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Original article

Critical endpoints in dynamic follow-up of anemia patients with percutaneous coronary intervention for acute coronary syndrome

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Abstract: *Introduction* — Identifying critical endpoints during long-term follow-up of patients with coronary artery disease (CAD) and anemia after percutaneous coronary intervention (PCI) would allow optimizing management tactics for this group of patients.
Objective — To investigate the risks of developing adverse cardiovascular complications in patients with anemia who underwent revascularization for acute coronary syndrome (ACS) and to assess the most significant factors affecting outcomes.
Material and Methods — The study included 298 patients with CAD who had undergone PCI at least two years before enrollment. A survey of patients and a retrospective analysis of their medical records were conducted. The outcome was a composite endpoint (death, myocardial infarction, stroke, transient ischemic attack). Kaplan-Meier curves were constructed to assess the effect of anemia on outcomes. To identify predictors of an adverse outcome, a Cox regression model was built.
Results — In the group of patients with ACS who underwent PCI, the incidence of anemia was 8.4%. The incidence of the composite endpoint in patients with anemia was 51.6%, which was significantly different from its value in patients without anemia after 400 days of follow-up (logrank test, $p<0.008$). After day 1,200, both groups exhibited similar dynamics of adverse outcomes. The following factors were statistically significantly linked to the risk of death within 24 months after PCI: left ventricular ejection fraction ($p=0.002$), anemia ($p=0.009$), and chronic kidney disease ($p=0.02$).
Conclusion — We demonstrated that anemia influenced the development of adverse outcomes from day 400 to day 1,200 of a follow-up. Some factors, such as left ventricular ejection fraction and the presence of chronic kidney disease, also had a high predictive power for adverse events.

Keywords: anemia, acute coronary syndrome, percutaneous coronary intervention.

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Introduction

Currently, anemia is recognized as one of the risk factors for death in patients with acute coronary syndrome (ACS), along with smoking, diabetes mellitus, hypertension, and dyslipidemia [1,2,3]. The prevalence of anemia among adults worldwide is quite high and amounts to 18–35% [4]. According to various sources, a reduction in hemoglobin content occurs in 10–30% of patients with coronary artery disease (CAD) [5,6]. It is worth noting that the leading position in the etiology of anemia is taken by iron deficiency (up to 80–90% of all cases) [7].

The negative impact of anemia on the development of cardiovascular events can be directly associated with the presence of myocardial hypoxia occurring against the background of a reduction in the number of red blood cells, a decrease in their functional ability to transport oxygen, as well as with changes in the vascular, platelet, and blood clotting components of hemostasis in this category of patients. There is evidence of the stimulating effect of ADP, released by altered erythrocytes, on platelet adhesion and aggregation, endothelial damage and activation of the blood clotting system components. [8,9,10]. It was previously shown that anemia was most common in women aged 40-49 years and men 60-69 years of age (20-21%) [11]. In men, the manifestation of anemia coincides with the age of onset of CAD, in particular ACS [12]. The presence of anemia in patients with CAD is associated with a more frequent development of hemodynamically significant occlusion of the coronary arteries simultaneously with a less frequent performance of revascularization procedures [13].

Considering the urgency of revascularization in ACS, the issue of following up patients with anemia after percutaneous coronary intervention (PCI) remains noteworthy. Available publications most often analyze either hospital mortality or five-year risks of patients with anemia and ACS [14,15]. However, in our opinion, it is of interest to monitor the dynamics of adverse events among patients with anemia in comparison with individuals without hematologic disorders. This would allow identifying critical endpoints in the long-term follow-up, as well as optimizing tactics

for the correction and monitoring of anemia in this group of high-risk patients.

Hence, the objective of our study was to investigate the risks of developing adverse cardiovascular complications in patients with anemia who underwent revascularization for ACS and to assess the most significant factors affecting outcomes.

Material and Methods

The single-center observational study included patients who underwent myocardial revascularization within the previous 24±1 months. Selected patients (n=298) were diagnosed with ACS and subjected to PCI between 1 March 2019 and 1 March 2020. During the period from 1 June 2021 to 1 June 2023, we conducted a survey of patients and a retrospective analysis of their medical records.

Data analysis was performed depending on the presence of anemia before the revascularization procedure and according to the World Health Organization (WHO) criteria (hemoglobin level <130 g/L in men and <120 g/L in women). A total of 273 patients without anemia and 25 patients with preoperative anemia were included in our study sample. Mean duration of a period between the PCI performance and the survey was 1,163 [1,121; 1,236] days. The outcome was a composite endpoint (death, myocardial infarction, stroke, transient ischemic attack).

Statistical data processing was carried out using Microsoft Office Excel 2007 and STATISTICA 6.0 (StatSoft, Inc., USA). Categorical data are presented as frequencies in the form of percentages. For normally distributed study samples, quantitative data are presented as a mean and a standard deviation (M±SD). For distributions other than normal, quantitative data are presented in the form of a median and an interquartile range, Me [25%; 75%]. To assess the normality of distribution, the Kolmogorov–Smirnov test was employed.

To compare qualitative variables (binary or proportions), the chi-squared test ($\chi 2$) was performed. Intergroup differences for quantitative variables were assessed based on the Mann–Whitney U test. The differences were assumed statistically significant at $p<0.05$. Kaplan-Meier curves were constructed to evaluate long-term patient survivorship.

To test the hypothesis about the effect of the investigated factor (anemia) on the prognosis of patients, the logrank test was employed, and the effect was considered statistically significant at $p<0.05$.

To assess the contribution of individual factors (including anemia) to the risk of death for patients after PCI in the long term, a Cox regression model was constructed. The model included the parameters that differed most between the groups of deceased and surviving patients, regardless of the significance level of the differences. Although the groups were comparable on key clinical parameters, the modeling also included left ventricular ejection fraction (LVEF), chronic kidney disease (CKD), and platelet count as the most significant predictors of mortality according to available published sources.

Results

The clinical characteristics of patients with ACS were initially analyzed, taking into account the presence or absence of anemia. The results are presented in *Table* 1.

Table 1. Comparative characteristics of patients with ACS and CCAD with and without anemia

Clinical characteristics	*Without anemia*	*With anemia*	*p*
Sample size, n	273	25	–
Age, M ± SD	63.9±9.4	67.8±7.2	0.043
DM, n (%)	73 (27.1%)	9 (29.03%)	0.59
CKD, n (%)	213 (78.02%)	20 (64.5%)	0.516
LVEF, %, Me [25%; 75%]	60 [55; 64]	62 [50; 64]	0.913
Hemoglobin, g/L, Me [25%; 75%]	148 [138; 157]	117 [112; 123]	<0.001
LDL at discharge, mmol/L, Me [25%; 75%]	2.6 [2; 3.5]	2.35[1.7; 3.4]	0.118
Statins, n (%)	205 (75.1%)	19 (61.3%)	0.743
P2Y12 receptor inhibitor, n (%)	63 (23.1%)	3 (9.7%)	0.457
ASA, n (%)	207 (75.8%)	14 (45.2%)	0.025
Beta blockers, n (%)	176 (64.5%)	17 (54.8%)	0.592
ACEI, n (%)	116 (42.5%)	12 (38.7%)	0.705
Nitrates, n (%)	24 (8.8%)	5 (16.1%)	0.003
Calcium channel blockers, n (%)	57 (20.9%)	7 (28.6%)	0.364

ACS, acute coronary syndrome; CCAD, Chronic Coronary Artery Disease; DM, diabetes mellitus; CKD, chronic kidney disease; LVEF, left ventricular ejection fraction; LDL, low-density lipoproteins; ASA, acetylsalicylic acid; ACEI, angiotensin-converting enzyme inhibitors; M±SD, mean ± standard deviation; Me [25%; 75%], median [25%; 75%]; *p*, Mann-Whitney U test yielding statistically significant results at $p<0.05$.

Table 2. Clinical data comparison between deceased and surviving patients with ACS who underwent myocardial revascularization

Clinical characteristics	*Surviving*	*Deceased*	*p*
Sample size, n	291	32	–
Male gender, n (%)	214 (73.5%)	27 (84.3%)	0.164
Age, M ± SD	64.2 ± 9.3	63.7 ± 7.8	0.886
DM, n (%)	73 (25.1%)	9 (28.1%)	0.691
MI in anamnesis, n (%)	131 (45%)	15 (46.9%)	0.815
CKD, n (%)	227 (78%)	28 (87.5%)	0.19
LVEF, %, Me [25%; 75%]	61 (55;64)	56 [47;64]	0.07
Anemia present, n (%)	24 (8.2%)	7 (21.9%)	0.012
Hemoglobin, g/L, Me [25%; 75%]	146 [134; 156]	148 [131; 159.5]	0.572
Platelets, 10^9/L, Me [25%; 75%]	241 [201; 289]	268 [215; 331]	0.188
TC, mmol/L, Me [25%; 75%]	4 [4; 6]	5 [3.5; 5]	0.62

DM, diabetes mellitus; MI, myocardial infarction; CKD, chronic kidney disease; LVEF, left ventricular ejection fraction; TC, total cholesterol; M±SD, mean ± standard deviation; Me [25%; 75%], median [25%; 75%]; *p*, Mann-Whitney U test yielding statistically significant results at $p<0.05$.

Table 3. Results of multivariate regression of clinical data based on patients with ACS who underwent PCI

Clinical characteristics	*Regression coefficient*	*Standard error*	*p*
Male gender, %	0.937	0.510	0.066
Age, years, abs.	-0.008	0.022	0.712
CKD (creatinine clearance <90 mL/min/1.73 m2), %	1.330	0.570	0.02
LVEF, %, abs.	-0.060	0.019	0.002
Anemia (hemoglobin <130 g/L in men, <120 g/L in women), %	1.160	0.555	0.009
Platelets, 10^9/L, abs.	0.002	0.002	0.168

ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; CKD, chronic kidney disease; LVEF, left ventricular ejection fraction.

In the group of patients with ACS who underwent PCI, the incidence of anemia was 8.4%. According to our study, on average, patients with ACS and anemia were older than patients with ACS but without anemia (67.8±7.2 y/o vs. 63.9±9.4 y/o, p=0.043). We also revealed that patients with ACS and anemia were less likely to take acetylsalicylic acid (45.2% vs. 75.8%, p=0.025), but took nitrates twice as often (16.1% versus 8.8%, p=0.003). For the

remaining studied clinical characteristics, we detected no significant differences between the compared groups (*Table* 1).

Next, we analyzed long-term prognoses in patients with acute forms of CAD depending on the anemia syndrome. The incidence of the composite endpoint in anemia patients with ACS and PCI (death + myocardial infarction + stroke + transient ischemic attack) within 24 months after revascularization was 51.6%. As shown in *Figure* 1, patients with anemia and ACS experienced fewer adverse outcomes in the first 400 days than patients without anemia. However, starting from day 400 to day 1,200, the situation for patients with anemia was worse than for patients without it. Moreover, after day 1,200, the incidence of adverse outcomes increased sharply, regardless of the hemoglobin level (logrank test, p=0.008). Moreover, after day 1,200, the incidence of adverse outcomes increased sharply in both groups, albeit being more pronounced in anemic patients (LogRankTest<0.001).

To elucidate the results obtained on the effect of anemia on the incidence of adverse events in the long term, we built a Cox regression model. We used it to identify factors increasing the risk of developing a composite endpoint in patients with ACS who underwent revascularization. To select factors for the model, the clinical characteristics of patients with and without the development of the composite endpoint were preliminary compared (*Table* 2).

We revealed statistically significant differences between the groups only in the proportion of patients with low hemoglobin *sensu* the WHO criteria (p=0.012). At lower values of LVEF, the differences were insignificant (p=0.07) but approached the cut-off significance value of 0.05. When constructing a statistical model, taking into consideration a relatively small sample size, we decided to include all parameters exhibiting differences between groups at a significance level of p<0.2 as factors, which was consistent with published data. Age was also included as a factor (even though p=0.886). Despite the fact that the resulting samples were comparable in terms of mean age, published sources considered it as the most significant predictor of death.

The results of multivariate regression analysis are presented in *Table* 3. The outcome of the built model was a composite endpoint (death + myocardial infarction + stroke + transient ischemic attack). The time that elapsed from PCI to the development of an adverse outcome was calculated. The grouping variable was anemia.

The constructed regression model demonstrated high predictive power: χ2 criterion=21.713, p=0.001. Factors, such as LVEF (p=0.002), anemia (p=0.009) and CKD (p=0.02), were significantly associated with the risk of death after PCI for ACS within 24 months.

Discussion

Our study demonstrated that anemia significantly affected survivorship over a period of 1.5 to 3.5 years of follow-up in patients who underwent PCI for ACS.

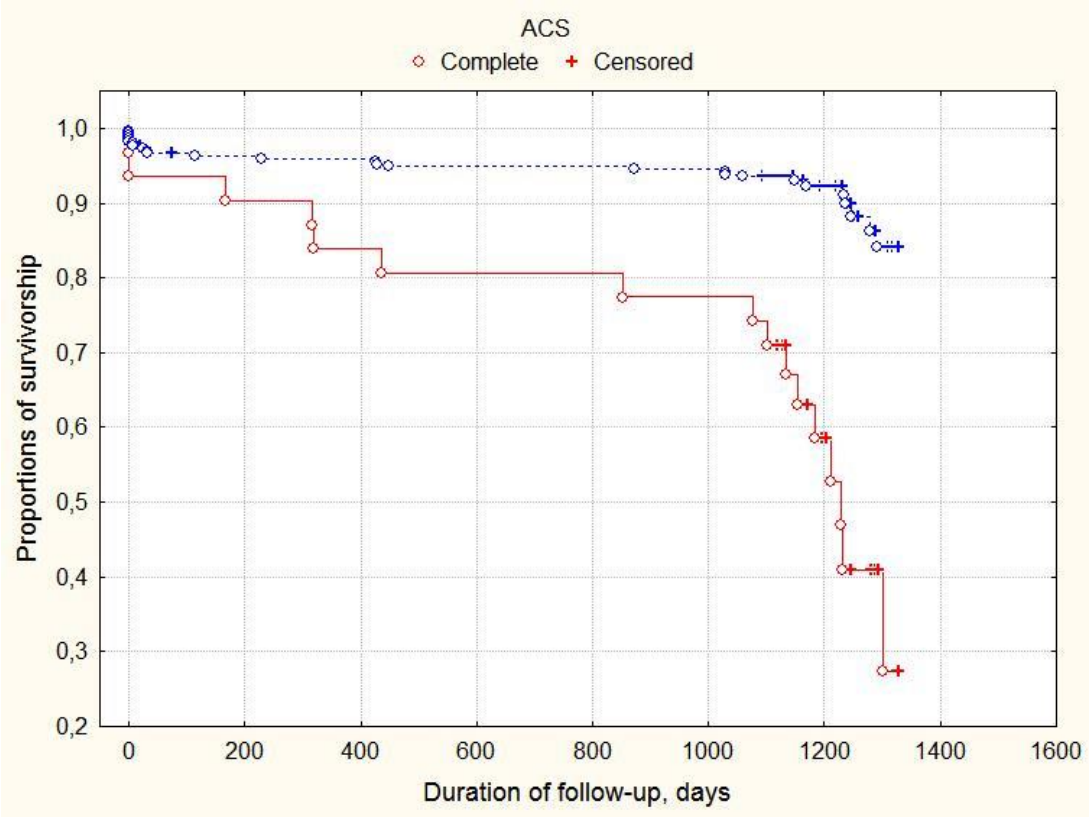

Figure 1. Kaplan-Meier curve of patients with ACS who underwent myocardial revascularization.
Patients with and without anemia are marked with red and blue, respectively; ACS, acute coronary syndrome.

On the one hand, tissue hypoxia during anemia is a trigger for the development of collateral circulation, which improves the short-term prognosis of anemia patients after acute coronary events [20]. However, in the long term, the more severe clinical status of these patients explains their lower survivorship. Our study showed that on average, anemia patients were older and had lower LVEF values. These data were consistent with results of other studies [21,22]. Also, anemia patients had a significantly higher need for nitrates, which once again pointed out the contribution of anemia to the development of myocardial ischemia [23].

The constructed regression model exhibited a high predictive power for such factors as the presence of anemia, LVEF, and the presence of CKD. However, there is published evidence that CKD can be both an aggravating factor for higher mortality in anemia patients [24,25] and an independent risk factor for adverse events, regardless of the initial hemoglobin level [26]. Progression of renal failure may be responsible for the rapidly declining survival rate of patients with and without anemia three years after revascularization.

It should be noted that our study included patients with anemia *sensu* the WHO criteria (less than 130 g/L in men and less than 120 g/L in women). Moreover, in actual clinical practice, treatment for anemia patients is usually prescribed when the hemoglobin level is less than 110 g/L. In the study group, the median hemoglobin level was 117 [112; 123] g/l; i.e., the vast majority of patients had hemoglobin values above 110 g/L. However, the outcomes of these patients differed significantly from those of patients with normal hemoglobin levels *sensu* the WHO criteria. Therefore, even a slight reduction in hemoglobin levels requires a closer doctor's attention.

Conclusion

In a study of the outcomes of patients with ACS who underwent revascularization, anemia was shown to have an impact on the long-term prognosis of these patients. The critical duration of the follow-up period was 400–1,200 days of observation, when the incidence of outcomes in anemia patients increased vs. patients without anemia. Moreover, starting from day 1,200 of the follow-up, survival rate sharply decreased in all patients, regardless of their hemoglobin level, albeit being more pronounced in anemic patients. Along with anemia, other factors (such as LVEF and the presence of CKD) had a high predictive power for adverse events.

Limitations of the study

The study is limited by the small sample size of the groups. The study did not examine the etiology of anemic syndrome since examination and treatment of patients with anemia was carried out at the place of their residence within the framework of established procedures and standards of medical care. Data on the actually received therapy, and the frequency and nature of outcomes were obtained from the words of patients or their relatives.

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References

1. Arant CB, Wessel TR, Olson MB, Bairey Merz CN, Sopko G, Rogers WJ, et al. Hemoglobin level is an independent predictor for adverse cardiovascular outcomes in women undergoing evaluation for chest pain: Results from the National Heart, Lung, and Blood Institute Women's Ischemia Syndrome Evaluation Study. *J Am Coll Cardiol* 2004: 43(11): 2009-2014. https://doi.org/10.1016/j.jacc.2004.01.038.
2. Kaiafa G, Kanellos I, Savopoulos C, Kakaletsis N, Giannakoulas G, Hatzitolios AI. Is anemia a new cardiovascular risk factor? *Int J Cardiol* 2015; 186: 117-124. https://doi.org/10.1016/j.ijcard.2015.03.159.
3. Astor BC, Coresh J, Heiss G, Pettitt D, Sarnak MJ. Kidney function and anemia as risk factors for coronary heart disease and mortality: The Atherosclerosis Risk in Communities (ARIC) Study. *Am Heart J* 2006; 151(2): 492-500. https://doi.org/10.1016/j.ahj.2005.03.055.
4. Safiri S, Kolahi AA, Noori M, Nejadghaderi SA, Karamzad N, Bragazzi NL, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990-2019: Results from the Global Burden of Disease Study 2019. *J Hematol Oncol* 2021; 14(1): 185. https://doi.org/10.1186/s13045-021-01202-2.
5. Gorohovskaya GN, Martynov AI, Yun VL, Petina MM. The modern view of general practitioner on the problem of iron deficiency anemia in patients with cardiovascular pathology. *Medical Council* 2020; (14): 70-78. Russian. https://doi.org/10.21518/2079-701X-2020-14-70-78.
6. Ye SD, Wang SJ, Wang GG, Li L, Huang ZW, Qin J, et al. Association between anemia and outcome in patients hospitalized for acute heart failure syndromes: Findings from Beijing Acute Heart Failure Registry (Beijing AHF Registry). Intern *Emerg Med* 2021; 16(1): 183-192. https://doi.org/10.1007/s11739-020-02343-x.
7. Baranov II, Salnikova IA, Nesterova LA. Clinical practice guidelines for the diagnosis and treatment of iron deficiency: the view from 2022. *Akusherstvo i ginekologiya: novosti, mneniya, obuchenie* 2022; 10(2): 56-64. Russian. https://doi.org/10.33029/2303-9698-2022-10-2-56-64.
8. Zhelobov VG, Tuev AV, Agafonov AV. Mechanisms of coagulative hemostasis disturbances at various pathogenetic types of anemias. *Tromboz, Gemostaz I Reologiya* 2017; (2): 64-68. Russian. https://doi.org/10.25555/THR.2017.2.0786.
9. Wischmann P, Kuhn V, Suvorava T, Muessig JM, Fischer JW, Isakson BE, et al. Anaemia is associated with severe RBC dysfunction and a reduced circulating NO pool: Vascular and cardiac eNOS are crucial for the adaptation to anaemia. *Basic Res Cardiol* 2020; 115(4): 43. https://doi.org/10.1007/s00395-020-0799-x.
10. Byrnes JR, Wolberg AS. Red blood cells in thrombosis. *Blood* 2017; 130(16): 1795-1799. https://doi.org/10.1182/blood-2017-03-745349.
11. Volkova SA, Mayansky NA, Borovkov NN, Balabanov AS, Egorova TV, Podsosova EV, et al. Hemogram values in working adult population. *Russian journal of hematology and transfusiology* 2008; 53(1): 21-27. Russian. https://www.elibrary.ru/item.asp?id=10335718&.
Oberoi M, Ainani N, Abbott JD, Mamas MA, Velagapudi P. Age considerations in the invasive management of acute coronary syndromes. *US Cardiology Review* 2022; 16: e14. https://doi.org/10.15420/usc.2021.29.
12. Huynh R, Hyun K, D'Souza M, Kangaharan N, Shetty PC, Mariani J, et al. Outcomes of anemic patients presenting with acute coronary syndrome: An analysis of the Cooperative National Registry of Acute Coronary Care, Guideline Adherence and Clinical Events. *Clin Cardiol* 2019; 42(9): 791-796. https://doi.org/10.1002/clc.23219.
13. González-Ferrer JJ, García-Rubira JC, Balcones DV, Gil IN, Barrio RC, Fuentes-Ferrer M, et al. Influence of hemoglobin level on in-hospital prognosis in patients with acute coronary syndrome. *Rev Esp Cardiol* 2008; 61(9): 945-952. English, Spanish. https://pubmed.ncbi.nlm.nih.gov/18775236.

14. Al-Hijji MA, Gulati R, Lennon RJ, Bell M, El Sabbagh A, Park JY, et al. Outcomes of percutaneous coronary interventions in patients with anemia presenting with acute coronary syndrome. *Mayo Clin Proc* 2018; 93(10): 1448-1461. https://doi.org/10.1016/j.mayocp.2018.03.030.
15. Vicente-Ibarra N, Marín F, Pernías-Escrig V, Sandín-Rollán M, Núñez-Martínez L, Lozano T, et al. Impact of anemia as risk factor for major bleeding and mortality in patients with acute coronary syndrome. *Eur J Intern Med* 2019; 61: 48-53. https://doi.org/10.1016/j.ejim.2018.12.004.
16. Moghaddam N, Wong GC, Cairns JA, Goodman SG, Perry-Arnesen M, Tocher W, et al. Association of anemia with outcomes among ST-segment-elevation myocardial infarction patients receiving primary percutaneous coronary intervention. *Circ Cardiovasc Interv* 2018; 11(12): e007175. https://doi.org/10.1161/CIRCINTERVENTIONS.118.007175.
17. Jung C, Rezar R, Wischmann P, Masyuk M, Datz C, Bruno RR, et al. The role of anemia on admission in acute coronary syndrome – An umbrella review of systematic reviews and meta-analyses. *Int J Cardiol* 2022; 367: 1-10. https://doi.org/10.1016/j.ijcard.2022.08.052.
18. Gao M, Zhang X, Qin L, Zheng Y, Zhang Z, Tong Q, et al. Discharge hemoglobin association with long-term outcomes of ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention. *Cardiovasc Ther* 2020; 2020: 8647837. https://doi.org/10.1155/2020/8647837.
19. Badoyan AG, Gorgulko AP, Khelimsky DA, Krestyaninov OV, Bergen TA, Naydenov RA, et al. The role of collateral circulation in maintaining and restoring left ventricular myocardial function and contemporary methods for its assessment. *Russian Journal of Cardiology* 2022; 27(8): 5164. Russian. https://doi.org/10.15829/1560-4071-2022-5164.
20. Guedeney P, Sorrentino S, Claessen B, Mehran R. The link between anemia and adverse outcomes in patients with acute coronary syndrome. *Expert Rev Cardiovasc Ther* 2019; 17(3): 151-159. https://doi.org/10.1080/14779072.2019.1575729.
21. Bolińska S, Sobkowicz B, Zaniewska J, Chlebińska I, Boliński J, Milewski R, et al. The significance of anaemia in patients with acute ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Kardiol Pol* 2011; 69(1): 33-39. https://pubmed.ncbi.nlm.nih.gov/21267962.
22. Solomon A, Blum A, Peleg A, Lev EI, Leshem-Lev D, Hasin Y. Endothelial progenitor cells are suppressed in anemic patients with acute coronary syndrome. *Am J Med* 2012; 125(6): 604-611. https://doi.org/10.1016/j.amjmed.2011.10.025.
23. Goodnough LT, Schrier SL. Evaluation and management of anemia in the elderly. *Am J Hematol* 2014; 89(1): 88-96. https://doi.org/10.1002/ajh.23598.
24. Shiraishi J, Kohno Y, Nakamura T, Yanagiuchi T, Hashimoto S, Ito D, et al. AMI-Kyoto Multi-Center Risk Study Group. Prognostic impact of chronic kidney disease and anemia at admission on in-hospital outcomes after primary percutaneous coronary intervention for acute myocardial infarction. *Int Heart J* 2014; 55(4): 301-306. https://doi.org/10.1536/ihj.13-367.
25. Rodrigues FB, Bruetto RG, Torres US, Otaviano AP, Zanetta DM, Burdmann EA. Effect of kidney disease on acute coronary syndrome. *Clin J Am Soc Nephrol* 2010; 5(8): 1530-1536. https://doi.org/10.2215/CJN.01260210.

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