative period

After the surgery, the patients were sedated, intubated, and placed in the intensive care unit according to the procedure for transporting patients from the operating block and treated according to all the principles of intensive care. Within 72 hrs after surgery, attention was paid to the course of treatment, the time of onset of AKI, its degree, and the eventual initiation of RRT. The following parameters were monitored daily: hourly and total diuresis, the use of vasoactive drugs, the use of diuretics, the number of hrs when arterial pressure was lower than normal preoperative pressure, number of hrs when MAP < 65 mmHg, laboratory data: BUN, blood creatinine, CyC, and glucose concentration, the concentration of electrolytes in blood (sodium, potassium, chlorine, magnesium), blood lactate level, acid-base status: pH, base excess (BE).

Acute Physiology and Chronic Health Evaluation (APACHE) II score on the first day and the Sequential Organ Failure Assessment (SOFA) score, ClCr, and GFR using plasma CyC (GFR CyC) concentrations were calculated for all three days.

BN ProSpect plasma protein analyzer – Siemens Healthineers Global, was used to measure CyC concentration (the method was nephelometric immunoassay: particle enhanced nephelometric immunoassay – PENIA), while serum creatinine was measured by Jaffe reaction.

Statistical analysis

Arithmetic means with standard deviation or median with the range including minimum and maximum values were used to describe the continuous numerical characteristics as a measure of central tendency. The estimation of the normality of continuous variables distribution was performed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Categorical variables were described using absolute and relative numbers.

Depending on the type and the normality of the distribution of variables, the differences between the studied groups were compared using appropriate parametric and non-parametric tests.

For the AKI development prediction model, all independent factors (variables) of preoperative and intraoperative status whose statistical significance was $p < 0.05$ were analyzed. To improve the clinical utility of the results obtained, continuous variables were transformed into dichotomous ones based on the maximum sum of sensitivity and specificity estimated by the receiver operating characteristic (ROC) analysis of curves and cut-off values obtained. Then, a univariate analysis was performed to check the statistical significance and to calculate the odds ratio (OR) and 95% confidence intervals (CIs). The collinearity of the examined variables was also verified using Pearson's correlation test and collinearity test. For the formation of the complete logistic regression model, all those variables were taken, which, after univariate analysis, were $p < 0.05$ and the value of probability coefficient greater than 2.

Logistic regression results are represented by a beta coefficient (Beta), standard error (SE), *p*-value, and probability coefficient with 95% CI. The ROC curve, the positive and negative values, and the sensitivity and specificity of the complete model were also calculated. The significant predictors of AKI development were those variables that reached $p < 0.05$.

IBM SPSS version 21 (Chicago, Illinois) was used for the statistical analysis. The results were presented in Tables and Figures; statistical significance was set at the *p*-value of less than 0.05.

Results

The total number of enrolled patients was 174. Preoperatively, 5 patients were excluded – two patients with CKD stage 3, two patients with ASA status IV, and one patient who refused to participate in this study. Intraoperatively, one patient was excluded because of the need for suprarenal cross-clamping. Postoperatively, 2 patients were excluded because of the need for re-operation and 26 because of missing data and noncompliance with the research protocol.

The total number of patients who completed the study was 140. Among them, 40 (28.56%) developed AKI; 32 (80%) of them developed AKIN 1, 6 (15%) AKIN 2, and only 2 (5%) AKIN 3 stage of the disease.

The mean age of the patients was 67.17 ± 6.53 years. Most patients were male (82.14%), with ASA status III (95.71%) and a mean BMI of 26.97 ± 5.28 kg/m^2. One hundred and thirteen (92.86%) patients had high blood pressure, 35 (25%) had COPD, 20 (14.28%) were diabetics, 15 (10.71%) had CVD, and 15 (10.71%) had CKD. One hundred and eleven (79.29%) patients underwent surgery for a diagnosed AAA and 29 (20.71%) for aortic occlusive disease (Leriche syndrome).

Univariate analysis revealed the differences at the $p < 0.05$ level between cases and controls in the sample for age, diagnosis, CKD, BUN, SCr, ClCr, CyC, GFR using plasma CyC, the use of acetylsalicylic acid or other antiplatelet drugs, oliguria in intraoperative period, the value of BE in-

traoperatively, colloid volume greater than 500 mL, the use of fresh frozen plasma (FFP) and resuspended erythrocytes (RE) intraoperatively, the total volume of fluid given intraoperatively greater than 59 mL/kg (Table 1).

Logistic regression was conducted to evaluate the impact of multiple independent factors on the likelihood of developing AKI. The model contained 11 independent variables: age, CKD, BUN, SCr, CyC, other antiplatelet drugs, oliguria, colloid volume, FFP and RE, and total fluid replacement volume (Table 2).

The whole model (with all predictors) was statistically significant, $\chi^2 = 74.753$, $p < 0.001$ (DF = 11, n = 140), which shows that the model distinguishes between the patients who developed AKI and those who did not. The model explains between 41.4% (R-squared Cox and Snell) and 59.3% (R-squared Nagelkerke) of the variance in AKI status and accurately classifies 87.9% of cases. As seen in the Table 2, only four independent variables made a unique statistically significant contribution to the model (CKD, CyC, colloid volume, and total fluid volume).

The strongest predictor of AKI development was a CyC concentration above 1.14 mg/L, with a probability ratio of 17.811. That shows that the patients who preoperatively have a CyC concentration above 1.14 mg/L are over 17 times more likely to develop AKI, with all other elements in the model being equal. A CKD with a probability factor of 8.569 is in second place, suggesting that patients with CKD are 8 times more likely to develop AKI, with all other factors in the model being equal. The OR for the colloid volume used intraoperatively and for total fluid volume is over 4. In other words, patients treated with a colloid volume greater than 500 mL or a total fluid volume greater than 59 were 4 times more likely to develop AKI, with all other factors in the model being equal. The classification table obtained from the logistic regression shows that this model correctly classifies 72.5% of the respondents who developed AKI (sensitivity). Correspondingly, this model accurately identified 94% of individuals who did not develop AKI (specificity). The positive predictive value was 82.9%, and the negative predictive value was 89.5%.

The ROC area under the curve (AUC) of the complete predictor model was 0.932, and the 95% CI was 0.889–0.971 (Figure 1, Table 3).

Table 1

The results of univariant logistic regression

Variable	Beta	SE	*p*-value	OR (95% CI)
Age (> 65 years)	1.471	0.462	0.001	4.352 (1.760–10.757)
Leriche syndrome	-1.099	0.575	0.048	0.333 (0.108–1.030)
CKD	2.209	0.621	< 0.001	9.103 (2.695–30.755)
BUN (> 6.15 mmol/L)	1.466	0.404	< 0.001	4.333 (1.964–9.561)
SCr (> 80 μmol/L)	1.054	0.394	0.007	2.868 (1.326–6.205)
ClCr (< 79 mL/min)	-1.439	0.399	< 0.001	0.237 (0.108–0.518)
Cystatin C (> 1.14 mg/L)	2.652	0.463	< 0.001	14.182 (5.721–35.155)
GFR (< 63 ml/min)	-2.351	0.469	< 0.001	0.095 (0.038–0.239)
Acetylsalicylic acid	-0.853	0.382	0.026	0.426 (0.201–0.902)
Other antiplatelet drugs	1.365	0.578	0.018	3.917 (1.263–12.148)
Oliguria	1.023	0.469	0.029	2.782 (1.109–6.796)
BE (mmol/L)	-0.161	0.078	0.039	0.851 (0.731–0.992)
Colloid (> 500 mL)	0.999	0.392	0.011	2.714 (1.259–5.851)
FFP	1.084	0.444	0.015	2.958 (1.239–7.059)
RE	1.466	0.474	0.002	4.333 (1.710–10.981)
Volume (> 59 mL/kg)	1.206	0.388	0.002	3.339 (1.559–7.149)

SE – standard error; OR – odds ratio; 95% CI – confidence interval; CKD – chronic kidney disease; BUN – blood urea nitrogen; SCr – serum creatinine; ClCr – creatinine clearance; GFR – glomerular filtration rate; BE – base excess; FFP – fresh frozen plasma; RE – resuspended erythrocytes.

Table 2

Results of multivariant logistic regression

Variable	Beta	SE	*p*-value	OR (95% CI)
Age (> 65 years)	0.565	0.676	0.403	0.569 (0.151–2.138)
CKD	2.148	0.922	0.020	8.569 (1.407–52.181)
Urea (> 6.15 mmol/L)	0.477	0.600	0.426	1.612 (0.497–5.223)
SCr (> 80 μmol/L)	0.156	0.655	0.812	1.169 (0.324–4.219)
Cystatin C (> 1.14 mg/L)	3.376	0.833	< 0.001	17.811 (4.581–69.252)
Other antiplatelet drugs	1.554	0.945	0.100	4.730 (0.742–30.166)
Oliguria	1.172	0.838	0.162	3.229 (0.625–16.690)
Colloid (> 500 mL)	1.489	0.705	0.035	4.432 (1.113–17.654)
FFP	0.964	0.717	0.179	2.622 (0.643–10.691)
RE	-0.396	0.792	0.617	0.673 (0.143–3.180)
Volume (> 59 mL/kg)	1.453	0.687	0.034	4.274 (1.112–16.424)

SE – standard error; OR – odd ratio; 95% CI – confidence interval; CKD – chronic kidney disease; SCr – serum creatinine; FFP – fresh frozen plasma; RE – resuspended erythrocytes.

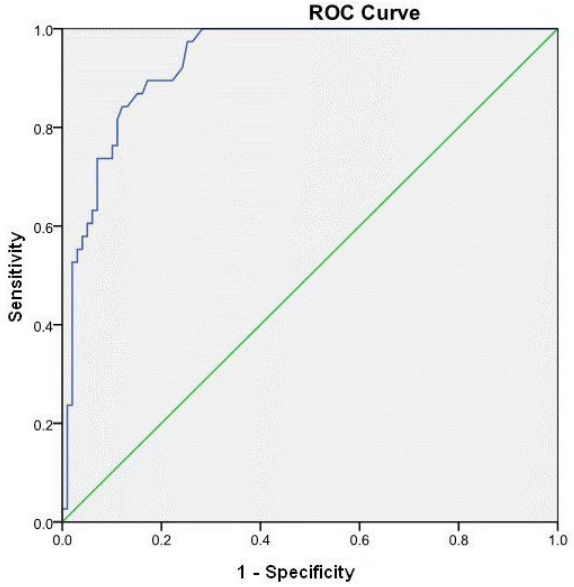


Fig. 1 – A receiver operating characteristic (ROC) curve of the complete logistic regression model.

Table 3

A receiver operating characteristic (ROC) curve analysis

AUC	SE	*p*-value	95% CI
0.932	0.022	< 0.001	0.889–0.971

AUC – area under the curve; SE – standard error; CI – confidence interval.

Discussion

Our results show that the incidence of AKI after elective aortic surgery is 28.56%, which is slightly higher compared to the literature data. The reason may be the use of different diagnostic criteria for AKI in our and other studies. We used a more sensitive AKIN classification, where the definition of AKI is not based on an increase in serum creatinine relative to the individual baseline value as in the RIFLE classification but on the initially measured value, and the change is observed within 48 hrs [14]. The incidence of AKI after elective AAA surgery varies from 1–28% depending on the study and the applied criteria [5, 15–17]. Bang et al. [18] showed in their study that AKI, according to AKIN criteria, was developed in 18.5% of patients and according to RIFLE criteria in 12.4% of patients after AAA surgery. In a study that included patients with AAA surgeries – endovascular, open, ruptured, and unruptured – the incidence of AKI in open surgery for unruptured aneurysms was 26.2%, while in ruptured aneurysms it was 48.1% [19]. Few papers investigated the incidence of AKI after aortic occlusive disease surgery. In a study evaluating AKI in elective open aortic surgery, the incidence was 22%, using RIFLE diagnostic criteria [5]. The average age of the examined patients in our study was 67.17 years (standard deviation – SD, 6.53), which is in accordance with the literature data. As age increases, so does the prevalence of the aneurysmal and aortic disease. The prevalence of AAA is about 5% in the population older than 65 years. Some studies have shown that the average age of the patients who underwent AAA surgery was 72 years [20, 21]. Our study included much more men – 115 (82.14%), than women, 25 (17.86%). The ratio between men and women was 4.6: 1, similar to the known literature data, where it is stated that the number of men exceeds the number of women among these patients, and the ratio is 4–6 : 1 [22, 23].

Demographic factors such as age and gender are closely related to the development of postoperative AKI. The occurrence of AKI as a complication in the postoperative period increases with age. The capacity of the kidneys to adapt to hemodynamic changes decreases with age [24]. Further, the renal blood flow and response to vasodilating factors decrease in old age [25]. Numerous studies have shown that the male gender is a risk factor for the development of postoperative AKI [26, 27]. However, in a recent prospective study that evaluated 9,400 patients after cardiac surgery, the female gender was shown to be a significant risk factor for the development of postoperative AKI [28]. Our study showed that there was no statistically significant difference in the distribution of the examined patients by groups according to gender. In the group of patients with AKI, there were 10 (25%) women and 30 (75%) men, while in the group of patients with no AKI, there were 15 (15%) women and 85 (85%) men.

From the examined potential predictors of AKI in the preoperative and intraoperative period, we found a total of 11 factors that had a statistically significant ($p < 0.05$) individual influence (Table 2). After the analysis of the potential risk factors, we obtained a final prediction model consisting of the presence of CKD, preoperative CyC concentration > 1.14 mg/L, intraoperative colloid replacement in a volume > 500 mL, and total intraoperative replacement volume > 59 mL/kg.

The strongest predictor of AKI development was the preoperative CyC concentration above 1.14 mg/L, with an OR of 17.811. That shows that patients with a preoperative CyC concentration above 1.14 mg/L are over 17 times more likely to get AKI, with all other factors equal in the model. CyC is an excellent marker of glomerular filtration rate: it is freely filtered through the glomeruli, completely reabsorbed in the proximal tubules, and not secreted by the renal tubules. It does not have as much interindividual variation and limitation as creatinine, e.g., due to the influence of muscle mass, diet, sex, and tubular secretion. Therefore, CyC is a better marker of GFR than creatinine [29, 30], especially in cases where there is a subclinical increase in creatinine, which is not a criterion for defining renal impairment by current definitions [29, 31, 32]. In our study, we found out that the preoperative value of CyC in the group of patients with AKI was statistically significantly higher, and the strength of the impact was assessed as extremely high. Specifically, the mean CyC concentration in the group of patients who did not receive AKI was 0.96 (SD = 0.27) mg/L, while in the group of patients who received AKI, it was 1.31 (SD = 0.25) mg/L. According to the ROC curve analysis, the concentration limit value for CyC was 1.14 mg/L. For this value, the maximum sensitivity index was 82.5%, and the specificity 76%. The

area under the curve was 0.830, and the 95% CI was 0.761–0.900. Seven (8.4%) out of 83 patients with a CyC concentration less than or equal to 1.14 mg/L developed AKI, and 33 (57.9%) of 57 patients with a CyC concentration greater than 1.14 mg/L developed AKI. According to our previous knowledge, there is no literature data on the examination of the predictive value of the preoperative concentration of CyC in vascular surgery. However, there is plenty of literature on the predictive value of preoperative CyC concentration in cardiac surgery [33, 34]. The reason could be the highest incidence of AKI after cardiac surgery. The literature data are in agreement with our results. A Translational Research Investigating Biomarker Endpoints in Acute Kidney Injury (TRIBE-AKI) study in 1,147 cardiac surgery patients demonstrated that preoperative CyC concentration was a better predictor of AKI after cardiac surgery than preoperative SCr and ClCr [35]. Turki et al. [36] confirmed in their research that preoperative, baseline, serum CyC value is a good predictor of AKI after cardiac surgery. All the above suggests that it would be rational to find out the preoperative value of CyC in risky surgery because it has been proven to be a good predictor of postoperative AKI.

In second place is the presence of CKD with an OR of 8.569. That suggests that patients with CKD are 8 times more likely to develop AKI, with all other factors equal in the model. CKD unequivocally increases the risk of acute renal damage, which is in line with numerous literature data [19, 37]. CKD significantly contributes to the formation of AKI and *vice versa* [38]. In our study, we included the patient with mild CKD (1st and 2nd degree) and excluded those with CKD 3rd, 4th, and 5th degrees. Of all the associated diseases, only a statistically significant difference between the examined groups was found for the presence of mild chronic renal failure. A statistically significantly higher number of subjects with CKD was observed in the group of patients with AKI. Of the 40 patients who developed AKI, 11 (27.5%) had a history of stage 1 or 2 CKD, and of the 100 who did not develop AKI, only 4 (4%) had CKD.

The probability ratio for intraoperative colloid replacement in a volume > 500 mL and the total intraoperative replacement volume > 59 mL/kg is over 4. That means that patients who received > 500 mL of colloidal solutions intraoperatively and who received a total replacement volume greater than 59 mL/kg are 4 times more likely to develop AKI. It was observed that in the group of patients who received a larger volume of colloidal solutions (from 501 mL to 1,000 mL), a statistically significantly higher number of patients developed AKI, 19 (47.5%), compared to patients who did not develop AKI, 25 (25%). This result agrees with previous research on the effect of hydroxyethyl starch (HES) solution on renal function. For decades, there has been a debate about intravenous fluid therapy on whether colloids or crystalloids are better or more harmful. There is no doubt that it will continue in the future. However, the detrimental effect of synthetic colloidal solutions on the kidneys is known [39]. Newer solutions have a lower molecular weight and a lower degree of substitution, the two changes that reduce accumulation and toxicity. We used 6% HES solutions with 130 kDa and a degree of substitution of 0.42 in a physiologically balanced solution. Many studies conducted to investigate the effect of HES solution on renal function in sepsis have shown that the use of HES solution is an independent risk factor for the development of AKI in severe sepsis [40] and that the usage of HES increases the need for RRT. The greater the cumulative dose of colloid, the greater the adverse effect [41]. Furthermore, a meta-analysis of ten studies examining this topic in critically ill septic patients showed that HES administration was associated with higher 90-day mortality, an increased risk of developing AKI, and a higher need for RRT [42]. The detrimental effect of HES solution on the kidneys and among surgical patients in the perioperative period has also been proven [43]. Intravenous fluid therapy is widely used for both the prevention and treatment of AKI in the belief that the most common cause of AKI is the prerenal component. On the other hand, the harmful effects of a fluid overdose can be emphasized in situations such as severe sepsis, major surgery, and trauma, which are predisposing factors for the development of AKI [44, 45].

Intravenous fluid therapy is the most exploited therapy for patients at risk of AKI. However, the harmful consequences of fluid therapy are being increasingly recognized. In fact, adequate fluid therapy in patients with AKI is the key to the treatment. The administration of crystalloid solutions increases the intravascular compartment, but over time it it and is distributed in the interstitial compartment. Renal interstitial edema worsens renal function. Because the kidney is an encapsulated organ, when congestion occurs, venous pressure also increases, along with intracapsular pressure, which all leads to a decrease in renal blood flow and GFR. Observational studies in critically ill patients have found a link between positive fluid balance and AKI [46, 47]. Moreover, excessive fluid intake results in visceral edema, which is a risk factor for the occurrence of intraabdominal hypertension. Elevated intraabdominal pressure increases renal venous pressure and decreases renal blood flow and GFR [48]. A conservative fluid replacement strategy is recommended with the goal of neutral and a negative fluid balance when hemodynamic stability is achieved. In patients with AKI, this strategy involves the earlier use of RRT in the initial phase of treatment, when a more liberal fluid replacement strategy is used [49]. In general, an individualized approach to each patient and goal-directed fluid therapy (GDT) are emphasized to avoid iatrogenic harmful fluid therapy [50].

The classification table of logistic regression shows that the final model accurately classified 72.5% of respondents who developed AKI (sensitivity). In addition, this model accurately identified 94% of individuals who did not develop AKI (specificity). The positive predictive value was 82.9%, and the negative predictive value was 89.5%. The ROC AUC of the complete predictor model was 0.932, and the 95% CI was 0.889–0.971. A Chinese study in 2017 on risk factors after AAA surgery showed a predictive score for AKI (WCR-DA score), which contains the following elements for elective surgeries: smoking, blood loss > 1 L, and antihyperten-

sive therapy. A score of 0 has a predicted risk of developing AKI of 2%, while a maximum score of 4 carries a risk of 78% [51]. A recent Korean study obtained its predictive model for the development of AKI after aortic surgery, which includes age > 60 years, decreased preoperative GFR, preoperatively reduced left ventricular systolic function, prolonged operative time, intraoperative oliguria, and intraoperative furosemide therapy [52]. In an Italian study comparing the incidence of AKI after endovascular and open elective operations on the infrarenal aorta, the development of AKI was significantly associated with smoking, hypertension, chronic renal failure, open aortic surgery, and arrhythmias [53].

Conclusion

Levels of preoperative CyC above 1.14 mg/L are a good predictor of AKI in patients undergoing elective infrarenal aortic surgery. These findings support the use of routine preoperative CyC measurements with all other important predictors.

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