

## RISK FACTORS FOR ANEMIA IN PATIENTS WITH CHRONIC HEART FAILURE

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### Abstract

This article discusses chronic heart failure (CHF) as a significant public health problem, which is characterized by high mortality, frequent rehospitalization of patients and, as a result, a high financial burden on the healthcare system. According to the recommendations of the European Society of Cardiology (ESC), HF is “a clinical syndrome characterized by typical complaints or symptoms such as shortness of breath, swelling of the legs and weakness, which are accompanied by such external manifestations or signs as increased pressure in the jugular vein, moist rales over lungs and peripheral edema as a result of abnormal cardiac structure and/or impaired cardiac function, which ultimately leads to decreased cardiac output and/or increased intracardiac pressure at rest or during stress.”

**Keywords:** anemia, cardiovascular disease, threshold hemoglobin level, currents.

### Relevance

In most diseases, anemia is a cause or consequence that accompanies the disease and in 95% of cases requires long-term treatment [1,2,3]. Anemia is a decrease in the number of red blood cells, often accompanied by a decrease in hemoglobin (Hb) levels or changes in the morphology of red blood cells and, as a consequence, is manifested by the presence of general weakness, chronic fatigue, difficulty concentrating and decreased productivity of the patient [4,5]. With anemia, physical activity decreases, the quality of life becomes unsatisfactory, and as a result, the root cause of adverse outcomes [6,7,8]. According to the World Health Organization (WHO) classification, anemia is defined as a decrease in hemoglobin levels of less than 120 g/l in women and less than 130 g/l in men [9]. Jandl proposed a threshold hemoglobin level of 142 g/l as a definition of anemia [10,11,12]. If we take into account the threshold value proposed by the WHO, it turns out that 22% of healthy people would be anemic [13]. Two databases played a major role in determining the hemoglobin concentration, which included 95% and 95.7% of healthy people. These are NHANES-III (the third national registry of health and nutrition surveys) in the USA and the Scripps-Kaiser database, which collects data for the period 1998-2002. [14]. Using the WHO classification of anemia, Sarnak et al. found that in the United States, among a healthy population aged 45-64 years, the prevalence of anemia was 9% (5% among men, 13% among women) [7]. While taking into account age, gender, and race, NHANES-III (National Health and Nutrition Examination Survey) showed that the prevalence of anemia was approximately 5% [6]. According to the Framingham study of 91,316 patients hospitalized with chronic heart failure (CHF), anemia, compared with hypertension and coronary artery bypass grafting, was a stronger predictor of the need for early

readmission [8]. It has been determined that anemia increases the load on the myocardium due to hemodynamic and neurohormonal changes, which can lead to pathological LV remodeling [9]. In the experiment, in animals that had severe anemia, the presence of LV hypertrophy and dilatation was noted [10,11].

### **Purpose of the study**

Patients with CHF who are susceptible to the development of anemia are mainly decompensated patients, often female, elderly, and those who have concomitant chronic kidney disease (CKD) and diabetes mellitus (DM) [12]. In such patients, the prevalence of anemia can reach 30-61%, and in the presence of fewer symptoms varies from 4 to 23% [13]. In 21 outpatient patients with CHF who received recommended therapy, the prevalence of anemia with Hb <120 g/l ranged from 8 to 15% [14].

**Age.** The incidence of anemia increases with age. Thus, in the USA, the level of anemia in women and men over 65 years of age is 11% and 10%, respectively [15], the proportion of anemic people doubles upon reaching 85 years of age [16]. The presence of anemia in elderly patients is accompanied by a worsening prognosis, including a decrease in reserves for physical activity, impaired consciousness, and a high probability of loss of consciousness [16].

**Floor.** When studying anemia in patients with HF, a relationship was found between the number of anemic women and the worsening degree of anemia [17]. According to T. Joo Yeo et al. The prevalence of anemia among women compared to men was higher in both the HF group (70.5% vs. 58.6%) and the control group (57.9% vs. 20.4%), which persisted even after adjustment by age, race, body mass index, comorbidity, and alcohol and cigarette use [18]. The ANCHOR study found that female gender ( $p=0.01$ ) was an independent predictor of decreased hemoglobin levels [19]. Chronic kidney disease (CKD). The interaction of CHF and CKD is due to the growing number of patients with CKD, including the most severe forms, and the predominance of vascular pathology as the etiological basis in the complex: atherosclerosis, arterial hypertension, diabetes mellitus [20]. CKD is defined when the glomerular filtration rate decreases to less than 60 ml/min/1.73 m<sup>2</sup> or in the presence of other markers of kidney damage, such as structural or functional pathologies with normal or reduced glomerular filtration rate [21]. In patients with CHF, CKD usually does not manifest itself clinically. Thus, only one out of four patients with a glomerular filtration rate (GFR) in the range of 15-59 ml/min/1.73 m<sup>2</sup> is aware of the presence of CKD [20], while at the same time, 30-50% of patients with CHF have a decrease in GFR <60 ml/min/1.73 m<sup>2</sup> [22]. The combination of CKD and anemia are the most common comorbid conditions in patients with CHF [17], in this regard, anemia is more common in patients with CHF with CKD than without CKD. The studies provided convincing indirect evidence about the role of the kidneys in the pathogenesis of anemia in patients with HF [23]. The combination of anemia, CHF and CKD



is called “cardiorenal anemia syndrome”, based on the theoretical assumption of the reciprocal negative effect of CHF and renal failure, anemia in this case is an aggravating factor [20]. Thus, severe anemia is an independent predictor of mortality in patients with CKD. However, on the practical side, there are gaps in understanding whether anemia is a marker of CKD or CHF, or a cardiovascular risk factor.

**Diabetes.** The prevalence of diabetes mellitus throughout the world is very high. In the United States, approximately 7% of the population has diabetes, which is approximately 20.8 million people [24]. A similar trend is observed in Europe. In Germany, the number of people with diabetes is 6.5 million (8.2%) [25]. In 2000 in Kazakhstan, this indicator was 0.72 per 100 thousand population, with a subsequent increase of 1.6 times by 2010 - 1.17 per 100 thousand population [26]. According to the NHANES-III analysis, the risk of developing anemia in the population with diabetes is two times higher than in persons without diabetes, the same as among the examined patients with renal failure [27]. PAERI clinical studies showed that anemia was detected in 53% of patients with diabetes with concomitant renal failure; in patients with renal failure only, this figure was 1.4 times lower and amounted to 39% [28]. The NEFRON study, which included 4000 patients with diabetes, showed that anemia develops when GFR is more than 60 ml/min/1.73 m<sup>2</sup>, but in the presence of albuminuria [29]. Anemia develops more often in patients with diabetic nephropathy compared to other types of nephropathies [30]. In the presence of diabetes, anemia can develop at the onset of the disease, when the production of erythropoietin (EPO) decreases, even if renal function is preserved, that is, the production of EPO decreases while the ability to synthesize it remains intact [31].

**Drugs.** The treatment of patients with CHF includes various groups of drugs. One of the basic groups of drugs is angiotensin-converting enzyme inhibitors (ACE) and angiotensin II receptor antagonists (angiotensin receptor blockers (ARBs)). A number of studies have demonstrated that taking ACE inhibitors causes or contributes to the progression of anemia in patients. In the SOLVD study, where a decrease was noted overall mortality, there was also a decrease in hematocrit and an increase in new cases of anemia in patients with CHF. Strikingly, among patients with new cases of anemia, the overall mortality was higher by 108%. In a study conducted in Spain with including 337 patients hospitalized with HF during a 20-month follow-up, there was no statistically significant relationship between anemia and ACE intake.<sup>30</sup> These drugs lead to pharmacological inhibition of the RAAS, thereby leading to a decrease in hematocrit, which is insignificant in the presence of normal renal function and more pronounced in the presence of CKD. Other drugs that contribute to the development of anemia are non-steroidal anti-inflammatory drugs, through the development of chronic blood loss, and also possibly by blocking prostaglandins that stimulate erythropoiesis.

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