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Prevalence of Iron Deficiency in Patients with Acute Decompensated Heart Failure

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ABSTRACT

Aim. The research aims to systematize current data on the prevalence, diagnosis, and clinical significance of iron deficiency (ID) in patients with acute decompensated heart failure (ADHF).

Materials and methods. A systematic analysis of studies from 2019 to 2024 in PubMed and eLibrary databases was conducted, including data from 6,500 patients with ADHF. Selection criteria were as follows: confirmed ADHF diagnosis, assessment of iron status using standard parameters (ferritin and transferrin saturation (TSAT)), and availability of clinical outcome data.

Results. To differentiate the type of iron deficiency, optimal diagnostics of simultaneous assessment of ferritin and TSAT levels requires: ferritin < 100 μg/L – absolute ID; ferritin 100–299 μg/L in combination with TSAT < 20% – functional ID. ID was found in 45–89% of ADHF patients and was associated with: more severe disease progression (functional class III-IV according to the New York Heart Association system in 68% of cases), elevated NT-proBNP levels (35% higher compared to non-ID patients), reduced exercise tolerance (six-minute walk test: 278±45 m vs 342±38 m in non-ID group).

Conclusion. Iron deficiency is an independent prognostic factor in ADHF. Early diagnosis and correction, particularly through intravenous ferric carboxymaltose administration, may improve clinical outcomes and reduce hospital readmission rates.

Keywords: heart failure, acute decompensated heart failure, iron deficiency, prevalence, clinical outcomes, prognosis

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Распространенность дефицита железа у больных с острой декомпенсацией сердечной недостаточности

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РЕЗЮМЕ

Цель. Систематизировать современные данные о распространенности, диагностике и клиническом значении дефицита железа (ДЖ) у пациентов с острой декомпенсацией сердечной недостаточности (ОДСН).

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Материалы и методы. Проведен систематический анализ исследований за период с 2019 по 2024 г. в базах PubMed и eLIBRARY, включающий данные 6 500 пациентов с ОДСН. Критерии отбора: подтвержденный диагноз ОДСН, оценка статуса железа по стандартным параметрам (ферритин, коэффициент насыщения трансферрина железом (КНТЖ)), наличие данных о клинических исходах.

Результаты. Для разграничения типа дефицита железа оптимальная диагностика требует одновременной оценки уровня ферритина и КНТЖ: ферритин менее 100 мкг/л – абсолютный ДЖ; ферритин 100–299 мкг/л в комплексе с КНТЖ менее 20% – функциональный ДЖ. Установлено, что ДЖ встречается у 45–89% пациентов с ОДСН и ассоциирован с более тяжелым течением заболевания (функциональный класс III–IV по классификации Нью-Йоркской кардиологической ассоциации в 68% случаев), повышением уровня N-концевого пропептида натрийуретического пептида типа B (в среднем на 35% по сравнению с пациентами без ДЖ), снижением толерантности к физической нагрузке (тест шестиминутной ходьбы: 278 ± 45 м против 342 ± 38 м в группе без ДЖ).

Заключение. Дефицит железа – независимый прогностический фактор при ОДСН. Его ранняя диагностика и коррекция, в частности внутривенным введением железа карбоксимальтозата, могут улучшить прогноз и снизить частоту повторных госпитализаций.

Ключевые слова: сердечная недостаточность, острая декомпенсация сердечной недостаточности, дефицит железа, распространенность, клинические исходы, прогноз

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

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INTRODUCTION

Heart failure (HF) represents one of the most significant challenges in modern cardiology. Its global prevalence ranges from 1 to 2% among the adult population, increasing with age: from less than 1% in individuals under 55 years to over 10% in those over 70 years. The true prevalence of HF is believed to be significantly higher, especially among patients with heart failure with preserved ejection fraction (HFpEF) [1].

In the Russian Federation, epidemiological studies indicate that the prevalence of chronic heart failure (CHF) in the general population reaches 7% (12.35 million people), including 4.5% of cases with clinically manifested CHF [2]. Particular attention is paid to patients with acute decompensated heart failure (ADHF), who have an extremely poor prognosis, high rates of readmission, and, consequently, impose significant financial burdens – making them a critical public health issue. The 5-year mortality rate following an ADHF episode can be as high as 75% [3, 4].

Numerous studies support the concept that hospitalization for ADHF often signifies a sharp turn in the natural history of HF. The rate of rehospitalization or death reaches 50% within 6 months after the initial ADHF event, which is considerably higher than the event rates observed after acute myocardial infarction [5, 6]. By 2030, the annual number of patients hospitalized with ADHF is projected to rise from 1.5 million to 8 million, with associated financial costs steadily increasing by over 50% compared to previous periods [7]. According to the independent Russian ORACUL-RF registry, following an ADHF hospitalization episode, the 30-day readmission rate was 31%, and all-cause mortality was 13%, increasing to 43% at one year of follow-up [8].

Iron deficiency (ID) and anemia are among the most common comorbidities in CHF, associated with an unfavorable prognosis, reduced exercise tolerance, and impaired quality of life [9]. ID is significantly more prevalent in HF patients than anemia, being diagnosed in 60% of outpatients and 80% of inpatients with HF. Literature data suggest that ID occurs in over 80% of hospitalized patients in Russia [10]. Recently, ID has come to be viewed not merely as a concomitant disease but as an integral component involved in the pathophysiology of HF

development and progression [11–13]. Growing evidence supports a key role for ID in adverse long-term outcomes in HF patients.

Optimal HF therapy, including a comprehensive pharmacological approach, contributes to a reduction in the frequency of ID, even without direct iron supplementation. However, despite a substantial number of conducted studies, the significance of ID in the post-ADHF patient population remains uncertain, posing a challenge for the scientific community to continue optimizing algorithms for timely diagnosis and effective correction strategies [14].

The aim of this review is to systematize current data on the prevalence of ID in patients with ADHF and to assess its impact on the disease course and outcomes. The article will review key studies conducted in this field and present data on the frequency of ID in this patient population.

MATERIALS AND METHODS

A systematic approach was chosen to review the literature on ID in patients with ADHF. The methodology included the following steps:

Formulating research questions: defining key questions the review should answer, including the prevalence of ID and its impact on patient status.

Study selection criteria: inclusion of studies published in Russian and English over the last 5 years (2019 to 2024). Works lacking empirical data or not relevant to the review topic were excluded.

Source search: utilizing medical databases, such as PubMed and eLibrary with specialized search queries, including keywords like "iron deficiency" and "acute decompensated heart failure."

Data collection and analysis: reviewing and synthesizing data from selected studies to identify common trends and differences in methodologies and results.

Results synthesis: integrating the obtained data into a unified analytical review reflecting the current state of knowledge on the problem.

IRON DEFICIENCY AND ITS SIGNIFICANCE IN HEART FAILURE

Iron is one of the most essential micronutrients, an integral component of many enzymes and proteins playing a central role in functions, such as cellular respiration, cell proliferation, biosynthesis of oxygen-transporting molecules, synthesis and repair of nucleic acids, and as a cofactor in numerous other enzymatic reactions [15, 16].

Iron deficiency is defined as "a health-related condition in which iron availability is insufficient to meet the body's needs and which can be present with or without anemia." In most clinical situations, diagnosing ID requires the determination of two parameters: serum ferritin level and transferrin saturation (TSAT) [17].

In patients with CHF, iron deficiency is defined as a serum ferritin level < 100 μg/L (absolute ID) or a ferritin level in the range of 100–299 μg/L (functional ID) in combination with transferrin saturation < 20%, alongside a decrease in serum iron to a level less than 13 μmol/L with TSAT < 20% [19]. According to the Russian Society of Cardiology Guidelines for CHF, all HF patients should undergo regular screening for anemia and ID with a complete blood count, measurement of serum ferritin concentration, and TSAT (Class of recommendation I, Level of evidence C) [2].

It is known that in the absence of inflammation or chronic disease, serum ferritin correlates with body iron stores, and a serum ferritin level of 100 μg/L corresponds to approximately 1g of tissue iron. In healthy individuals, a ferritin level below 30 μg/L and TSAT below 16% define iron deficiency [9]. In inflammation, including HF, the ferritin level is non-specifically elevated as an acute-phase reactant, making the identification of absolute or functional ID challenging [20]. For this reason, various clinical trials on ID correction in HF patients have used ferritin levels < 100 μg/L or < 300 μg/L if TSAT < 20% to identify patients with absolute and functional ID [21, 22].

Ferritin is the primary storage protein for iron in tissues. There is a direct correlation between iron stores in the reticuloendothelial system and the serum ferritin level, allowing the latter to be used as a marker of iron reserves. A serum ferritin level < 30 μg/L indicates low iron stores and is diagnostic for ID in patients without chronic inflammatory or infectious diseases [20]. However, the properties of ferritin as an acute-phase protein mean its level increases in inflammatory conditions, such as chronic kidney disease, HF, liver disease, and cancer. Consequently, higher threshold ferritin concentrations are used to define ID in HF patients

compared to healthy individuals. Under these conditions, ferritin levels within the normal range differ from those mentioned above (Table 1).

Table 1

Diagnostic Criteria for Iron Deficiency [20]

Condition	Serum ferritin, μg/L	TSAT, %
Preoperative Iron Deficiency	CRP <5 mg/L: <30 CRP >5 mg/L: <100	<20
Iron Deficiency in HF	<100	<20 (if serum ferritin is 100–299 μg/L)
Iron Deficiency in CKD	CKD Stage C3–C5: ≤100 CKD Stage C5D: ≤200	≤20

Note. TSAT – transferrin saturation, HF – heart failure, CKD – chronic kidney disease, CRP – C-reactive protein

In chronic inflammatory or infectious diseases, measuring serum ferritin alone may not always suffice to diagnose ID. Under these circumstances, calculating TSAT is also necessary. Transferrin saturation represents the ratio of serum iron to total iron-binding capacity, expressed as a percentage, and reflects the proportion of active sites on serum transferrin occupied by iron atoms [27]. TSAT values < 20% are accepted as thresholds for diagnosing ID in chronic somatic-symptom diseases, such as HF or chronic kidney disease (Table 1).

Some studies emphasize the more significant role of TSAT compared to ferritin as a key indicator of ID and adverse outcomes [14, 23]. For instance, the 2021 study by P. Palau et al. assessed the association between potential markers of ID – TSAT and serum ferritin – and the risk of readmission (RA) within 30 days or death in patients with ADHF. Over 30 days, 177 events (10.4%) were recorded (95 deaths and 85 HF-related readmissions). After multivariate adjustment, lower TSAT was associated with an increased risk of short-term events (p = 0.009), while no such association was found for ferritin levels (HR 1.00; 95% CI 0.99 1.00, p = 0.347) [23].

These diagnostic criteria for ID in HF patients are presented in the 2021 European guidelines, which is consistent with the opinion of Russian experts [20]. It is important to remember that serum iron concentration can exhibit significant diurnal variations in HF patients; therefore, this laboratory parameter cannot be used independently to diagnose ID in this patient category.

Another proposed marker, suggested as an accessible and cost-effective tool for identifying ID in ADHF patients, is reticulocyte hemoglobin content (Ret-He) [24]. Reticulocytes now offer a rapid way to assess iron status. Unlike mature erythrocytes, which have a lifespan of 120 days, reticulocytes are renewed in the bone marrow every 2–4 days. This feature provides current data on the quality of the cellular pool and iron availability at the time of testing, unlike a standard complete blood count, which reflects the state of hematopoiesis with a significant time delay. Unlike traditional parameters (serum iron, ferritin, and transferrin), Ret-He levels are not influenced by inflammatory processes, making it a reliable indicator of current iron bioavailability.

Dynamic monitoring of this parameter allows for an objective assessment of the effectiveness of therapy for ID states: an increase in Ret-He values indicates a positive response to treatment [25]. A unified Ret-He threshold value of 32.4 pg for ID screening, based on two criteria (TSAT < 20% and serum ferritin <100 μg/L), underscores its potential as a universal indicator for diagnosing ID in this patient population. This approach may improve clinical outcomes in patients hospitalized with ADHF by enabling faster, more accurate, and accessible determination of ID, both in the inpatient setting and during subsequent outpatient visits [24].

PREVALENCE OF IRON DEFICIENCY AMONG ADHF PATIENTS

The first studies exploring the relationship between ID and HF appeared in the scientific literature in the late 20th century. However, a deeper understanding of this link and its clinical significance became a subject of active investigation only in the early 21st century. Since 2010, following large-scale clinical trials and meta-analyses, the topic of ID in HF has seen significant development. These works have provided a better understanding of the mechanisms through which ID affects myocardial function and its role in HF progression [26–28].

One of the key studies addressing ID in ADHF patients was work by international researchers published in 2019. In this study conducted at a leading medical center, ID was diagnosed based

on a serum ferritin level < 100 μg/L or TSAT < 20% with a ferritin level of 100–299 μg/L. Among the 503 included patients, 270 (55%) had heart failure with preserved ejection fraction (HFpEF), 160 (33%) had heart failure with reduced ejection fraction (HFrEF), and 57 (12%) had HFmrEF. ID was identified in 54% of patients with HFrEF and 56% of patients with HFpEF. The authors emphasized the high prevalence of ID among ADHF patients, regardless of HF type [29].

In 2023, the study "Ferric Carboxymaltose in Patients with Acute Decompensated Heart Failure and Iron Deficiency: A Real-Life Study" investigated the efficacy of ID correction using ferric carboxymaltose in ADHF patients. Among 104 hospitalized patients (mean age 84 years, 53.5% with HFpEF), 90 underwent a complete iron status assessment. ID was diagnosed in 73 (81.1%) patients [30].

In 2022, data covering the period from January 2013 to December 2018 were published, showing that among 1,863 patients hospitalized with ADHF (both HFrEF and HFpEF), 840 (45%) had laboratory signs of ID (absolute or functional), meeting the inclusion criteria [31].

In the study by D.H.Van Dalen et al. (2022), the prevalence and dynamics of ID in ADHF patients were examined. At hospitalization (T0), ID was detected in 71.8% of patients (44.1% had absolute ID, 27.7% – functional ID). After clinical stabilization prior to discharge (T1) and 10 ± 6 weeks post-discharge (T2), ID persisted in 56.4% and 50.3% of patients, respectively. Absolute ID persisted from T0 to T2 in 66% of patients, whereas functional ID resolved in 56% of patients. Ferritin, transferrin saturation, and serum iron levels increased significantly from T0 to T1 and from T1 to T2, even without iron supplementation. The authors concluded that ID was highly prevalent in ADHF patients but may resolve spontaneously during treatment in some. Absolute ID resolved more often, while functional ID frequently resolved with ADHF therapy [32].

In the study by K.AlAayedi (2023), current practices for diagnosing and treating ID in hospitalized ADHF patients with HFpEF were evaluated. Among 111 patients, 74% (82) had their iron status analyzed, and ID was diagnosed in 63% (52) of them according to European Society of Cardiology (ESC) criteria. Among patients with ID, 54% (28) also had anemia. ID correction was prescribed to 34 out of 52 patients (65%), indicating insufficient clinician awareness of the importance of treating ID [36].

In the retrospective multicenter study "Iron Deficiency and Short-term Adverse Events in Patients with Decompensated Heart Failure" (P. Palau et al., 2021), which included 1,701 patients, ID was identified in 1,246 (73.3%) patients according to the ESC definition [23].

The research conducted by V.Yu.Mareev et al. demonstrated a high prevalence of ID among HF patients. In an extensive analysis encompassing 498 patients (198 women and 300 men), ID was detected in 83.1% of those examined. Patients with ID were older and had more pronounced functional myocardial changes: median age was 70.0 [63.0; 79.0] years compared to 66.0 [57.0; 75.2] years in the non-ID group (p = 0.009). Notably, anemia was diagnosed in only 43.5% of patients with ID, highlighting the independence of these two conditions [33]. In the study by Smirnova et al., the prevalence of iron deficiency was analyzed among 294 patients with chronic heart failure (mean age 71.3±0.4 years) hospitalized due to decompensation in coronary artery disease and/or arterial hypertension, and worsening HF symptoms. The results demonstrated a progressive decrease in serum iron levels and transferrin saturation with increasing NYHA functional class. Iron deficiency was diagnosed in 72% of examined patients (n = 213), with a pronounced gender imbalance (78% of cases in women vs. 22% in men). The combination of ID and anemia was observed in 25% of cases, whereas isolated anemia without ID was found in 16% [34].

In the study by E.A.Smirnova et al., data from 80 patients with ADHF revealed a high prevalence of ID – 80% of cases. Absolute ID was diagnosed in 82.8% of patients, while functional ID was observed in only 17.2% of cases. Concomitant anemia of varying severity was detected in 35% of those examined: mild degree was registered in 64.3%, moderate and severe – in 25 and 10.7% of patients, respectively. Importantly, in 89.3% of cases, anemia was iron-deficient, while anemia of chronic disease occurred in only 10.7% of cases. The combination of ID and anemia was noted in

31.2% of patients, while normal iron metabolism and hemoglobin levels were recorded in only 16.3% of patients [10].

The study conducted by Zh.D. Kobalava et al. investigated the prevalence and prognostic significance of ID in patients with ADHF. The results showed that the frequency of ID ranged from 70% to 89% depending on the diagnostic criteria used. Using Criterion A (ferritin level < 100 μg/L or ferritin 100–299 μg/L in combination with TSAT < 20%), ID was detected in 89% of patients, including absolute ID in 153 (69%) and functional ID in 46 (20%). Criterion B (TSAT < 20% and serum iron level < 13 μmol/L) showed ID in 70% of patients [35].

Analysis of data obtained from 223 ADHF patients demonstrated that according to Criterion A, ID without anemia was observed in 106 (47%) patients, ID with anemia – in 93 (42%), and anemia without ID – in 9 patients (4%). Fifteen (7%) patients had normal hemoglobin and serum iron metabolism markers. Using Criterion B, ID without anemia was identified in 77 (35%) patients, ID with anemia – in 79 patients (35%), and anemia without ID – in 24 cases (11%). Forty-three (19%) patients had no abnormalities in hemoglobin content or serum iron metabolism markers. The study underscores the high prevalence of ID among ADHF patients and its independence from the presence of anemia. The authors also noted that the choice of diagnostic criteria significantly affected ID detection rates, highlighting the need for standardized diagnostic approaches [14, 35].

Studies show that ID is a common condition among patients with ADHF. Across various studies, the prevalence of ID ranges from 45% to 89% (Table 2).

IMPACT OF IRON DEFICIENCY ON CLINICAL PARAMETERS

According to the available data, patients with ADHF and concomitant ID have distinct clinical characteristics indicating a more severe disease course and a less favorable prognosis.

1. Patients with ID cover a shorter distance in the six-minute walk test (6MWT) compared to patients without ID, indicating worse physical endurance.

Data from the Russian multicenter cross-sectional screening study (2023) determined that the mean 6MWT distance in CHF patients with concomitant ID was 155.9 ± 84.0 m versus 239.6 ± 82.7 m in the group without iron metabolism disorders (p = 0.01) [10]. These results are corroborated by the study of V.Yu.Mareev et al. (2022), which also found a significant reduction in the 6MWT distance in ID (250 [170;320] m vs. 299 [210;358] m in the non-ID group, $p < 0.001$) [33].

2. Patients with ID have lower scores on the visual analog scale (VAS), indicating a lower quality of life.

As shown by the study by E.A. Smirnova et al., organized by the Russian Heart Failure Society, the mean VAS score in the ID patient group was 36.4 ± 16.3 versus 46.3 ± 20.7 in the group without iron metabolism disorders (p = 0.036), indicating a substantial deterioration in quality of life associated with concomitant ID [10].

3. The level of N-terminal pro-B-type natriuretic peptide (NT-proBNP) is significantly higher in patients with ID, which may indicate more pronounced heart failure symptoms.

In the study led by V.Yu. Mareev et al. (2022), it was shown that each 100 pg/mL increase in NT-proBNP level was associated with an increased likelihood of having ID (OR 1.006 [1.002–1.011], p = 0.0152) [33]. These data correlate with the results of E.A. Smirnova et al., where patients with ID had significantly higher NT-proBNP levels (5,155.5 [3,267.3;9,786.3] pg/mL) compared to the group without ID (2,055.5 [708.8; 2,839] pg/mL, $p < 0.001$). Interestingly, the presence of concomitant anemia did not have an additional impact on NT-proBNP levels in patients with ID (5,683.0 [3,494.5; 7,863.5] pg/mL in ID with anemia vs. 5,110.0 [2,779.0; 10,140.0] pg/mL in isolated ID, p = 0.799) [10].

Additional evidence of the link between ID and HF progression and myocardial fibrosis was obtained in the study by Zh.D. Kobalava et al. (2022). In this work, patients with ID had significantly higher levels of C-reactive protein (15.1 mg/L vs. 6.2 mg/L in the control group, $p < 0.001$), NT-proBNP (5,422 pg/mL vs. 2,380 pg/mL, $p < 0.001$), and soluble suppression of tumorigenicity 2 receptor (sST2) (59.6 ng/mL vs. 42 ng/mL, p = 0.02). The observed elevation in sST2, a specific marker of myocardial fibrosis, is of particular significance. The obtained data suggest that patients with ID

Table 2

Prevalence of Iron Deficiency Among Heart Failure Patients

Study	Number of Patients	Age (years)	ID Prevalence, %	Anemia Prevalence, %	ID & Anemia Co-prevalence, %
Factors Associated with Iron Deficiency in Patients with Chronic Heart Failure.M.P. Smirnova et al. (2023) [34]	213 (Women – 166 (78%), Men – 47 (22%))	71.3±0.4	72	22.4	25
Prevalence of Iron Deficiency in Patients with Chronic Heart Failure in the Russian Federation. Data from an Observational Cross-sectional Study. Failure.M.P. et al. (2022) [33]	510	70 [63; 79]	83.1	40.4	43.5
Prognostic Significance of Different Iron deficiency Criteria in Patients with Decompensated Heart Failure. Zh.D.Kobalava et al. (2022) [35]	223	73 [65; 82]	Criterion (1) ferritin < 100 ng/mL or 100–299 ng/mL with TSAT < 20%* Criterion (2) TSAT < 20% and serum iron < 13 μmol/L By Criterion (1): 89% (Absolute ID – 69%, Functional ID – 20%) By Criterion (2): 70%	By Criterion (1): 4% By Criterion (2): 11%	By Criterion (1): 42% By Criterion (2): 35%
Prevalence and Clinical Significance of Iron Deficiency in Patients with Acute Decompensated Heart Failure. E.A.Smirnova et al. (2023) [10]	80 (62.5% men)	68.4±11.1	80	35	31.2
Iron Deficiency in Acute Decompensated Heart Failure. A.Beale et al. (2019) [29]	503 (43% women) HFpEF (55%) HFrEF (33%) HFmrEF (12%)	78 ± 11	Overall ID –57% (of which 54% HFrEF, 56% HFpEF) *Absolute ID –38%* *Functional ID – 18%*	–	–
Ferric Carboxymaltose in Patients with Acute Decompensated Heart Failure and Iron Deficiency: A Real-Life Study. F. Capone et al. (2023) [30]	90 HFpEF – 53.5%	84	81.1	66.7	69.9
IV Sodium Ferric Gluconate Complex in Patients Hospitalized Due to Acute Decompensated Heart Failure and Iron Deficiency". I. Borreda et al. (2022) [31]	1,863	74.28 [65.42; 81.55]	45	–	–
Iron deficiency and short-term adverse events in patients with decompensated heart failure. P. Palau et al. (2021) [23]	1,701	76 [68; 82]	73.3	–	–
The Burden of Iron Deficiency in Heart Failure: Therapeutic Approach. D.H.Van Dalen et al. (2022) [32]	692	78 [70; 84]	At hospitalization (T0): 71.8% At discharge (T1): 56.4% 10 ± 6 weeks post-discharge (T2): 50.3% Absolute ID persisted in 66% from T0 to T2. Functional ID resolved in 56%	–	–
An Audit of Iron Deficiency in Hospitalized Heart Failure Patients: A Commonly Neglected Comorbidity K.AlAayedi (2023) [36]	82	>18	63	–	54

Note. SAT – transferrin saturation, ID – iron deficiency, ADHF – acute decompensated heart failure, HFrEF – heart failure with reduced ejection fraction, HFmrEF – heart failure with mid-range ejection fraction, HFpEF – heart failure with preserved ejection fraction.

exhibit more pronounced myocardial remodeling compared to patients without iron metabolism disorders. These results align with the general trend observed in the study by T.B. Pecherina et al., where sST2 and NT-proBNP demonstrated high prognostic value for assessing the risk of myocardial fibrosis [18, 35].

4. Significantly more patients with ID have NYHA functional class IV heart failure, indicating a more severe disease course.

Studies show that ID correlates with CHF functional class. Research by Zh.D.Kobalava et al. (2022) and E.A. Smirnova et al. (2023) found that patients with ID had higher NYHA functional classes [10, 35]. M. Smirnova and P. Chizhov identified ID in 68% of patients with NYHA functional class III-IV CHF and in 58% of patients with stage IIB–III CHF according to the Strazhesko-Vasilenko classification [34].

5. According to the EUROQOL GROUP EQ-5D questionnaire, patients with ID more frequently experience difficulties with mobility and daily activities and report significant discomfort.

Within the Russian multicenter screening study, analysis of the EUROQOL EQ-5D questionnaire data revealed that patients with ID experienced significantly more pronounced limitations: 41.3% reported an inability to walk independently (vs. 6.3% in the non-ID group, $p < 0.001$) and 49.2% reported significant difficulties in daily activities (vs. 18.8%, $p < 0.01$). The presence of ID was associated with more severe clinical manifestations of CHF, reduced exercise tolerance, and a substantial deterioration in quality of life indicators [10].

6. Patients with ID more frequently present with edema, pulmonary rales, hydrothorax, and other manifestations of heart failure.

According to data from the study by E.A. Smirnova, patients with ID had significantly more frequent signs of congestion in the pulmonary circulation (46.9% of cases) manifesting as cardiac asthma (43.8%) and pulmonary edema (6.3%), as well as pronounced symptoms of systemic congestion (96.9% of cases), including lower extremity edema (84.4%), hydrothorax (65.6% vs. 31.3% in the non-ID group; $p = 0.012$), ascites (29.7%), hydropericardium (18.8%), and anasarca (15.6%, with a complete absence of this symptom in patients without ID) [10].

7. Patients with ID receive higher initial doses of intravenous diuretics, which may be associated with a more severe condition.

In the study conducted by E.A. Smirnova et al., ID was more common in patients with frailty, which also required the prescription of higher initial doses of intravenous diuretics. These data underscore the need for an individualized treatment approach for this patient category, with special attention to ID correction, to improve treatment outcomes and quality of life [10].

8. The length of hospital stay (LOS) for patients with ID is slightly higher, but the difference is insignificant and comparable to patients without ID.

A 2023 Russian study assessed the prognostic significance of ID in patients suffering from ADHF. ID was associated with an increased risk of readmission and death, once again emphasizing the importance of considering this parameter [14]. In a 2009 study by international colleagues (published in 2019), the problem of ID in ADHF patients was examined. The study aimed to characterize ID and determine its association with dyspnea class, length of hospitalization, biomarker levels, and echocardiographic parameters of diastolic function in patients with reduced and preserved left ventricular ejection fraction.

Among the 503 enrolled patients, 270 (55%) had HFpEF, 160 (33%) had HFrEF, and 57 (12%) had HFmrEF. ID was identified in 54% of HFrEF patients and 56% of HFpEF patients. In the HFpEF patient group, ID was associated with increased LOS (11 ± 7.7 days vs. 9 ± 6 days in patients without ID, $*p* = 0.036$) and remained an independent predictor of increased LOS after adjusting for comorbidities, age, and ID status. The finding of increased LOS specifically in HFpEF patients, which was not observed in HFrEF patients, is particularly significant. This may indicate a more pronounced role of ID in the pathogenesis of HFpEF [29].

The work by K. AlAayedi also evaluated the significance of ID in hospitalized ADHF patients with HFpEF: the mean length of hospitalization for patients with ID was 13.8 days versus 11.2 days for patients without ID [36]. These findings highlight the need for further study of ID as a potential therapeutic target in the treatment of ADHF, especially in patients with HFpEF, and

could significantly impact clinical practice and the direction of future research in cardiology.

CONCLUSION

The conducted analysis has shown that ID is an extremely prevalent (45–89% of cases) and clinically significant condition in patients with ADHF. Differentiating between absolute and functional iron deficiency against the background of chronic inflammation characteristic of HF poses a particular diagnostic challenge, necessitating the use of comprehensive criteria that include not only traditional parameters (ferritin and transferrin saturation) but also modern markers, such as soluble transferrin receptors, hepcidin, and reticulocyte hemoglobin.

Intravenous iron administration, particularly ferric carboxymaltose, has demonstrated efficacy in reducing the risk of hospital readmissions and improving patients' functional capacity. However, questions remain regarding the long-term impact of ID correction on survival, optimal treatment regimens for different HF phenotypes, and the role of new biomarkers in predicting structural and functional myocardial changes. Promising directions for future research include investigating the mechanisms of ID influence on remodeling processes, developing personalized diagnostic and treatment algorithms considering individual HF course characteristics, and assessing the cost-effectiveness of ID screening in routine clinical practice.

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