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Structure of Anemic Syndrome in Patients with Chronic Forms of Coronary Artery Disease

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The purpose of the study was to determine the incidence and characteristic features of anemia in elderly and senile patients with chronic forms of coronary artery disease.

Materials and methods. 1,993 case reports of patients with chronic forms of coronary artery disease with comorbid anemia were analyzed retrospectively. All patients were diagnosed with chronic coronary artery disease (stable angina pectoris of II-III functional classes, diffuse or focal (post-infarction) cardiosclerosis). Average age of investigated patients was 79.5 ± 5.24. Comorbid anemia was diagnosed in case of hemoglobin level below 130 G/l in males and 120 G/l in females. The patients were randomized by gender, age and form of coronary artery disease.

Results and discussion. Among all examined patients with coronary artery disease anemia is found in nearly 70% of cases, which coincides with the literature data. In people after 60 anemia is more common in men than in women, while in young and middle-aged patients anemic syndrome is more typical in females. Only in less than hundred case reports the diagnosis of anemia was recorded in the final clinical diagnosis during patients' discharge from the hospital, in another cases low hemoglobin level was not taken into consideration by physicians. Approximately only one-third of all cases of severe anemia was not diagnosed in a hospital and no appropriate correction of hemoglobin level was performed. Incidence of anemia does not depend on the form of the chronic coronary artery disease (stable angina pectoris or cardiosclerosis). In most patients with coronary artery disease comorbid anemia is of normochromic and normocytic character. Along with progression of the severity of the comorbid anemia, statistically significant increase of the hospitalization period is observed. In patients with coronary artery disease and comorbid anemia the frequency of hospitalizations per year is also increased along with anemia degree of severity progressing.

Conclusion. Chronic forms of coronary artery disease in elderly and senile patients in 69.89% of cases are complicated by comorbid anemia of different degrees of severity. In older patients with coronary artery disease, anemic syndrome is most often caused by respiratory diseases, stomach ulcer and duodenal ulcer, cancer of different localization. In most patients with coronary artery disease comorbid anemia is of normochromic and normocytic character. Comorbid anemia in patients with coronary artery disease contributes to the prolongation of the patients' in-hospital treatment and increasing of the frequency of hospitalizations due to the main disease throughout the year.

Keywords: cardiovascular disease, coronary artery disease, anemia.

Introduction. Cardiovascular diseases have been among the leading causes of mortality in Ukraine for many years [1]. An important role in their occurrence belongs to the negative "achievements" of modern society: hypodynamia, increased caloric content of food products, chronic mental stress. The indicated well-known factors contribute to the unceasing increase in the incidence of coronary artery disease (CAD), arterial hypertension, obesity, diabetes mellitus, dyslipidemia.

Clinical trials convincingly point to the important role of the reduced hemoglobin level in the progression of the diseases of the cardiovascular system. Anemia is recognized as an independent predictor of a high risk of fatal cardiovascular events developing during 6 years in non-cardiovascular patients, especially those aged 45–64. In the PRAISE study in patients with severe chronic heart failure with decreased hematocrit to 25.4–37.4%, the risk of sudden death was 52% higher than with its high value (46.1–58.8%). In addition, the reduction of this figure by 1% below 25.4% was accompanied by an increase in the risk of mortality by 11%.

Anemia is associated with increased all-cause hospitalization and mortality in community-dwelling individuals above the age of 65 years. In primary care offices higher prevalence of anemia is associated with advancing age and comorbidities, such as essential hypertension, hypothyroidism, chronic kidney disease, malignancy, rheumatologic disease, congestive

heart failure, and coronary artery disease [2]. In the large population with stable CAD low hemoglobin is an independent predictor of mortality, cardiovascular events, and major bleeds. Persisting or new-onset anemia is a powerful predictor of cardiovascular and non-cardiovascular mortality [3, 4].

The purpose of the study was to determine the incidence and characteristic features of anemic syndrome (AS) in patients with CAD of elderly and senile age.

Materials and methods. Retrospective analysis of the 1,993 patient records of illnesses was carried out. Patients were undergoing inpatient treatment in the cardiological department of the Regional Hospital for Disabled Soldiers of the Great Patriotic War (Chernivtsi, Ukraine) from January to December 2014. All patients were diagnosed with chronic CAD, which was represented by stable angina pectoris of functional classes II-III (according to the classification of the Canadian Association of Cardiologists, 1976), as well as diffuse and focal (post-infarction) cardiosclerosis. The age of the patients ranged from 60 to 96 years (average age was 79.5 ± 5.24 years). Comorbid anemia was diagnosed in case of hemoglobin level below 130 G/l in males and 120 G/l in females (WHO's Recommendations, 2003).

Distribution of patients by age is given in **Fig. 1**. The data from 252 elderly patients (60–74 years old) – 12.64% and 1,700 senile patients (75–89 years old) – 85.30% were analyzed. In addition, the investigation included records of the hospitalized patients over 90 years old (2.06%). Gender distribution of the patients is represented in **Fig. 2**.

The study conforms to the Helsinki Declaration (1997), the Convention on Europe on Human Rights and Biomedicine (1997), the International Code of Medical Ethics (1983), ICHGSP (2002).
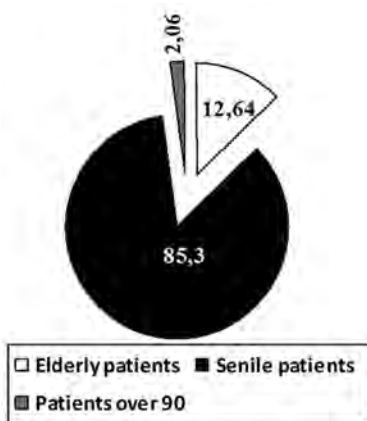

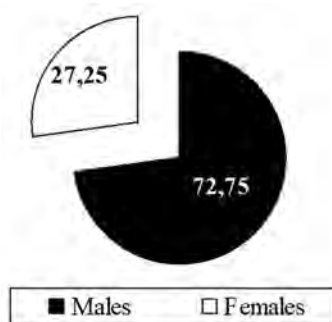**Fig. 1** – Age distribution of the patients with CAD, %

Fig. 2 – Gender distribution of the patients with CAD, %

Results and discussion. Among all examined patients, AS was found in 69.89% (1,393 cases), which coincides with the literature data [3, 4]. Among male patients, anemia occurred in 1,120 cases, which was 77.24%, among women – in 273 cases (50.28%). It was established that in people after 60 anemia is more common in men than in women, whereas it is a well-known fact that in adolescents and young adults AS occurs more frequently in females.

Mild anemia (hemoglobin level 90–120 (130) G/l) was the most frequent comorbid pathology in patients with CAD (1,317 cases, 94.54%). Moderate degree of anemia severity (hemoglobin level 70–90 G/l) occurred in 65 cases (4.67%). In 11 CAD patients severe anemia (hemoglobin level less than 70 G/l) was found (0.79%). Among males, mild anemia was detected in 1,065 cases (95.09%), moderate anemia – in 49 cases (4.37%), severe anemia – in 6 cases (0.54%). In women, anemia of mild degree occurred in 92.31% (252 cases), moderate – 5.86% (16 cases), severe degree – 1.83% (5 cases).

Only in less than hundred case reports the diagnosis of AS was recorded in the final clinical diagnosis during patients' discharge from the hospital. Mild anemia was documented as a separate diagnosis in only 37 patients among 1,317 (2.81%) (**Fig. 3**). Moderate anemia was present as a separate diagnosis in about 2/3 of all cases (in 42 patients out of 65). Approximately only one-third of all cases (36.36%) of severe anemia were not diagnosed in a hospital and no appropriate correction of hemoglobin level was performed (**Fig. 4).**
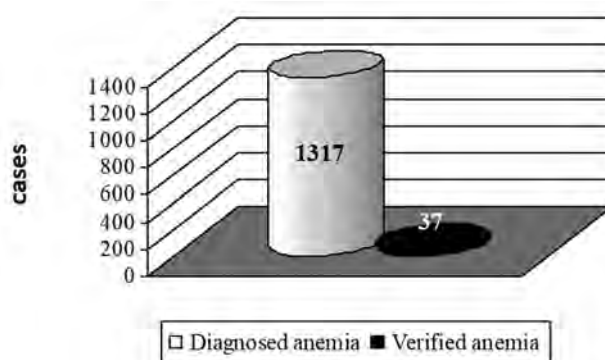

Fig. 3 – Frequency of mild anemia verification in patients with CAD

This issue was surprising for us as it is a well-known fact that low hemoglobin is an independent predictor of mortality, cardiovascular events, and major bleeds. Persisting or new-onset anemia is also a powerful predictor of cardiovascular and non-cardiovascular mortality [3]. Major adverse cardiac events are important causes of morbidity and mortality in CAD patients, detection and treatment of the risk factors, including anemia, are critical to improve health
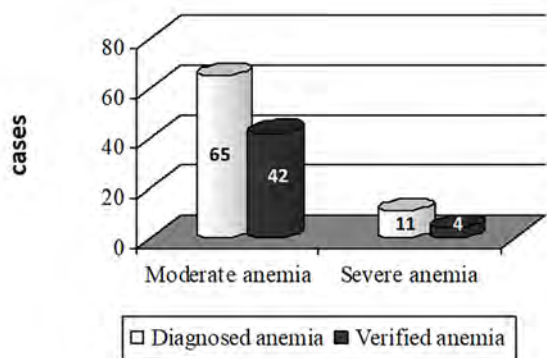
Fig. 4 – Frequency of moderate and severe anemia verification in patients with CAD

and longevity of patients with CAD [5]. Thus it is necessary to pay doctor's attention to the control of patient's hemoglobin level and its correction.

Table 1 – Dependence of the frequency of anemic syndrome on the form of chronic CAD

Form of CAD	Stable angina pectoris		Cardiosclerosis	
Anemia	+	-	+	-
Absolute number	753	219	640	381
%	77.47	22.53	62.68	37.32

Comparing the incidence of the comorbid anemia depending on the form of chronic CAD, we have found out that anemia in approximately equal percent of cases complicated the course of stable angina pectoris and post-infarction or diffuse cardiosclerosis (**Table 1**).

Comparing the degree of saturation of erythrocytes with hemoglobin, the hyperchromic character of anemia (color index > 1.05) was detected in 22 patients (1.58%), hypochromic (color index < 0.86) – in 116 patients (8.33%). In most cases anemia in patients with CAD was of normochromic character – 1,255 cases (90.09%) (**Fig. 5**).
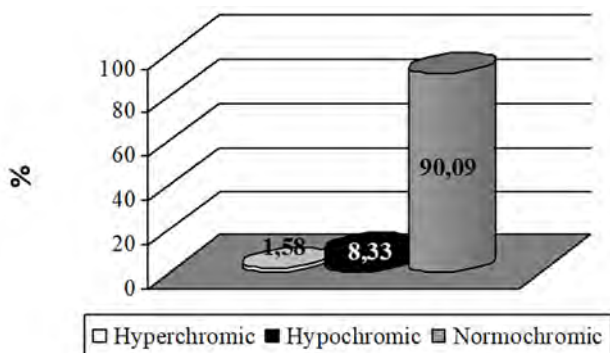

Fig. 5 – Morphological characteristics of anemia in patients with chronic forms of CAD

To determine the morphological characteristics of AS in patients with chronic forms of CAD, erythrocytes

mean corpuscular volume (MCV) was calculated. Mild macrocytosis (MCV = 95–108 fl) was detected only in several cases – 19 patients (1.36%), microcytosis (MCV < 80 fl) – in 157 patients (11.27%), normocytosis was found in 1,217 cases (87.37%) (**Fig. 6**).
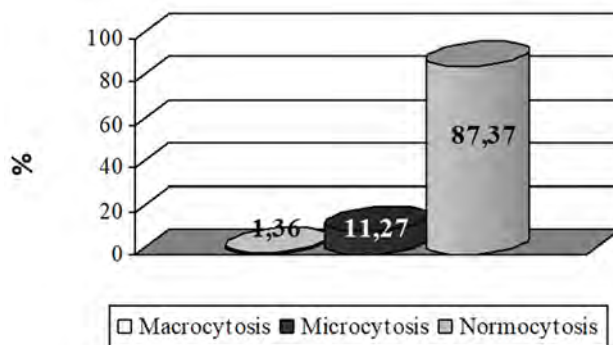

Fig. 6 – Morphological characteristics of anemia in patients with chronic forms of CAD

Thus, in most patients with CAD comorbid anemia is of normochromic and normocytic character. We may predict that anemia in case of CAD is anemia of chronic disease and the mechanisms, pathophysiology, and treatment of anemia in such patient is complex [6]. Without treatment hemodynamic changes found in the acute anemic state may contribute to progressive arterial wall and left ventricular hypertrophy if the anemic state persists chronically. The American College of Physicians recommends using a restrictive red blood cell transfusion strategy (trigger hemoglobin threshold of 7 to 8 g/dL compared with higher hemoglobin levels) in hospitalized patients with coronary heart disease [7].

The average duration of the in-hospital treatment of the patients with CAD without anemia was 16.14 ± 0.03 days. Along with progression of the severity of the comorbid anemia, statistically significant increase of the hospitalization period was observed. So, if CAD was accompanied by mild anemia, the average in-hospital treatment duration was 18.23 ± 0.050 days, moderate anemia – 20.02 ± 0.077, severe anemia – 21.03 ± ± 0.100. In patients with CAD and comorbid anemia, the frequency of hospitalizations per year has been also increased. Thus, among all patients with CAD without anemia, 85.50% of the patients were hospitalized twice a year due to main disease, 43.01% – three times per year, 24.33% – four times per year, 0.33% – more than four times. On the other hand, in the case of CAD with concomitant anemia, 94.54% of patients were admitted to the hospital twice a year, 55.20% – three times, 33.17% – four times, 3.88% – more often.

Among all analyzed cases in the largest number of them (79.83%) CAD and anemia were comorbid with chronic obstructive pulmonary disease, 28.14% of patients suffered from peptic ulcer of stomach and

duodenum, 4.31% of patients had oncological pathology of various localization, in 20.32% of cases anemia and CAD were isolated.

Conclusion and prospects for further research. Chronic forms of coronary artery disease in elderly and senile patients in 69.89% of cases are complicated by comorbid anemia of different degrees of severity. In older patients with CAD, anemic syndrome is most often caused by respiratory diseases (79.83%), stomach ulcer and duodenal ulcer (28.14%), cancer of different localization (4.31%). Concomitant anemia in patients with CAD contributes to the prolongation of the patients' in-hospital treatment and increasing of the frequency of hospitalizations due to the main disease throughout the year.

Perspectives of further investigations. Due to high incidence of comorbid course of anemia and chronic forms of CAD as well as increased mortality and fatal and non-fatal cardiovascular complications in these patients, search of possibilities of anemic syndrome correction is nowadays a crucial issue.

References

1. Kovalenko VM, Lutay MI, Sirenko YuM, Sychov OS. *Cardio-vascular diseases. Classification, standards of diagnosis and treatment*. 2016). 189 s. [Ukrainian]

2. Gandhi SJ, Hagans I, Nathan K, Hunter K, Roy S. Prevalence, comorbidity and investigation of anemia in the primary care office. *J Clin Med Res*. 2017;9(12):970-980. PMID: 29163729. PMCID: PMC5687900. doi: 10.14740/jocmr3221w

3. Kalra PR, Greenlaw N, Ferrari R, Ford I, Tardif JC, Tendera M, et al. Hemoglobin and change in hemoglobin status predict mortality, cardiovascular events, and bleeding in stable coronary artery disease. *Am J Med*. 2017 Jun;130(6):720-730. PMID: 28109968. doi: 10.1016/j.amjmed.2017.01.002

4. Nappi J. Anemia in patients with coronary artery disease. *Am J Health Syst Pharm*. 2003;60(14 Suppl 3):S4-8. PMID: 12908376. doi: 10.1093/ajhp/60.suppl_3.S4

5. Tsai IT, Wang CP, Lu YC, Hung WC, Wu CC, Lu LF, et al. The burden of major adverse cardiac events in patients with coronary artery disease. *BMC Cardiovasc Disord*. 2017 Jan 4;17(1):1. PMID: 28052754. PMCID: PMC5210314. doi: 10.1186/s12872-016-0436-7

6. Rymer JA, Rao SV. Anemia and coronary artery disease: pathophysiology, prognosis, and treatment. *Coron Artery Dis*. 2018 Mar;29(2):161-167. PMID: 29280914. doi: 10.1097/MCA.0000000000000598

7. Qaseem A, Humphrey LL, Fitterman N, Starkey M, Shekelle P; Clinical Guidelines Committee of the American College of Physicians. Treatment of anemia in patients with heart disease: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2013 Dec 3;159(11):770-779. PMID: 24297193. doi: 10.7326/0003-4819-159-11-201312030-00009

СТРУКТУРА АНЕМІЧНОГО СИНДРОМУ У ХВОРИХ З ХРОНІЧНИМИ ФОРМАМИ ІШЕМІЧНОЇ ХВОРОБИ СЕРЦЯ

Павлюкович Н. Д., Павлюкович О. В., Шупер В. О.

Резюме. *Мета дослідження*: визначення частоти та можливого генезу анемії у хворих похилого та старечого віку з хронічними формами ішемічної хвороби серця.

Матеріали та методи. Ретроспективно проаналізовано 1993 історії хворих на хронічні форми ішемічної хвороби серця із коморбідною анемією, які були госпіталізовані впродовж року в стаціонар з приводу основного захворювання.

Результати. Серед усіх обстежених хворих на хронічні форми ішемічної хвороби серця анемічний синдром був виявлений майже в 70% випадків. У осіб після 60 років анемія частіше зустрічається у чоловіків, ніж у жінок, тоді як у осіб молодого та середнього віку анемічний синдром частіше діагностують у жінок. Лише в менш ніж ста випадках діагноз анемії був зафіксований в остаточному клінічному діагнозі під час виписки пацієнтів із стаціонару. Частота анемії у обстежених хворих не залежить від форми хронічної ішемічної хвороби серця (стабільна стенокардія напруги чи дифузний/постінфарктний кардіосклероз). У більшості хворих на хронічну ішемічну хворобу серця коморбідна анемія має нормохромний і нормоцитарний характер. Поряд із прогресуванням ступеня тяжкості коморбідного анемічного синдрому спостерігається статистично достовірне збільшення терміну госпіталізації хворих з приводу основного захворювання. У пацієнтів із ішемічною хворобою серця та коморбідною анемією частота госпіталізацій на рік також збільшується.

Висновки. Хронічні форми ішемічної хвороби серця у хворих похилого та старечого віку в 69,89% випадків ускладнюються коморбідною анемією різного ступеня тяжкості. У літніх хворих на ішемічну

хворобу серця анемічний синдром найчастіше зумовлений захворюваннями органів дихання, виразковою хворобою шлунка та дванадцятипалої кишки, раком різної локалізації. У більшості хворих на ішемічну хворобу серця коморбідна анемія має нормохромний і нормоцитарний характер. Супутній анемічний синдром у хворих на хронічну ішемічну хворобу серця сприяє подовженню тривалості перебування хворого у стаціонарі та збільшенню частоти госпіталізацій з приводу основного захворювання впродовж року.

Ключові слова: серцево-судинні захворювання, ішемічна хвороба серця, анемія.

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