

PREVALENCE OF IRON DEFICIENCY AND ANEMIA IN PATIENTS ADMITTED TO HOSPITAL WITH CHRONIC HEART FAILURE

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Anemia and iron deficiency (ID) are important and common comorbidities that often coexist in patients with heart failure (HF). Both conditions, together or independently, are associated with poor clinical status and worse outcomes. Whether anemia and iron deficiency are just markers of heart failure severity or whether they mediate heart failure progression and outcomes and therefore should be treated is not entirely clear. The prevalence of anemia in patients with HF (defined as hemoglobin <13 g/dL in men and <12 g/dL in women) is ≈30% in stable and ≈50% in hospitalized patients [1,4,10]. It has been acknowledged that iron plays an important role in oxygen transport, as well as in cell growth and proliferation. In recent years, more insight has been gained into iron physiology and the regulation of cellular iron homeostasis [2] Iron deficiency occurs, for example, when the dietary intake is inadequate, during times of digestive blood loss or menstrual periods or during states that excessively increase iron requirements, particularly during childhood growth or pregnancy. However, in patients with chronic illnesses, iron may become unable to be immobilized as a consequence of chronic inflammation, thus leading to functional iron deficiency. Many studies have shown that iron deficiency is very common in patients with heart failure (HF), and its prevalence increases with increasing New York Heart Association class [5,7,8]. Approximately half of all patients with HF have either absolute iron deficiency or functional iron deficiency defined as transferrin saturation <20% and serum ferritin 100–300 µg/L, and this finding is only partly associated with the presence of anemia. Indeed, many HF patients present with iron deficiency, many with anemia and some of these with both [3,11].

The aim of our research was to study prevalence and clinical impact of ID and anemia in HF patients admitted to the cardiology department of our hospital.

Material and methods. We studied 133 patients with HF who have been admitted to hospital since September 2019: 78 (58.6%) patient had ID (latent iron deficiency), 55 (42.4%) with HF and without ID were included in the control group. All patients aged 18 years and older were eligible, provided a left ventricular ejection fraction of 45% or less was documented on echocardiography during the enrolment visit and signs and symptoms of chronic heart failure were present. All patients gave written informed consent. Exclusion criteria were coronary interventions of any kind within the past 6 months and planned coronary interventions, evidence of acute or chronic infectious or inflammatory conditions from routine laboratory assessment, malignant disease or gastric or duodenal ulcer with or without active bleeding.

Patient baseline assessment included a standardized HF history regarding HF etiology (classified as ischemic or non-ischemic) and co-morbidities. All patients underwent a standardized clinical evaluation, including physical examination, determination of NYHA class, determination of body weight. Blood samples were drawn from an antecubital vein in the morning for the assessment of a full blood count and clinical chemistry, includ-

ing parameters of iron metabolism - serum ferritin and kidney function (creatinine).

Renal dysfunction was diagnosed if the glomerular filtration rate (eGFR) was below 60 ml/min/1.73 m², diabetes mellitus, if patients reported a history of diabetes or were on anti-diabetic drugs, and chronic obstructive pulmonary disease (COPD), if patients were on anti-obstructive pharmacotherapy or reported that COPD had been previously diagnosed. Anemia was defined according to World Health Organization criteria as hemoglobin level <120 g/l in women and <130 g/l in men. ID was defined as serum ferritin <100 µg/l. Assessment of exercise capacity was performed by a 6-min walk test. Exercise capacity was categorized as reduced, if patients performed below the median walking distance during 6-min walk test.

Continuous variables are given as means with standard deviations. Non-normally distributed variables (serum ferritin, serum creatinine, serum C-reactive protein) were log-transformed to achieve normal distribution before analysis. Student's t test was used to test for between-group differences. P values of <0.05 were considered statistically significant.

Results and discussion. Baseline characteristics are given in Table 1.

As can be seen from the Table, ID was present in 78(58.6%) patients. None of the patients had a history of iron supplementation of any kind. Most patients in both groups are men, patients with ID were elderly, with mean age of 75.2±8.2 and 68.1±7.1 in group without ID. There was no significant difference between body weight in groups. In both groups, most patients had arterial hypertension: 59 (75%) and 42(76%) respectively. More patients with ID had diabetes mellitus: 26(33.3%) and 14 (25.5%) respectively. HF etiology was predominantly ischemic in both groups: 49 (62.8%) and 34 (61.8%) respectively. The NYHA distribution was 9% and 16.4% for NYHA class II, 74.4% and 69.1% for class III, and 16.7 and 27.3% for class IV. So, most patients were with NYHA class III (74.4% and 69.1% respectively). But patients with ID had significantly low LVEF: 38.1±6.9 and 42.7±4.3.

No differences were recorded for body weight, diastolic blood pressure, platelets, eGFR or serum creatinine (all $p>0.05$). No such differences were found regarding hypertension and chronic obstructive pulmonary disease.

70 (52.6%) patients from 133 presented with anemia. None of the patients had received blood transfusion for the treatment of anemia. Patients with anemia were more likely to have concomitant ID than non-anemic patients ($p<0.05$), and anemia and ID were concomitantly present in 52 (74.3%) of the patients, Table 2.

There was a highly significant association between hemoglobin and serum ferritin in patients with ID, but in patients without ID, this association was only of borderline significance ($p=0.03$). No corresponding associations were noted between hemoglobin, C-reactive protein, or serum creatine after splitting the data set into patients with vs. without ID. The presence of anemia, ID, or both was associated with significantly higher NYHA class.

Table 1. Baseline characteristics of HF patients with ID versus without ID

Characteristics	Patients with ID N=78	Patients without ID N=55	P
Age (years)	75.2±8.2	68.1±7.1	<0.05
Male gender (%)	55	58	
Body weight (kg)	83.8±8.1	81.1±7.8	0.16
Heart rate (min)	77.6±7.5	74.6±7.3	<0.05
Systolic BP (mmHg)	126±17.4	131±19.2	<0.05
Diastolic BP (mmHg)	71.1±7.2	71.6±7.2	0.16
Hypertension (%)	59 (75%)	42(76%)	0.16
Renal dysfunction (%)	32 (41%)	11 (20%)	<0.05
COPD (%)	13 (16.7%)	9(16.4%)	0.16
Diabetes mellitus (%)	26(33.3%)	14 (25.5%)	<0.05
Ischemic etiology (%)	49 (62.8%)	34 (61.8%)	0.26
NYHA class II	7 (9%)	9 (16.4%)	<0.05
NYHA class III	58 (74.4%)	31 (69.1%)	<0.05
NYHA class IV	13 (16.7%)	15 (27.3%)	0.16
LVEF (%)	38.1±6.9	42.7±4.3	<0.05
Anemia (%)	61 (78.2%)	9 (16.4%)	<0.05
Hemoglobin (g/l)	107.8±5.8	132±3.6	<0.05
Platelets (10 ³ /L)	280.5±50.4	291.1±24.7	0.13
Iron (μmol/L)	2.98±1.1	12.8±5.3	<0.05
Serum ferritin (μg/l)	68.4±11.8	297±12.6	<0.05
Serum creatinine (μmol/L)	104.4±26.5	102.8±17.7	0.1
eGFR (ml/min 1.73m ²)	56.9±5.2	58.2±7.1	0.1
CRP (mg/dl)	4.5±1.2	4.2±0.9	<0.05

Table 2. Clinical characteristics in patients with anemia or without it

Characteristics	Patients with anemia n=70	Patients without anemia n=63	P
ID	52 (74.3%)	26 (25.7%)	P<0.05
NYHA III	58 (82.9%)	31 (49.2%)	P<0.05
NYHA IV	17 (24.3%)	11 (17.5%)	P<0.05
Creatinine	103.6±11.4	103.1±10.2	P>0.05
CRP	4.1±1.3	4.08±1.1	P>0.05

Table 3. 6-min walk distance

Characteristics	Distance - m	% of expected distance for healthy persons
Anemia	205.3±5.2*	41.2±2.4*
No anemic	224.7±7.1*	54.6±3.1*
NYHA II	223.6±6.2*	53.5±4.2*
NYHA III	181.2±5.9*	39.3±1.4*
Men	231.2±2.6*	44.5±3.2*
Women	194.6±3.1*	38.2±1.9*
eGFR<60 ml/min	218.9±7.2*	50.2±0.8*
eGFR>60 ml/min	188.7±3.5*	40.3±3.2*
LVEF <40	195.6±4.6*	41.4±3.3*
LVEF >40	182.3±5.5*	38.8±2.0*

*P<0.05

A total 77 (57.9%) underwent 6-min walk test: 52 patients with ID and 25 – without ID. (Table 3).

In both groups was decreased average distance walked and percentage of expected distance for healthy persons.

We found that gender, NYHA class, LVEF, the presence of anemia, eGFR all predicted lower exercise capacity.

Prevalence and possible consequences of ID complicating HF have more recently been attracting increasing attention. Among more than 500 ambulatory patients with stable HF, Jankowska et al. found an ID rate of 32 and 57% in anemic and non-anemic subjects, respectively [6]. Schou et al. using the same cut-off criteria as Jankowska et al. to define ID, found among Danish outpatients with characteristics similar to our study (25% female, NYHA III-IV, mean LVEF 32%) an ID prevalence of 45% and thus very comparable to our findings [9]. Our findings regarding ID prevalence are thus in accordance with published data from several clinical cohorts. Our results also correspond to a recent report from the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF) [9]. Remarkably, and also in line with our observations, exercise capacity decreased in parallel to decreasing hemoglobin levels in SICA-HF. Furthermore, exercise capacity proved significantly lower in 19% of the patients who presented with both, anemia and ID, compared with those with either ID or anemia.

Conclusion. Our study demonstrated high prevalence of both anemia and ID in patients with chronic heart failure. Despite high prevalence, ID was previously unknown in patients. Given the clinical relevance, treatability, and independent association with reduced exercise capacity, ID should be defined in patients with chronic heart failure.

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SUMMARY

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Anemia and iron deficiency (ID) are important and common comorbidities that often coexist in patients with heart failure (HF). Both conditions, together or independently, are associated with poor clinical status and worse outcomes. The aim of our research was to study prevalence and clinical impact of ID and anemia in HF patients attending cardiology department of our hospital.

We studied 133 patients with HF who have been admitted to hospital since September 2019: 78 (58.6%) patient had ID, 55 (42.4%) with HF and without ID were included in the control group. Patient baseline assessment included a standardized HF history regarding HF etiology (classified as ischemic or non-ischemic) and co-morbidities. All patients underwent a standardized clinical evaluation, including physical examination, determination of NYHA class. Blood samples were drawn for the assessment of a full blood count and clinical chemistry, including iron and serum ferritin and kidney function (creatinine). Assessment of exercise capacity was performed by a 6-min walk test. ID was present in 78(58.6%) patients. 70(52.6%) patients from 133 presented with anemia. Most patients in both groups are men, patients with ID were elderly, in both groups, most patients had arterial hypertension, more patients with ID had diabetes mellitus, HF etiology was predominantly ischemic in both groups, most patients were with NYHA class III, patients with ID had significantly low LVEF. No differences were recorded for body weight, diastolic blood pressure, platelets, eGFR or serum creatinine, no such differences were found regarding hypertension and chronic obstructive pulmonary disease. There was a highly significant association between hemoglobin and serum ferritin in patients with ID, but in patients without ID, this association was only of borderline significance. The presence of anemia, ID, or both was associated with significantly higher NYHA class. We found that gender, NYHA class, LVEF, the presence of anemia, eGFR all predicted lower exercise capacity.

Keywords: Iron deficiency, Anemia, Exercise capacity, Heart failure, Prevalence.

РЕЗЮМЕ

ДЕФИЦИТ ЖЕЛЕЗА И АНЕМИИ У ПАЦИЕНТОВ, ГОСПИТАЛИЗИРОВАННЫХ С ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ

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Анемия и дефицит железа (ДЖ) - значимые и распространенные коморбидности, которые часто сосуществуют у пациентов с сердечной недостаточностью (СН). Оба состояния вместе или по отдельности связаны с плохим клиническим статусом и неблагоприятным исходом.

Целью исследования явилось определение распространенности и клинического воздействия дефицита железа и анемии у пациентов с сердечной недостаточностью.

Наблюдались 133 пациента с СН, которые находились в клинике с сентября 2019 г.: у 78 (58,6%) пациентов отмечался ДЖ, 55 (42,4%) пациентов с СН, без дефицита железа составили контрольную группу. Базовая оценка пациентов включала стандартизованную историю сердечной недостаточности относительно этиологии, классифицируемой как ишемическая или неишемическая, и сопутствующих заболеваний. Все пациенты прошли стандартизованную клиническую оценку, включая физическое обследование, определение функционального класса по NYHA. Для оценки общего анализа крови и биохимии, в том числе железа, ферритина и функции почек (креатинин) забирали образцы крови. Оценку толерантности к физической нагрузке проводили посредством теста 6-минутной ходьбы. ДЖ отмечался у 78 (58,6%) пациентов. Из 133 пациентов у 70 (52,6%) выявлена анемия. Большинство пациентов в обеих группах были мужчины, имели артериальную гипертензию и сахарный диабет, этиология СН в обеих группах была преимущественно ишемической. 89 пациентов имели СН III функционального класса по NYHA. Пациенты с ДЖ имели значительно низкую фракцию выброса левого желудочка (LVEF). Различий по массе тела, диастолическому кровяному давлению, тромбоцитам, eGFR или креатинину сыворотки не зарегистрировано. Существует весьма значительная связь между показателями гемоглобина и ферритина сыворотки крови у пациентов с ДЖ, однако у пациентов без ДЖ эта связь имела только пограничное значение. Анемия,

ДЖ или оба ассоциируются со значительно более высоким классом NYHA. Авторами выявлено, что пол, класс NYHA, LVEF, наличие анемии, eGFR прогнозируют более низкую толерантность к физической нагрузке.

რეზიუმე

რკინის დეფიციტის და ანემიის სისშირე გულის ქრონიკული უკმარისობის მქონე ჰოსპიტალიზებულ პაციენტებში

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ანემია და რკინის დეფიციტი მნიშვნელოვან თანმხლებ პათოლოგიას წარმოადგენს გულის უკმარისობით პაციენტებში. ორივე ერთად ან ცალ-ცალკე ასოცირებულია კლინიკური მდგომარეობის გაუარესებასთან და დაავადების ცუდ გამოსავალთან.

კვლევის მიზანს წარმოადგენდა რკინის დეფიციტის და ანემიის სისშირის შესწავლა გულის ქრონიკული უკმარისობით ჰოსპიტალიზირებულ პაციენტებში. გამოკვლეულია 133 პაციენტი გულის უკმარისობით: 78 (58,6%) აღენიშნებოდა რკინის დეფიციტი, 55 (42,4%) პაციენტმა რკინის დეფიციტის გარეშე შეადგინა საკონტროლო ჯგუფი. პაციენტებს ჩატარდათ კლინიკურ-ლაბორატორიული კვლევები, დატვირთვის მიმართ ტოლერანტობა განისაზღვრა 6-წუთიანი სიარულის ტესტით. რკინის დეფიციტი აღენიშნა 78 (58,6%) პაციენტს, ანემია – 70 (52,6%). პაციენტთა უმრავლესობა იყო მამაკაცი, რკინის დეფიციტის მქონე პაციენტები უფრო ასაკოვანი იყვნენ და უფრო ხშირი იყო მათში შაქრიანი დიაბეტი და გულის უკმარისობის III ფუნქციური კლასი, უფრო დაბალი მარცხენა პარკუჭის განდევნის ფრაქცია. რკინის დეფიციტის მქონე პაციენტებში სარწმუნოდ დაბალი იყო ჰემოგლობინის და ფერიტინის დონე, ხოლო ანემიასთან ამ მახვეუბლების კავშირის სარწმუნოობა უფრო დაბალი იყო. რკინის დეფიციტი და ანემია ერთად და ცალ-ცალკე სარწმუნოდ ასოცირდებოდა გულის უკმარისობის მაღალ ფუნქციურ კლასთან. კვლევამ გამოავლინა პაციენტთა სქესის, გულის უკმარისობის ფუნქციური კლასის, ანემიის, eGFR კავშირი ფიზიკური დატვირთვის მიმართ დაბალ ტოლერანტობასთან.