The relationship between iron-deficient patients with acute heart failure and the New York Heart Association (NYHA) classes and left ventricular ejection fraction (LVEF)

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Abstract

Introduction: iron deficiency is common in patients with heart failure and is also recognized as a risk factor for worsening symptoms, impaired quality of life and a poor prognosis in this population. The objective of this study was to describe the clinical characteristics of patients with heart failure and explore an association between serum iron levels and the *New York Heart Association* (NYHA) functional classes and left ventricular ejection fraction (LVEF).

Method: this was an observational, analytical, cross-sectional study of hospitalized patients from the mideastern integrated healthcare services subnetwork in Bogotá, Colombia. Sociodemographic, clinical and laboratory variables were analyzed using univariate and bivariate analysis and simple logistic regression to calculate the odds ratio (OR).

Results: a total of 139 patients hospitalized during the study period yielded a 43% prevalence of heart failure with mildly reduced LVEF; the average age was 53 years and 67.6% were male, with comorbidities like atrial fibrillation (23.2%), coronary disease (59%) and dyslipidemia (27.9%). Altogether, 57.2% of the patients had iron deficiency. The factors associated with NYHA III and IV were male sex (OR: 2.8; 95% CI: 1.17;6.97), chronic obstructive pulmonary disease (OR: 2.7; 95% CI: 1.03;7.23), and iron deficiency (OR: 1.92; 95% CI: 1.13;3.25).

Conclusions: most patients with iron deficiency and heart failure had a mildly reduced LVEF, anemia, low ferritin levels and low transferrin saturation. The need to measure the iron kinetics profile of all patients with decompensated heart failure is stressed. The factors associated with NYHA classes III and IV as well as reduced ejection fraction were male sex, chronic obstructive pulmonary disease, hemoglobin < 13 g/dL, and a history of coronary disease. **(Acta Med Colomb 2024; 49. DOI: https://doi.org/10.36104/amc.2024.3091).**

Keywords: heart failure, iron deficiency, *New York Heart Association*, anemia.

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Introduction

Heart failure (HF) is one of the main causes of cardiovascular death in Colombia (1). The prevalence of HF in Colombia is approximately 2.3% (2). A significant increase in the number of hospitalizations for decompensated HF has been reported over the last decade, secondary to coronary syndromes, arrhythmias, hypertension, pulmonary thromboembolism and infections, among others (1, 3).

Iron deficiency with or without anemia plays an important role in patients with HF. Even with apparently adequate levels of ferritin, almost 73% of patients with anemia have iron deficiency (4). Therefore, iron deficiency without anemia must be defined as serum ferritin less than 100 ng/L or ferritin between 100-300 mg/L with less than 20% transferrin saturation. These levels are present in 37% of patients with HF and are associated with higher rates of mortality and long-term complications (5).

In light of this, when patients with HF have persistent symptoms, iron deficiency should be suspected as a possible cause, although there are other associations not previously studied (6). Therefore, the objective of this study was to describe the clinical characteristics and explore an association between iron deficiency levels and the New York Heart Association (NYHA) functional classes and left ventricular ejection fraction (LVEF) of patients with decompensated HF.

Materials and method

Type of study

This was a cross-sectional analytical observational study of patients hospitalized in the integrated central-eastern

healthcare sub-network in Bogotá, Colombia, from January through December 31, 2021.

Study population

Patients eligible for enrollment in the study were identified through a search of the following International Classification of Diseases, 10th edition (ICD-10) codes: heart failure (HF) (I50x), congestive heart failure (I500), complications and descriptions of heart disease (I51x), left ventricular failure (I501), and unspecified heart failure (I509). Patients who, due to a diagnostic coding error, did not have an ICD-10 code but did have an HF diagnosis reported in the medical chart were also included.

Inclusion and exclusion criteria

The inclusion criteria were: 1) patients over the age of 18 with a diagnosis of decompensated HF. The definition of decompensated HF referred to patients with signs and symptoms of HF. The following procedures were accepted as diagnostic methods: echocardiography or magnetic resonance imaging or catheterization recording the LVEF. 2) Hospitalized patients with laboratory tests showing ferritin and transferrin saturation levels. Iron deficiency was defined as ferritin <100 ng/L, low transferrin saturation as <20%, and functional iron deficiency as ferritin between 100 and 299 mg/L, with a transferrin saturation <20%.

The exclusion criteria were: pregnant patients, breastfeeding patients, heart transplant patients, patients who had received intravenous (IV) iron saccharate or ferric carboxymaltose replacement within the last six months or a transfusion within the last two months, and patients with acute inflammation identified by signs and symptoms (SIRS plus an infection site) with ferritin greater than 1,000 ng/dL.

Variables and statistical analysis

The measured variables included demographic and clinical characteristics (sex, age, marital status, history of diabetes mellitus, atrial fibrillation, smoking, coronary disease, dyslipidemia, chronic kidney disease, chronic obstructive pulmonary disease, valvular heart disease, stroke, and obstructive sleep apnea. Laboratory parameters were included such as kidney function, lipid profile, TSH, NYHA LVEF, AHA stage, TIBC, transferrin saturation, ferritin, transferrin and total iron). The medical treatment for HF was also included. The iron deficiency stage was determined by the iron kinetics profile indicated by serum ferritin (ng/dL), transferrin saturation, TIBC, transferrin and total iron levels.

The STATA® 15 program was used. Descriptive statistics were run for clinical and sociodemographic variables. The LVEF and NYHA frequencies were presented as measures of central tendency and proportions. Qualitative variables were presented as absolute and relative frequencies, and measures of central tendency and dispersion were used for quantitative variables, according to the distribution of the analyzed data evaluated with the Chi square test. Average and standard deviation were used when they met the criteria for normality; otherwise, the median and interquartile range were applied. After classifying the variables, a Chi square test of association was run between the NYHA classification and LVEF in patients with iron deficiency hospitalized for decompensated HF with or without anemia. Subsequently, logistical regression was run with its respective odds ratio (OR).

An exploratory analysis was done of the association between the iron kinetics profile with HF and the NYHA classification, as well as LVEF and anemia, which was evaluated using the Chi square or Fisher's exact test. A $p < 0.05$ was used to accept the null hypothesis and $p > 0.05$ to reject the null hypothesis. An exploratory subgroup analysis was also done to compare patients with HF and mortality.

Sample size and sampling

The sample size was calculated from a finite sampling frame, the finite master sample frame; data was collected from the sub-network's annual reports of chronic diseases, with a prevalence of decompensated HF with iron deficiency of 0.79% based on the HEART-FID (7) study, for a power of 80% and a 0.05 level of significance using the EPIDAT 3.1 statistical program, obtaining a resultant number of patients with HF, with 20% expected losses to follow up, of 139 patients in the sample. The entire sample was collected at Hospital Santa Clara.

Ethical considerations

The protocol was approved by the ethics committee at the referral center involved in the study, under the "no risk study" category (CODE:MI-GC-FT-004. Initiation memorandum N#10 issued on July 12, 2023). The ethical principles established for the Declaration of Helsinki were followed; therefore, patients' personal data was not collected.

Results

A total of 500 patients were collected from the medical chart database between January 01 and December 31, 2021. Of these, 361 patients did not meet the inclusion criteria, and therefore 139 patients were included and analyzed in the study. This process is shown in Figure 1. The sociodemographic characteristics of patients with HF with preserved LVEF, mildly reduced LVEF and reduced LVEF in the institution were distributed as follows: the average age ranged from 53-83 years, with an average age of 68 years. The proportion of males was 67.6%. For marital status, the most representative category was single, with 71.1%, followed by married (13%), cohabiting (9.26%), widowed (5.56%) and separated (3.7%).

Out of the total population, 41% had type 2 diabetes mellitus as a comorbidity, with an average glycosylated hemoglobin of 6.2% (SD±1.5), followed by atrial fibrillation, at 23.2%. Other highly prevalent diseases included

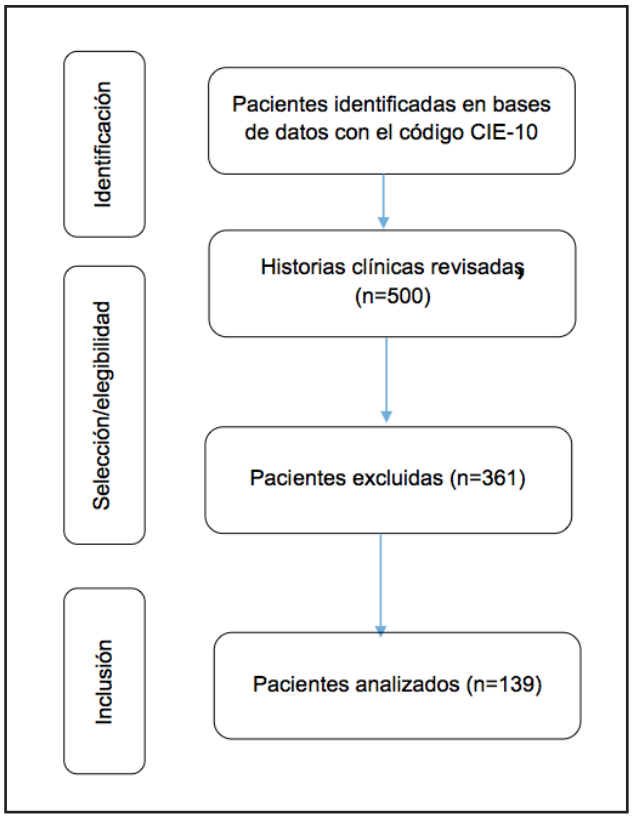

Figure 1. *Sociodemographic and clinical characteristics of patients with heart failure.*

smoking (41%), coronary disease (59%), dyslipidemia (27.9%), chronic obstructive pulmonary disease (46%), chronic kidney disease (26.6%), a history of stroke (12%) and obstructive sleep apnea (2%) (Table 1).

The most commonly found valvular heart diseases were mitral regurgitation (mild, moderate, severe) 27%, followed by aortic regurgitation (mild, moderate, severe) 5%, and tricuspid regurgitation (mild, moderate, severe) 5% (Table 1).

The clinical variables described included systolic arterial pressure (SAP), with an average of 113 mmHg (SD±21 mmHg), diastolic arterial pressure 71.2 mmHg (SD±15.1 mmHg), heart rate 76.5 bpm (SD ± 16 bpm), average weight 63.4 kg (SD±10.5 kg), and height 160.5 cm (SD±15.4 cm), with an average body mass index of 24 kg/m^2 (SD± 6.96 kg/m^2) (Table 1).

Of the patients diagnosed with HF, 21.1% were classified as AHA B, 71.7% as AHA C, and 6.52% as AHA D. Regarding NYHA classification, 20.1% were classified as NYHA I, 38.8% as NYHA II, 30.9% as NYHA III and 10% as NYHA IV (Table 1).

The reported laboratory parameters included a GFR of 64.5 mL/min/1.73 m^2 (SD ± 31.9 mL/min/1.73 m^2) and total cholesterol ranging from a minimum of 100 mg/d to a maximum of 200 mg/100 mL, with an average of 150 mg/100 mL. Likewise, HDL cholesterol had an average of 37.6 mg/100 mL (SD+/-15.1 mg/100 mL), LDL cholesterol had an average of 82.6 mg/100 mL (SD ± 43.7 mg/100 mL) and TG cholesterol had an average of 122.4 mg/100 mL (SD ± 72.8 mg/100 mL) (Table 1).

The patient description showed hemoglobin levels of 12.2 g/dL (SD±2.8g/dL), an average TSH of 8.8 U/L (SD±25.4 U/L) and C-reactive protein levels of 4.0 mg/dL (SD±6.7). The average LVEF of the 139 patients was 44% (SD±16.1%) (Table 1).

The iron kinetics profile showed ferritin levels at 117.4 mg/dL (SD+/-94.3 mg/dL), 17.1% transferrin saturation (SD ±10%), 258% average TIBC (SD ± 59%), transferrin levels at 190.2 mg/dL (SD±49.2), and total iron at 50.7 mg/dL (SD±36.3 mg/dL). With these values, approximately 57.2% of the patients with HF were found to have iron deficiency and began inpatient intravenous iron replacement (Table 1).

Treatment for patients with HF with preserved, mildly reduced and reduced LVEF included beta blockers for 86.9%, angiotensin converting enzyme (ACE) inhibitors for 27% or angiotensin II receptor blockers (ARBs) for 23.2%, sodium-glucose cotransporter-2 (SGLT-2) inhibitors for 51.4%, angiotensin receptor-neprilysin inhibitors (ARNIs) for 31.1%, aldosterone receptor antagonists (MRAs) for 34%, diuretics for 48.5%, calcium channel blockers (CCBs) for 23.9%, and amiodarone for 7.97%. Patients with dyslipidemia were treated with statins in 72.4% of cases, dual antiplatelet therapy with a P2Y12 receptor inhibitor in 17.4% and acetylsalicylic acid in 30%. Altogether, 5.07% of the patients with HF had an implantable cardioverter defibrillator (ICD), and 2.17% had cardiac resynchronization therapy (CRT) (Table 1).

The iron kinetics profile, considering the definition of iron deficiency in the inclusion criteria, showed ferritin levels <100 ng/dL in 53.4% of the patients with reduced LVEF, 66.6% of those with mildly reduced LVEF and 63% of the patients with preserved LVEF. Ferritin levels between 100-300 ng/dL with transferrin saturation <20% were reported in 83.3% of patients with reduced ejection fraction, 33% of those with mildly reduced ejection fraction and 83.6% of those with preserved ejection fraction, with a statistically significant difference (p= 0.03) (Table 2).

The univariate logistic regression analysis showed that the male sex (OR:3.20;1.51;7.14) behaved as a risk factor for developing iron deficiency; when the other variables were compared, they did not show significant differences. Table 3 shows the results of the logistic regression with their respective ORs or confidence intervals.

After the previous exploration, a multivariate analysis was run with the main objective of identifying the sociodemographic and clinical (ejection fraction and NYHA functional class) associations with iron deficiency. Based on the results of the logistic regression model analysis, for patients with NYHA III and IV classifications, the male sex (OR: 2.8; 95% CI: 1.17;6.97), chronic obstructive pulmonary disease (OR: 2.7; 95% CI: 1.03;7.23) and iron deficiency (OR: 1.92; 95% CI: 1.13;3.25) had a statistically significant association (Table 4).

Table 1. *Sociodemographic and clinical characteristics of patients with heart failure.*

Name of the variable	Reduced ejection fraction (<40%) n=54	Mildly reduced ejection fraction (41-50%) n=9	Preserved ejection fraction (>50%) n=76	*p*
Sex: male (%)	44(81.4)	6(66.6)	43(56.8)	0.012
Age (SD)	68.5(12.0)	66.6(13.5)	68.2 (15.7)	0.89
Marital status (%)				
Single	35(64.8)	7 (77.7)	54(71)	0.46
Married	9(16.6)		10(13.1)	
Separated	2(3.7)			
Widowed	3(5.56)		6(7.89)	
Cohabiting	5(9.26)	2(22.2)	6(7.89)	
Comorbidities				
Type 2 diabetes mellitus (%)	21(38.8)	6(66.6)	19(25)	0.02
HbA1c% (SD)	6.4(1.51)	6,28(0.8)	6.3(1.5)	
Atrial fibrillation (%)	9 (16.6)	3(33.3)	15(19.7)	0.502
Smoking (%)	19(35.1)	5(55.5)	34(44.7)	0.379
Coronary disease (%)	38(70.3)	3(33.3)	18(23.6)	0.000
Dyslipidemia (%)	18(31.4)	4(44.4)	17(23.2)	0.311
Chronic obstructive pulmonary disease (%)	20(37.0)	5(55.5)	39(51.32)	0.23
Chronic kidney disease (%)	16(29.6)	4(44.4)	17(22.3)	0.29
Valvular heart disease (%)	51(94.4)	7(87.5)	57(78)	0.03
Mild mitral regurgitation	12(23.5)	3(42.8)	16(28)	
Moderate mitral regurgitation	21(41.1)	1(14.2)	16(28)	
Severe mitral regurgitation	10(19.6)	2(28.5)	2(3.51)	
Mild aortic regurgitation	3(5.88)		6(10.5)	
Moderate aortic regurgitation	3(5.88)		5(8.77)	
Severe aortic rergurgitation	1(1.96)		1(1.75)	
Mild tricuspid regurgitation			3(5.26)	
Moderate tricuspid regurgitation			3(5.26)	
Severe tricuspid regurgitation	1.96)	1(14.2)	5(8.77)	
Stroke (%)	7(12.9)		9(11.8)	0.524
Obstructive sleep apnea syndrome (%)	1(1.85)		3(3.95)	0.677
Clinical variables				
Systolic arterial pressure mmHg (SD)	107(18)	115(11)	116(23)	0.678
Diastolic arterial pressure mmHg (SD)	69(13)	68.1(13)	73(16)	0.295
Heart rate bpm (SD)	74(14)	79.2(12	77(17)	0.846
Weight kg (SD)	64.3(8.7)	66.4(12.9)	62,4(11.4)	0.502
Height m (SD)	1.62(0.6)	1.62(0.4)	1.59(0.2)	0.616
BMI kg/m^2 (SD)	24.9(4.6)	25(4.8)	24.9(8.4)	0.953
NYHA Class I (%)	4(7.41)		24(31.5)	
NYHA Class II (%)	18(33.3)	5(55.5)	31(40.7)	
NYHA Class III (%)	22(40.7)	4(44.4)	17(22.3)	
NYHA Class IV (%)	10(18.5)		4(5.26)	
AHA Stage A (%)			1(1.33)	
AHA Stage B (%)	1(1.85)		28(37.3)	
AHA Stage C (%)	44(81.4)	9(100)	46(61.3)	
AHA Stage D (%)	9(16.6)			

... Continuation... **Table 1.** *Sociodemographic and clinical characteristics of patients with heart failure.*

Name of the variable	Reduced ejection fraction (<40%) n=54	Mildly reduced ejection fraction (41-50%) n=9	Preserved ejection fraction (>50%) n=76	*p*
Laboratory variables				
Creatinine mg/dL(SD)	1.68(1.4)	1.3(0.66)	1.4(2)	0.976
GFR (SD)	59(30)	59.8(29.5)	68.6(33.3)	0.457
HDL mg/dL (SD)	36.7(16.1)	39.8(8.6)	38(15.3)	0.339
LDL mg/dL (SD)	92.1(40.8)	78.7(50,6)	75.3(44.2)	0.456
TC mg/dL (SD)	153.8(47.4)	150.5(58.4)	147.2(52.3)	0.848
TG mg/dL (SD)	117.4(60.5)	107(79.3)	129.2(81.4)	0.433
Hgb g/dL (SD)	12.6(2.7)	12.9(2.6)	11.9(2.8)	0.245
TSH mg/dL (SD)	4.9(7.5)	4.4(3.7)	12.2(33.6)	0.441
LVEF % (SD)	26.1(8.3)	45.4(3)	57.8(2.7)	0
C-reactive protein mg/dL (SD)	2.9(4.8)	3.8(5.7)	4.8(8.0)	0.306
Iron kinetics profile of patients with heart failure				
Ferritin ng/dL (SD)	135.3(112)	160(141)	99.3(68.4)	0.125
Transferrin saturation (SD)	17.5(12.7)	23.4(7.31)	16(7.83)	0.636
TIBC (%)	282.2(61)	245.1(52.6)	249.3(66.5)	0.09
Transferrin mg/dL (SD)	205.6(51.3)	177.8(52.4)	177.3(43.2)	0.65
Total iron mg/dL (SD)	54.8(44.6)	61.3(19.6)	45.1(27.7)	0.634
Iron defiency criteria (%)	26(57.7)	3(42.8)	34(58.6)	0.725
Iron replacement (%)	29(60.4)	3(42.8)	35(60.3)	0.659
Treatment of patients with heart failure				
Beta blockers (%)	54(100)	8(88.8)	58(77.3)	0.001
ACE inhibitors (%)	6(11.1)	2(22.2)	19(25.3)	0.13
ARBs (%)	5(9.2)	2(22.2)	25(33.3)	0.006
SGLT-2 inhibitors (%)	39(72.2)	8(88.8)	24(32)	0
Trimetazidine (%)	6(11.1)			0.008
ARNIs (%)	30(55.5)	2(22.2)	11(14.6)	0
MRAs (%)	22(44.4)	5(55.5)	18(24)	0.02
Diuretics (%)	30(55.5)	3(33.3)	34(45.3)	0.332
Ivabradine (%)	1(1.85)			0.457
CCBs (%)	12(22.2)	1(11.1)	20(26.6)	0.547
Amiodarone (%)	5(9.26)		6(8)	0.637
Isosorbide dinitrate (%)			1(1.33)	0.655
Statins (%)	47(87.04)	7(77.7)	46(61.3)	0.005
P2Y12 receptor inhibitors (%)	15(27.7)	1(11.1)	8(10.6)	0.03
ASA (%)	28(51.8)	3(33.3)	11(14.6)	0
Anticoagulants (%)	18(33.3)	4(44.4)	18(24)	0.294
Warfarin	2(11.1)	1(25)	6(33.3)	0.582
Apixaban	8(38.8)	2(50)	8(44.4)	
Dabigatran			1(5.56)	
Enoxaparin	3(16.6)			
Unfractionated heparin	2(11.1)		1(5.56)	
Rivaroxaban	4(22.2)	1(25)	2(11.1)	
ICD (%)	5(9.26)		2(2.6)	0.187
CRT (%)	3(5.56)			0.092
Pacemaker (%)	1(1.85)		1(3.3)	0.905
PCI (%)	17(31.4)	3(33.3)	9(12)	0.018
Death (%)	12(22.2)		8(10.5)	0.07

Table 2. Iron deficiency profile of patients with decompensated heart failure.

Name of the variable	Reduced ejection fraction (<40%) n=54	Mildly reduced ejection fraction (41-50%) n=9	Preserved ejection fraction (>50%) n=76	p
Ferritin levels < 100 ng/dL (%)	23(53.4)	4(66.6)	36(63.1)	0.58
Ferritin levels 100-300 ng/dL with transferrin saturation <20%	35(83.3)	3(33)	41(83.6)	0.003

Table 3. *Univariate analysis in iron deficient patients with heart failure*.

Results	With iron deficiency (n=76)	Without iron deficiency (n=63)	OR (95% CI)
Male sex (%)	42 (66.6)	51(80)	3.20 (1.51;7.14)
Age (SD)	67 (14)	69.2(14.3)	0.98 (0.95;1.01)
Diabetes mellitus (%)	21 (33.3)	25(35.8)	1.02 (0.50;2.07)
Atrial fibrillation (%)	13 (20.6)	14(18.4)	1.15 (0.49;2.67)
Smoking (%)	22 (34.9)	36 (47.3)	0.59 (0.30;1.18)
Coronary disease (%)	24 (38.1)	35 (46)	0.72 (0.36;1.42)
Dyslipidemia (%)	13 (21.6)	25 (32.8)	0.56 (0.25;1.22)
Chronic obstructive pulmonary disease (%)	25 (39.6)	39 (51.3)	0.62 (0.31;1.22)
Chronic kidney disease (%)	17 (26.9)	20 (26.3)	1.03 (0.48;2.20)
Valvular heart disease (%)	55 (90.1)	60 (81.0)	2.13 (0.76;5.95)
Stroke (%)	8 (12.7)	8 (10.5)	1.23 (0.43;3.50)
LVEF (SD)	43.7 (16.4)	45.5 (16)	1.05 (0.93;1.19)
TSH (SD)	6.78 (11.6)	10.4 (32.2)	0.92 (0.84;1.01
Hgb (SD)	12 (2.86)	12.4 (2.76)	1.18 (0.48;2.89)
NYHA Class III-IV (%)	26 (53.5)	19 (46.3)	0.28 (0.05;14.8)
CRP (SD)	3.52 (6.0)	4.49 (7.3)	0.87(0.73;1.05)
Mortality (%)	6 (9.5)	14(18.4)	0.46 (0.16;1.29)

Table 4. Multivariate analysis between iron deficient patients with decompensated heart failure with or without anemia and the NYHA classification and LVEF.

NYHA Class III-IV		
Result	**OR**	**95% CI**
Sex: male	2.8	1.17;6.97
Chronic obstructive pulmonary disease	2.7	1.03;7.23
Iron deficiency	1.92	1.13;3.25
Hemoglobin <13 g/dL	1.10	0.91;1.33
Reduced ejection fraction <50%		
Result	**OR**	**95% CI**
Sex: male	3.20	1.51;7.14
Age under 65 years	0.96	0.93;0.98
History of coronary disease	5.80	2.33;14.4
Hemoglobin <13 g/dL	1.26	1.00;1.59
Treatment of reduced ejection fraction <50%		
Result	**OR**	**95% CI**
Beta blockers	0.89	0.82;0.96
Sodium-glucose cotransporter-2 (SGLT-2) inhibitors	0.94	0.92;0.96
Angiotensin receptor-neprilysin inhibitors (ARNIs)	0.93	0.91;0.96
Aldosterone receptor antagonists (MRAs)	0.97	0.95;0.99
Diuretics	0.97	0.95;0.99
P2Y12 receptor inhibitors	0.96	0.93;0.99
Acetylsalicylic acid (ASA)	0.95	0.92;0.97
Interventional cardiology procedures (ICPs)	0.97	0.94;0.99

For patients with total iron over 40 mg/dL, a statistically significant association was found with NYHA III and IV classifications (OR: 0.80; 95% CI: 0.60;0.97). No statistically significant association was found in patients with HF and anemia (Hgb < 13 g/dL) (OR: 1.10; 95% CI: 0.91;1.33) (Table 4).

For patients with mildly reduced and reduced ejection fractions (LVEF < 50%), a statistically significant association was found with the male sex (OR: 3.20; 95% CI: 1.51;7.14), a history of coronary disease (OR: 5.80; 95% CI: 2.33;14.4) and anemia (Hgb < 13 g/dL) (OR: 1.26; 95% CI:1.00;1.59), as risk factors. Protective factors were age under 65 years (OR: 0.96; 95% CI: 0.93;0.98) and SAP greater than 120 mmHg (OR: 0.98; 95% CI: 0.96;099) (Table 4).

Discussion

The main objective of this study was to describe the sociodemographic and clinical characteristics of a population of 139 patients admitted to the emergency room for decompensated HF over the period of one year.

The prevalence of iron deficiency in patients with HF was 57.2%, which was greater than reported in a recent study by Deichl et al., which ranged from 35 to 50% (7). The average age of patients with HF was 68.2 years and ranged from 54 to 82 years; most were men (66.9%), and the most prevalent marital status was "single," similar to the data found in the RECOLFACA and North American studies (6, 8).

This study presents similar data, with the main prior conditions in patients with HF being type 2 diabetes mellitus, atrial fibrillation, smoking, coronary disease, dyslipidemia, chronic obstructive pulmonary disease, valvular heart dis-

ease and chronic kidney disease, and this is more evident in the group of patients with mildly reduced and reduced HF (<50%). Shanhzeb et al.'s findings (9) are similar to what is described in our study.

Patients with HF with iron deficiency and anemia were in NYHA classes II, III and IV; 40% of the patients were in NYHA III and IV, and 48.5% were in AHA Stages C and D. This study shows similar data, finding that 29.8 and 4.7% were in NYHA III and IV, and 94.5 and 5% were in Stages C and D, according to the latest RECOLFACA registry (8).

This study showed that patients with HF with reduced, mildly reduced or preserved LVEF had received iron replacement. This could be due to the coexistence of patients with HF and anemic syndrome or chronic kidney disease, conditions which can accelerate progression to an advanced clinical presentation with regard to LVEF and NYHA. These findings are consistent with the clinical practice guidelines recorded by the FAIR-HF, IRON-HF and CONFIRM-HF studies, which support the administration of intravenous iron in patients with iron deficiency and HF. Therefore, we emphasize the need to begin IV iron replacement in patients with iron deficiency and HF, either before hospital discharge or as part of outpatient treatment, in order to improve symptoms like the NYHA classification and six-minute walk test (10-12).

The factors associated with patients classified as NYHA III/IV were: the male sex (OR 2.8), chronic obstructive pulmonary disease (OR 2.7), transferrin saturation < 20% (OR 1.92), and total iron > 40 mcg/dL (OR 0.80). However, we did not find a statistically significant association between NYHA III/IV and anemia (OR 1.10; 95% CI:0.91;1.33). Aldeano et al. had similar findings (13).

In the context of this study, the factors associated with LVEF reduction in patients with HF with reduced and mildly reduced LVEF were the male sex (OR 3.20) and a history of coronary disease (OR 5.80). On the other hand, no association was found between reduced LVEF and factors like SAP greater than 120 mmHg (OR 0.98) and age under 65 years (OR 0.96), which coincides with the risk factors described by Lee et al. (14).

Likewise, a statistically significant association was found between LVEF <50% and anemia (OR 1.26; 95% CI:1.00;1.59).

Finally, further exploration indicated that the results of the pharmacological treatment used in patients with HF with mildly reduced and reduced LVEF were statistically significantly associated with the use of several medications, including beta blockers (OR 0.89), SGLT-2 inhibitors (OR 0.94), ARNIs (OR 0.93) MRAs (OR 0.97), diuretics (OR 0.97), P2Y12 receptor inhibitors (OR 0.96), ASA (OR 0.95) and ICPs (OR 0.97). These results are in line with the guidelines and recommendations established by the European HF guidelines and the American HF guidelines which recommend treatment according to the patients' specific clinical conditions (15, 16).

Study limitations

This limitation precludes establishing a clear causal relationship (cause-effect or effect-cause), which makes it hard to distinguish precisely between risk factors and prognostic factors in patients with acute HF and iron deficiency. Furthermore, obtaining data through the medical chart system (dynamic) may introduce information bias secondary to the lack of reliable information in the medical charts and a possible referral center bias due to being a public institution whose population has significant financial limitations as well as challenges in adherence and outpatient follow up.

Conclusions

This is one of the first studies in a population with decompensated HF with anemia and iron deficiency, contributing valuable information on the local behavior of the disease. The most common comorbidities in HF with reduced and mildly reduced LVEF with anemia and iron deficiency were hypertension, type 2 diabetes mellitus, and atrial fibrillation, among others.

We also found that risk factors like the male sex, chronic obstructive pulmonary disease, transferrin saturation < 20%, hemoglobin < 13 g, and a history of coronary heart disease can be associated as risk factors for a reduced ejection fraction and Stage III and IV NYHA classification. These findings highlight the importance of early evaluation of patients with HF in order to implement actions to prevent the onset of the disease and limit its progression to more advanced stages with irreversible damage.

References

1. **Gomez E.** Capitulo 2. Introduccion, epidemiologia de la falla cardiaca e historia de las clinicas de falla cardiaca en Colombia. *Rev Colomb Cardiol*. 2016;23:6–12.
2. **Urbich M, Globe G, Pantiri K, Heisen M, Bennison C, Wirtz HS, et al.** A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014-2020). *Pharmacoeconomics*. 2020;38:1219–36.
3. **Gaviria A, Muñoz NJ, Ruiz F, Ospina ML.** Carga de enfermedad por enfermedad crónicas no transmisibles y discapacidad en Colombia. *Observatorio Nacional de Salud*. 2015; pag 1-239.
4. **Enjuanes C, Bruguera J, Grau M, Cladellas M, Gonzalez G, Meroño O, et al.** Iron Status in Chronic Heart Failure: Impact on Symptoms, Functional Class and Submaximal Exercise Capacity. *Rev Esp Cardiol*. 2016;69:247–55.
5. **Jankowska EA, Rozentryt P, Witkowska A, Nowak J, Hartmann O, Ponikowska B, et al.** Iron deficiency: an ominous sign in patients with systolic chronic heart failure. *Eur Heart J*. 2010;31:1872–80.
6. **González-Costello J, Comín-Colet J.** Iron deficiency and anaemia in heart failure: understanding the FAIR-HF trial. *Eur J Heart Fail*. 2010;12:1159–62.
7. **Deichl A, Edelmann F.** Improvement of exercise and functional capacity and quality of life in patients with heart failure by iron therapy. *Front Cardiovasc Med*. 2023;10: 1-8.
8. **Gómez-Mesa JE, Saldarriaga CI, Echeverría LE, Luna P.** Colombian heart failure registry (RECOLFACA): methodology and preliminary data. *Rev Colomb Cardiol*. 2021;28:217–30.
9. **Khan MS, Samman A, Vaduganathan M, Greene SJ, Alrohaibani A, Anker SD, et al.** Trends in prevalence of comorbidities in heart failure clinical trials. *Eur J Heart Fail*. 2020;22:1032–42.
10. **Ponikowski P, van Veldhuisen DJ, Comin-Colet J, Ertl G, Komajda M, Mareev V, et al.** Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency. *Eur Heart J*. 2015;36:657–68.
11. **Ponikowski P, van Veldhuisen DJ, Comin-Colet J, Ertl G, Komajda M, Mareev V, et al.** Rationale and design of the CONFIRM-HF study: a double-blind, randomized, placebo-controlled study to assess the effects of intravenous ferric

carboxymaltose on functional capacity in patients with chronic heart failure and iron deficiency. *ESC Hear Fail*. 2014;1:52–8.

12. **Anker SD, Colet JC, Filippatos G, Willenheimer R, Dickstein K, Drexler H, et al.** Rationale and design of Ferinject® Assessment in patients with IRon deficiency and chronic Heart Failure (FAIR-HF) study: a randomized, placebo-controlled study of intravenous iron supplementation in patients with and without anaemia. *Eur J Heart Fail*. 2009;11:1084–91.
13. **Alcaide-Aldeano A, Garay A, Alcoberro L, Jiménez-Marrero S, Yun S, Tajes M, et al.** Iron Deficiency: Impact on Functional Capacity and Quality of Life in Heart Failure with Preserved Ejection Fraction. *J Clin Med*. 2020;9, 1-12.
14. **Lee MP, Glynn RJ, Schneeweiss S, Lin KJ, Patorno E, Barberio J, et al.** Risk Factors for Heart Failure with Preserved or Reduced Ejection Fraction Among Medicare Beneficiaries: Application of Competing Risks Analysis and Gradient Boosted Model. *Clin Epidemiol*. 2020;12:607–16.
15. **McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al.** Guía ESC 2021 sobre el diagnóstico y tratamiento de la insuficiencia cardiaca aguda y crónica. *Rev Española Cardiol*. 2022;75:523, 1-114.
16. **A. HP, Biykem B, David A, A. AL, J. BJ, M. CM, et al.** 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary. *J Am Coll Cardiol*. 2022;79:1757–80.