A.S. Korostelev, A.F. Potapov, A.A. Ivanova, P.I. Zakharov, A.V. Bulatov

PREDICTING ACUTE KIDNEY INJURY IN CAD PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

DOI 10.25789/YMJ.2020.70.06

УДК 616-06

The aim of the study was to identify the risk predictors of developing acute kidney injury (AKI) and to create an AKI prognosis chart for patients with coronary artery disease (CAD) undergoing off-pump coronary artery bypass grafting.

The study covered 210 patients with coronary artery disease (mean age of 58.4 ± 6.3 years, 173 (82.4%) men and 37 (17.6%) women) who underwent off-pump coronary artery bypass grafting. The signs of AKI after the surgery were observed in 89 (42.4%) patients. Out of the numerous factors, 17 most significant signs of the risk of developing AKI were selected using the Wald test.

Using the identified signs, we built models (1) and (2) for predicting the probability of developing AKI with the sensitivity of 81% and specificity of 91%.

We also revealed increased probability of developing AKI by 7.83 times (95% CI: 4.2-14.7) in patients with concomitant metabolic syndrome (MS).

Keywords: coronary artery disease, metabolic syndrome, off-pump coronary artery bypass grafting, acute kidney injury, risk predictors, prediction model.

Kidney failure and various degrees of AKI in patients with coronary artery disease undergoing coronary artery bypass grafting remains one of the challenges in cardiac surgery and cardiovascular anesthesiology [4]. The AKI developed in the postoperative period leads to a changed patient treatment tactic, prolonged treatment duration and significantly worse prognosis, increasing the hospital mortality rate of such patients to 26.3% [1]. In addition, several research results indicate the highest risk of perioperative renal complications in patients with comorbid pathologies, including concomitant MS [3].

With the goal of improving treatment outcomes, the differentiated and patient-oriented approach is a current trend in medicine. From this perspective, the identification of objective prognostic risk criteria for developing AKI is of great applied value.

The aim of the present study was to identify the risk predictors of developing AKI and to create an AKI prognosis chart for patients with CAD undergoing off-pump coronary artery bypass grafting.

Materials and Methods. A retro- and prospective, longitudinal observational study was conducted. The retrospective stage of the study included analysis of medical records of 90 inpatients, prospective - examination and treatment of 210 patients with coronary artery disease (173 (82.4%) men, 37 (17.6 %) women) who underwent myocardial revascularization by coronary artery bypass grafting and mammary coronary artery bypass surgery off-pump. Mean age of patients was 58.4 ± 6.3 years. All surgeries were performed at the Sakha (Yakutia) Republic's Hospital No. 1 - National Center of Medicine in the period 2016-2020.

The diagnostics of the cardiovascular system functional status was carried out in accordance with the 2014 ESC/EACTS Guidelines on Myocardial Revascularization [11]. MS was diagnosed using the criteria from the Clinical Guidelines of the Ministry of Health of the Russian Federation [6].

Under the ASA (American Society of Anesthetists) classification, all the patients were assigned ASAPS Class 3 and Class 4. The anesthetic and postoperative managements were carried out following the management protocols of patients undergoing off-pump coronary artery bypass grafting [5].

The diagnostics of the functional status of kidneys, assessment of the degree of renal dysfunction, AKI and assessment of its severity were carried out following the KDIGO (Kidney Disease Improving Global Outcomes) Clinical Guidelines [12].

The processing of statistical data was performed using SPSS Statistics, version 23, and included: at different stages of the study, calculating the mean value and standard deviation assuming a normal distribution (M ± SD), the median and interquartile range (Me, IQ RQ3-Q1); conducting a logistic regression analysis to develop an AKI prediction model; and determining the two-tailed criterion of Student's t-test for comparing mean values of two independent groups, and the Mann-Whitney criteria for a nonparametric test. The statistical significance was set at $p < 0.05$.

Results and Discussion. In the postoperative period, the signs of AKI were observed in 89 (42.4%) patients. To predict postoperative AKI in patients with coronary artery disease, we studied 104 factors that were considered from the perspective of increasing or decreasing the risk of kidney injury. Using a statistical analysis, we identified 72 factors that have a statistically significant relationship with the risk of developing AKI. At the next stage, out of these factors, 17 signs were selected by

KOROSTELEV Aleksandr Sergeevich – anesthesiologist-resuscitator, Department of Anesthesiology, Resuscitation and Intensive Care (Cardiology), State autonomous institution of the Sakha Republic (Yakutia) "Republic's Hospital No. 1 - National Center of Medicine." Address: 677000, Sakha Republic (Yakutia), Yakutsk, ul. Oyunskogo, 27. Tel/fax. +7 (4112) 363489. Mob. +7-924-763-9300. E-mail: bezbazaroff@inbox.ru; **POTAPOV Aleksandr Filippovich** – Doctor of Medical Sciences, Head, Department of Anesthesiology, Resuscitation and Intensive Care with Emergency Care Course, Faculty of Post-graduate Studies for Doctors, Institute of Medicine, Federal state educational institution of higher professional education "M.K.Ammosov North-Eastern Federal University". **IVANOVA Albina Ammosovna** – Doctor of Medicine, Associate Professor, Department of Anesthesiology, Reanimation and Intensive Care, Institute for Post-graduate Medical Training, Ammosov North-Eastern Federal University. **ZAKHAROV Petr Ivanovich** – Doctor of Medical Sciences, chief external expert in cardiovascular surgery, Head, Cardiovascular Surgery Department, Clinical Center, State autonomous institution of the Sakha Republic (Yakutia) "Republic's Hospital No. 1 - National Center of Medicine." **BULATOV Alkviad Valentinovich** – Candidate of Medical Sciences Head, Department of Anesthesiology, Resuscitation and Intensive Care (Cardiology), State autonomous institution of the Sakha Republic (Yakutia) "Republic's Hospital No. 1 - National Center of Medicine."

the Wald stepwise backward elimination method (Table 1).

The Table demonstrates that along with the values of blood creatinine, GFR and proteinuria, which are mandatory in assessing renal function [3, 4, 17], we selected the factors whose role in the development and course of AKI has been confirmed by numerous studies. These are anthropometric data [11, 8], smoking [10], a number of hemodynamic parameters [9, 2], blood sugar [11, 14, 15] and lipids [7,10,16,18], as well as the intake of statins, which have nephroprotective effect [18].

The inclusion of the presented risk factors for developing AKI made it possible to create a prediction model (1) for determining the probability of developing AKI in each case:

$$PAKI = 1/(1 + e^{-z}),$$

where: PAKI – the probability of developing AKI, expressed in %; e^{-z} – the natural logarithm base (Euler's number) = 2.71828.

The following risk factors are to be used to calculate z:

$$z = -28.561 + 0.09*X_{age} + 0.2*X_{BMI} + 1.5*X_{smoking} - 1.2*X_{statins} + 0.07*XEF - 1.9*X_{LVEDd} + 0.1*X_{GFR} + 0.09*X_{creatinine} + 2.0*X_{proteinuria} + 0.3*X_{HbA1c} + 0.3*X_{glucose} + 0.09*X_{Hb} - 0.2*X_{Ht} - 0.3*X_{TC} + 1.1*X_{TG} - 3*X_{HDL} + 1*X_{LDL} \quad (1),$$

where: X_{age} – age (years); X_{BMI} – body mass index (kg/m^2); $X_{smoking}$ – smoking factor (0 – non-smokers, 1 – smokers); $X_{statins}$ – the intake of statins in therapeutic doses (0 – does not take, 1 - takes); X_{EF} – ejection fraction (%); X_{LVEDd} – left ventricular end diastolic dimension (cm); X_{GFR} – glomerular filtration rate (ml/min/1.73m^2); $X_{creatinine}$ – serum creatinine (μmol/l); $X_{proteinuria}$ – proteinuria (mg/d); X_{HbA1c} – glycated hemoglobin (%); $X_{glucose}$ – blood glucose level (μmol/l); X_{Hb} – hemoglobin level (g/l); X_{Ht} – hematocrit (%); X_{TC} – total cholesterol (μmol/l); X_{TG} – triglycerides (μmol/l); X_{HDL} – high-density lipoproteins (μmol/l); X_{LDL} – low-density lipoproteins (μmol/l); - 28.561 – a constant.

The assessment of the probability of developing AKI in CAD patients was carried out as follows: with a value of PAKI > 50 %, the patient was assumed the high-risk group of kidney injury, while with PAKI < 50% – the low-risk group. The sensitivity of the obtained model was 81%, specificity – 91%, with the total percentage of diagnostic efficiency at 86.7%.

Based on the values of the regression coefficients, all of the listed factors are directly related to the probability of developing AKI in the postoperative period. The obtained regression model (1) is statistically significant (p = 0.001) and, based on the value of the Nigelkerk coefficient of determination, it takes into account 73.5% of the factors signaling the probability of developing AKI in the postoperative period.

In order to adapt this model (1) for application in the routine clinical practice, and also taking into account the complex mathematical calculation of logistic regression, we transformed it using the multiple linear regression. The value of the probability of AKI development, expressed as a percentage, served as a dependent variable, and we introduced the same 17 indicators used in model (1) as factor variables. As a result, the following equation was created (Model 2):

$$YAKI\ (\%) = 0.7*X_{age} + 2.3*X_{BMI} + 14*X_{smoking} - 16*X_{statins} + 0.1*X_{EF} - 18.5*X_{LVEDd} + 0.4*X_{GFR} + 0.6*X_{creatinine} + 13*X_{proteinuria} + 3*X_{HbA1c} + 2.7*X_{glucose} + 0.9*X_{Hb} - 2.4*X_{Ht} - 2.5*X_{TC} - 2*X_{TG} - 24*X_{HDL} + 12.2*X_{LDL} - 105 \quad (2),$$

Where: YAKI (%) – the probability of developing AKI in %; - 105 – a constant (baseline probability of AKI without the factors included in the Model); values of 0.7; 2.3; 14; 16, etc. – regression coefficients determining how much the AKI risk will increase with a certain risk factor.

The created prediction regression model (2) was characterized by a direct, statistically significant correlation of the probability of AKI (p = 0.001) and had a strong relationship of the factors on the Chaddock scale (rxy = 0.940). Based on the value of the Nigelkerk determination coefficient R^2, Model (2) takes into account 88.3% of the most significant factors determining the probability of AKI in the postoperative period. The sensitivity of the model remained high and made 81%, specificity – 91%.

The conducted ROC (Receiver Operating Characteristic) analysis confirmed high diagnostic value of the created model (2). The area under the ROC – AUC (area under curve) was 0.94 ± 0.14 (95% CI 0.91-0.97), dividing value of prognostic function (cut-off) – 50% (Fig.).

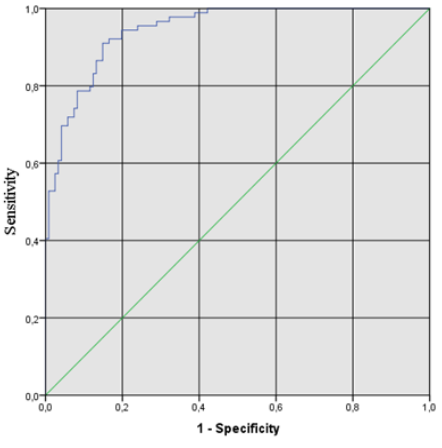
Assuming that the AKI predictors include all the signs characteristic of MS, we carried out a separate analysis of the AKI incidence in patients with concomitant MS. The statistical analysis showed that the probability of developing AKI with concomitant MS increases by 7.83 times (95% CI: 4.2-14.7) (Table 2).

Table 1

Factor having established relationship with the AKI risk in CAD patients

Characteristics	With AKI (n=89)	Without AKI (n=121)	p
Age, years, (M±SD)	59.1±5.9	57.8±6.6	0.154
BMI, kg/m2, (M±SD)	31.1±4.1	26.8±5.0	< 0.001*
Smoking, n (%)	63 (70.8%)	26 (29.2%)	< 0.001*
LVED, cm, (M±SD)	4.9 ± 0.4	4.9±0.4	0.159
EF, %	58.5±6.0	59.6±6.24	0.871
GFR/min/1.73m2, (M±SD)	71.5 ±14.2	77.9 ± 14.1	0.001*
Serum creatinine, μmol/l (Me [Q1-Q3])	101.0 [88.0-122.0]	89.0 [88.0-99.0]	< 0.001*
Proteinuria, mg, (Me [Q1-Q3])	0.3 [0.1-1.0]	0.1 [0-0.2]	< 0.001*
Fasting plasma glucose, μmol/l (Me [Q1-Q3])	8.0 [7.0-9.0]	5.5 [4.5-7.75]	< 0.001*
HbA1c,%	6.5 [5.25-7.0]	4.0 [4.0-4.5]	< 0.001*
Hb, g/l (M±SD)	140.0±8.1	137.1±8.8	0.016*
Ht, %, (Me [Q1-Q3])	35.0 [33.0-38.0]	37.0 [34.0-43.0]	< 0.001*
Total cholesterol, μmol/l, (M±SD)	6.5 [5.25-7.25]	5.5 [4.25-7.0]	0.001*
Triglycerides, μmol/l, (M±SD)	1.63±0.3	1.43±0.3	< 0.001*
HDL cholesterol, μmol/l, (Me [Q1-Q3])	1.36±0.27	1.32±0.29	0.357
LDL cholesterol, μmol/l, (Me [Q1-Q3])	2.35±0.64	1.84±0.7	< 0.001*
Atorvastatin, 20 мг, n (%) 80 мг, n (%)	61 (68.5%) 28 (31.5%)	41 (33.9%) 80 (66.1%)	< 0.001*

Note: BMI - body mass index; LVED - the final diastolic size of the left ventricle; LVEF - left ventricular ejection fraction; GFR - glomerular filtration rate; TC - total cholesterol; TG - triglycerides; HDL - high density lipoproteins; LDL - low density lipoproteins. In the tables 1-2 * - differences in the indicators are statistically significant (p <0.05).



ROC-curve characterizing the correlation between the probability of developing AKI and the prognostic function Yaki % in Model (2).

serum creatinine of 159 μmol/l, and decreased urine output of less than 0.5 ml/kg/h.

Conclusion. Therefore, in our study, signs of AKI were observed in 42.4% of the patients with coronary artery disease, and the probability of its development with concomitant MS increased by 7.83 times. Predicting AKI and assessing the risk of its development should become mandatory for patients with coronary artery disease prior coronary artery bypass grafting. Assessing the probability of developing AKI will allow adjusting the program of preoperative preparation of patients, thereby reducing the number of complications in the postoperative period and improving the results of treating patients of this complex category.

Table 2

Evaluation of the AKI incidence in patients with concomitant MS

Presence/absence of AKI	Patients with MS (n=106)		Patients without MS (n=104)		p*	OR; 95% CI
	Abs.	%	Abs.	%		
Signs of AKI	69	65.1	20	19.2	<0.001	7.83; 4.2-14.7
No signs of AKI	37	34.9	84	80.8		

Upon completion of the study, we created a chart for practitioners "Assessing the risk of developing AKI in patients with coronary artery disease undergoing CABG", including the discussed predictors. Here is a clinical example of calculating the probable risk of AKI in a patient with coronary artery disease and MS:

Patient M., 66, was admitted for a surgery to treat coronary artery disease with concomitant MS. The indicators at admission: BMI – 32 kg/m²; smokes a pack of cigarettes a day; LVEDd – 4.4 cm, EF – 55%; GFR – 71 ml/min/1.73 m², blood creatinine – 126 μmol/l, proteinuria – 0.9 mg; HbA1c – 6.4%; blood glucose – 7.2 μmol/l; Hb – 124 g/l, Ht – 32%; TC – 6.6 μmol/l, HDL – 2.4 μmol/l, LDL – 3.1 μmol/l, TG – 1.9 μmol/l; has been taking Atorvastatin 20 mg for 2 months.

The calculation estimated the risk of AKI in the patient exceeding 50%, which indicated a high risk of developing AKI. The prediction was later confirmed. 48 hours after the surgery, the patient showed signs of AKI: decreased GFR of 59 ml/min/1.73 m², increased

References

1. Искендеров Б. Г., Сисина О.Н. Факторы риска и исходы острого повреждения почек у пациентов с сохранной функцией почек, подвергнутых аорто-коронарному шунтированию. *Нефрология*. 2013;3:7-63. [Iskenderov BG, Sisina ON. Risk factors and outcomes of acute kidney injure in patients with intact renal function underwent coronary artery bypass grafting. *Nefrologiya*. 2013; 3:7- 63. (In Russ.).]

2. Кобалава Ж.Д., Моисеев В.С. Концепция кардиоренальных и метаболических соотношений в современной профилактической кардиологии. *Кардиоваскулярная терапия и профилактика*. 2008;4: 4-7. [Kobalava ZD, Moiseev VS. The concept of cardiorenal and metabolic relationships in modern preventive cardiology. *Kardiovaskulyarnaya terapiya i profilaktika*. 2008; 4: 4-7. (In Russ.).]

3. Мельник А.А. Метаболический синдром и риск хронической болезни почек. *Почки*. – 2017; 6:(2): 80-90. [Melnik AA. Metabolic syndrome and risk of chronic kidney disease. *J. Pochki*. 2017; 6(2): 80 – 90. (In Russ.).]

4. Миролюбова О.А., Алексеева М.А., Яковлева А.С., Шонбин А.Н. [и др.] Острое повреждение почек после аортокоронарного шунтирования на работающем сердце: прогнозирование исходов. *Нефрология и диализ*. 2014;16(3): 350-358. [Mirolyubova OA, Alekseeva MA, Yakovleva AS, Shonbin AN. [et al.] Acute kidney injury after CABG without cardiopulmonary bypass: prediction of outcomes. *Nefrologiya i dializ*. 2014;16(3): 350-358. (In Russ.).]

5. Хенсли А.Ф., Мартин Д.Е., Грэвли Г.П. Практическая кардиоанестезиология. 5-е изд. — М.: «*Медицинское информационное агентство*», 2017. [Frederick A. Hensley Jr., Donald E. Martin, Glenn P. Gravlee. A practical approach to cardiac anesthesia. *Medicinskoe informacionnoe agentstvo*. 5th ed., transl. version. (In Russ.).]

6. Рекомендации по ведению больных с метаболическим синдромом: *клинические рекомендации МЗ РФ*; 2013: 42. [Clinical guidelines for the management of patients with metabolic syndrome. *RF Ministry of Health care*; 2013: 42. (In Russ.).]

7. Chen SC, Hung CC, Kuo MC. [et al.] Association of dyslipidemia with renal outcomes in chronic kidney disease. PLoS One; 2013; 8(2):556.

8. Burden R, Tomson C. Identification, management and referral of adults with chronic kidney disease: concise guidelines. *Clin. Med*. 2005; 5:635–642.

9. Ronco C, McCullough P, Anker S. [et al.] Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative. *Eur. Heart J*. 2010; 3:703-711.

10. Yamamoto R, Nagasawa Y, Shoji T [et al.] Cigarette smoking and progression of IgA nephropathy. *Am. J. Kidney Dis*. 2010; 56:313–324.

11. Despres J.-P. Abdominal obesity: the most prevalent cause of the metabolic syndrome and related cardiometabolic risk. *Eur. Heart J*. - 2006; 8 (suppl. B): 4-12.

12. Windecker S, Kolh P, Alfonso F. [et al.] ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur. Heart J*. 2014;35(37): 619-2541.

13. Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int*. (Suppl) 2012; 2:1-138.

14. Chen J, Muntner P, Hamm L. [et al.] Insulin resistance and risk of chronic kidney disease in nondiabetic US adults. J. Am. Soc. *Nephron*.- 2003;14:469-477.

15. Kurella M, Lo JC, Chertow GM. Metabolic syndrome and the risk for chronic kidney disease among nondiabetic adults. J. Am. Soc. *Nephrol*. 2005;16: 2134-2140.

16. Urazlina CE, Zhdanova TV, Nazarov AV [et al.] Lipid metabolism in patients with chronic renal failure. *Ural Medical Journal*. 2011; 2(80): 6-122.

17. Peterson JC. Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study . *Ann. Intern. Med*. 1995; 123:754–762.

18. Song-jian H. Qiang Liu, Hua-qiu Li, Fang Tian, Shi-yu Chen. Role of statins in preventing cardiac surgery-associated acute kidney injury: an updated meta-analysis of randomized controlled trials. *Ther. Clin. Risk Manag*. 2018; 14: 475–482.