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DIAGNOSTIC AND TREATMENT METHODS

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RISK OF ACUTE KIDNEY INJURY IN PATIENTS WITH ISHEMIC HEART DISEASE AND CONCOMITANT METABOLIC SYNDROME AFTER ON-PUMP CORONARY BYPASS GRAFTING

The aim of the research was to study the incidence and risk factors of developing AKI, its patterns in patients with CHD and concomitant MS after the coronary artery bypass grafting off-pump.

Materials and methods. The study covered two groups: patients with CHD and MS (the main group, n=82); and patients with CHD but without MS (the control group, n=51). Here are the inclusion criteria for the study: CHD with HF of Class III-IV; normal left ventricular ejection fraction (LVEF) - 55% and above; 45-69 years of age. The exclusion criteria were as follows: complications during and after the surgery, diabetes mellitus, kidney diseases, low LVEF (<54%), over 70 years of age. The criteria for MS: central obesity, arterial hypertension, increased triglycerides (≥1.7 mmol/L), and impaired glucose tolerance (IGT).

Results. Signs of AKI were detected in 61 (45.9%) patients, out of which 56 (68.3%) patients had MS. The patients with MS demonstrated initial reduced in GFR (71.2 ± 13.2 ml/ min/1.73 m^2), with its values reducing further on the 2nd day to 55.2 ± 14 ml/min/1.73 m^2 and the low values remaining on the 10th day after the surgery (69.5 ± 12.8 ml/min/1.73 m^2). The patients with MS had longer artificial lung ventilation (17.1 ± 9.1 hours against 10.8 ± 8.6 in the control group, p <0.01), longer stay at ICU (4.1±1.7 days against 2.9±0.9 in the control group, p<0,01) and in the hospital (24.3±3.2 days against 21.39±2.3 in the control group, p<0.015), and higher mortality (5.4% against 1.9% in the control group). The statistically reliable risk factors were revealed: the patient's age (p<0.01), high-density lipoprotein in blood (p <0.01), total cholesterol (p<0.039), and creatinine (p<0.01).

Conclusion. The presence of MS is a factor contributing to the high probability of AKI development after coronary artery bypass grafting off-pump (68.3% of the cases), which requires monitoring of the renal function during perioperative period, as well as prevention of AKI in patients with CHD and concomitant MS.

***Keywords*:** coronary heart disease, coronary artery bypass grafting off-pump, metabolic syndrome, risk factors, acute kidney injury.

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Relevance. Coronary heart disease (CHD) is a leader among all causes of death in the world [1]. At present, myocardial revascularization by artery bypass surgeries is a common solution for CHD. However, despite its high efficiency, there surgeries are accompanied by various undesirable dysfunctions of organs and systems in the organism, as well as the development of severe complications, including acute kidney injury (AKI) [2]. The recent data show that after coronary artery bypass grafting, AKI is observed in 17.5 % of cases [3], leading to a changed patient treatment tactic, prolonged treatment duration and significantly worse prognosis, with hospital mortality rate increasing from 7.6 % to 26.3% [2].

It has been established that MS is one of the negative factors contributing to renal dysfunction in patients with cardiovascular pathologies [4]. Typically, patients with MS are overweight and suffer from dyslipidemia, insulin resistance, and arterial hypertension [5]. Due to a high risk of developing various complications in the postoperative period, this category of patients constitutes a serious medical, social, and economic challenge of the present time [2, 4].

The comparison of the data from different researchers on AKI after bypass surgeries demonstrates a wide scatter of the incidence and outcomes of treating this complication. This is explained by the fact that they use different criteria of evaluating kidney injuries, present heterogeneous age groups of patients, sometimes do not take into account the presence of chronic kidney diseases, or cover different methods of surgeries – bypass grafting with mechanical ventilation or off-pump.

In this regard, the study of the incidence and predictors of developing AKI, its patterns in patients with CHD and concomitant MS having undergone coronary artery bypass grafting off-pump is relevant.

The aim of the research was to study the incidence and risk factors of developing AKI, its patterns in patients with CHD and concomitant MS after the coronary artery bypass grafting off-pump.

Materials and methods. The study covered 133 patients (104 men and 29 women), aged 45-69 (mean age of 58.2±6.4 years). All the patients underwent semi-elective coronary artery bypass grafting off-pump at the Sakha (Yakutia) Republic's Hospital No. 1 - National Center of Medicine in the period 2017-2020. During the postoperative period, the patients were supervised and treated at the Anesthesiology, Reanimation and Intensive Therapy Unit (ARITU).

The diagnostics of AKI and evaluation of its severity was done in accordance with the Kidney Disease Improving Global Outcomes (KDIGO) Guidelines [9]. The calculation of the glomerular filtration rate (GFR) was done with the CKD-EPI formula (Chronic Kidney Disease Epidemiology Collaboration) [10] before the surgery, on Day 1, 2, 3, and 10 following the surgery.

The continuous sampling of all the patients was divided into two groups: Group 1 – 82 patients with CHD and concomitant MS (main group); and 51 patients with CHD without MS (control group).

The inclusion criteria for the study were as follows: diagnosed CHD with HF of Class 3 and 4; normal left ventricular ejection fraction (LVEF) – 55% and above; 45-69 years of age.

The exclusion criteria were as follows: complications during and after the surgery (major bleeding, repeated exploration, perioperative myocardial infarction, and stroke), diabetes mellitus of Type 1 and 2, kidney diseases, and low LVEF (<54%).

The criteria for MS: waist over 80 cm in women and over 94 in men, systolic blood pressure >140 and diastolic – above 90 mm Hg, increased level of triglycerides (≥1.7 mmol/l), IGT – an increased level of plasma glucose in 2 hours after the load of 75 g of anhydrous glucose with the oral glucose tolerance test ≥7.8 and <11.1 mmol/l, under the condition that the level of fasting plasma glucose makes less than 7.0 mmol/l [1].

All the patients fell into Class 3 and 4 under the classification of anesthesiology risks by the American Society of Anesthetists (ASA).

All the patients were measured and their body mass indexes (BMI) were calculated. Before the surgery, the patients underwent standard tests: ECG, holter monitoring, duplex vascular scans. Two-three weeks before the surgery, they had a selective coronary angiography (SCAG), angiography of major and peripheral arteries. Laboratory tests: general clinical (complete blood count and urinalisys, coagulogram, biochemistry tests, lipid profile, finding out the acid-base balance and blood electrolytes, glycemic profile). The tests were run on the following stages: *Stage 1* – before the surgery; *Stage 2* – Day 1 after the surgery; *Stage 3* – Day 2 after the surgery; *Stage 4* – Day 3 after the surgery; *Stage 5* – Day 10 after the surgery.

The anesthetic managements of all the patients was carried out under cardio anesthesiology standards following the management protocol of patients undergoing coronary artery bypass grafting off-pump.

The type of the study is retrospective and prospective, longitudinal observational.

The processing of the 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); a logistic regression analysis to assess the predictors of reduced GFR; the

Table 1

The indicators and dynamics of laboratory-instrumental and clinical data in the studied groups (M±SD)

Indicators	All patients (n=133)	Patients with MS (n = 82)	Patients without MS (n=51)	p
Overweight BMI>25 kg/m^2	29.7±4.8	32.4±3.26	25.3±3.7	0.297
HbA1c, %	4.99±1.0	5.44±1.08	4.27±0.6	<0.01
EuroSCORE index, %	8.95±2.83	9.55±2.99	7.92±2.23	<0.01
Surgery duration, min.	156.5±18.9	157.43±20.2	155.1±16.7	0.496
Number of bypasses, Me(IQR)*	1(1;1)	1(1;1)	1(1;1)	0.895
Number of bypasses, n (%)				
1 bypass	115 (86.5)	70 (85.4)	45 (88.2)	
2 bypasses	17 (12.8)	12 (14.6)	5 (9.8)	
3 bypasses	1 (0.8)	-	1 (2)	
LVEF, %				
before surgery	59.9±6.1	59.6±5.2	60.3±7.5	<0.01
after surgery (Day 2)	60.8±6.1	60.4±6.25	61.5±6.6	0.036
Microalbuminuria, mg/day				
before surgery	18.6±13.7	22.4±13.1	12.64±12.6	0.387
Urea, mmol/l				
before surgery	7.5±1.4	7.6±1.3	7.2±1.56	0.243
Day 1 after surgery	8.9±2.2	9.3±2.3	8.1±1.71	0.002
Day 2 after surgery	9.6±2.7	10.3±2.8	8.4±1.9	0.001
Day 3 after surgery	9.6±2.8	10.0±3.1	8.92±2.0	0.011
Day 10 after surgery	8.2±1.9	8.3±2.0	8.0±2.0	0.341
Creatinine, μmol/l				
before surgery	96.6±16.5	100.4±17.8	90.5±12.18	0.012
Day 1 after surgery	96.3±15.7	119.6±20.3	100.9±13.2	<0.01
Day 2 after surgery	119.6±29.7	130.4±29.2	102.2±21.4	0.013
Day 3 after surgery	111.1±26.3	120.0±26.1	96.7±19.8	0.081
Day 10 after surgery	96.3±15.7	102.1±14.7	87.1±12.6	0.971
Osmolarity, mOsm/l				
before surgery	279.8±10.1	283.2±6.4	274.5±12.4	<0.01
Day 1 after surgery	286.4±10.4	291.4±7.6	278.8±9.9	0.279
Day 2 after surgery	288.7±11.0	292.7±10.3	283.4±10.1	0.159
Day 3 after surgery	285.5±10.5	289.8±6.6	279.8±12.4	<0.01
Day 10 after surgery	279.4±12.3	283.6±6.3	272.7±16.1	<0.01

Note: * Me, IQR – the median, interquartile range Q3-Q1.

two-tailed criterion of Student's t-test for comparing the mean values of two independent groups, and the x^2 criterion for comparing the dichotomous variables. The statistical significance was set at $p < 0.05$

Results and Discussion. Out of 133 patients covered in the study, the signs of AKI were observed in 61 (45.9%) patients. The changes in the excretory function of the kidneys were registered as early as on Day 1 after the surgery and reached the maximum on Day 2. The two studied groups demonstrated significant differences. In the control group, the sign of AKI under the KDIGO criteria were observed in 5 (9.8%) patients only, whereas in the group of the patients with MS the signs manifested in 56 (68.3 %) of the patients. Indeed, the analysis of the concomitant MS contribution to the development of AKI in the patients revealed their definite relation: the odds ratio (OR) = 12.9; confidence interval (CI) = 4.6–36.0; $x^2 = 31.153$ ($p<0.05$).

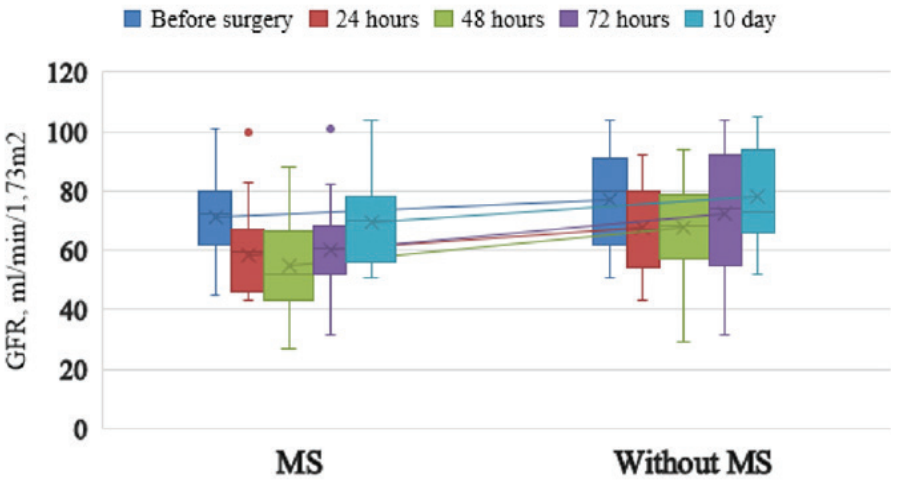
Table 1 and Figure present the detailed comparative analysis of the values obtained in the laboratory research and instrumental analysis on the patients in the studied groups.

In the preoperative period, the study groups demonstrated significant baseline differences ($p<0.05$) in the values of the adverse outcome index of coronary artery bypass grafting (EuroSCORE index), glycosylated hemoglobin (HbA1c), LVEF, creatinine and blood osmolarity. For instance, before the surgery, the blood creatinine level in the patients with MS was 100.4±17.8 μmol/l, in the control group – 90.5±12.2 μmol/l ($p<0.012$). The exceptions were BMI ($p=0.297$) and albuminuria level ($p=0.387$) (Table 1).

The most pronounced changes in the indices were observed in the both groups on Day 2 after the surgery, when the maximum level of increased blood creatinine was noted. The patients with MS also demonstrated a more pronounced increase in creatinine, which reached 130.4±29.2 μmol/l.

The postoperative dynamics of GFR, as an objective predictive criterion of AKI, confirms the above dynamics of the creatinine level in blood at the different stages of treatment (Figure).

In the patients with MS, in contrast to the patients in the control group, an initial decrease in GFR was observed in the preoperative period – 71.2±13.2 ml/min/1.73 m^2 ($p<0.01$). After the surgery, it decreased further, reaching 55.2±14 ml/min/1.73 m^2 on Day 2, which is 1.3 times lower than the initial values ($p<0.01$). In the following days, there was an increasing trend; however, on Day 10 after the surgery, the GFR level remained below the initial values – 69.5±12.8 ml/min/1.73 m^2. It can be seen that similar dynamics in the level of GFR in the postoperative period is also characteristic of the patients in the control group, which indicates the need for mandatory monitoring of the renal function and targeted prevention of its disorders for all patients with coronary artery disease having undergone bypass grafting.



Glomerular filtration rate dynamics in the studied groups (M±SD).

Given the obvious relationship between MS and decreased renal function, as well as the presence of numerous risk factors for the development of AKI with MS, it is of interest to identify the key factors among them. In order to determine the main predictors of a decrease in GFR in patients with MS, we performed a regression analysis of a number of AKI factors (Table 2).

Among the presented risk factors for AKI, the statistical significance of the factors was revealed: the patient's age ($p<0.01$), the level of high-density lipoproteins (HDL) in blood ($p<0.01$), total cholesterol ($p<0.039$), and creatinine ($p<0.01$). All other factors were of no statistical significance (Table 1). Obviously, the risk factors for the development of AKI also include the specifics of a certain surgery (duration, number of bypasses, technical difficulties) and anesthetic support (for example, unstable hemodynamics). However, we excluded the cases with a complicated course of surgical intervention and anesthesia from our study.

The treatment outcomes of the patients in the studied groups demonstrated significant differences (Table 3).

The duration of mechanical ventilation in the patients with MS in the postoperative period was 17.1±9.1 hours against 10.8±8.6 hours in the control group ($p<0.01$).

The duration of treatment of the patients with MS at ARITU and in-patient ward was 4.1±1.7 and 24.3±3.2 days, respectively, which also reliably exceeds the duration of treatment of the patients in the control group ($p<0.01$).

The mortality in the patients with MS made 5.4%, in the patients without MS – 1.9%.

Conclusions. In our study, the patients with coronary heart disease who underwent bypass surgery off-pump

Table 2

The regression analysis of the main predictors of a decrease in GFR in patients with MS (M±SD)

AKI risk factors	GFR 89-60 ml/min/1.73m2 (n=26)	GFR < 60 ml/min/1.73m2 (n=56)	p
Age, years	55.0±7.0	59.4±6.5	<0.01
BMI, kg/2	31.3±3.2	33.5±2.9	0.094
Osmolarity of blood plasma, mOsmol/l	284.0±7.6	282.0±5.6	0.819
HDL, mmol/l	1.68±0.23	1.49±0.2	<0.01
LDL, mmol/l	2.53±0.36	2.5±0.5	0.486
Total cholesterol, mmol/l	6.75±1.2	6.94±1.26	0.039
Triglycerides, mmol/l	1.78±0.2	1.71±0.3	0.599
Creatinine, μmol/l	97.8±15	101.9±20.6	<0.01
LVEF, %	61±5.9	60.2±5.9	0.551

Table 3

The treatment outcomes of the patients in the studied groups (M±SD)

Indicator	All patients (n=133)	Patients with MS (n=82)	Patients without MS (n=51)	p
Duration of MV at ARITU, hours	14,7±9,4	17,1±9,1	10,8±8,6	<0,01
Duration of treatment, bed/days at ARITU at in-patient ward	 3,6±1,6 23,2±3,1	 4,1±1,7 24,3±3,2	 2,9±0,9 21,39±2,3	 <0,01 0,015
Mortality, abs (%)	5(4)	4(5,4)	1(1,9)	<0,01

manifested early signs of AKI in 45.9% of the cases, with the signs most pronounced on Day 2 after the surgery. The signs of AKI in the patients without MS were noted in 9.8% of the cases, whereas with concomitant MS, they were observed far more often – in 68.3% of the patients. In this case, unlike the patients in the control group, the patients with MS were characterized by both an initial decrease in GFR (71.2 ± 13.2 ml/min/1.73 m^2) and its low values on Day 10 after the surgery (69.5 ± 12.8 ml/min/1.73 m^2).

Among the risk factors for AKI, the statistical significance of the factors was revealed: the patient's age ($p<0.01$), the level of high-density lipoproteins (HDL) in blood ($p<0.01$), total cholesterol ($p<0.039$), and creatinine ($p<0.01$).

Thus, the management of patients with coronary heart disease and concomitant MS who underwent surgical treatment, in particular bypass surgery off-pump, requires a special approach, a mandatory assessment of the initial state of the renal function, and the implementation of measures for the targeted prevention of the kidney decreased function in pre- and postoperative periods.

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