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# Significance of its Markers in Early Diagnosis of Acute Kidney Damage in Myocardial Infarction

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**Abstract:** The article examines the issues of early detection of acute kidney injury in the acute phase of myocardial infarction, and a comparative analysis of NGAL, KIM-1 and cystatin C indicators is carried out. ROC analysis showed that NGAL (AUC=0.84, p<0.001) and KIM-1 (AUC=0.81, p<0.001) were 0.81, which was the second most significant change after NGAL. Cystatin C (AUC=0.81, p<0.001) was highly significant in acute kidney injury, but its sensitivity and specificity were low compared with NGAL.

**Keywords:** Myocardial infarction, acute kidney injury, biomarkers, glomerular filtration, creatinine, neutrophil gelatinase.

## Introduction

Acute kidney injury is one of the complications of myocardial infarction and, according to some literature, is observed in 10-60% of patients [3,5]. The addition of renal dysfunction significantly worsens the course of myocardial infarction, increases the risk of death and increases the cost of treatment. [1].

The development of acute renal failure in myocardial infarction is associated with a decrease in perfusion and filtration in the kidneys as a result of a decrease in cardiac output [6]. At the same time, damage to the renal tubules further complicates the process [7].

As is known, creatinine is widely used to detect it. However, for a number of reasons (patient age, gender, muscle mass, etc.), it does not allow for early diagnosis of changes in the functional state of the kidneys. Therefore, in recent years [12], the use of highly sensitive specific biomarkers has made it possible to detect changes in the kidneys early [4,9]. However, their diagnostic criteria have not been studied in detail so far.

As is known, myocardial infarction, which is one of the clinical forms of acute myocardial infarction, occurs suddenly, its symptoms are well studied, and standards for the treatment of various clinical forms have been created. In this case, it is important to study the risk factors leading to it and the damage to other internal organs in this serious disease [23].

Acute kidney injury is a serious complication of myocardial infarction and, according to literature data, is observed in 10-60% of cases. Its addition leads to a more severe course of the disease, an increased risk of death, and increased efforts for treatment [1].

Recent studies have shown that acute kidney injury following myocardial infarction is a risk factor for both immediate and long-term adverse outcomes. The 10-year mortality rate from myocardial infarction in mild acute kidney injury is 15%, in moderate acute kidney injury 23%, and in severe acute kidney injury 33% [7].

In order to standardize the diagnosis of acute kidney injury and assess its severity, the Acute Dialysis Quality Initiative (ADQI) group (2004) recommended the RIFLE (Risk Injusy Failure Loss, End-stage renal disease) classification system [17].

In 2007, this classification was simplified, and in its simpler form, acute kidney injury was divided into three stages, and the duration of diagnosis was extended to 48 hours. The criteria were later called the Acute Kidney Injury Network (AKIN) [18].

Therefore, the study of markers confirming acute kidney injury is of great practical importance. Biological markers are used in practice to assess the risk of developing the disease or its diagnosis, and to assess the effectiveness of treatments [19].

As is known, the most widely used biomarkers in practice are blood creatinine levels and albuminuria. Although they indicate the progression of renal dysfunction, changes are observed in the late stages of this complication. [22].

In recent years, cystatin-C has become a widely used biomarker for the assessment of renal dysfunction, along with glomerular filtration rate. This protein consists of 122 amino acids, has a molecular weight of 13 kDa, and is an inhibitor of cysteine proteases. Cystatin-C is present in all body fluids, including urine [20], and its stability protects the body from uncontrolled proteolysis. Unlike creatinine, cystatin-C production is not dependent on a number of factors, including age, sex, tumor growth, excess muscle mass, and inflammation. However, some studies have shown that its high levels are also associated with male gender, height, and excess body weight [16]. Cystatin-C diffuses into the tubule lumen and is completely metabolized in its proximal part. Therefore, it can be concluded that its blood level is inversely proportional to glomerular filtration rate.

Available data suggest that the use of creatinine in parallel with cystatin-C in the diagnosis of renal dysfunction is appropriate. The Epidemiology of Kidney Disease (CKD-EPI) has conducted studies on the diagnostic value of the combination of creatinine and cystatin-C when the eGFR is less than 60 ml/min/1.73 m2 [24].

When eGFR is measured together with creatinine and cystatin-C, the risk of death from all causes, including cardiovascular disease, increases in parallel when the value is less than 85 ml/min/1.73 m2 [25].

Therefore, studies show that estimation of glomerular filtration rate using cystatin-S and creatinine is reliable in diagnosing renal dysfunction. Also, blood creatinine, cystatin-C values, and urine albumin-to-creatinine ratio risk stratification and more clearly confirm the development of renal failure [27].

Neutrophil gelatinase-associated lipocalin (NGAL) is a 25 kDa protein consisting of 128 amino acids. In biological fluids, NGAL is mainly found in the monomeric form. In animals with ischemic nephrotoxic acute renal failure, elevated levels of this protein were detected in their serum and urine. Therefore, NGAL has been considered a primary biomarker of ischemic kidney damage. This protein is mainly produced in the ascending limb of the renal tubule of Henle and the collecting ducts [28].

Currently, NGAL is not only a reliable marker of acute kidney injury, but also has been shown to be important in the diagnosis of SCD in experiments conducted in two types of rats [26]. It has also been shown to increase in the blood of patients with rapidly developing SCD [14]. In addition, elevated levels of NGAL in the blood and urine have been found in several other kidney diseases, including IgA nephropathy, autosomal polycystic kidney disease, and diabetic nephropathy [15].

KIM-1 is a transmembrane lipoprotein with a molecular weight of 90 kDa and contains extracellular mucin and immunoglobulin domains. Its levels are unchanged in normally

functioning kidneys but are elevated in the proximal tubules after ischemia. The extracellular domain of KIM-1 is readily detected in the urine shortly after ischemic kidney injury [13].

In rats, KIM-1 depletion from renal epithelial cells causes interstitial inflammation with fibrosis, leading to death, anemia, proteinuria, hyperphosphatemia, and hypertension. This finding may provide a useful insight into the mechanisms underlying human kidney disease [21].

Therefore, the persistent production of KIM-1 is a sign of the development of renal fibrosis, a mechanical connection between acute and chronic damage, and an increase in SCC. Although in retrospective observation of patients with proteinuria associated with diabetes mellitus, elevated urinary KIM-1 levels were noted, they normalized after taking angiotensin-converting enzyme inhibitors or a low-salt diet. This confirms that this lipid protein may play an important role in assessing the effectiveness of treatment [10,11].

Although a number of studies have been conducted in recent years on the importance of the above-mentioned biochemical markers in the early detection of renal dysfunction in the acute period of myocardial infarction, they have not been studied in a comparative manner. Troponins, which are considered important diagnostic markers of myocardial infarction, are reported in the literature to be altered not only in this disease, but also in a number of other pathological conditions, including nephropathies. From this point of view, the study of the relationship between troponin and other markers of renal dysfunction is of great practical importance.

Objectives of the study: Comparative study of changes in renal glomeruli and tubules in the acute period of myocardial infarction using cystatin-C, neutrophil gelatin-associated lipocalin-NGAL and kidney damage molecules - KIM-1.

**Materials and methods**

Based on the set goals and objectives, our study involved 60 patients diagnosed with acute myocardial infarction treated in the cardioresuscitation department of the Multidisciplinary Clinic of the Tashkent Medical Academy in 2024 - the main group, and 30 patients treated in the cardiology department and diagnosed with stable angina pectoris of functional classes III-IV - the control group. The main group of patients consisted of 38 (63.3%) men and 22 (36.7%) women. The average age was 60.5±7.4. The control group included 16 men and 14 women, and their average age was 63.6±5.9 years.

The main group of patients was also divided into two subgroups based on electrocardiographic changes. The first group consisted of 32 patients with electrocardiographic S-T segment elevation, and their average age was 57.4±3.68. Of these, 23 were men and 9 were women. The second group consisted of 28 patients with no electrocardiographic ST-segment elevation, with a mean age of 63.8±2.87 (13 women, 15 men). Patients were prescribed standard treatment for acute myocardial infarction (antiischemic, ACE inhibitor or sacubitril/valsartan, β-blockers, statin, antiplatelet agents, anticoagulants).

The control group included 30 patients with stable angina pectoris functional class III-IV. This group of patients received standard treatment for ischemic heart disease.

Determination of laboratory parameters. Complete blood count. The main part of the complete blood count was performed on the “Mythic-22” Orphee, (Switzerland) hematological analyzer. It determined the hemoglobin content, erythrocyte, leukocyte, platelet, and hematocrit indices. The leukocyte formula was stained with the Romanovsky-Giemza method and counted under a “BAUSCH-LOMB” (Russia) microscope. Erythrocyte sedimentation rate was determined by Panchenko's apparatus in a 100 mm tube with blood mixed with 5% sodium citrate solution.

Blood biochemical parameters - serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, glucose, urea, creatinine, total protein, potassium, sodium, blood lipid spectrum analysis were performed on a Mindry BA-88 biochemical analyzer using reagents from the Human company (Germany). Serum cystatin C levels were determined using

an ELISA method on a semi-automatic Mindray MR 96A device. Detection range: 0.313-20 ng/ml, Sensitivity: 0.188 ng/ml.

Serum NGAL levels were determined using the ELISA method on a semi-automatic Mindray MR 96A device. Detection range: 0.313-20 ng/ml, Sensitivity: 0.188 ng/ml.

Serum NGAL levels were determined using the ELISA method on a semi-automatic Mindray MR 96A device. Detection range: 0.156-10 ng/ml, Sensitivity: 0.094 ng/ml.

**Results and Discussions**

It is known that among cardiovascular diseases, myocardial infarction stands out from other diseases by its acute onset and multiple complications. Especially in patients with ST-segment elevation (STEMI) and non-ST-segment elevation (NSTEMI) myocardial infarction, if acute kidney injury is not detected in time, this condition can lead to a sharp deterioration in their general condition. As we noted above, in recent years, the importance of biomarkers such as NGAL, KIM-1 and Cystatin-C in the diagnosis of acute kidney injury in medicine has been increasing. The main advantages of these biomarkers are that their levels increase in serum or are excreted in urine at early stages of kidney damage, that is, before creatinine levels. Taking the above into account, we studied the levels of NGAL, KIM-1 in urine and Cystatin-C in serum in patients with myocardial infarction. The results are presented in Table 1 below.

**Table 1.Changes in laboratory indicators of kidney dysfunction in patients with acute myocardial infarction**

| № | Indicators | with ST segment elevation, n=32 | No ST segment elevation, n=28 | Control group, n=30 | P (difference between groups 1 and 2) |
|---|---|---|---|---|---|
| 1 | NGAL, ng/ml | 483.1±34.57 | 315.3±32.5 | 124.7±21.8 | $P_{1-2}<0.01$<br>$P_{1-3}<0.001$<br>$P_{2-3}<0.001$ |
| 2 | KIM 1, ng/ml | 4.363±0.147 | 2.713±0.089 | 2.1±0.1 | $P_{1-2}<0.001$<br>$P_{1-3}<0.001$<br>$P_{2-3}<0.01$ |
| 3 | Cystatin C, mg/l | 1.318±0.034 | 1.157±0.034 | 1.3±0.04 | $P_{1-2}<0.01$<br>$P_{1-3}>0.05$<br>$P_{2-3}<0.01$ |

As shown in the table, the level of NGAL (lipocaine 2) in urine in patients with myocardial infarction with S-T segment elevation was 483.1±34.57 ng/ml and in those without S-T elevation, it was 315.3±32.5 ng/ml. When comparing them, a significant (P<0.01) statistical difference was found. KIM-1 indicators were 4.363±0.147 ng/ml in the first group and 2.713±0.089 ng/ml in the second group, with a high (P<0.001) significant difference between them.

Serum Cystatin C indicators were 1.318±0.034 mg/l and 1.157±0.034 mg/l, respectively, with a significant (P<0.01) difference. In order to assess the degree of acute kidney injury in both groups, glomerular filtration rate, calculated by serum cystatin-C, was also evaluated. In patients with S-T segment elevation, glomerular filtration rate was 62±3.6 ml/min per 1.72 m2 of body surface area and in patients without S-T segment elevation, it was 70.5±4.2 ml/min per 1.72 m2 of body surface area. When comparing them, no statistically significant differences were found. In the control group, the level of NGAL in urine was 124.7±21.8 ng/ml, KIM 1 indicators were 2.1±0.1 ng/ml, and serum Cystatin C was 1.3±0.04 ng/ml. The high levels of cystatin C in this group of patients may be associated with the higher incidence of chronic kidney disease in these patients.

In addition, in order to predict the occurrence, severity, and outcome of acute kidney injury in patients with myocardial infarction, we evaluated the relationship between troponin, which is generally recognized as its main marker in serum, and markers of acute kidney injury using correlation and regression analyses. Figure 1 below shows the correlation between troponin and NGAL in patients with acute myocardial infarction.

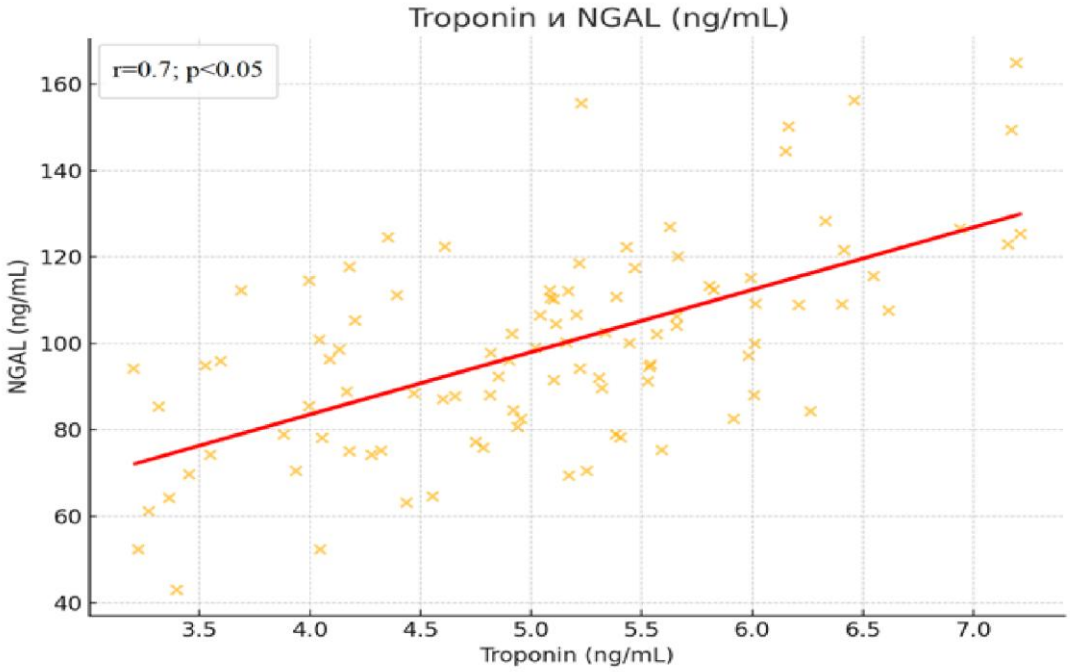


**Figure 1.** Correlation between troponin levels and NGAL in patients with acute myocardial infarction**.**

As shown in the figure, a strong positive correlation was found between serum troponin levels and NGAL (r=0.7, p<0.05). This relationship suggests that elevated troponin levels are an indirect marker of acute kidney injury.

In the next step, the correlation between KIM-1 levels and troponin in our patients was analyzed and is presented in Figure 2.

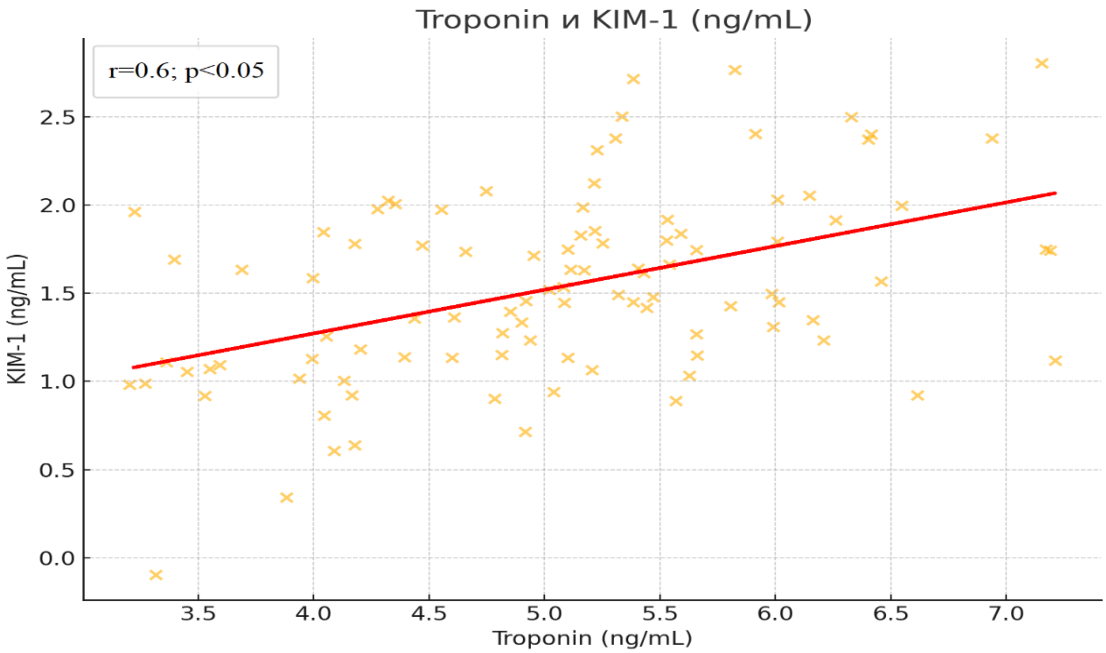


**Figure 2.** Correlation between troponin and KIM-1 levels in patients with myocardial infarction**.**

As shown in this figure, a moderately strong positive correlation was observed between troponin indicators and KIM-1 ($r=0.6$, $p<0.05$). The obtained result confirms the increase in KIM-1, which is considered one of the markers of acute kidney injury in the urine, in parallel with troponin indicators.

It is known that numerous studies have confirmed that cystatin C is a reliable marker of kidney injury and that the calculated glomerular filtration rate determined by it is of great importance in assessing the functional state of the kidneys. From this point of view, it is of practical importance to study the relationship between troponin levels in the blood and cystatin-C in the detection of renal dysfunction. Taking this into account, we studied the relationship between these two markers and presented in Figure 3.

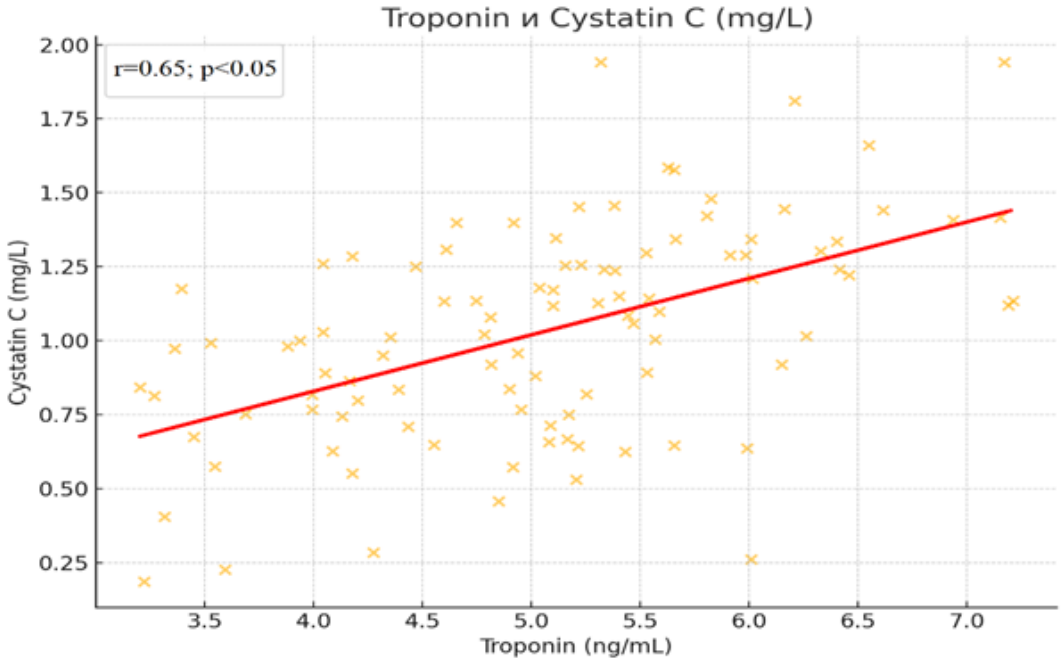


**Figure 3.** Correlation between troponin levels and cystatin C in patients with myocardial infarction**.**

A moderately strong positive correlation was observed between serum cystatin-C and troponin ($r=0.65$, $p<0.001$) in patients with myocardial infarction. This indicates that elevated serum troponin levels exacerbated existing renal dysfunction in patients as a result of hypoxia resulting from myocardial infarction.

Taking the above into account, we conducted a ROC analysis to determine the reliability of the studied markers in diagnosing acute kidney injury. The results are presented in Figure 4.

As shown in the figure, the ROC analysis revealed that NGAL (AUC=0.84, $p<0.001$) was the most reliable marker for acute kidney injury in patients with myocardial infarction. In this analysis, KIM-1 (AUC=0.81, $p<0.001$) was second only to NGAL, with a significant change of 0.81. Cystatin C (AUC=0.81, $p<0.001$) was found to have a high significance in acute kidney injury, but its sensitivity and specificity were low compared to NGAL.

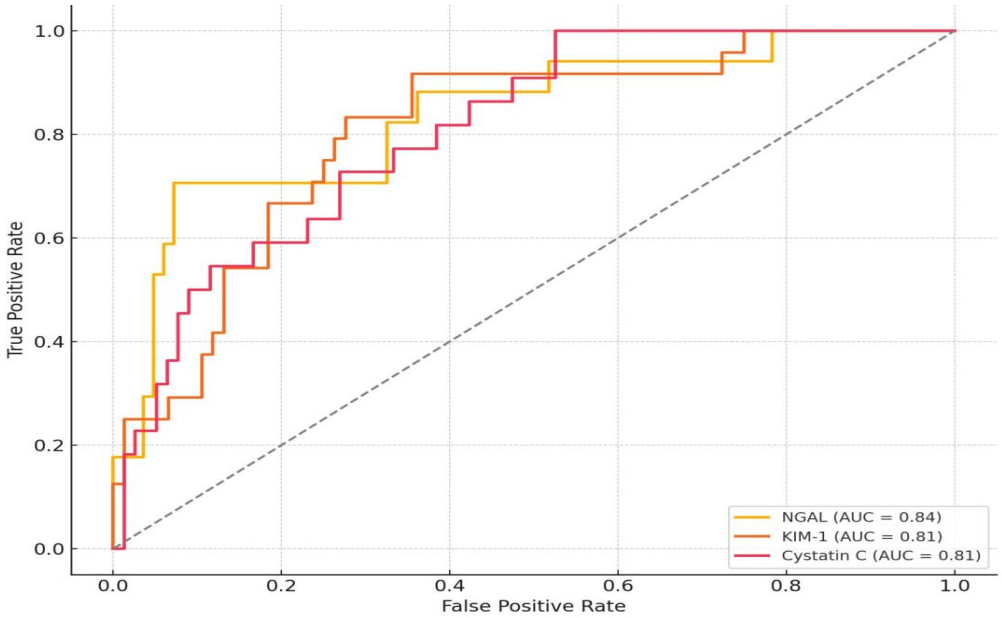


**Figure 4.** Comparative analysis of studied biomarkers in the diagnosis of acute kidney injury in myocardial infarction**.**

## Conclusion

A slight increase in the above-mentioned markers in patients with myocardial infarction indicates a high probability of developing acute kidney injury. Indeed, the kidneys are the most commonly affected target organ in patients with acute myocardial infarction. The results we have found in our study confirm this. In this group of patients, the presence of any concomitant diseases accelerates the process in the kidneys and leads to the development of acute kidney injury. Therefore, the detection of the above-mentioned markers in the acute period of the disease requires dynamic monitoring of the functional state of the kidneys and the implementation of nephroprotective therapy.

## References:

1. Avdoshina S.V., Villevalde S.V., Efremovtseva M.A., Kabalova J.D. Znachenie biomarkerov v diagnostike i opredeleni i prognoza ostrogo pochechnogo povrezdeniya u bolnyx s strym koronarnym syndromom bez pedema segmenta ST. // Vestnik Rossiyskogo universiteta drujby narodov. – 2014. – №1. – S. 92-95.
2. Demchuk O.V., Sukmanova I.A. Prognozirovanie chastoty razvitiya khronicheskoy bolezny chek u patsentiov s infarktom myocarda i otrym poverjdeniem chek. // Russian Cardiology Journal. – 2023. –28(6): 5247. https://doi.org/10.15829/1560-4071-2023-5247.
3. Zaitseva V.P., Nanchikeeva M.L., Bulanov NM. // Nephrology and dialysis. – 2013; (4): 369.
4. Kobalava J.D., Villevalde S.V., Efremovtseva M.A., Moiseev V.S. Biomarkers acute kidney injury: contemporary perspectives and prospects // Sweat. arch. – 2014. – №6. – S. 88-93.
5. Menzorov M.V., Shutov A.M., Serov V.A. and dr. Ostroe poverjdenie pochek u bolnyx infarktom myocarda s pod'emom segmenta ST. // Nephrology, 2012; (1): 40-(4).
6. Menzorov M.V., Shutov A.M., Makeeva E.R., Serov V.A., SaenkoYu.V., Strakhov A.A. Acute kidney injury and vnutrigospitalnaya lethality in patients with acute myocardial infarction in the ST segment. // Fundamental research. – 2012. – №12. – S. 100-103.
7. Menzorov M.V., Shutov A.M., Serov V.A. i dr. Ostroe poverjdenie pochek u bolnyx infarktom myocarda s pod'emom segmenta ST. // Nephrology. – 2012; (1): 40-4.

8. Muradov A.M., Komilov T.T., Faizulloev H.T., Muradov A.A., Shumilina M.V. Characteristics of the functional kidney and the heart infarct of the heart and depending on the stage of the acute kidney injury. // Vestnik postlediplomnogo obrazovaniya v sphere zdravohraneniya. – 2021 – №4. – S.11-19.
9. Ray S.I. Acute pochechnoe povrejdenie. Sovremennye aspektydiagnostiki, prophylactici i lecheniya. Medical alphabet. // Neotlojnaya meditsina. – 2013. – №4. – S. 43-50.
10. Rozanova V.A., Palenkina L.V., Simonova O.V. The role of new biomarkers in the alteration of lung tissue and early diagnosis of chronic kidney disease (literature review). Kirovsky gosudarstvennyy meditsinskiy universitet Minzdrava Rossii, Kirov, // Russia, 2019. DOI 10.24411/2220-7880-2019-10042.
11. Chaulin A.M., Duplyakov D.V. Increased cardiac troponin, not associated with acute coronary syndrome. Chast 1 // Cardiology: novelty, mnenia, obuchenie. – 2019. –T. 7. –№2. –S. 64-70.
12. Braunwald, E. Biomarkers in heart failure. // N Engl J Med. – 2008. – T. 358 (20). – P. 2148-2159.
13. Bansal, A., & Nigoskar, S. Determination of serum KIM-1 in patients with chronic kidney injury. Asian Journal of Medical Sciences. – 2023;14(8), – 56-59. Retrieved from https://www.nepjol.info/index.php/AJMS/article/view/53228.
14. Danquah, M., Owiredu, W.K.B.A., Jnr, B.A.E. et al. Diagnostic value of neutrophil gelatinase-associated lipocalin (NGAL) as an early biomarker for detection of renal failure in hypertensives: a case–control study in a regional hospital in Ghana. BMC //Nephrol 24, 114 (2023). https://doi.org/10.1186/s12882-023-03120-6
15. Ding H, He Y, Li K, Yang J, Li X, Lu R, et al. Urinary neutrophil gelatinase-associated lipocalin (NGAL) is an early biomarker for renal tubulointerstitial injury in IgA nephropathy. // Clinical Immunology. –2007; 123(2): – P. 227-234.
16. Dharnidharka V.R. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. American J. of Kidney Diseases. – 2002; – 40 (2): – P. 221-226.
17. Chenoweth, C.E. Urinary tract infections / C.E. Chenoweth, S. Saint // Infectious Disease Clinics of North America. – 2011. – №25. – P. 103-115.
18. Englberger, L. Clinical accuracy of RIFLE and Acute Kidney Injury Network (AKIN) criteria for acute kidney injury in patients undergoing cardiac surgery / L. Englberger, R.M. Suri, Z. Lee et al. // Crit. Care. – 2011. – №15. –P. 16.
19. Etzioni R, Urban N, Ramsey S, McIntosh M, Schwartz S, Reid B, et al. The case for early detection. // Nature Reviews Cancer. – 2003; 3 (4): – P. 243-252.
20. Hellerstein S. The ratio of urinary cystatin C to urinary creatinine for detection of decreased GFR. // Pediatric Nephrology. – 2004; 19 (5): – P. 521–525.
21. Humphreys BD, Hu F, Sabbisetti V, Grgic I, Naini SM, Wang N, et al. Chronic epithelial kidney injury molecule-1 expression causes murine kidney fibrosis. // J. of Clinical Investigation. –2013; 123(9): – P. 4023-4035.
22. Levey AS, Cattran D, Friedman A, Miller WG, Sedor J, Tuttle K, et al. Proteinuria as a surrogate outcome in CKD: report of a scientific workshop sponsored by the National Kidney Foundation and the US Food and Drug Administration. // American J. of Kidney Diseases. – 2009; 54 (2): – P. 205-226.
23. Thygesen K, Alpert JS, Jaffe AS, et al. ESC Scientific Document Group. // Fourth universal definition of myocardial infarction (2018). Eur Heart J. – 2019; 40:237-69.

24. Inker LA, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, et al. Estimating glomerular fi ltration rate from serum creatinine and cystatin. // The New England J. of Medicine. – 2012; 367 (1): – P 20-29.

25. Shlipak MG, et al. Cystatin C versus creatinine in determining risk based on kidney function. // The New England J. of Medicine. – 2013; 369 (10): – P. 932-943.

26. Viau A, El Karoui K, Laouari D, Burtin M, Nguyen C, Mori K, et al. Lipocalin 2 is essential for chronic kidney disease progression in mice and humans. // J. of Clinical Investigation. – 2010; 120(11): – P 4065-4076.

27. Wasung ME, Chawla LS, Madero M. Biomarkers of renal function, which and when? // Clinica Chimica Acta. – 2015; 438: – P. 350-357.

28. Zang XJ, An SX, Feng Z et al. In vivo mechanism study of NGAL in rat renal ischemia-reperfusion injury. // Genetics and molecular research. – 2014; –13 (4): – P. 8740-8748.