Iron Deficiency in Heart Failure

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Background and Objective of the Survey

Iron deficiency (ID) is increasingly recognized as a common comorbidity in patients with heart failure (HF) and is associated with poor outcomes. The role of iron in HF goes beyond its traditional function in oxygen transport, as it is essential for cellular metabolism, mitochondrial function, and myocardial contractility. In HF, ID contributes to reduced exercise tolerance, impaired quality of life, increased hospitalizations, and mortality. Mechanisms underlying the impact of ID in HF include alterations in myocardial structure and function, impaired energy metabolism, and activation of neurohormonal pathways. Furthermore, ID can exacerbate HF-related symptoms such as fatigue and dyspnea, leading to decreased functional capacity and poor prognosis. Iron deficiency in HF may occur due to multiple factors, including inadequate dietary intake, gastrointestinal bleeding, impaired absorption, and systemic inflammation. Recognizing and treating ID in HF patients has emerged as an important therapeutic strategy to improve symptoms, quality of life, and clinical outcomes. Intravenous iron supplementation has shown benefits in HF patients with ID, including improvements in exercise capacity, quality of life, and hospitalization rates. Overall, addressing iron deficiency represents a promising approach to optimize management and outcomes in patients with heart failure.

The objective of the survey is:

To evaluate the role of iron deficiency in heart failure

Methodology of the Survey

A survey was conducted to evaluate the role of iron deficiency in heart failure. A total of 150 doctors from India participated in the survey.

Step 1: A literature search was done on the topic. Below topics were covered in the literature search

- Introduction
- Importance of Diagnosing and Treating Iron Deficiency in Patients with Heart Failure
- Assessment for Iron Deficiency
- Treatment of Iron Deficiency in Patients with Heart Failure
- Trials of Intravenous Iron Supplementation in HF
- Potential Safety Concerns with Intravenous Iron Therapies

Step 2: A survey questionnaire was prepared based on the literature search. The survey form was shared through the digital medium with physicians across India.

Step 3: Their responses were analyzed and the findings are provided in this survey analysis booklet.

Literature Review

1. Introduction[1]

Heart failure (HF) impacts in the region of 26 million people across the world and due to the ageing population its prevalence is still increasing. Although there have been advances to prevent and treat HF, it is still associated with substantial rates of mortality and morbidity as well as diminished patient quality of life (QoL).

HF is defined as a syndrome characterised by cardinal symptoms, for example fatigue, breathlessness and ankle swelling, which may occur alongside signs including peripheral oedema, increased jugular venous pressure and crackles in the lung. HF is caused be an abnormality of the heart, which may be functional and/or structural, resulting in increased pressure in the heart and/or a deficient cardiac output while resting and/or exercising.

Iron deficiency is an important and frequent comorbid condition in patients with HF. In these patients, it independently predicts mortality and morbidity, and is also associated with impaired exercise capacity and reduced QoL. The recently updated 2021 European Society of Cardiology (ESC) guidelines on HF acknowledge the importance of iron deficiency among patients with HF and also provide specific recommendations for diagnosing and appropriately treating the condition. However, iron deficiency remains under-recognised and under-treated in clinical practice, likely due in part to a lack of practical guidance for clinicians that can be easily followed.

There are three main goals when treating patients with HF with reduced ejection fraction (HFrEF): (1) lessening mortality; (2) preventing recurrent hospitalisations due to HF worsening; and (3) improving functional capacity, clinical status and QoL. Clinical trial evidence has shown that correcting iron deficiency with supplementary IV iron addresses two of the aforementioned treatment goals (reducing recurrent hospitalisations due to HF, and improving HF symptoms, functional status, and QoL). Hence, correction of iron deficiency in patients with HFrEF is recommended to improve these clinical outcomes.

The majority of patients with HF are managed primarily by general internal medicine physicians who play a crucial role in screening, diagnosing and subsequently treating iron deficiency. This article aims to provide a summary of iron deficiency in HF, along with

practical guidance for its diagnosis and appropriate treatment. It aims to address the frequently asked questions of 'Why', 'Who', and 'How' to diagnose and appropriately treat iron deficiency in patients with HF.

2. Importance of Diagnosing and Treating Iron Deficiency in Patients with Heart Failure[1]

2.1. Role of Iron and the Impact of Iron Deficiency

Iron deficiency is a clinical condition where the available iron is inadequate to fulfil the needs of the body. Iron has a critical role in the function of every cell in the human body. As an essential component of respiratory chain proteins in mitochondria, iron is key for cellular energy generation. While iron is most widely recognised for its role in the transport of oxygen as a vital constituent of haemoglobin (Hb), it also has a major role in non-haematopoietic tissues, such as cardiac and skeletal muscle, which are dependent on iron for oxygen storage, mitochondrial energy production and many other cellular processes. Thus, iron deficiency *per se*, even in the absence of anaemia (i.e., at a normal Hb level), can be harmful. Experimental studies show that iron deficiency directly weakens the ability of human cardiomyocytes to contract in vitro, and that this can be corrected by iron repletion. In patients who have chronic HF (CHF), iron deficiency can be associated with breathlessness on exertion, increased fatigue, reduced exercise capacity, poorer health-related QoL, worse HF symptoms, increased HF hospitalisation and higher mortality. These adverse effects are independent of anaemia in patients who have HF and iron deficiency. Furthermore, anaemia does not affect these adverse outcomes in HF when corrected for iron deficiency and other prognostic markers, although patients with both iron deficiency and anaemia have worse outcomes. Importantly, treatment of iron deficiency with intravenous (IV) iron is associated with improved functional status among patients with HF, even when Hb is normal.

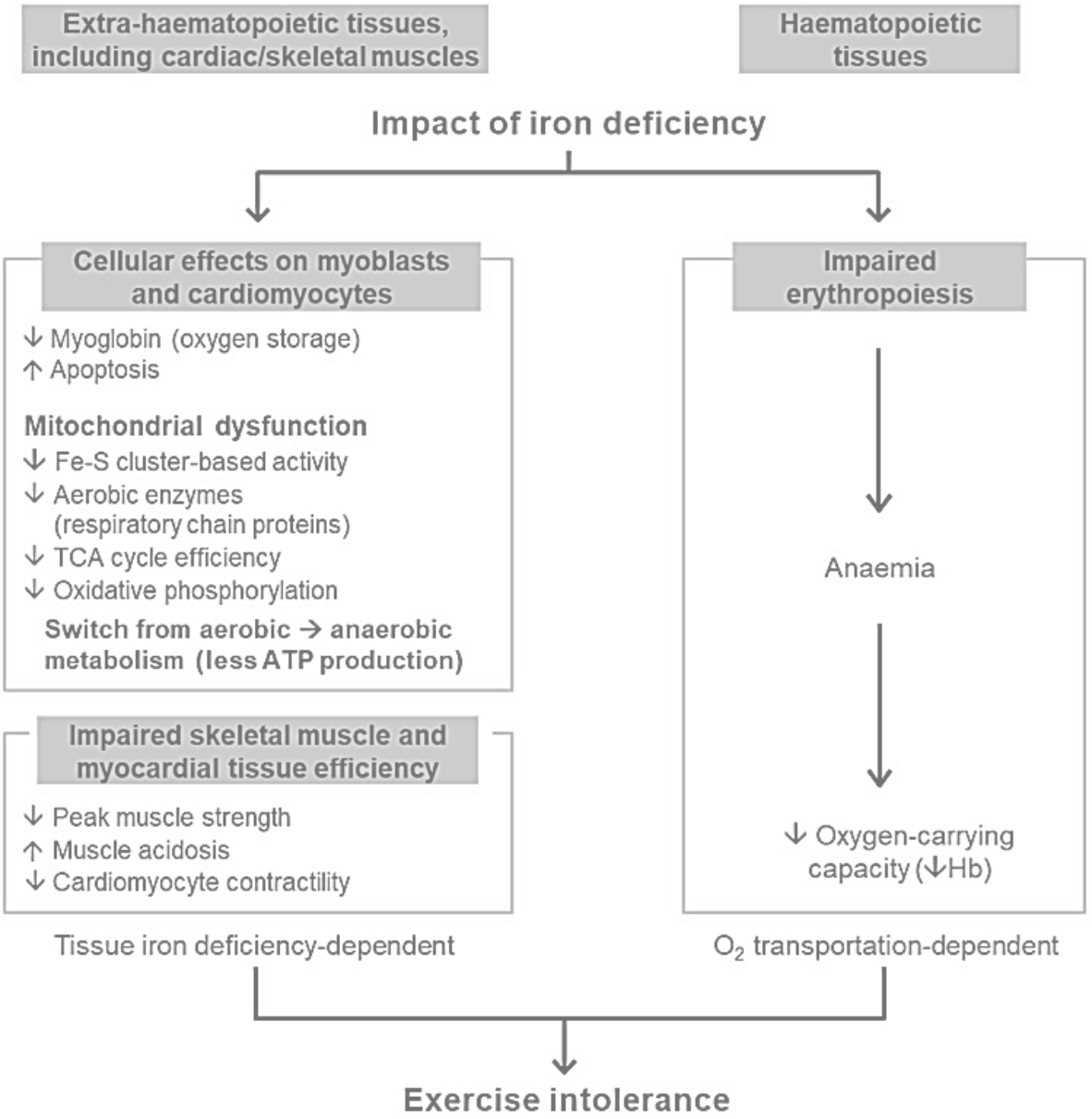


Figure 1. Role of iron in the body and detrimental impact of iron deficiency.

ATP, adenosine triphosphate; Fe-S, iron–sulphur; Hb, haemoglobin; TCA, tricarboxylic acid.

2.2. Iron Deficiency Prevalence in Patients with Heart Failure

Iron deficiency is one of the most commonly seen comorbid conditions in patients who have HF, with studies reporting that approximately 40−70% of patients with CHF have iron deficiency, regardless of their ejection fraction. Iron deficiency also has a prevalence of up to 80% in patients with acute HF (AHF). Additionally, the prevalence of iron deficiency increases

in severe HF (i.e., with higher New York Heart Association [NYHA] class) and when anaemia is present.

2.3. Iron Deficiency Causes in Patients with Heart Failure

The aetiology of iron deficiency in HF is complex and multifactorial, with contradictory evidence on the precise cause(s). Factors that may contribute to iron deficiency include reduced appetite, co-administration of proton pump inhibitors, occult gastrointestinal blood loss and comorbidities such as chronic kidney disease and inflammatory activity. Since hepcidin is tightly regulated by inflammatory activation as part of the antibacterial response mechanism and HF is a condition of increased inflammatory activation, patients with HF may have high levels of circulating hepcidin. Hepcidin inhibits iron absorption by binding to ferroportin, causing sequestration of iron in the reticuloendothelial system and reducing the available useable iron. There is some evidence that, as HF progresses and iron deficiency develops, the circulating hepcidin levels may become low in patients with CHF.

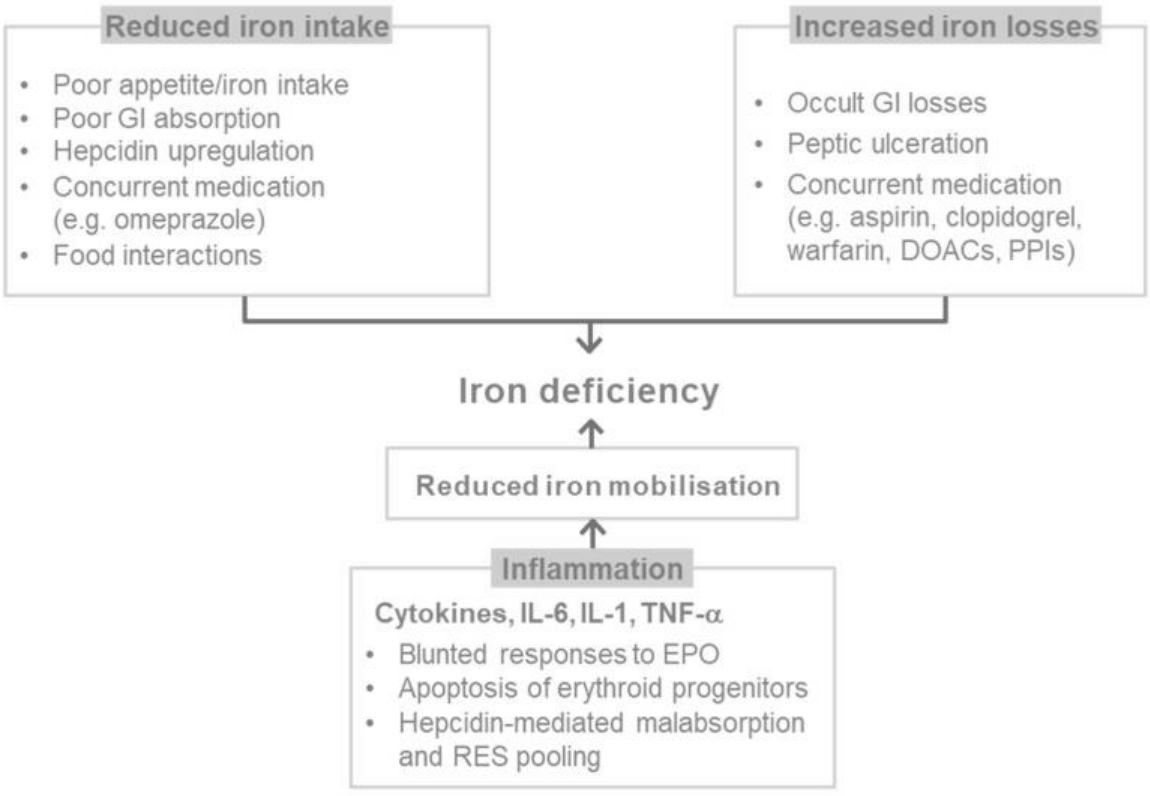


Figure 2. Causes of iron deficiency in heart failure.

DOAC, direct oral anticoagulant; EPO, erythropoietin; GI, gastrointestinal; IL, interleukin; PPI, proton-pump inhibitor; RES, reticuloendothelial system; TNF-α, tumour necrosis factor alpha.

3. Assessment for Iron Deficiency[1]

3.1. Who and When to Screen for Iron Deficiency?

The 2021 ESC HF guidelines recommend that every patient with HF should be periodically assessed for iron deficiency (and anaemia) including carrying out a full blood count, and measuring both serum ferritin concentration and transferrin saturation (TSAT) (recommendation class I, evidence level C); plasma iron level is not an adequate mirror of iron deficiency. This recommendation is a noteworthy update to the 2016 ESC HF guidelines since screening was previously only recommended for new cases of HF. Among the routine blood tests for comorbidities recommended for patients with suspected CHF, iron status (TSAT and ferritin) should also be tested (recommendation class I, evidence level C). Furthermore, determination of iron status (TSAT and ferritin) is recommended at pre-discharge in patients with AHF. We previously published comprehensive practical recommendations related to diagnosing, treating and monitoring patients with HF and iron deficiency in line with the 2016 ESC HF guidelines. In this article, we have updated our recommendations in line with the 2021 ESC guidelines and recent trial findings, and recommend that clinicians should periodically evaluate iron deficiency and anaemia in all patients with HF regularly as part of the clinical evaluation (i.e., one to two times per year), depending on the iron deficiency severity and HF. Iron status should also be checked in patients with suspected CHF, ambulatory patients or outpatients with worsening HF, and after hospitalisation for AHF.

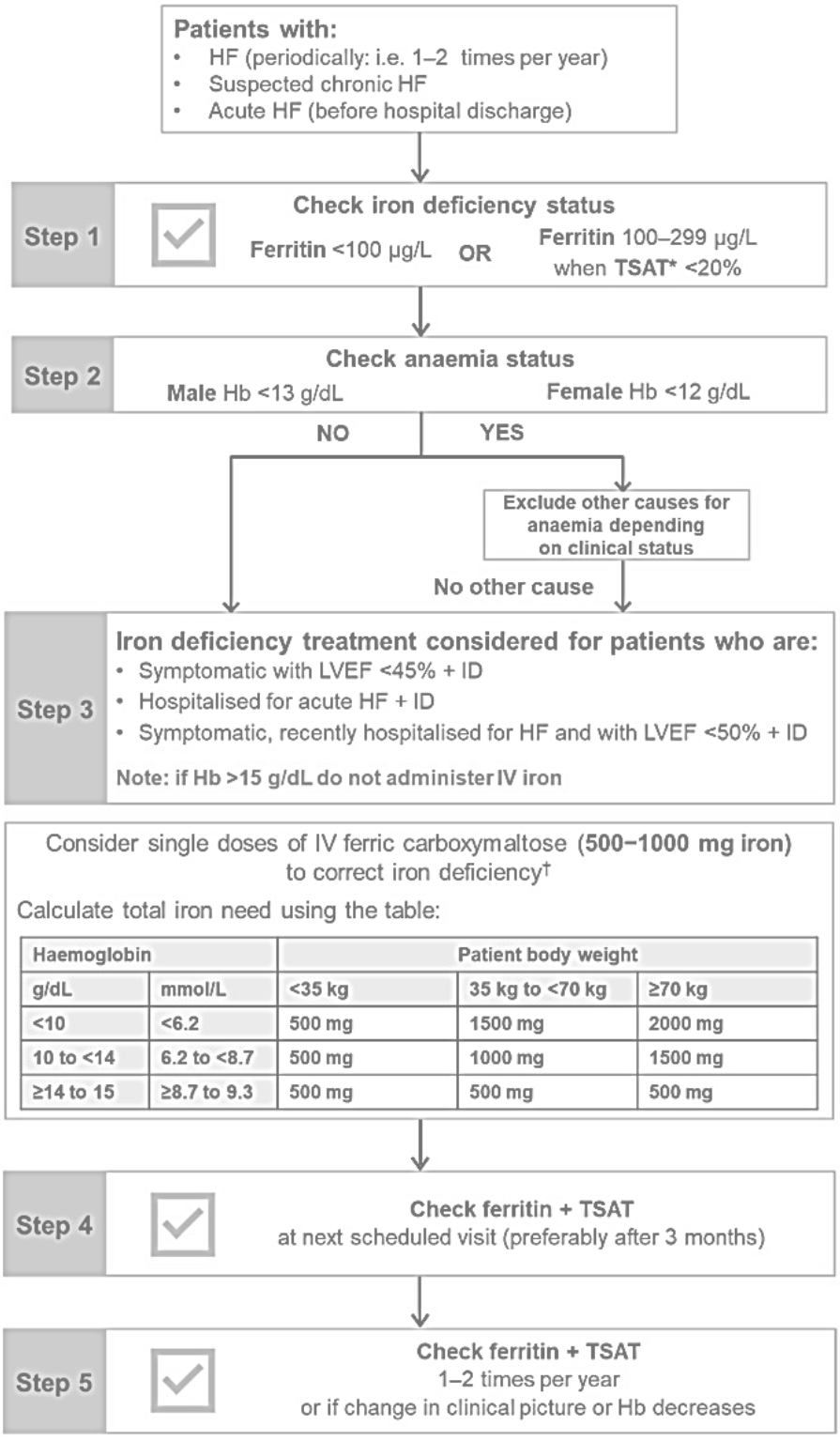


Figure 3. Algorithm showing screening, diagnosing, treating and monitoring for iron deficiency in patients with HF

* TSAT = (concentration of serum iron/total capacity to bind iron) × 100. † Note: The use of ferric carboxymaltose has not been assessed in paediatric patients, and therefore treatment with ferric carboxymaltose is not advised in children less than 14 years of age. Full prescribing information can be found in the latest Summary of Product Characteristics. Hb, haemoglobin; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ID, iron deficiency; IV, intravenous; LVEF, left ventricular ejection fraction; TSAT, transferrin saturation.

3.2. How to Diagnose Iron Deficiency in Patients with Heart Failure

Iron status can easily be determined by measuring two readily available blood biomarkers: ferritin and TSAT. Ferritin is a protein for storing iron within cells that is found in every cell type. Serum ferritin concentration is a surrogate marker for the total iron stored in healthy individuals. TSAT is an indicator of the amount of iron circulating in the body that is available to supply metabolising cells and is defined as the percentage (%) of transferrin which is bound to iron.

In patients with HF, iron deficiency should be diagnosed when serum ferritin is <100 µg/L or TSAT is <20% when serum ferritin is 100–299 µg/L. Two different thresholds are used since serum ferritin may be increased in response to inflammation, such as that seen in CHF, since it is an acute-phase reactant and can therefore appear to fall inside the normal range of 100–300 µg/L. In this situation, a TSAT value of <20% is used to confirm the iron deficiency diagnosis. In line with the 2021 ESC HF guidelines, ferritin and TSAT should be assessed at the same time to ensure the correct diagnosis of iron deficiency is made.

Although lower ferritin thresholds (e.g., <30 µg/L) are used for diagnosis of iron deficiency in other disease areas, it is important to use the thresholds specified above for the diagnosis of iron deficiency in patients who have HF. It is also critical to note that other laboratory parameters, such as mean values of corpuscular volume, corpuscular Hb and corpuscular Hb concentration are not reliable markers of iron deficiency status, so should not be used for determining iron deficiency status in patients who have HF. Furthermore, the measurement of only serum iron should not be utilised as an iron deficiency marker, since serum iron concentrations may differ considerably between individual patients with HF and can also display large diurnal fluctuations. When evaluating iron status, it is also important to check for

the presence of anaemia, which should be diagnosed using the Hb thresholds of <12 g/dL in females and <13 g/dL in males.

4. Treatment of Iron Deficiency in Patients with Heart Failure[1]

Given the serious clinical impact of iron deficiency on patients with HF, it is vital that if diagnosed, this condition is treated.

4.1. Recommendations for Correcting Iron Deficiency

The 2021 ESC HF guidelines recommend that IV FCM should be considered for the treatment of iron deficiency in:

- Symptomatic patients who have a left ventricular ejection fraction (LVEF) < 45% to alleviate symptoms, improve exercise capacity and QoL (recommendation class IIa, evidence level A)
- Pre- and post-discharge follow-up of patients hospitalised for AHF to improve symptoms and reduce rehospitalisation (recommendation class IIa, evidence level B)
- Symptomatic patients recently hospitalised for HF with LVEF < 50% to lessen the risk of HF hospitalisation (recommendation class IIa, evidence level B).

These recommendations were determined from the results of the FAIR-HF, CONFIRM-HF, EFFECT-HF and AFFIRM-AHF trials described in more detail below.

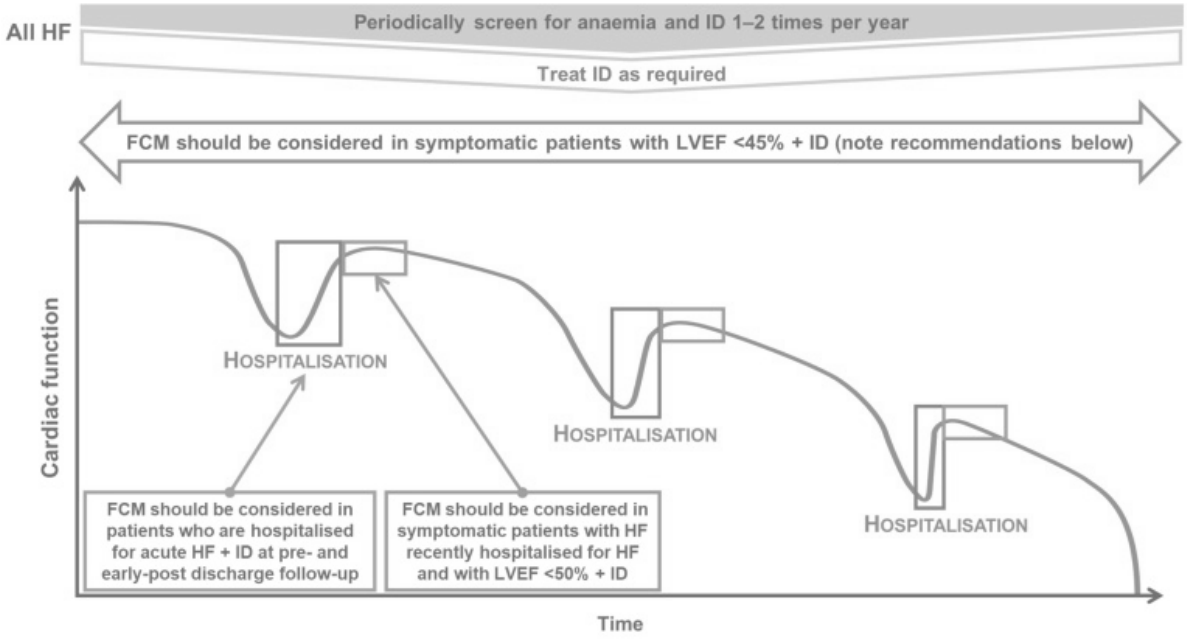


Figure 4. Screening and treatment of iron deficiency across the HFrEF continuum.

Iron deficiency determined by a ferritin <100 µg/L or TSAT <20% when ferritin is 100–299 µg/L; and anaemia determined by a Hb <13 g/dL in males and <12 g/dL in females. TSAT = (serum iron concentration/total iron-binding capacity) × 100. FCM, ferric carboxymaltose; Hb, haemoglobin; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ID, iron deficiency; LVEF, left ventricular ejection fraction; TSAT, transferrin saturation.

4.2. Evidence on the Therapeutic Management of Iron Deficiency

Ferric carboxymaltose (FCM), a precision-engineered nanomedicine with a characteristic clinical profile, is the most extensively studied IV iron in randomised controlled clinical trials of patients with CHF. Therefore, the majority of the evidence-base for IV iron in HF applies to IV FCM and, as such, FCM is the only iron formulation specifically recommended for the treatment of iron deficiency in the 2021 ESC HF guidelines.

The largest randomised controlled trials to evaluate FCM in patients who were iron-deficient and had stable CHF (LVEF ≤ 45%) were the FAIR-HF , CONFIRM-HF , EFFECT-HF and AFFIRM-AHF studies. A summary of the designs and key efficacy and safety findings of these trials is shown in .

Table 1. Design and key results from the FAIR-HF, CONFIRM-HF, EFFECT-HF and AFFIRM-AHF clinical trials of IV FCM in patients with HFrEF who have iron deficiency.

	FAIR-HF	CONFIRM-HF	EFFECT-HF	AFFIRM-AHF
Design, duration and number of patients who received treatment per arm	Double-blind, placebo-controlled, randomised; 24 weeks FCM: 305 Placebo: 154	Double-blind, placebo-controlled, randomised; 52 weeks FCM: 152 Placebo: 152	Open-label, SoC-controlled, randomised; 24 weeks FCM: 88 SoC: 86	Double-blind, placebo-controlled, randomised; 52 weeks FCM: 559 Placebo: 551
Key inclusion criteria	NYHA class II (LVEF ≤ 40%) or III (LVEF ≤45%) Hb 9.5–13.5 g/dL ID (ferritin <100 µg/L or 100–299 µg/L + TSAT <20%)	NYHA class II/III (LVEF ≤ 45%) BNP >100 pg/mL and/or NT-proBNP >400 pg/ml Hb <15 g/dL ID (ferritin <100 µg/L or 100–300 µg/L + TSAT < 20%)	NYHA class II/III (LVEF ≤ 45%) BNP >100 pg/mL and/or NT-proBNP >400 pg/ml Hb <15 g/dL ID (ferritin <100 µg/L or 100–300 µg/L + TSAT < 20%) Peak VO_2 10–20 mL/kg/min (reproducible)	Hospitalised for acute HF, treated with at least 40 mg IV furosemide (or equivalent) LVEF < 50% ID (ferritin <100 µg/L or 100–299 µg/L + TSAT <20%)
Dosing regimen	Dose determined by Ganzoni formula FCM equivalent to 200 mg	FCM equivalent to 500–3500 mg iron for iron repletion (baseline and	FCM equivalent to 500–1000 mg iron for iron repletion (baseline and	FCM equivalent to 500–1000 mg at baseline and Week 6 for iron repletion;

	iron/week for iron repletion then Q4W for maintenance	Week 6); 500 mg iron for maintenance (Weeks 12, 24, 36) if iron deficiency still present	Week 6) based on screening Hb and weight; only given at Week 6 if <70 kg and Hb <10 g/dL or ≥70 kg and Hb <14 g/dL; 500 mg iron for maintenance (Week 12) if iron deficiency still present	500 mg iron for maintenance at Weeks 12 and 24 for patients in whom ID persisted and for whom Hb was 8–15 g/dL
Mean cumulative iron dose/ total number of injections	NA/ Median 6 (3–7) during iron repletion phase	1500 mg/>75% of patients receiving FCM needed 2 injections maximum to correct and sustain iron parameters during the study	1204 mg/42% received 1, 55% received 2, and 3.3% received 3 FCM administrations	1352 mg/80% of patients received 1 or 2 FCM administrations during the treatment phase (i.e., up to Week 24)
Treatment effect on iron-related parameters	FCM vs. placebo at Week 24 (mean ± SE) • - Serum ferritin: 312 ± 13 vs. 74 ± 8 µg/L • - TSAT: 29 ± 1 vs. 19 ± 1%	Mean treatment effect (baseline-adjusted) difference for FCM vs. placebo at Week 52: • - Serum ferritin: 200 ± 19 µg/L	FCM vs. control (SoC) at Week 24: • - Serum ferritin: 283 ± 150 vs. 79 µg/L • - TSAT: 27 ± 8 vs. 20.2%	Compared with placebo, serum ferritin and TSAT both rose with FCM by week 6 and continued to be significantly higher at week 52

	• - Hb: 130 ± 1 vs. 125 ± 1 g/L (p < 0.001 for all)	• - TSAT: 5.7 ± 1.2% • - Hb: 1.0 ± 0.2 g/dL (p < 0.001 for all)	• - Hb: 13.9 ± 1.3 vs. 13.2 ± 1.4 g/dL (p < 0.05 for all)	
Primary endpoint results	Changes in PGA and NYHA functional class at Week 24 for FCM vs. placebo • - PGA: patients reported being much or moderately improved: 50% vs. 28% (OR 2.51; 95% CI, 1.75 to 3.61; p < 0.001) • - NYHA functional class I/II: 47% vs. 30% placebo (odds ratio for improvement by one class, 2.40; 95% CI, 1.55 to 3.71, p < 0.001)	LS means ± SE 6 MWT distance at Week 24 for FCM vs. placebo • - 18 ± 8 vs. −16 ± 8 metres (difference FCM vs. placebo: 33 ± 11 metres, p = 0.002)	Primary analysis LS means change from baseline in peak VO_2 at Week 24 for FCM vs. control (SoC) • - −0.16 ± 0.387 vs. −1.19 ± 0.389 mL/min/kg (p = 0.020) Sensitivity analysis in which missing data were not imputed for control vs. control: • - −0.16 ± 0.37 vs. −0.63 ± 0.38 mL/min/kg (p = 0.23)	Composite of total HF hospitalisations and CV deaths up to 52 weeks after randomisation for FCM vs. placebo: • - 293 primary events (57.2 per 100 patient-years) vs. 372 (72.5 per 100 patient-years) (RR: 0.79, 95% CI 0.62–1.01, p = 0.059) • - Pre-COVID-19 sensitivity analysis: 274 primary events (55.2 per 100

				patient-years) vs. 363 (73.5 per 100 patient-years) (RR: 0.75, 95% CI 0.59–0.96, p = 0.024)
Key secondary endpoint results	Significant improvement (p < 0.001) with FCM vs. placebo in: • - Self-reported PGA at Weeks 4 and 12 • - 6 MWT distance at Weeks 4, 12, and 24 • - QoL (EQ-5D visual assessment) at Weeks 4, 12, and 24 • - Overall KCCQ score at Weeks 4, 12, and 24	Significant improvements in PGA, NYHA class and 6 MWT with FCM vs. placebo: • - PGA at Week 12 (p = 0.035) Week 24 (p = 0.047), Weeks 36 and 52 (both p < 0.001) • - NYHA class at Week 24 (p = 0.004) and Weeks 36 and 52 (both p < 0.001) • - 6 MWT difference in changes at Week 36 (42 metres with 95% CI of 21–62, p < 0.001)	Significant improvements in NYHA class and PGA with FCM vs. control: • - NYHA class at weeks 6, 12 and 24 (with imputation; all p < 0.05) • - PGA at Weeks 12 and 24 (with imputation; p < 0.05) Note: effect of FCM vs. control on NYHA class and PGA without imputation (observed values) were similar	Total CV hospitalisations and CV deaths with FCM vs. placebo • - 370 vs. 451 (RR: 0·80, 95% CI 0·64–1.00, p = 0.050) CV deaths FCM vs. placebo • - 77 (14%) vs. 78 (14%) (HR: 0.96, 95% CI 0.70–1.32, p = 0.81) Significantly lower number HF hospitalisations with FCM vs. placebo • -

		and Week 52 (36 metres with 95% CI of 16–57, $p < 0.001$) • - Fatigue score at Week 12 ($p = 0.009$), Week 24 ($p = 0.002$) and Week 36 ($p < 0.001$), and Week 52 ($p = 0.002$)		217 vs. 294 (RR 0.74; 95% CI 0.58–0.94, $p = 0.013$) Significant treatment benefits with IV FCM vs. placebo for time to first hospitalisation or CV death • - 181 (32%) vs. 209 (38%) (HR: 0.80, 95% CI 0.66–0.98, $p = 0.030$)
Safety endpoint results	FCM vs. placebo (incidence per 100 patient-years at risk) • - All deaths: 3.4 % vs. 5.5% • - Deaths with CV cause: 2.7% vs. 5.5% • -	FCM vs. placebo (incidence per 100 patient-years at risk) • - All deaths: 8.9 % vs. 9.9% • - Deaths with CV causes: 8.1% vs. 8.5% • - Deaths, due to HF worsening: 3.0% vs. 2.1%	FCM vs. control (SoC) • - All deaths: 0 (0%) vs. 4 (4.7%) • - Hospitalisations: 37 (42.0%) vs. 21 (24.4%) • ◦ Due to worsening HF: 13 (14.8%) vs. 13 (15.1%) • ◦	FCM vs. placebo • - Serious adverse events: 250 (45%) vs. 282 (51%) • - Cardiac disorder events: 224 (40%) patients with 391 events vs. 244 (44%) patients with 453 cardiac disorder events.

	Deaths, due to HF worsening: 0% vs. 4.1% • - Hospitalisations with CV cause: 10.4% vs. 20.0% • - Hospitalisations for worsening HF: 4.1% vs. 9.7%	• - Hospitalisations, CV cause: 16.6% vs. 26.3% • - Hospitalisations due to worsening HF: 7.6% vs. 19.4%	Due to other CV reason: 13 (14.8%) vs. 3 (3.5%) • ◦ Due to non-CV reason: 11 (12.5%) vs. 4 (4.7%)	• - Treatment discontinued prematurely: 157 (28%) vs. 160 (29%) (modified intention-to-treat population)

6 MWT, 6-min walk test; AFFIRM-AHF, Study to Compare Ferric Carboxymaltose With Placebo in Patients With Acute Heart Failure and Iron Deficiency; BNP, brain natriuretic peptide; CONFIRM-HF, Ferric CarboxymaltOse evaluatioN on perFormance in patients with IRon deficiency in coMbination with chronic Heart Failure; CI, confidence interval; CV, cardiovascular; EFFECT-HF, Effect of Ferric Carboxymaltose on Exercise Capacity in Patients With Iron Deficiency and Chronic Heart Failure; EQ-5D, EuroQol-5 Dimension; FAIR-HF, Ferinject assessment in patients with IRon deficiency and chronic Heart Failure; FCM, ferric carboxymaltose; Hb, haemoglobin; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HR, hazard ratio; ID, iron deficiency; IV, intravenous; KCCQ, Kansas City Cardiomyopathy Questionnaire; LS, least squares; LVEF, left ventricular ejection fraction; NA, not available; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; PGA, patient global assessment; Q4W, every four weeks; OR, odds ratio; QoL, quality of life; RR, rate ratio; SE, standard error; SoC, standard of care; TSAT, transferrin saturation.

The FAIR-HF study assessed whether treatment with FCM provided a significant improvement of the two primary endpoints: functional capacity as assessed by NYHA functional score and patients' self-reported perception of wellbeing (Patient Global Assessment [PGA]). This treatment benefit was evident after only 4 weeks of treatment with FCM and was sustained for the duration of the 24-week study. FCM treatment was beneficial for the reduction of HF

symptoms, and in improving functional capacity and QoL. The treatment benefits of FCM were comparable among patients either with or without anaemia. FCM was well tolerated, and rates of adverse events, serious adverse events, and death were similar in both the FCM and placebo groups.

The CONFIRM-HF study evaluated the longer-term efficacy and safety of FCM. In this study, FCM significantly prolonged the Week 24 6-min walk test (6 MWT) distance (a difference of 33 ± 11 metres between the FCM and placebo groups [$p = 0.002$]), and this treatment effect was maintained until Week 52. Patients treated with FCM also achieved benefits to their PGA, NYHA class, QoL and fatigue score, compared with those receiving placebo. These improvements were statistically significant from Week 24 onwards, and the treatment benefits lasted up to 1 year. Patients treated with FCM were also found to have a significantly reduced risk of hospitalisation due to HF worsening compared with those in the placebo group (hazard ratio [HR]: 0.39 [95% confidence interval (CI) 0.19–0.82], $p = 0.009$). The mean dose received by patients was 1500 mg of iron over the 12-month study period, and >75% of the patients needed a total of two injections of FCM for correction and maintenance of iron parameters. Analysis of safety outcomes found that the frequency of adverse events and deaths were comparable between the two treatment groups.

The EFFECT-HF study evaluated whether FCM could improve exercise intolerance, based on the assessment of alteration in peak VO_2 from baseline to Week 24. FCM had a favourable effect on peak VO_2, compared with the control (treatment with standard of care), regardless of baseline anaemia status, and also significantly improved PGA score and NYHA functional class of patients in the study. In this study FCM was mostly well tolerated; there were no hypersensitivity reactions to FCM nor cases of hypophosphataemia reported.

Although the initial randomised, placebo-controlled clinical trials established that IV FCM treatment improved symptoms, functional capacity and health-related QoL of HFrEF patients with iron deficiency, they were not planned or sufficiently powered to assess the treatment effects on hard outcomes, such as hospitalisations and mortality. However, meta-analyses of FCM vs. placebo randomised controlled trials of patients with CHF who have iron deficiency, including the CONFIRM-HF and FAIR-HF studies, indicated that IV FCM treatment reduced the risk of all-cause death or cardiovascular (CV) hospitalisation, CV death or HF hospitalisation, and all-cause/CV death or recurrent CV/HF hospitalisations as combined endpoints .

Subsequently, the AFFIRM-AHF study evaluated the FCM treatment effect when initiated as early as hospital discharge on mortality and morbidity of patients who were hospitalised due to acute decompensated HF with LVEF < 50% and iron deficiency. Overall, 1108 patients with HF randomised to treatment with FCM (n = 558) or placebo (n = 550) for up to 24 weeks were considered in the analysis. The study reported 293 primary events in the FCM vs. 372 in the placebo groups (rate ratio [RR]: 0.79, 95% CI 0.62−1.01, p = 0.059) for the primary composite endpoint of total hospitalisations for HF and CV deaths for up to 52 weeks, failing to reach the standard statistical significance level of 5%. The secondary endpoint analyses showed that treatment with FCM significantly reduced the risk of HF hospitalisations by 26% compared with placebo (RR: 0.74, 95% CI 0.58–0.94; p = 0.013), and this treatment benefit was observed for anaemic and non-anaemic patients. Statistically significant treatment benefits with FCM therapy vs. placebo were also observed for the composite endpoint of time to first HF hospitalisation or CV death (HR: 0.80, 95% CI 0.66–0.98, p = 0.03) and for days lost due to HF hospitalisations and CV death (RR: 0.67, 95 CI 0.47–0.97; p = 0.035). Additionally, patients in the AFFIRM-AHF study receiving FCM also had significantly greater improvements in the Kansas City Cardiomyopathy Questionnaire (KCCQ) compared with patients receiving placebo: adjusted mean differences (95% CI) at Week 4 were 2.9 (0.5–5.3, p = 0.018) for overall summary score (OSS) and 2.8 (0.3–5.3, p = 0.029) for clinical summary score (CSS), and at Week 24 were 3.0 (0.3–5.6, p = 0.028) for OSS and 2.9 (0.2–5.6, p = 0.035) for CSS. Treatment with FCM was well tolerated by patients in AFFIRM-AHF and there were no unexpected safety findings.

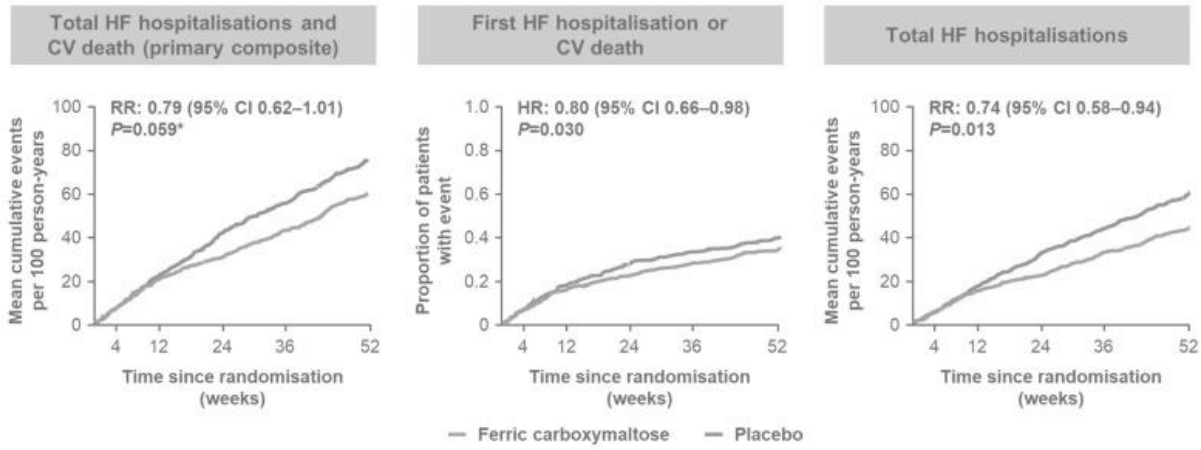


Figure 5. Key primary and secondary outcome results from AFFIRM-AHF

* AFFIRM-AHF primary endpoint narrowly missed statistical significance. AFFIRM-AHF, Study to Compare Ferric Carboxymaltose With Placebo in Patients With Acute Heart Failure and Iron Deficiency; CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; RR, rate ratio.

4.3. Safety and Tolerability of FCM

Evidence from clinical trials has shown that FCM is well tolerated by patients with HF and has a favourable safety profile. The most commonly reported adverse drug reactions in patients who received FCM in clinical trials and real-world practice (occurring in ≥1% to 10% patients) were dizziness, flushing, headache, hypertension, hypophosphataemia, injection-/infusion-site reactions and nausea. Anaphylactoid/anaphylactic reactions are rare (≥1/10,000 to <1/1000) and fatalities have been reported. Moderate or severe hypophosphataemia has more commonly been reported in patients treated with FCM within the cardiology therapy area (9.9%) than the neurology and gastroenterology therapy areas (39% and 47.1%, respectively), but hypophosphataemia does not result in serious clinical outcomes for most patients across the populations studied. Although a higher incidence of hypophosphataemia has been reported with FCM in certain patient subgroups, such as those who have had a kidney transplantation, hypophosphataemia was reported at the same frequency in patients with HF who received FCM or placebo (0.2% in each arm) in the AFFIRM-AHF trial. However, it should be noted that the product label specifies that serum phosphate levels should be monitored in those patients who receive multiple higher-dose injections of FCM or receive FCM long term, and in those patients with pre-existing factors that put them at risk for hypophosphataemia.

4.4. Oral Iron Substitution

Utilisation of oral iron for repletion of deficient iron in patients with HF was specifically evaluated in the 16-week, single, randomised, double-blind, placebo-controlled IRONOUT HF clinical trial. This study assessed the effect of oral iron polysaccharide supplementation at a high dose on exercise capacity among patients with HFrEF (LVEF < 40%) and iron deficiency. Compared with placebo, high-dose oral iron polysaccharide failed to increase exercise capacity, with no significant improvement in the primary endpoint of peak oxygen

consumption (peak VO_2) or in 6 MWT distance over 16 weeks. The study also showed that oral iron polysaccharide therapy provided negligible recovery of stored iron among patients treated with oral iron therapy. Overall, the IRONOUT HF study findings demonstrated that supplementation with oral iron polysaccharide is not an effective strategy for iron deficiency treatment in patients with HFrEF, and consequently the 2021 ESC HF guidelines do not recommend oral iron use in patients with HF.

4.5. Which Patients with Heart Failure Should Receive IV Iron?

FCM treatment benefit has been confirmed by multiple clinical trials in HFrEF. The FAIR-HF, CONFIRM-HF and EFFECT-HF studies involved patients with stable CHF and NYHA class II/III who had a LVEF ≤ 45%. The AFFIRM-AHF study involved patients with iron deficiency who had an LVEF < 50% and had stabilised following an episode of AHF. A series of prespecified subgroup analyses of the AFFIRM-AHF study showed a consistent effect of FCM on the composite primary outcome across multiple subgroups. While there were interesting observations in terms of the rate ratios when patients were stratified by chronic kidney disease stage, HF aetiology, and HF history, subgroup analyses are of limited power, and therefore, no definitive conclusions can be made on the basis of the subgroup analyses of the AFFIRM-AHF study.

Little is known about iron deficiency in HF with preserved ejection fraction (HFpEF), and a treatment benefit with IV iron has not been determined in patients with HFpEF since these patients were excluded from previous trials. The aim of the FAIr-HFpEF clinical trial, which is currently underway, is to assess the safety and efficacy of IV iron in patients with HFpEF who are iron deficient with or without anaemia.

Table 2. Ongoing randomised controlled studies assessing the effect of treatment with IV iron on mortality and morbidity outcomes among patients with HF and iron deficiency.

Study Name	Study Design and Duration	Patient Population/Key Inclusion Criteria	IV Iron Intervention/Dose	Primary Endpoint
FAIR-HF2	Double-blind, parallel-group, randomised, placebo-controlled trial	1200 patients with HFrEF Key inclusion criteria: • - Age ≥18 years • - CHF for ≥12 months • - Iron deficiency	1000 mg FCM followed by optional 500–1000 mg within the first 4 weeks (up to 2000 mg), followed by administration of 500 mg FCM Q4M, unless Hb >16.0 g/dL or ferritin >800 µg/L	Combined rate of HF hospitalisations and CV deaths after ≥12 months of follow-up
FAIR-HFpEF	Single-blind, parallel-group, randomised, placebo-controlled trial	200 patients with HFpEF Key inclusion criteria: • - Age ≥18 years • - LVEF ≥ 45% • - Ambulatory ≥7 days with NYHA class II/III • - Diuretic treatment • -	750 mg FCM given as an infusion over 15 min in 100 mL NaCl	The change in 6-min walking distance measured in meters from baseline to end of study

		Atrial fibrillation in 2 out of 4 patients • - Either hospitalized with an HF diagnosis within 1 year of randomisation or with sinus rhythm and increased plasma natriuretic peptides • - Hb >9.0 g/dL and ≤14.0 g/dL • - Iron deficiency (ferritin <100 µg/L or TSAT <20% when ferritin 100–299 µg/L)		
HEART-FID	Double-blind, parallel-group, randomised (1:1), placebo-controlled trial	3068 patients with stable HFrEF Key inclusion criteria: • - Age ≥18 years • - Stable HF (NYHA class II–IV) on optimal background therapy	FCM two undiluted bolus doses (15 mg/kg bw) seven days apart to a maximum 750 mg single dose of and a maximum 1500 mg combined dose Q6M as required by iron indices	Composite of: • - Incidence of death after 1 year • - Incidence of hospitalisation for HF after 1 year • -

		• - LVEF ≤ 40% • - Iron deficiency (ferritin <100 µg/L or TSAT <20% when ferritin 100 to 300 µg/L) • - Either documented hospitalisation for HF in the past year prior to randomisation OR elevated NT-proBNP within 90 days prior to randomisation		Change in 6 MWT distance at 6 months
IRONMAN	Open-label, randomised, standard of care-controlled trial	1300 patients Key inclusion criteria: • - Age ≥18 years • - LVEF < 45% within the previous 2 years using any conventional imaging modality • - NYHA class II–IV • -	Iron (III) isomaltoside 1000	CV mortality or hospitalisation for worsening HF

		Iron deficiency: ferritin <100 ug/L and/or TSAT < 20% • - Evidence of high risk HF with expectation of survival to discharge including hospitalisation for HF currently or within the past 6 months, OR outpatients in atrial fibrillation with NT-proBNP >1000 ng/L or in sinus rhythm with NT-proBNP >250 ng/L (or BNP 300 pg/mL or >75 pg/mL, respectively)		

6 MWT, 6-min walk test; bw, body weight; CHF, chronic heart failure; CV, cardiovascular; FCM, ferric carboxymaltose; Hb, haemoglobin; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro b-type natriuretic peptide; NYHA, New York Heart Association; Q4M, every four months; Q6M, every six months; TSAT, transferrin saturation.

It should also be noted that parenteral iron must be used cautiously in cases with acute or chronic infection, asthma, atopic allergies or eczema. Additionally, in patients with ongoing

bacteraemia, it is recommended that IV FCM treatment should be stopped. Furthermore, a benefit–risk assessment should be carried out in patients who have a chronic infection which considers erythropoiesis suppression.

4.6. How to Administer IV Ferric Carboxymaltose and Monitor Patients after Treatment

As previously described, administration of IV FCM treatment is based on the patient's iron need calculated using their weight and Hb. FCM can be administered by IV injection as a slow undiluted bolus (at a rate of 100 mg per minute, or 1000 mg over 15 min), or an infusion that requires dilution. As an infusion, FCM should not be over-diluted to ensure its stability is maintained. The maximum recommended cumulative FCM dose is 1000 mg of iron equivalent to 20 mL FCM per week. IV iron should only be administered in the immediate vicinity of staff trained to assess and treat anaphylactic reactions, and in a location where full resuscitation facilities are available. Following every IV iron injection, observation of the patient for any adverse effects is required for a minimum of 30 min.

Iron status should then be re-assessed after three months following iron replacement and further repletion provided as required. As indicated, patients should also be evaluated for loss of blood. It is important to avoid early re-assessment of iron status (i.e., occurring within four weeks of the administration of IV iron) since ferritin markedly increases following such administration, and therefore ferritin levels should not be used early on to indicate iron status. In agreement with the 2021 ESC HF guidelines, this working group recommends periodically and regularly evaluating iron deficiency and anaemia in all patients with HF as part of clinical evaluation (i.e., one to two times per year, depending on the severity of iron deficiency and HF). Anaemia and iron deficiency should also be evaluated when HF is decompensated, or when symptoms continue even though a patient has received optimised background treatment for HF. IV iron should then be administered as needed.

4.7. Evidence for Erythropoiesis-Stimulating Agent Therapy

The 2021 ESC HF guidelines state that in HF, erythropoiesis-stimulating agent (ESA) treatment of anaemia is not recommended in cases where there are no other indications for this therapy (recommendation class III). This was determined on the basis of findings from a sizeable randomised clinical trial showing that darbepoetin-alpha did not reduce the risk of HF

hospitalisations or all-cause mortality, and the risk of thromboembolic events was found to be increased in patients with HFrEF and mild-to-moderate anaemia.

4.8. Ongoing Research on IV Irons in HF

Prospective, randomised, controlled clinical trials are currently ongoing to investigate the benefit of IV iron on mortality and morbidity outcomes among patients with HF who have iron deficiency, and are expected to read out within the next two years. These include the FAIR-HF2, FAIR-HFpEF, HEART-FID , IRONMAN trials, which are evaluating the effects of IV iron vs. placebo among iron-deficient patients with stable CHF.

5. Trials of Intravenous Iron Supplementation in HF[2]

Iron is an essential nutrient that is necessary for oxygen delivery and metabolic homeostasis, and patients with HFrEF are at risk of developing absolute and functional ID. There are now 4 randomized clinical trials that have evaluated the effect of intravenous FCM in patients with ID and HFrEF. All 4 trials were relatively small and short-term, and the majority of patients were White and European. The FAIR-HF, CONFIRM-HF, and EFFECT-HF trials collectively demonstrated that intravenous FCM in ambulatory patients with HFrEF and ID improves symptoms, as measured by functional capacity (6-minute walk test), New York Heart Association classification, and subjective assessment. The most recent trial, AFFIRM-AHF, demonstrated that intravenous FCM modestly reduces total HF hospitalizations in a high-risk population of patients with ID admitted for acute HF. No effect on cardiovascular death was seen in pre– or post–coronavirus disease 2019 (COVID-19) analyses.

All 4 trials defined ID in HFrEF using the criteria of serum ferritin <100 ng/mL (absolute ID) or serum ferritin 100 to 300 ng/mL with serum transferrin saturation <20% (functional ID), regardless of the presence or absence of anemia. It is interesting that these criteria were not derived from patients with HFrEF but rather adopted from patients with ID and chronic kidney disease (CKD). However, CKD is associated with uremia-mediated inflammation, increased levels of hepcidin, and decreased renal production of erythropoietin requiring erythropoiesis-stimulating agents, none of which are seen in HFrEF. Given the differences in ID pathophysiology between CKD and HFrEF, it is unclear whether these serum markers

accurately diagnose ID in HFrEF patients, particularly functional ID. In addition, patients with HFrEF and coexisting CKD have complex iron metabolism, which requires additional study. Indeed, in FAIR-HF and CONFIRM-HF, the median ferritin levels were 39 ng/mL and 46 ng/mL respectively, both significantly lower than the ferritin cutoff of 100 ng/mL. In AFFIRM-AHF, the benefits of intravenous FCM were also more pronounced in patients with ferritin <100 ng/mL.

These trials demonstrate that ID is an important comorbidity in HFrEF and that treatment of true ID in HFrEF improves symptoms and modestly reduces hospitalizations. Although these are important end points, HFrEF therapies are most impactful when the therapy improves survival and significantly reduces nonfatal HF events. In addition, it remains to be seen whether intravenous iron improves myocardial function or alters the natural history of HFrEF.

6. Potential Safety Concerns with Intravenous Iron Therapies[3]

The symptomatic benefits of intravenous iron supplementation in patients with HFrEF with true ID should be balanced with the potential safety concerns associated with iron excess. Although oral iron absorption is tightly regulated by the effects of hepcidin and rarely leads to iron excess, intravenous iron introduces large amounts of non–transferrin-bound iron, which bypasses regulatory mechanisms and can cause iron overload.

The accumulation of unbound iron can be detrimental to cells and tissues by catalyzing reactive oxygen species. In rodent models, intravenous iron infusions were associated with increased oxidative stress and progression of atherosclerosis. In healthy human volunteers, intravenous iron resulted in transient endothelial dysfunction and biomarkers of oxidative stress. The toxic effects of intravenous iron may be particularly important to consider in the setting of (1) infection, because many infectious agents thrive on iron, and (2) patients with coronary artery disease with vulnerable or high-risk plaques, in whom the pro-oxidative effects of iron may theoretically promote plaque rupture.

It is also important to note that although certain patients with HFrEF may be systemically ID, they may simultaneously have increased myocardial iron. Reductions in myocardial iron reduce oxidative stress and cardiotoxicity in rodent models of cardiac injury, suggesting that targeted therapies that replenish systemic iron yet specifically reduce myocardial iron may be

beneficial. Questions also remain about the long-term safety of intravenous iron in HFrEF, particularly in patients who receive repeated intravenous iron infusions. The follow-up periods of the 4 trials mentioned ranged from only 16 to 52 weeks, and data are lacking on the long-term effects of intravenous iron on ventricular remodeling, inflammation, and survival.

References:

1. Sindone A, Doehner W, Manito N, et al. Practical Guidance for Diagnosing and Treating Iron Deficiency in Patients with Heart Failure: Why, Who and How?.*J Clin Med*. 2022;11(11):2976.
2. Sawicki KT, Ardehali H. Intravenous Iron Therapy in Heart Failure With Reduced Ejection Fraction: Tackling the Deficiency. Circulation. 2021;144:253–55.

Survey Form

1) In your clinical practise, how many patients with heart failure do you treat in a month?

a) <5
b) 5-10
c) 10-15
d) >15

2) In your clinical practise, which test is routinely done to diagnose a patient with heart failure?

a) ECG
b) NT pro-BNP
c) CT, MRI

3) What is the most common type of heart failure observed in your clinical practise?

a) Heart Failure with preserved Ejection Fraction (HFpEF)
b) Heart Failure with mildly reduced Ejection Fraction (HFmrEF)
c) Heart Failure with reduced Ejection Fraction (HFrEF)

4) In your clinical practise, do you consider treating iron deficiency in patients with Heart Failure?

a) Yes
b) No

5) In your clinical practice, what percentage of patients with Heart Failure are diagnosed with Iron Deficiency?

a) <25%
b) 25-50%
c) 51-75%
d) >75%

6) In your clinical practice, when do you initiate IV Iron Therapy in a patient with HF?

a) If Hb is less than normal
b) If patient's S. Ferritin is < 100 microgram/l, and normal Hb
c) If S. Ferritin is 100 - 299 microgram/l when Transferrin Saturation (TSAT) is <20%, and normal Hb

7) In your opinion, what do you consider to be the benefits of managing iron deficiency in patients with Heart Failure?

a) Alleviate Heart Failure Symptoms
b) Improve quality of life
c) Reduce the risk of Heart failure hospitalization

8) Which IV iron formulation do you prefer for treatment of iron deficiency in patients with Heart Failure?

a) Ferric Carboxymaltose
b) Iron Sucrose
c) Iron Isomaltoside
d) Iron derisomaltose

9) In your opinion, what do you think is the primary reason for lesser adoption of iron supplementation in patients with Heart Failure?

a) Lack of Awareness to look for Iron Deficiency in HF patients
b) Undiagnosed iron deficiency
c) Frailty of the patients with heart failure

10) In your clinical practise, what percent of patients with heart failure achieved symptomatic relief following IV iron supplementation?

a) 10-20%
b) 20-50%
c) >50%

11) In what type of heart failure would you prefer using IV iron supplementation, for alleviating symptoms of heart failure?

a) HFpEF
b) HFmrEF
c) HFrEF

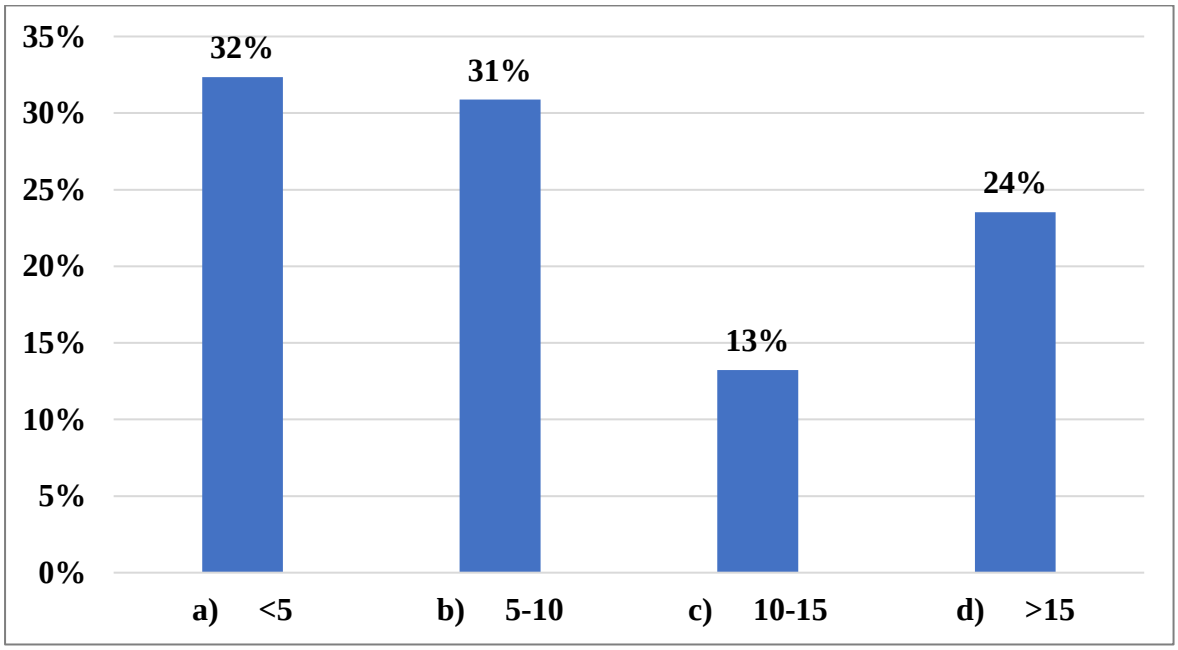
12) How would you rate the improvement in quality of life of a patient with heart failure and iron deficiency after IV iron supplementation?

a) No change
b) Average Improvement
c) Good Improvement
d) Very Good Improvement

Survey Findings

1) In your clinical practise, how many patients with heart failure do you treat in a month?

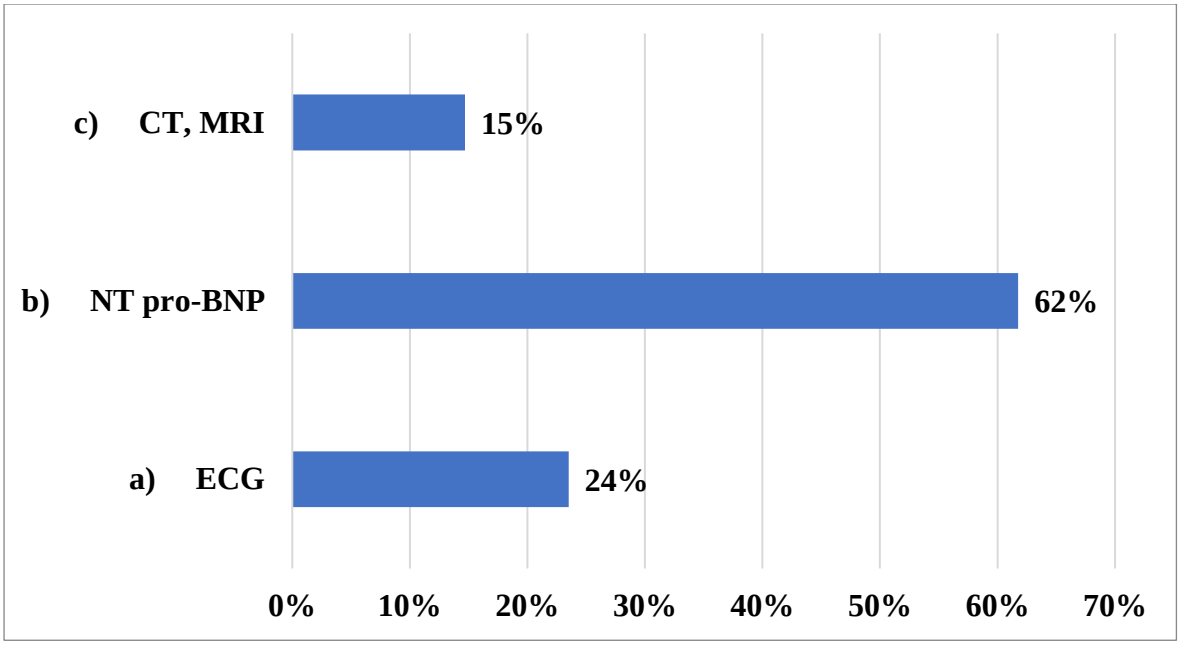
a) <5
b) 5-10
c) 10-15
d) >15



In the clinical practice of 32% of doctors, they treat <5 patients with heart failure in a month.

2) In your clinical practise, which test is routinely done to diagnose a patient with heart failure?

a) ECG
b) NT pro-BNP
c) CT, MRI



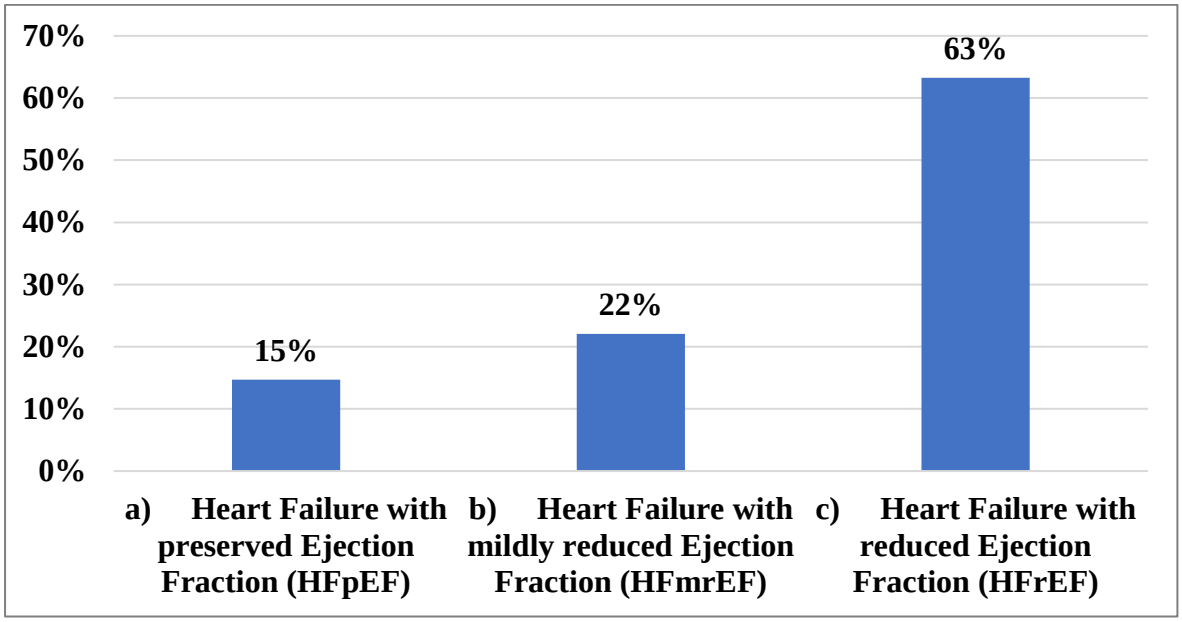
According to majority of doctors, NT pro-BNP test is routinely done to diagnose a patient with heart failure.

3) What is the most common type of heart failure observed in your clinical practise?

a) Heart Failure with preserved Ejection Fraction (HFpEF)

b) Heart Failure with mildly reduced Ejection Fraction (HFmrEF)

c) Heart Failure with reduced Ejection Fraction (HFrEF)

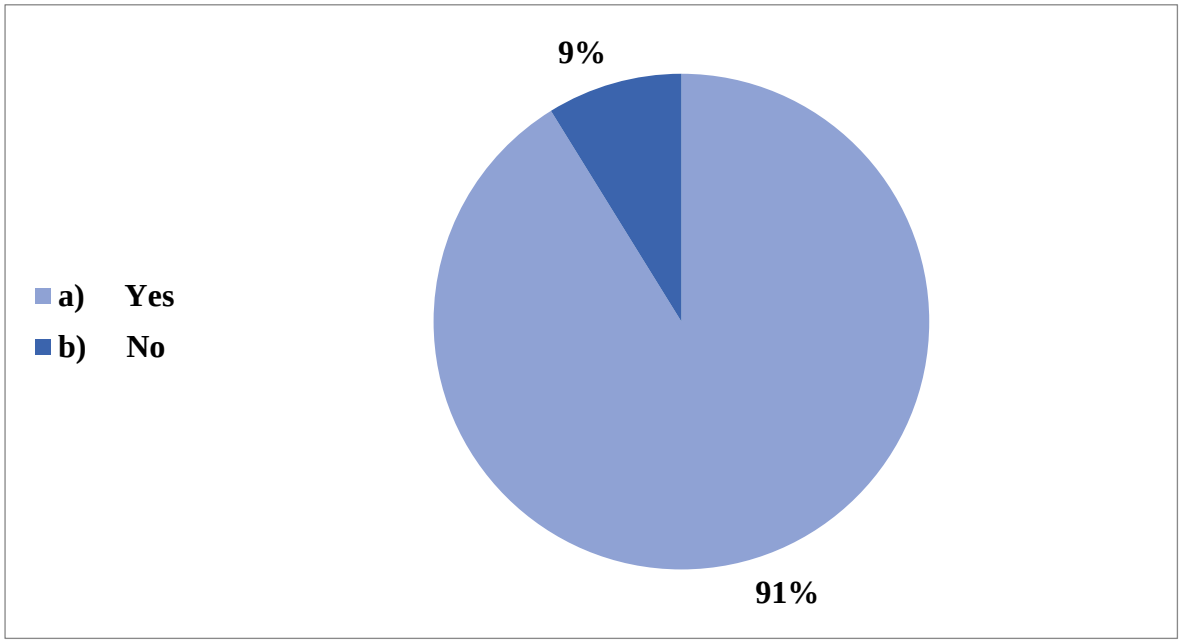


According to 63% of doctors, the most common type of heart failure observed in their clinical practice is heart failure with reduced Ejection Fraction (HFrEF).

4) In your clinical practise, do you consider treating iron deficiency in patients with Heart Failure?

a) Yes

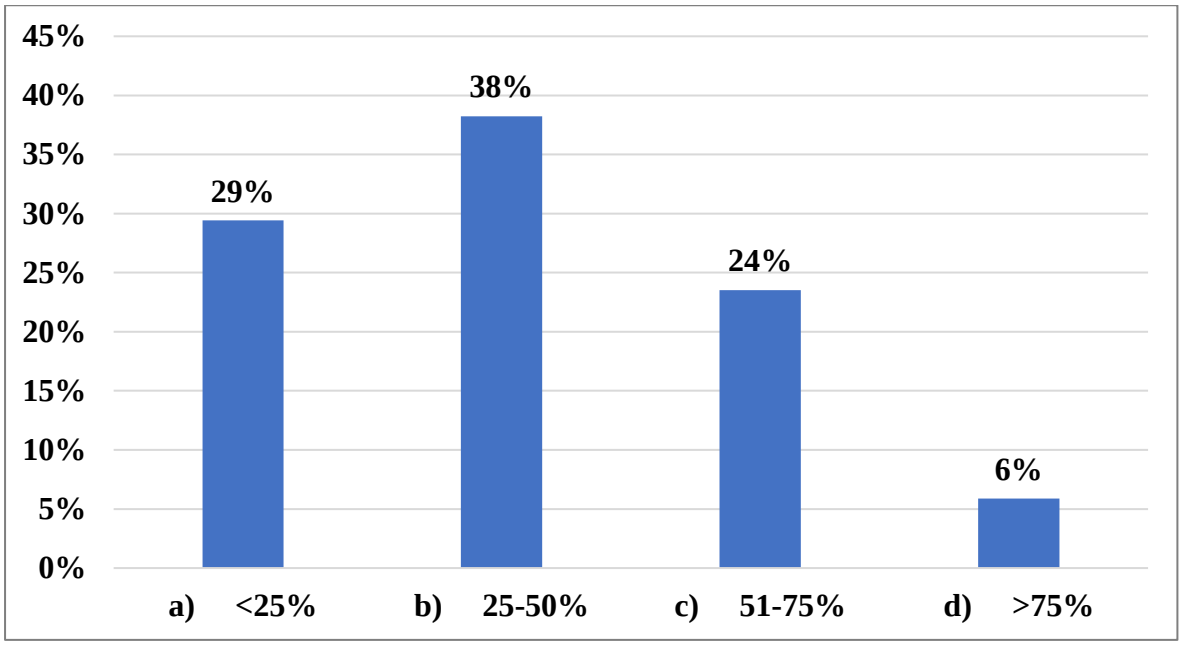
b) No



Majority of doctors, 91%, consider treating iron deficiency in patients with heart failure.

5) In your clinical practice, what percentage of patients with Heart Failure are diagnosed with Iron Deficiency?

a) <25%
b) 25-50%
c) 51-75%
d) >75%



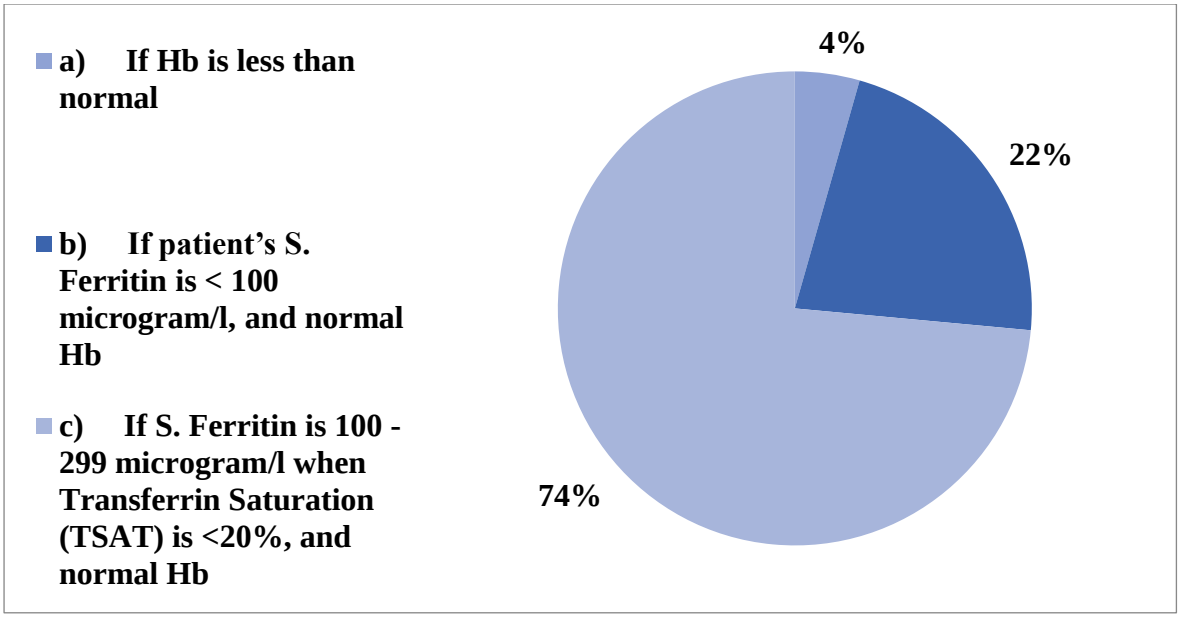
According to 38% of doctors, 25-30% of patients with heart failure are diagnosed with iron deficiency.

6) In your clinical practice, when do you initiate IV Iron Therapy in a patient with HF?

a) If Hb is less than normal

b) If patient's S. Ferritin is < 100 microgram/l, and normal Hb

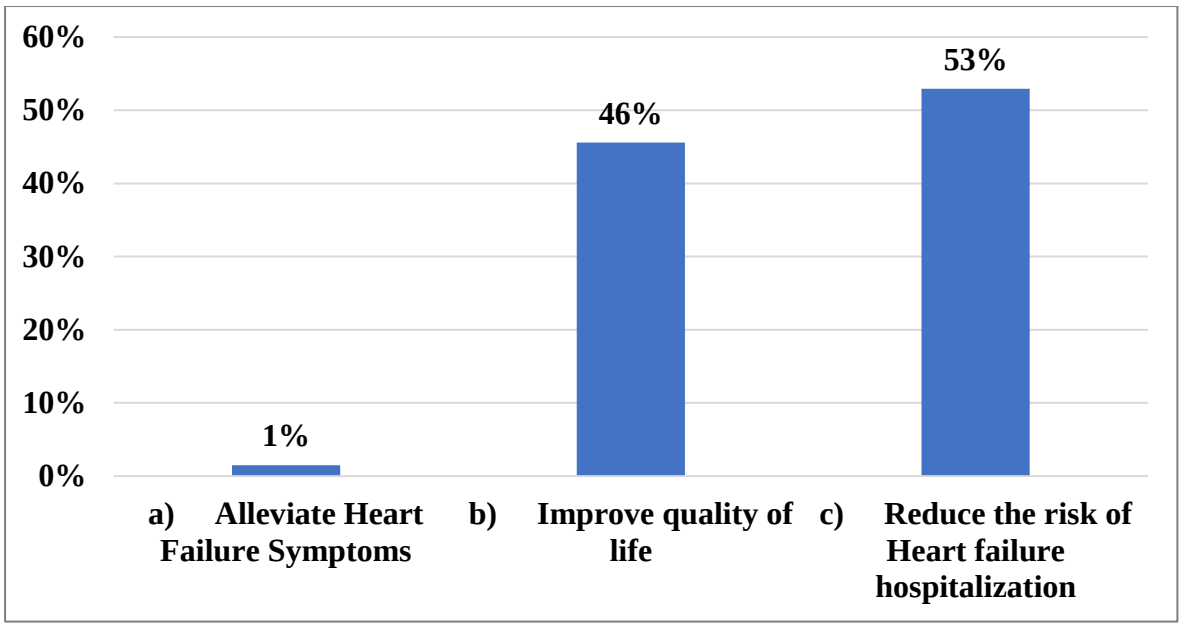
c) If S. Ferritin is 100 - 299 microgram/l when Transferrin Saturation (TSAT) is <20%, and normal Hb



Majority of doctors (74%) initiate IV Iron Therapy in a patient with HF if S. Ferritin is 100 - 299 microgram/l when Transferrin Saturation (TSAT) is <20%, and normal Hb.

7) In your opinion, what do you consider to be the benefits of managing iron deficiency in patients with Heart Failure?

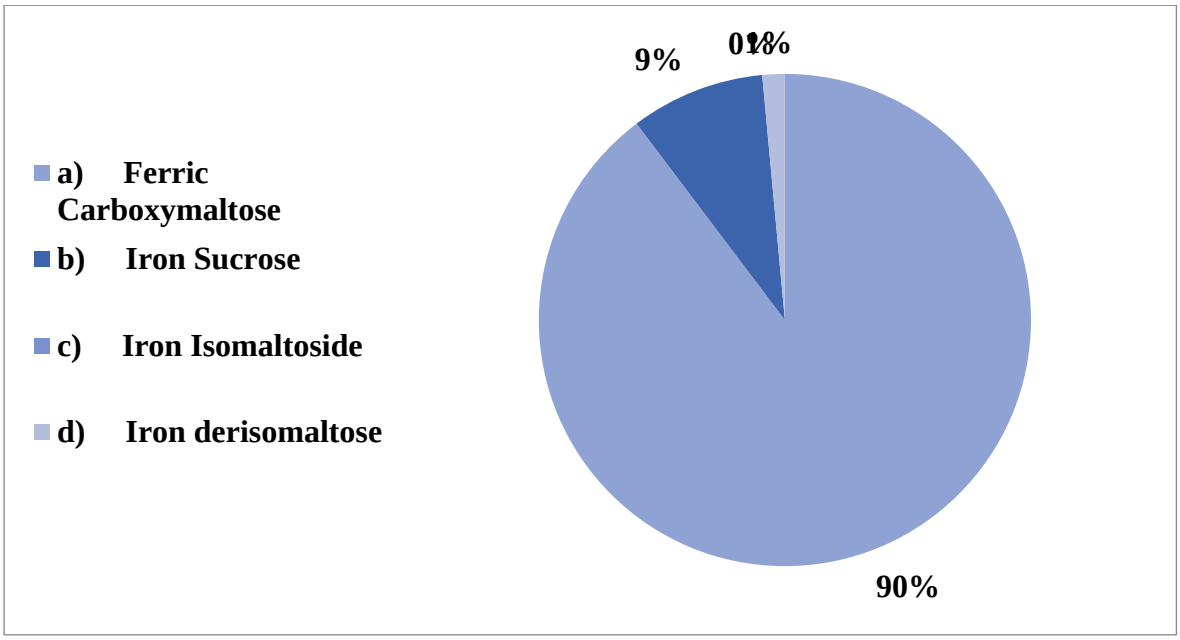
a) Alleviate Heart Failure Symptoms
b) Improve quality of life
c) Reduce the risk of Heart failure hospitalization



53% of doctors consider reducing the risk of heart failure hospitalization to be the benefits of managing iron deficiency in patients with heart failure.

8) Which IV iron formulation do you prefer for treatment of iron deficiency in patients with Heart Failure?

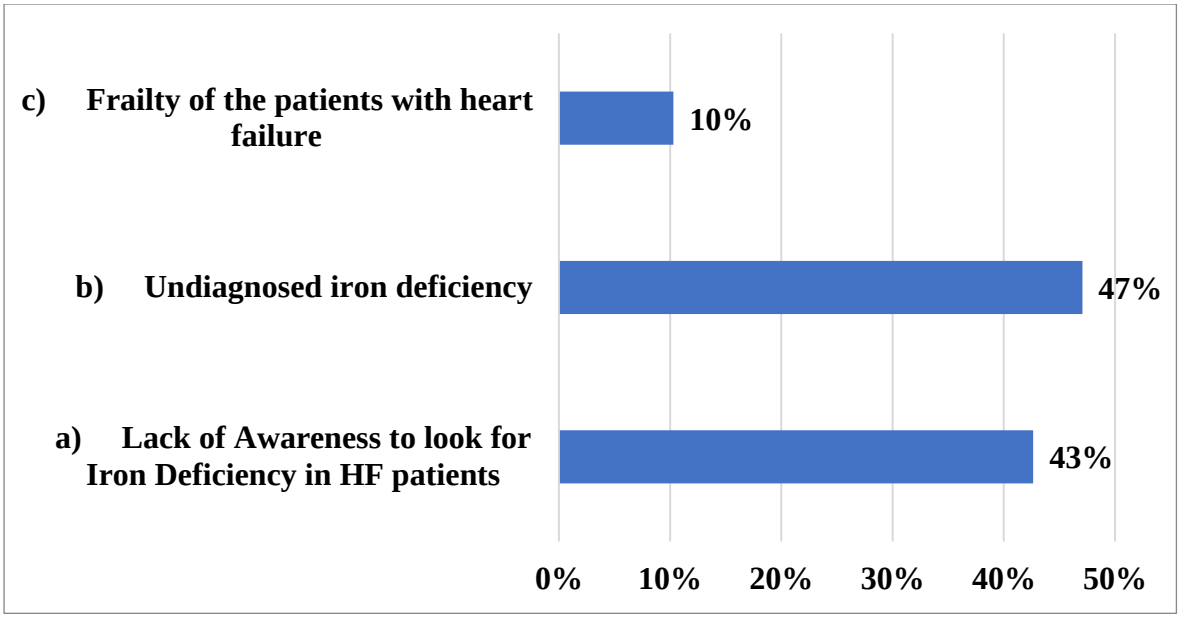
a) Ferric Carboxymaltose
b) Iron Sucrose
c) Iron Isomaltoside
d) Iron derisomaltose



Majority of doctors prefer Ferric Carboxymaltose for treatment of iron deficiency in patients with heart failure.

9) In your opinion, what do you think is the primary reason for lesser adoption of iron supplementation in patients with Heart Failure?

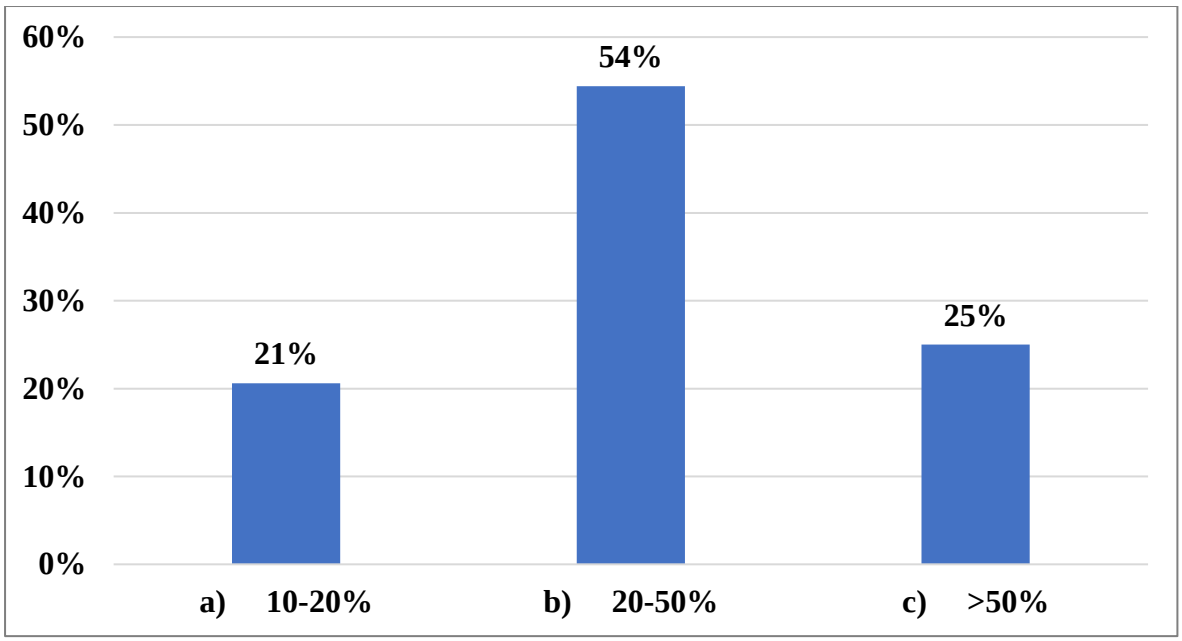
a) Lack of Awareness to look for Iron Deficiency in HF patients
b) Undiagnosed iron deficiency
c) Frailty of the patients with heart failure



47% of doctors think undiagnosed iron deficiency think is the primary reason for lesser adoption of iron supplementation in patients with heart failure.

10) In your clinical practise, what percent of patients with heart failure achieved symptomatic relief following IV iron supplementation?

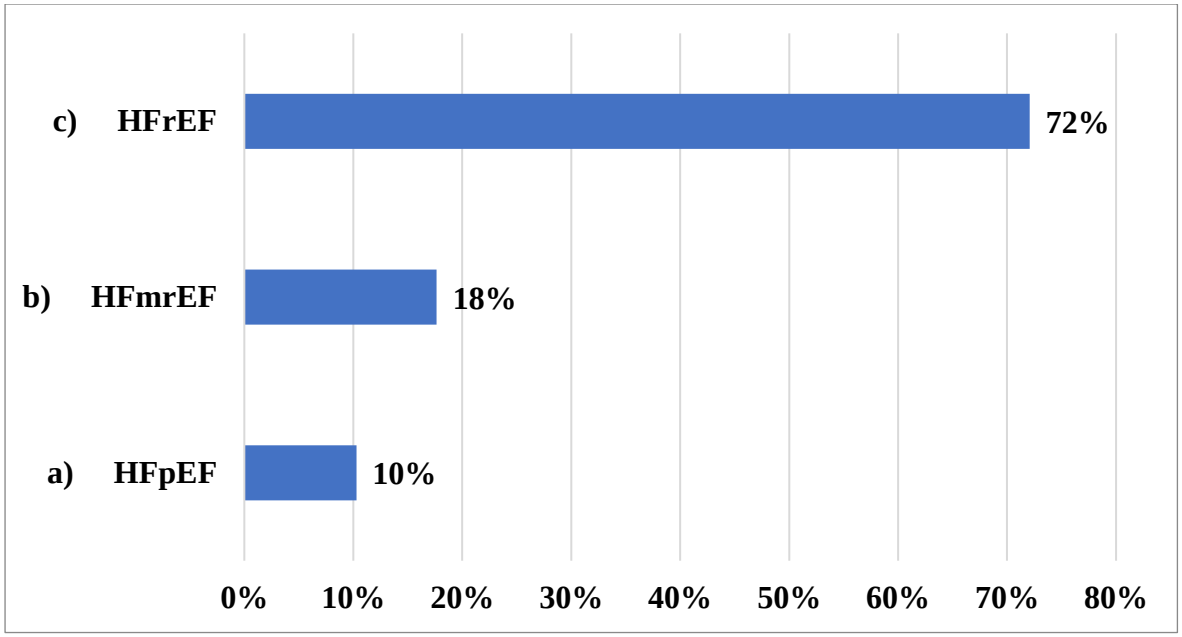
a) 10-20%
b) 20-50%
c) >50%



According to 54% of doctors, 20-50% of patients with heart failure achieved symptomatic relief following IV iron supplementation.

11) In what type of heart failure would you prefer using IV iron supplementation, for alleviating symptoms of heart failure?

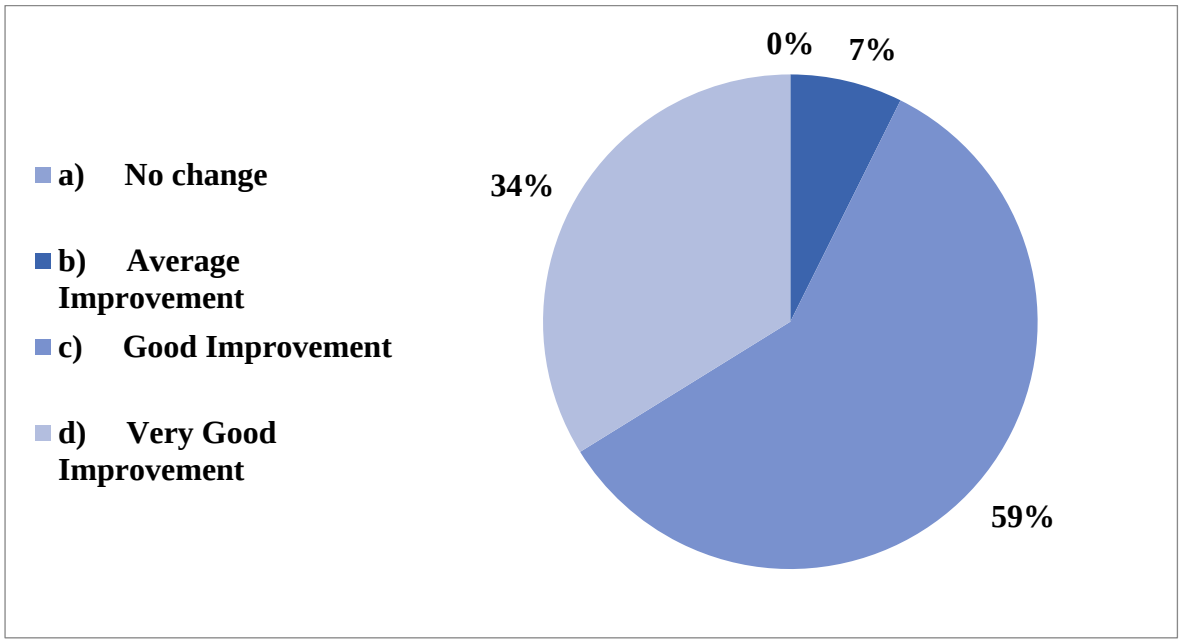
a) HFpEF
b) HFmrEF
c) HFrEF



Majority of doctors would prefer HFrEF type of heart failure for using IV iron supplementation, for alleviating symptoms of heart failure.

12) How would you rate the improvement in quality of life of a patient with heart failure and iron deficiency after IV iron supplementation?

a) No change
b) Average Improvement
c) Good Improvement
d) Very Good Improvement



59% of doctors rate the improvement in quality of life of a patient with heart failure and iron deficiency after IV iron supplementation as good.

Summary

- In the clinical practice of 32% of doctors, they treat <5 patients with heart failure in a month.
- According to majority of doctors, NT pro-BNP test is routinely done to diagnose a patient with heart failure.
- According to 63% of doctors, the most common type of heart failure observed in their clinical practice is heart failure with reduced Ejection Fraction (HFrEF).
- Majority of doctors, 91%, consider treating iron deficiency in patients with heart failure.
- According to 38% of doctors, 25-30% of patients with heart failure are diagnosed with iron deficiency.
- Majority of doctors (74%) initiate IV Iron Therapy in a patient with HF if S. Ferritin is 100 - 299 microgram/l when Transferrin Saturation (TSAT) is <20%, and normal Hb.
- 53% of doctors consider reducing the risk of heart failure hospitalization to be the benefits of managing iron deficiency in patients with heart failure.
- Majority of doctors prefer Ferric Carboxymaltose for treatment of iron deficiency in patients with heart failure.
- 47% of doctors think undiagnosed iron deficiency think is the primary reason for lesser adoption of iron supplementation in patients with heart failure.
- According to 54% of doctors, 20-50% of patients with heart failure achieved symptomatic relief following IV iron supplementation.
- Majority of doctors would prefer HFrEF type of heart failure for using IV iron supplementation, for alleviating symptoms of heart failure.
- 59% of doctors rate the improvement in quality of life of a patient with heart failure and iron deficiency after IV iron supplementation as good.

Consultant Opinion

Market Opportunities:

The survey reveals that a significant proportion of doctors treat a relatively low number of heart failure patients each month. This indicates a potential market opportunity for pharmaceutical companies to develop and market innovative treatments for heart failure that can address the needs of a broader patient population.

Value for Healthcare Professionals:

The routine use of the NT pro-BNP test for diagnosing heart failure highlights its value for healthcare professionals in accurately assessing and managing the condition. Continued education and training on the appropriate use of diagnostic tests can further enhance the diagnostic process and improve patient outcomes.

Adverse Effect Management:

Adverse effects associated with iron deficiency treatment, such as iron supplementation, need to be carefully managed to optimize patient safety and tolerability. Healthcare professionals should be educated on effective adverse effect management strategies, and patients should be closely monitored for any adverse reactions.

Withdrawal Management:

Strategies for managing iron deficiency in patients with heart failure, such as initiating IV iron therapy based on specific laboratory parameters, should be standardized to ensure consistent and effective treatment outcomes. Clear guidelines and protocols can assist healthcare professionals in making informed decisions regarding iron deficiency management.

Market Positioning:

Pharma companies can position iron supplementation products, such as Ferric Carboxymaltose, as preferred treatment options for iron deficiency in patients with heart failure. Emphasizing the benefits of these treatments, such as reducing the risk of heart failure hospitalization and improving quality of life, can help differentiate them in the market.

Personalized Treatment Decisions:

Tailoring iron deficiency management strategies to the specific type of heart failure observed in patients, such as heart failure with reduced ejection fraction (HFrEF), can optimize treatment outcomes and improve patient adherence. Healthcare professionals should consider individual patient characteristics and disease severity when making treatment decisions.

Improving Patient Outcomes:

Improving patient outcomes in heart failure and iron deficiency management requires a multifaceted approach, including routine screening, early diagnosis, personalized treatment, and patient education. Collaboration between healthcare professionals and pharmaceutical companies can help develop comprehensive care pathways that prioritize patient-centered care and optimize treatment outcomes.

In conclusion, there are significant opportunities to improve patient care in the management of heart failure and iron deficiency by focusing on standardized diagnostic and treatment protocols, effective adverse effect management, and personalized treatment decisions. Pharma companies can leverage these insights to develop targeted interventions and innovative solutions that address the unmet needs of patients with heart failure and iron deficiency, ultimately leading to improved patient outcomes and quality of life.

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

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Weston Medical Education Foundation of India

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