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# Risk assessment of contrast-induced acute kidney injury in patients with acute myocardial infarction after coronary angiography and percutaneous coronary intervention

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**Aim.** To assess the risk of contrast-induced acute renal injury (CI-AKI) in patients with acute myocardial infarction in a highly specialized hospital after coronary angiography.
**Material and methods.** The study sample included 502 patients who were treated in the cardiology department of a specialized hospital. CI-AKI was established by an increase in creatinine >26 μmol/L within 48 hours after percutaneous coronary intervention (PCI) with radiopaque contrast agents or an increase in creatinine >50% within a week after PCI. A multistage statistical analysis was used to search for possible predictors of CI-AKI.
**Results.** In total, CI-AKI was diagnosed in 57 (11,3%) patients. Based on the analysis performed, 3 significant predictors of CI-AKI were identified: patient's age, contrast medium volume (ml/kg) and anemia (presence/absence). An equation for assessing the risk of CI-AKI in patients after PCI has been created.
**Conclusion.** A simple scale for assessing the CI-AKI risk makes it possible to identify a category of patients who requires preventive measures to reduce iatrogenic complications and mortality.

**Keywords:** contrast-induced acute kidney injury, coronary angiography, acute myocardial infarction, radiopaque agents, predictors.

**Relationships and Activities:** none.

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Contrast-induced acute kidney injury (CI-AKI) is a dangerous complication of angiographic procedures due to the direct and indirect effect of iodine-containing contrast medium on the renal tissues, which are currently widely used in emergency and elective cardiology [1, 2]. The inpatient development of CI-AKI increases the patient's hospitalization period and also increases mortality [3, 4]. According to modern concepts, CI-AKI is diagnosed in the presence of one of the following indicators after the introduction of contrast medium: a) an increase in the serum creatinine level relative to the baseline value by 26 μmol/l or more in the period of 48 hours; b) an increase in the serum creatinine level by 50% or more relative to the baseline value in the period of 1 week; c) decrease in urine output >0,5 ml/kg/h in the period of 6 hours or more [5, 6]. Currently, three main pathophysiological mechanisms of CI-AKI development known as follows: a) medullary renal hypoxia due to a decrease in the level of vasodilators (prostaglandins, nitric oxide) and an increase in the level of vasoconstrictors (adenosine and endothelin); b) direct cytotoxic effect of a contrast medium on the proximal renal tubules, where the detrimental effect of free radicals and hyperoxia is emphasized; c) induction of apoptosis of renal tubular epithelial cells [7, 8].

Coronary angiography (CAG) and percutaneous coronary intervention (PCI) are vital manipulations in patients with acute myocardial infarction (AMI) in a highly specialized hospital. Recently, the number of PCI has increased in elderly patients, and the safety and outcomes of revascularization have improved [9]. This disease is relevant in modern medical literature. In particular, many researchers were looking for risk factors for CI-AKI, among which are the patient's age, female sex, anemia, diabetes, increased erythrocyte sedimentation rate, hypotension, congestive heart failure, volume of injected contrast agent, intra-aortic balloon counter-pulsation, chronic kidney disease, etc. Based on the found risk factors, models have been created allowing to reveal patients at high risk of CI-AKI [10-13].

Given the urgency of the problem, we tried to reveal easily accessible predictors of CI-AKI in patients with AMI in a specialized hospital.

## Material and methods

The study included 502 patients, who in 2014-2017 were treated in the cardiology department of the N. S. Karpovich Krasnoyarsk Interdistrict Clinical Emergency Hospital. CI-AKI was established based on a creatinine increase >26 μmol/L within 48 hours after PCI using contrast agents; another criterion for CI-AKI verification was a creatinine increase >50% within a week after PCI. The sample did not include patients with stage 5 chronic kidney disease, as well as patients who required investigations with contrast agents for reasons unrelated to PCI. The patients who were diagnosed with shock, decreased ejection fraction <40%, high central venous pressure >120 mm Hg were excluded. Upon admission, all patients underwent electrocardiography, laboratory tests, including a complete blood count, biochemical blood tests (creatinine, electrolytes, troponin, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatine kinase-MB, lipid profile, C-reactive protein, glucose). All patients were diagnosed with AMI, which is an indication for urgent CAG and consideration of further PCI. During the entire period of stay in the cardiac intensive care unit, urine output and serum creatinine levels (after 12 hours, 24 hours, 48 hours, 3, 5, 7 days and at discharge) were monitored. In cases of increased creatinine levels, hydration with low volume of 0,9% sodium chloride solution was performed under the monitoring of central venous pressure was performed.

Patients with verified CI-AKI who were included in the sample were randomly divided into 2 groups in a 4:1 ratio: training and testing, respectively. The search for predictors was initially based on univariate statistical analysis methods. The variables selected as a result of univariate methods from the general sample were included in the training group, from which, in turn, 100 samples were randomly generated, followed by logistic regression. For each of the generated samples, the predictors were evaluated step by step in order to be selected for the final model. The final sample included 3 variables that were significant ($p<0,001$) in more than 90% of the generated samples.

One of the selected variables is a categorical one with two values — "yes" and "no", while the other two are presented as the interval variables. To calculate the risk of CI-AKI, the obtained regression coefficients were used in combination with the corresponding values of predictors. Using logistic regression, the odds ratio (OR) was calculated with 95% confidence intervals for each predictor.

The adequacy of obtained regression model was confirmed by regression model adequacy tests ($P>0,57$) with random sample generation based on the available sample [14]. The sample size for presented logistic regression model can be considered acceptable based on numerous publications devoted to this problem [15]. Statistical analysis and data visualization were performed using the software package and the language "R". Normally distributed variables are presented as mean and standard deviation (s). Non-normally distributed variables

**Table 1**

**Clinical characteristics of patients with verified CI-AKI**

| Factor | Patients (n=57) |
|---|---|
| Male sex | 49% |
| Age (years) | 72,2±9,1 |
| Weight (kg) | 74,5±7,8 |
| Anemia | 44% |
| Diabetes | 83% |
| Hypertension | 90% |
| Combination of diabetes and hypertension | 85% |
| Congestive heart failure | 13,9% |
| Prior myocardial infarction | 33% |
| Myocardial infarction | 75% |
| Dyslipidemia | 39% |
| Diuretic use | 70% |
| Peripheral arterial atherosclerosis | 10% |
| Rheumatic heart disease | 5% |
| Baseline creatinine value (μmol/L) | 101,7±55,7 |
| Intra-aortic balloon counterpulsation | 4% |
| Contrast volume (ml) | 136,2±57,9 |

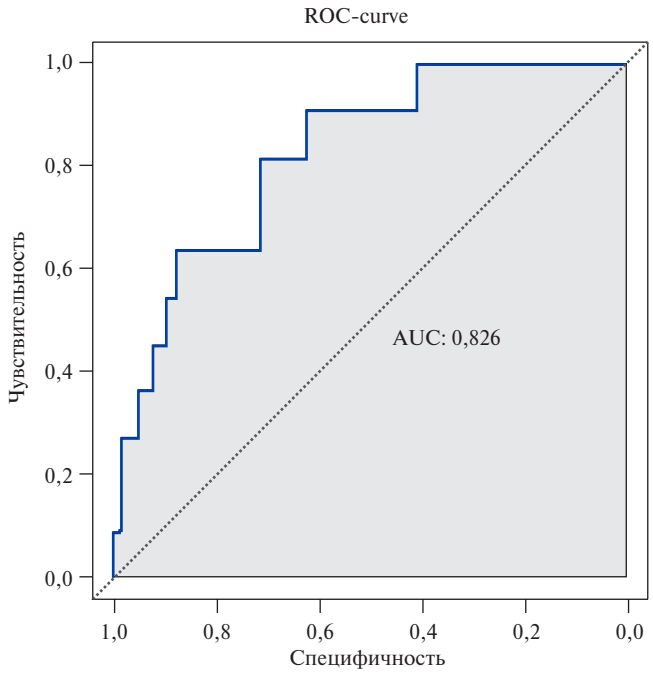


**Figure 1.** ROC-curve of logistic analysis of the risk for CI-AKI in patients with AMI.

are presented as a median (Me) and 25% and 75% quartiles (Q1; Q3).

The study was conducted in accordance with good clinical practice (GCP) standards The study was approved by the Local Ethics Committee of the V. F. Voino-Yasenetsky Krasnoyarsk State Medical University.

## Results

The main clinical characteristics of patients with verified CI-AKI included in the sample are presented in Table 1. The mean age of patients in the group with established CI-AKI was 72,2 years, while 35 (63%) patients were over 70 years old. The distribution of male and female patients was approximately the same (Table 1). The average creatinine level on admission was 101,7 μmol/L.

In the study sample, 57 patients with CI-AKI were verified. Variables such as age, anemia, and contrast volume in milliliters per kilogram of body weight were identified as predictors. Variable "anemia" is presented as categorical, while other variables were used as continuous values. The Hosmer-Lemeshow test with $\chi^2$ of 3,3 (p=0,2) confirmed the adequacy of created model.

C-statistics with the creating a ROC-curve showed a high proportion of objects with selected features (area under the ROC-curve =0,82) (Figure 1).

Based on the conducted multivariate study, we created a risk assessment scale for CI-AKI in patients with PCI, which includes 3 predictors as follows: age (OR, 0,06, p<0,01), anemia (OR, 2,23, p<0,01) and the volume of contrast medium per unit of body weight (ml/kg) (OR, 0,43, p<0,01). Table 2 shows that the largest proportion in the risk assessment scale for CI-AKI and the widest value of the confidence interval belongs to anemia, which is explained by the fact that this variable has a binomial character. In the group of patients with established CI-AKI, out of 52 patients, anemia was diagnosed in 23 patients (44%). In the group of patients without CI-AKI, the proportion of patients with anemia was 52% (n=163). The lower value of regression coefficient of the "age" variable is explained by its higher values in the interval value — 64,3±11,9. In addition, the average for sample of patients with CI-AKI was 72,2±9,1, while it was 63,2±11,9 in the rest of patients. The presented difference is significant, which is confirmed by the t-test of normally distributed samples (t=5,33, p<0,0001). The proportion of patients over 70 years old in the CI-AKI group was 63% (n=55), while in patients without CI-AKI — 26% (n=113). The contrast volume had the highest value of 4,6 ml/kg and the median of 1,4 (1; 2). The variable "contrast volume" was characterized by a deviation from the normal distribution with positive asymmetry both in the general sample and in the groups of patients with/

**Table 2**

**Multivariate predictors of the risk for CI-AKI after PCI**

| Variable | Regression coefficient | Odds ratio | 95% interval | P |
|---|---|---|---|---|
| Age | 0,06 | 1,06 | 1,03-1,10 | <0,01 |
| Anemia | 0,80 | 2,23 | 1,03-4,78 | <0,01 |
| Contrast volume (ml/kg) | 0,43 | 1,55 | 1,01-2,35 | <0,01 |

without CI-AKI, on the basis of which this variable is presented as a median (Me) and percentiles (Q1; Q3). In the group of patients with CI-AKI, the average value of contrast medium volume was 1,7 (1,2; 2,5), while in patients without CI-AKI — 1,4 (1,0; 1,9). The difference between the presented values is significant, which is confirmed by the Mann-Whitney U test (p=0,04).

Multivariate logistic regression revealed coefficients, on the basis of which the equation for assessing the risk of CI-AKI in patients with PCI was created:

dCI-AKI=1/(1+exp (7,613-0,43906*CV-0,06764* *Age-0,80557*A)),

where dCI-AKI is the likelihood of developing CI-AKI, CV — contrast volume (ml/kg), A — anemia as follows: presence — 1, absence — 0.

The following scale is proposed for assessing the degree of risk for CI-AKI in patients with angiography and PCI.

- ⩽5% — Low risk
- 5,1%-15% — Moderate risk
- 15,1%-50% — High risk
- >50% — Very high risk

## Discussion

There are some studies with certain predictors, on the basis of which models for assessing the risk of CI-AKI are created, while the set of CI-AKI predictors in different works is different [10-13].

In the present study, a number of significant variables were identified that allow assessing the risk of CI-AKI: anemia, age and contrast medium volume injected, depending on the patient's body weight. Numerous studies on the risk of CI-AKI considered the elderly and senile age of patients as a rather high risk for CI-AKI, which is confirmed by this work [11, 13]. In a number of studies, age >70 years was used as the threshold value for CI-AKI risk [10, 12]. The presented study confirms this statement by the fact that in the group of patients with established CI-AKI, the proportion of patients over 70 years old was 63%. It is known that the most common diseases of old age are a consequence of age-related weakening of defense mechanisms, which allows the action of exogenous factors to be realized. This study showed a relatively high probability of CI-AKI in patients over 80 years old, which was 22-33,5% in the range of 80-89 years, and in patients in the range of 90-92 years — 33,6-38,6%. The presented results undoubtedly require a special approach to patients of older age groups when using contrast-enhanced X-ray investigations. The volume of injected contrast agent is also considered in many works as a predictor of CI-AKI, while this parameter was presented differently: contrast volume per body surface area, contrast volume per mass unit, total volume of injected contrast [10-12]. Multivariate analysis in our study showed a significance of the variable of contrast volume per unit of body weight in ml/kg. It was also noted that if the contrast medium volume is >3,5 ml/kg in patients over 70 years old, the probability of CI-AKI is >25%, which makes it possible to classify these patients to a high-risk group. In contrast to the two above-mentioned predictors of CI-AKI, the variable "anemia" as a predictor of CI-AKI is presented comparatively less frequently in available publications. However, in the presented study, this variable was noted as a significant predictor of CI-AKI. In particular, on the basis of multivariate logistic regression, the presence of anemia in patients aged over 70 years of age with a volume of injected contrast medium >3,5 ml/kg increases the risk of CI-AKI up to 44%. The graphs presented show the risk of CI-AKI based on identified predictors (Figure 2a and 2b).

The presented risk assessment scale for CI-AKI in patients after CAG and PCI can be used to assign patients to a certain risk group, which will increase the potential for reducing the CI-AKI risk by applying appropriate treatment procedures. Despite the fact that multivariate analysis showed a high significance of the found CI-AKI predictors, it should be noted that due to the retrospective design of the study and a limited access to other possible predictors, it is very likely that we did not identify other important etiopathogenetic factors of CI-AKI development. It should also be noted that the current model for assessing the risk of CI-AKI was based on the CI-AKI criterion "an increase in creatinine levels within 48 hours and within a week", and cannot be used in relation to other criteria.

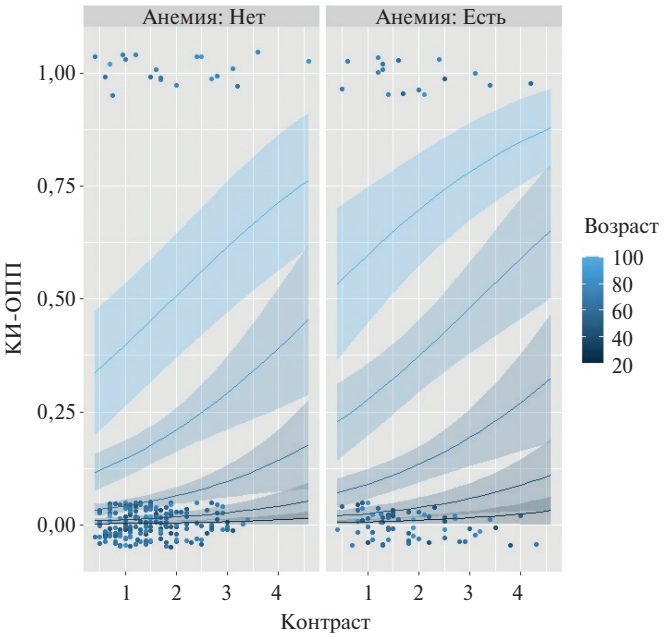


**Figure 2a.** The likelihood of developing CI-AKI depending on contrast volume (mg/ml), anemia and age.

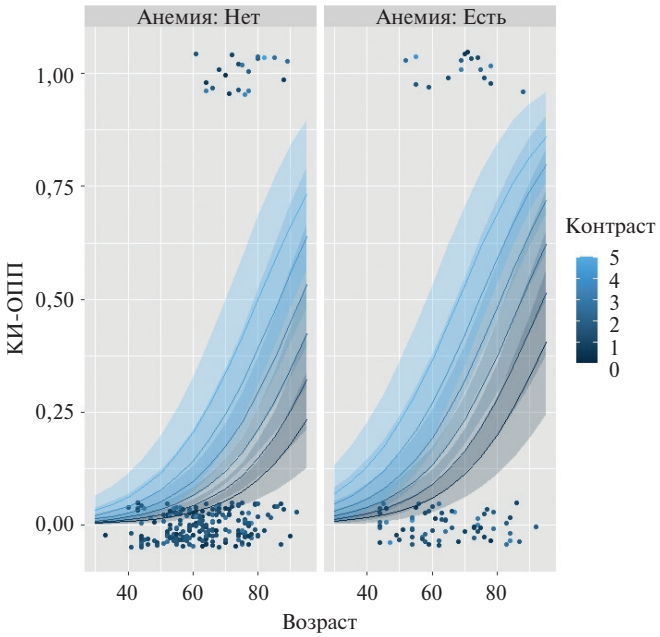


**Figure 2b.** he likelihood of developing CI-AKI depending on contrast volume (mg/ml) and anemia.

## Conclusion

CI-AKI is a common complication of CAG in patients with AMI in a specialized hospital. A simple scale for assessing the CI-AKI risk makes it possible to identify a category of patients who require preventive measures to reduce iatrogenic complications and mortality.

**Relationships and Activities:** none.

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