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Peculiarities of the Course of Acute Coronary Syndrome in Anemia According to the Registry of the Regional Vascular Center of the Ryazan Region

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ABSTRACT

INTRODUCTION: Anemia not only negatively affects the course and prognosis of acute coronary syndrome (ACS), but can also influence the choice of treatment. It seems relevant to study the regional features of the course and prognosis of ACS in combination with anemia.

AIM: To study the incidence and severity of anemia in patients with ACS, the features of the course and outcomes of ACS in patients with anemia according to the registry of the Regional Vascular Center of the Ryazan Region.

MATERIALS AND METHODS: A retrospective analysis of the ACS registry data for 2019 was performed, which included 242 patients: group 1 — patients with anemia (n=52; 21.5%), group 2 — patients without anemia (n=190; 78.5%). All analyzed data were obtained from the medical records of the inpatients.

RESULTS: Eighty five percent of patients in group 1 had mild, 11% — moderate, and 4% — severe anemia. Patients with ACS in combination with anemia were older (p=0.0001). There were more women in the anemia group (p <0.001), these patients more often had a history of myocardial infarction (p <0.001), stroke (p=0.03), angina (p=0.009); they had lower blood pressure (p=0.002 for systolic and p=0.0004 for diastolic), glomerular filtration rate (p=0.0005), left ventricular ejection fraction (p=0.01). Killip class II heart failure was more often recorded in the presence of anemia (p=0.009), the risk of in-hospital mortality according to the GRACE scale was also higher in patients with anemia (p <0.001). Coronary angiography and percutaneous coronary intervention were more often performed in the group with ACS without anemia (p <0.001 and p=0.005 respectively). In-hospital mortality in patients with anemia exceeded that in patients without anemia (17.3% versus 7.9%, p=0.04). Mild anemia was predominant among deceased patients (80.0%).

CONCLUSION: According to the ACS registry of the Regional Vascular Center for 2019, anemia was detected in 21.5% of patients, with mild anemia predominating. Patients with ACS and anemia more often had angina pectoris, postinfarction cardiosclerosis and stroke in history, and according to the GRACE scale, a higher risk of hospital mortality. They were less likely to undergo coronary angiography and percutaneous coronary intervention compared to patients with ACS without anemia. Hospital mortality was higher in the ACS group with anemia; among the deceased, mild anemia predominated.

Keywords: acute coronary syndrome; anemia; registry; hospital mortality.

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Особенности течения острого коронарного синдрома при анемии по данным регистра Регионального сосудистого центра Рязанской области

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АННОТАЦИЯ

Введение. Анемия не только негативно влияет на течение и прогноз острого коронарного синдрома (ОКС), но может влиять и на выбор лечения. Представляется актуальным изучить региональные особенности течения и прогноза ОКС в сочетании с анемией.

Цель. Изучить частоту встречаемости и тяжесть анемии у пациентов с ОКС, особенности течения и исходов ОКС у пациентов с анемией по данным регистра Регионального сосудистого центра Рязанской области.

Материалы и методы. Проведен ретроспективный анализ данных регистра ОКС за 2019 год, в который включены 242 пациента: 1-я группа — пациенты с анемией (n=52; 21,5%), 2-я группа — пациенты без анемии (n=190; 78,5%). Все анализируемые данные получены из медицинских карт стационарного больного.

Результаты. 85% пациентов 1-й группы имели легкую, 11% — среднюю и 4% — тяжелую степень анемии. Пациенты с ОКС в сочетании с анемией были старше (p=0,0001). В группе с анемией было больше женщин (p <0,001), в анамнезе эти пациенты чаще имели инфаркт миокарда (p <0,001), инсульт (p=0,03), стенокардию напряжения (p=0,009); у них был ниже уровень артериального давления (p=0,002 для систолического и p=0,0004 для диастолического), скорости клубочковой фильтрации (p=0,0005), фракции выброса левого желудочка (p=0,01). Сердечная недостаточность Killip II класса чаще регистрировалась при наличии анемии (p=0,009), риск госпитальной летальности по шкале GRACE также был выше у пациентов с анемией (p <0,001). Коронароангиография и чрескожное коронарное вмешательство чаще проводились в группе с ОКС без анемии (p <0,001 и p=0,005 соответственно). Госпитальная летальность пациентов с анемией превосходила таковую у пациентов без анемии (17,3% против 7,9%, p=0,04). Среди умерших пациентов преобладала анемия легкой степени (80,0%).

Заключение. По данным регистра ОКС Регионального сосудистого центра за 2019 год анемия, была выявлена у 21,5% пациентов, преобладала анемия легкой степени. Пациенты с ОКС и анемией в анамнезе чаще имели стенокардию напряжения, постинфарктный кардиосклероз и инсульт, а по шкале GRACE более высокий риск госпитальной летальности. Им реже проводились коронароангиография и чрескожное коронарное вмешательство по сравнению с пациентами с ОКС без анемии. Госпитальная летальность была выше в группе ОКС с анемией, среди умерших преобладала анемия легкой степени.

Ключевые слова: острый коронарный синдром; анемия; регистр; госпитальная летальность.

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INTRODUCTION

Cardiovascular diseases are the main cause of mortality in all categories of the adult population not only in the Russian Federation, but also in many countries around the world. One of most serious pathologies — acute coronary syndrome (ACS), is the leading cause of hospitalization in emergency departments. Many conditions are known to aggravate the course and prognosis of ACS, including anemia of various genesis, which can have a prognostic role in the development of short-term and long-term complications in myocardial infarction (MI) [1]. According to epidemiological data, 32.9% of the world's population suffer from anemia, which indicates the widespread prevalence of this pathology [2]. According to the independent ACS RECORD registry, which included 796 patients from 18 hospitals in 13 Russian cities, hemoglobin value below 110 g/l was an independent predictor of in-hospital death. In addition, patients with anemia and ACS were less likely to undergo diagnostic and therapeutic coronary procedures [3].

A decrease in the blood hemoglobin level is one mechanism of the development of the clinical and pathogenetic variant of type 2 MI, associated with a decrease in oxygen supply to the myocardium [4]. Anemic syndrome often accompanies many chronic diseases, including cardiologic ones, leading to aggravation of the course and progression of the main disease [5]. This problem is especially relevant for elderly patients, who in most cases have several chronic diseases that have a mutually aggravating effect [3].

Thus, in patients with ACS, the baseline hemoglobin level determines the prognosis [6]. In this regard, it seems relevant to study the regional characteristics of the course and prognosis of ACS in combination with anemia.

The **aim** of this study to incidence and severity of anemia in patients with ACS, the characteristics of the course and outcomes of ACS in patients with anemia according to the registry of the Regional Vascular Center of the Ryazan Region.

MATERIALS AND METHODS

The study was conducted at the Emergency Cardiology Department of the Ryazan Regional Clinical Hospital. A retrospective analysis of the ACS registry data for 2019 was conducted, which included 242 patients hospitalized with ACS from January 1, 2019 to December 31, 2019.

The patients were divided into two groups:

- ***group 1*** — 52 patients with anemia at the time of hospitalization (21.5%);

- ***group 2*** — 190 patients without anemia (78.5%).

All analyzed data (demographic, anamnestic, clinical, laboratory and instrumental) were obtained from the medical records of inpatients.

Statistical analysis of the data was performed using the Statistica 10.0 application package (Stat Soft Inc., USA). Descriptive statistics methods were used. The frequency of occurrence of a feature or event is presented in absolute values (n) and proportions (%). The normality of distribution was determined using the Kolmogorov–Smirnov test. Continuous values, the distribution of which differed from normal, are presented as a median (Me) and interquartile range [Q1; Q3]. The statistical significance of differences between these values in the groups was assessed using the nonparametric Mann–Whitney criterion. Comparison of discrete values was performed using the χ^2 criterion with a Yates continuity correction, Fisher's exact test. Differences were considered statistically significant at p <0.05.

RESULTS

The hemoglobin level in group 1 was 111.5 [101.5; 117.0] g/l, in group 2 — 146 [137; 155] g/l; 85% of patients in group 1 had mild, 11% — moderate, and 4% — severe anemia. In women with anemia, the hemoglobin level positively correlated with body weight (r=0.43, p <0.05) and with the platelet level (r=0.79, p <0.05). In men with anemia, positive correlations were found with the left ventricular ejection fraction (EF) (r=0.43, p <0.05) and the platelet level (r=0.76, p <0.05). Thrombocytopenia in group 1 was recorded in 7 patients (13.5%), in group 2 only in one case (0.5%, p <0.001).

Patients with ACS and anemia were significantly older (78.0 [69.5; 82.5] years versus 66 [59.0; 75.0] years, p=0.001). Thus, there were 2 times more elderly patients in this group than in the group without anemia (p <0.001). There were also more women in the group with anemia (p <0.001). In the ACS group without anemia, males (64.21%) and elderly people (42.1%, Table 1) prevailed. More common associated clinical conditions in the group with anemia were MI (p <0.001), stroke (p=0.03), and angina pectoris (p=0.009). No statistically significant differences were found in the analyzed risk factors for cardiovascular diseases. When assessing previous pharmacotherapy, it was found that patients in group 1 (with anemia) more often took acetylsalicylic acid (ASA) preparations (p=0.001).

In terms of the frequency of the main complaints on admission to the hospital, no statistically significant differences were found between the groups: pain syndrome or its retrosternal equivalent (80.8% in the group with anemia and 78.4% in the group without anemia, p >0.05), pain syndrome or its equivalent in another location (7.7% and 6.8% respectively, p >0.05), syncope (0.0% and 0.53% respectively, p >0.05). Patients with anemia tended to have a higher frequency of dyspnea (26.9% and 16.3%, p >0.05) and weakness (46.2% and 41.1%, p >0.05).

The distribution of patients by the severity of acute heart failure according to Killip classification is presented

Table 1. Comparative characteristics of clinical and demographic indicators (n (%)) in patients with acute coronary syndrome with and without anemia

Parameter	Patients with anemia	Patients without anemia	*p*
Gender			
Male	29 (44.2)	68 (64.2)	*<0.001*
Female	23 (55.8)	122 (35.8)	*<0.001*
Age			
Young	0	6 (3.1)	*<0.001*
Middle	2 (3.8)	55 (29.0)	*<0.001*
Elderly	21 (40.4)	80 (42.1)	0.820
Old	28 (53.8)	47 (24.7)	*<0.001*
Longevity	1 (2.0)	2 (1.1)	0.800
Associated clinical conditions			
Arterial hypertension	49 (94.2)	181 (95.3)	0.490
Type 2 diabetes mellitus	9 (17.3)	29 (15.3)	0.880
Myocardial infarction in history	30 (57.7)	50 (26.3)	*<0.001*
Percutaneous coronary intervention in history	8 (15.4)	21 (11.1)	0.540
Exertion angina in history	47 (90.4)	139 (73.2)	*0.009*
Stroke	8 (15.4)	10 (5.3)	*0.03*
Peripheral artery diseases	2 (3.9)	8 (4.2)	0.630
Chronic heart failure	51 (98.1)	176 (92.6)	0.149
Chronic lung diseases	7 (13.5)	13 (6.8)	0.210
Risk factors for cardiovascular diseases			
Obesity	10 (19.2)	64 (33.7)	0.067
Smoking	6 (11.5)	46 (24.2)	0.070

in Table 2. The proportion of patients with Killip class II was statistically significantly higher in the group of ACS with anemia.

In the group of patients with anemia, the body mass index was lower (27.0 [24.3; 28.7] kg/m^2 versus 27.7 [25.3; 37.9] kg/m^2, p=0.035), the systolic blood pressure level on admission was lower (130 [110; 140] mmHg versus 140 [122; 150] mmHg, p=0.002), and the diastolic blood pressure level on admission was lower (79 [70; 82] mmHg versus 80 [80; 90] mmHg, p=0.0004).

The creatinine level on admission was higher in patients with anemia (p=0.026). The glomerular filtration rate (GFR) according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula was 51.7 [34.2; 65.9] ml/min/1.73 m^2 in group 1 and 63.0 [49.9; 75.3] ml/min/1.73 m^2 in group 2 (p=0.001. Due to the lack of information on the duration of the GFR decrease in the ACS registry, it is impossible to talk about the presence of chronic kidney disease in all cases.

In an electrocardiographic examination, patients with anemia showed a tendency toward a higher frequency of ST segment depression (40.4% versus 35.8%, p >0.05), the formation of a pathological QS complex (15.4% versus 10.5%, p >0.05). The groups were comparable in the incidence of ST segment elevation (40.4% versus 40.5%, p >0.05).

According to the results of transthoracic echocardiography, left ventricular EF in group 1 was 50.0 [45.5; 53.0]%, in group 2 — 52 [48; 57]% (p=0.01). In group 1, patients with left ventricular EF of 40–49% (44.2%) predominated, while in group 2, left ventricular EF ≥50% (59.5%) was more often recorded.

Patients with ACS and anemia more often had the final clinical diagnosis of *unstable angina* (26.9% versus 20.0%, p=0.7). The incidence of Q-wave MI and non-Q-wave MI did not show statistically significant difference (50.0% versus 53.2%, p >0.05 and 23.1% versus 26.8%, p >0.05 respectively).

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At the next stage, the complication rate was analyzed depending on the presence of anemia with MI as an outcome of ACS (n=190, Table 3). Moderate left ventricular failure was more common in MI without anemia (p=0.023), and pulmonary edema in MI with anemia (p=0.093). Rupture of the free wall of the left ventricle was recorded with equal frequency (2.6%).

Bleeding was recorded in two patients, in both cases on admission: minimal uterine bleeding in a 55-year-old female patient without anemia and clinically significant gastrointestinal bleeding in a patient with anemia that required transfusion of platelet mass and resulted in death.

Table 2. Presence and severity of acute heart failure (n (%)) in patients with acute coronary syndrome with and without anemia

Severity class in Killip classification	Group 1	Group 2	*p*
I	39 (75.0)	172 (90.5)	0.070
II	11 (21.1)	14 (7.4)	*0.009*
III	0	3 (1.6)	0.800
IV	2 (3.9)	1 (0.5)	0.200

Table 3. Incidence of MI complications (n (%)) in patients with and without anemia

Complication	Myocardial infarction with anemia	Myocardial infarction without anemia	*p*
n	38	152	
Moderate left ventricular failure	31 (81.5)	142 (93.4)	*0.023*
Pronounced pulmonary edema	6 (15.7)	9 (5.9)	0.093
Cardiogenic shock	1 (2.6)	1 (0.6)	>0.05
Rupture of free wall of left ventricle	1 (2.6)	4 (2.6)	>0.05

Non-ST-segment elevation ACS was recorded in 51.9% of patients in group 1 and in 43.2% of patients in group 2. When assessing the risk of hospital mortality on the GRACE (Global Registry of Acute Coronary Events) scale in the subgroup of patients with ACS, the following data were obtained: on average, patients with anemia had statistically significantly higher scores (134 [118; 152] points versus 108 [87; 125] points, p <0.001), with a smaller proportion of patients with low risk (18.5% versus 49.4%, p=0.008) and a higher proportion of patients with high risk (40.7% versus 15.7%, p=0.006).

Diagnostic coronary angiography and percutaneous coronary intervention (PCI) were performed more often in the group of patients with ACS without anemia (64.7% versus 34.6%, p <0.001 and 54.2% versus 30.7%, p=0.005, respectively). No complications of PCI were recorded. The frequency of successful revascularization (TIMI 3) was comparable: 93.7% in group 1 and 87.1% in group 2 (p >0.05). Upon discharge, patients without anemia were more often prescribed ASA (p=0.009), and patients with anemia — clopidogrel (p=0.003). Hospital mortality in patients with anemia exceeded that in patients without anemia (17.3% versus 7.9%, p=0.04). Among the deceased patients, mild anemia was prevalent (80.0%), and in both groups, Q-wave MI was prevalent (77.7% and 76.9% respectively).

DISCUSSION

Our analysis of the data from the ACS Registry of the Regional Vascular Center (based on the Regional Clinical Hospital) in Ryazan for 2019 showed the incidence of anemia of 21.5%, which is comparable to the data from the RECORD registry (2007–2008) — 29.0% [3]. In our study, mild anemia significantly predominated, accounting for 85.0%, in other studies, mild anemia also predominated:

for example, in the German MONICA/KORA registry study (2011), its incidence was 64.7% [7]. In the group with anemia and ACS, patients are older, and female patients are more common, which is confirmed by the data of A. Rai et al. (2020) [1]. The high incidence of previous MI in patients with ACS and anemia is also confirmed by other studies [1, 6, 8–10].

In the clinical presentation of ACS in patients with anemia, a *tendency* to a higher frequency of complaints of shortness of breath and weakness has been recorded, which may be associated not only with cardiovascular pathology, but also with anemia.

Of attention is the incidence of mild anemia — 85.0%, which, according to the authors, reflects insufficient attention of outpatient physicians to a mild decrease in hemoglobin level. Also noteworthy is a high frequency of thrombocytopenia in the ACS group with anemia (p <0.001), which, in turn, can be accompanied by the development of posthemorrhagic anemia and worsen the prognosis of ACS. At the same time, the platelet level positively correlated with the hemoglobin level, regardless of gender.

Echocardiographic examination showed differences in the left ventricular EF value depending on the presence of anemia in patients. This can be explained by the fact of the coronary blood flow resource being limited not only by atherosclerosis of the coronary vessels, but also by a decrease in the oxygen capacity of blood. The pumping function of the heart decreases due to a decrease in the reserve capacities of the myocardium, which contributes to the aggravation of the course of heart failure. Anemia is a risk factor for the development of chronic heart failure, including acute decompensated heart failure [11]. According to our data, in men with anemia, the hemoglobin level directly correlated with the left ventricular EF.

The ACS registry data do not allow us to determine the duration of renal damage in patients with ACS, while the level of GFR according to the CKD-EPI formula was lower in patients with anemia. A decrease in GFR may reflect chronic kidney disease, therefore, the genesis of anemia can be partly explained by a decrease in erythropoietin synthesis. On the other hand, an acute frustration of renal perfusion in a patient with ACS can lead to both the progression of chronic kidney disease and the development of acute cardiorenal anemia syndrome, which is associated with poorer short-term and long-term outcomes [12].

As part of regular previous therapy, patients with anemia more often took ASA drugs, which does not exclude the existence of a source of blood loss in the gastrointestinal tract. Endoscopic search for a source of bleeding in ACS is limited by contraindications. In this regard, patients with anemia were probably more often prescribed clopidogrel upon discharge from hospital.

According to the ACS Registry, patients with anemia underwent coronary angiography and PCI significantly less frequently. A large number of studies have shown that performing PCI with a decreased hemoglobin concentration significantly increases post-procedural mortality, leads to the development of major adverse cardiac events (MACE), recurrent MI, and bleeding; however, the optimal strategy for treating anemia in such patients remains uncertain [13–16]. At the same time, the presence of anemia as a pathogenetic factor for type 2 MI does not exclude the presence of atherothrombosis, which is characteristic of type 1 MI [14].

Patients with anemia are susceptible to developing complications of MI in hospital [1, 6]. Thus, S.J. Brener et al. (2017) showed that adverse outcomes increased nonlinearly with decreasing the baseline hemoglobin level; baseline hemoglobin level and anemia were independent predictors of a major bleeding and death in ACS [6]. In our study, MI in patients with anemia was more often complicated by the development of pulmonary edema; statistically significant differences were not obtained due to the relatively small number of observations of patients with anemia.

The presence of anemia is associated with worsening of both short-term and long-term outcomes in patients with MI [7, 9, 17–22]. According to the study by V. Tripathi et al. (2021), anemia is a significant predictor of 30-day rehospitalization in patients with type 2 MI [17]. M.G. Colombo et al. (2018) showed an increased risk of mortality in MI in patients with anemia, regardless of its severity [7]. According to our data, hospital mortality in anemia exceeds mortality of patients without anemia (p=0.04). To note, mild anemia prevailed among the deceased, therefore, identifying individuals with cardiovascular diseases and even with a mild decrease in hemoglobin levels will allow timely correction of anemia and, possibly, improve the prognosis for such patients.

Limitations of the study: a relatively small sample size, which, nevertheless, was able to demonstrate the features of the course and prognosis of ACS in anemia.

CONCLUSION

According to the 2019 acute coronary syndrome registry of the Regional Vascular Center, anemia was detected in 21.5% of patients, with mild anemia predominating. Patients with acute coronary syndrome and anemia in history more often had angina, post-infarction cardiosclerosis and stroke, and according to the GRACE scale, a higher risk of in-hospital mortality. They were less likely to undergo coronary angiography and percutaneous coronary intervention compared to patients with acute coronary syndrome but without anemia. In-hospital mortality was higher in the acute coronary syndrome group with anemia, among those who died mild anemia predominated.

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ADDITIONAL INFORMATION

Author contributions. O.M. Uryasyev; A.V. Solovyeva — concept of the study, editing; I.A. Filkina — collection and analysis of material, writing the text; S.B. Aksentyev; A.S. Sapitsyna — collection and analysis of material. All authors approved the manuscript (the publication version), and also agreed to be responsible for all aspects of the work, ensuring proper consideration and resolution of issues related to the accuracy and integrity of any part of it.

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