

OPEN ACCESS

ISSN (O) 3023-3593 | (Print: 3023-3585)

RESEARCH ARTICLE



Sustained Haematological and Cardiac Responses Following Intravenous Ferric Carboxymaltose in Iron-Deficient Heart Failure with Reduced Ejection Fraction: A 12-Month Prospective Observational Study

Durga Prasad Verma¹ | Avaneesh Shukla² | Padala Sai Venkatesh^{3*} | Nishant Kanodia⁴ **Abstract**

Introduction: Iron deficiency is a prevalent comorbidity in heart failure with reduced ejection fraction (HFrEF), and significant in causing anaemia, reducing exercise performance, and heart failure pathology. Ferric carboxymaltose (FCM) intravenously administered can restore iron levels and is not dependent on the digestive system. The study aim to analyse the changes in various physiological parameters following the administration of FCM.

Method: The study was a prospective observational study was conducted among 103 adult patients of chronic symptomatic HFrEF (NYHA II-III, LVEF <40%) with iron deficiency at HIMS, Uttar Pradesh. Patients were underwent with the FCM through intravenous route along with the conventional treatment for heart failure. The hematological, iron, cardiac, and renal markers were measured at baseline and after 3, 6, and 12 months of follow-up.

Results: The result findings showed the mean values of haemoglobin at baseline were 10.0 ± 1.5 g/dL, ferritin 59 ± 41 ng/mL, TSAT $17.2 \pm 6.3\%$, and LVEF $31.7 \pm 4.5\%$. Following 12 months of therapy, haemoglobin increase to 12.2 ± 1.2 g/dL, ferritin 293 ± 75 ng/mL, TSAT $30.1 \pm 6.5\%$, and LVEF $41.5 \pm 5.8\%$ (all $p < 0.001$). NT-proBNP reduced from 1905 to 1620 pg/mL, and NYHA III patients from 41 to 15.

Conclusion: The study concluded that the FCM therapy was related with the improved iron status, haemoglobin, LVEF, NT-proBNP, and functional class for 12 months, without the reduction in the renal parameters.

Key words: Heart failure with reduced ejection fraction, Ferric carboxymaltose, Iron deficiency, Transferrin saturation, Left ventricular ejection fraction

1 | INTRODUCTION

In patients with HFrEF, there is ongoing neurohormonal activation, myocardial dysfunction, increasing filling pressures of the ventricles, and decreasing exercise capacity. Patients with HFrEF are still susceptible to recurrent congestion,

functional deterioration and hospitalisation despite improvement in guideline-directed medical therapy. Iron deficiency has become a significant, non-haemoglobin-related, potentially modifiable comorbidity in this group of patients, due to its impact on cellular oxygen use, mitochondrial energy generation, and skeletal muscle oxidative metabolism,

¹ Assistant professor, Department of Medicine ,Hind Institute of Medical Sciences ,Ataria, Sitapur Uttar Pradesh, India .

² Assistant professor ,Department of Pediatrics,Hind Institute of Medical Sciences, Ataria, Sitapur, Uttar Pradesh India .

³ PG Resident , Department of Medicine, Hind Institute of Medical Sciences ,Ataria Sitapur, Uttar Pradesh India .

⁴ Professor,Department of Medicine Hind Institute of Medical Sciences Ataria Sitapur, Uttar Pradesh, India.

Address correspondence to: Padala Sai, Venkatesh, PG Resident , Department of Medicine, Hind Institute of Medical Sciences ,Ataria Sitapur, Uttar Pradesh India ,

Sustained Haematological and Cardiac Responses Following Intravenous Ferric Carboxymaltose

resulting in an independent contribution to exercise intolerance [1,2]. Guidelines for heart failure list ID as consistent with either a serum ferritin level $<100 \mu\text{g/L}$ or a ferritin level $100\text{--}299 \mu\text{g/L}$ and a transferrin saturation $<20\%$ [2,3]. This is especially important in heart failure, where inflammation can lead to sequestration of iron in addition to the relative reduction in absolute iron stores.

ID is common among people with CHF and is more frequent as the severity of CHF progresses. Importantly, patients with or without overt anaemia may have consequences. Iron-dependent mitochondrial enzymes are involved in oxidative phosphorylation, energy production in myocytes, and oxygen transport; therefore, decreased availability of iron in the cell is likely to affect the performance of the myocardium and skeletal muscle before a significant decrease in haemoglobin level is detected clinically [1,4]. ID has also been reported to be associated with decreased functional capacity, poor health-related quality of life, and risk of adverse clinical events in HFrEF. These have led the focus in treatment from correcting anaemia to restoring systemic and tissue iron availability.

Oral iron replacement is modestly effective in the treatment of HFrEF. The IRONOUT-HF trial showed that oral Iron polysaccharide did not result in a significant improvement in exercise capacity, despite elevating some iron parameters in blood, which suggests that gastrointestinal absorption and iron utilisation are suboptimal in the inflammatory and haemodynamically complex setting of HF [5]. IV iron is thus an alternative, pharmacologically different, approach that avoids the intestinal absorption process and can quickly replace the available iron stores.

Ferric carboxymaltose, a stable intravenous iron formulation, has been well tested in the HFrEF and ID population. Treatment with FCM was shown to provide clinically relevant benefits in patient-reported global status, New York Heart Association functional class, 6-minute walk distance, and health-related quality of life in the FAIR-HF trial, both with and without anaemia [6]. The CONFIRM-HF study then continued these findings for 52 weeks, which showed that 6-minute walk distance continued to improve and that benefits were seen for NYHA class, fatigue and quality of life [7]. The results indi-

cated that iron repletion could have long-term beneficial functional effects beyond short-term correction of laboratory abnormalities.

The clinical value of IV iron has since been included in the current heart failure guidelines. The 2023 European Society of Cardiology focused update suggests using IV iron in symptomatic HFrEF or heart failure with mildly reduced ejection fraction to improve symptoms and quality of life, and that FCM or Ferric Derisomaltose may also be used to decrease the risk of heart failure hospitalisation [2,3]. But it is still unknown what the magnitude and stability of the haematological and cardiac responses will be in normal clinical use. Randomised trials have varied in patient selection, timing of treatment, baseline anaemia, severity of heart failure and definitions of heart failure outcomes. Further, the large HEART-FID trial failed to show that multiple doses of FCM improved its composite primary endpoint of death, heart failure hospitalisation and 6-minute walk distance, highlighting the difference between enhancing iron status or functional status and actual improvements in clinically relevant issues [8].

Therefore, a prospective observational 12-month follow-up study of FCM-treated patients with HFrEF and ID assumes clinical significance. Longitudinal monitoring of haemoglobin, ferritin, TSAT and cardiac or functional parameters can help to determine whether there are ongoing biological and clinical benefits after the early treatment phase beyond iron repletion. This real-world data can be used to help clarify the findings of the randomised trials by describing treatment response in normal clinical practice and determining the relationship between sustained iron availability and cardiac functional recovery.

2 | METHOD

Research design

The study was a prospective, observational design to analyse the haematological and cardiac responses which was followed by the intravenous ferric carboxymaltose among heart failure patients. The study was conducted in the Department of General Medicine, Hind Institute of Medical Sciences (HIMS), Mau, Ataria, Sitapur, Uttar Pradesh, India

for 12 months which was followed by the FCM therapy. The study selected 103 patients presented with the chronic heart failure admitted from the medicine outpatient clinics and medical/cardiology wards. Several predefined criteria were considered for the patient selection. Baseline and follow up evaluation include the hemoglobin, ferritin, TSAT, TIBC, LVEF, NT-proBNP, NYHA functional class, serum creatinine, and eGFR. Both verbal and informed consent required for the study.

Inclusion criteria

- Patients age should be more than 12 years of age of both of the gender
- Informed consent is required
- Patients with chronic symptomatic heart failure, NYHA class II or III were included
- Patients with LVEF <40% on transthoracic echocardiography were included
- Patients with the deficiency of iron on the basis of the reduction of the ferritin/serum iron, low TSAT, and/or elevated TIBC were included

Exclusion criteria

- Patients with LVEF $\geq 41\%$ including the HFmrEF (41–49%) and HFpEF ($\geq 50\%$) were excluded
- Patients those who were participated in the clinical trial within the previous 3 months
- Those who were with the intravenous iron therapy within the previous 4 weeks were excluded

Procedure

Patients were selected based on consent and specific criteria. All participants underwent with the baseline demographic, anthropometric, and clinical assessment, including age, gender, occupation, weight, BMI, blood pressure, NYHA functional class, and relevant comorbidities. Cardiac evaluation included transthoracic 2-D echocardiography for LVEF estimation and serum NT-proBNP measurement. Laboratory investigations included hemoglobin, MCV, serum ferritin, serum iron, TSAT, and TIBC were

performed and recorded. Patients continued with the standard guideline-directed medical therapy for HFrEF, while those meeting the biochemical criteria for iron deficiency received intravenous ferric carboxymaltose (FCM). The total iron deficit was estimated by the use of the modified Ganzoni formula, and FCM was administered at 500–1000 mg per infusion under hospital supervision with vital-sign monitoring and post-infusion observation. Follow-up assessments were performed at 3, 6, and 12 months, repeating hematological, iron, cardiac, and NYHA parameters. All information was recorded in a standardized master chart.

Statistical analysis

Means $\pm$ SD/median (IQR) and frequency distribution were used to demonstrate the data of continuous and categorical variables respectively. Parametric or non-parametric tests were used to compare pre and post treatment values of variables. Categorical variables were analysed by the use of the Chi-square test. Multivariate regression analysis was performed. P value less than 0.05 was maintained for statistical significance. Statistical analysis was conducted by SPSS version 27.

3 | RESULTS

howed that largest proportion of patients were noted in the 50–59-year age group (31.1%), which was followed by 60–69 years (26.2%) and 40–49 years (20.4%), and 8.7% of cases were in the age group of 30–39 years. Males were 65.0% of the sample and females were 35.0%. 27.2% were farmers which were followed by the housewives (24.3%) and labourers (21.4%) and private employees reported for 12.6%. The distribution of BMI reported 59.2% with normal BMI, while 26.2% were overweight, 8.7% obese, and 5.8% underweight. 61.4 ± 10.0 kg was the mean value of body weight, with 60.6 kg as the median, within the range of 41.0–83.6 kg, which highlighted the variation of the body weight.

Figure 1 showed the distribution of the systolic blood pressure noted with the concentration of values between the 110 and 140 mmHg. 110–120 mmHg showed the highest rate of frequency, consisting of

27 participants (26.2%), which were followed by the 120–130 mmHg category along with 26 patients. 18 participants (17.5%) were in the 130–140 mmHg, while 13 participants (12.6%) were in the 100–110

Sustained Haematological and Cardiac Responses Following Intravenous Ferric Carboxymaltose

Table 1. Distribution of Study Participants According to Sociodemographic and Anthropometric Characteristics

Domain	Category / Parameter	Number (n)	Percentage (%) / Value
Age Group (years)	30–39	9	8.7
	40–49	21	20.4
	50–59	32	31.1
	60–69	27	26.2
	≥70	14	13.6
	Total	103	100
Gender	Male	67	65
	Female	36	35
	Total	103	100
Occupation	Farmer	28	27.2
	Laborer	22	21.4
	Housewife	25	24.3
	Private Employee	13	12.6
	Others	15	14.6
	Total	103	100
BMI Category	Underweight (<18.5)	6	5.8
	Normal (18.5–24.9)	61	59.2
	Overweight (25–29.9)	27	26.2
	Obese (≥30)	9	8.7
	Total	103	100
Weight (kg)	Mean	—	61.4
	Standard Deviation	—	10
	Median	—	60.6
	Range	—	41.0–83.6

mmHg. 10 participants (9.7%) were noted with systolic blood pressure in the range between 140 and 150 mmHg. 90–100 mmHg and 150–160 mmHg were observed with lowest frequencies including 6

(5.8%) and 3 (2.9%) patients. Systolic blood pressure was less than 130 mmHg among 57 participants (55.3%), while 31 participants (30.1%) showed the blood pressure above of 130 mmHg.

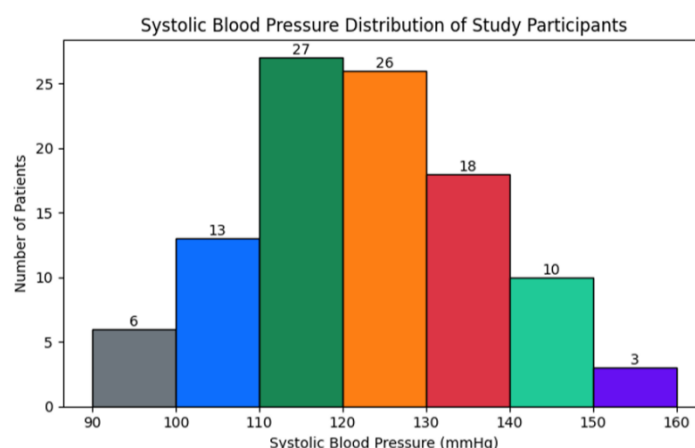


Fig. 1: Distribution of Study Participants According to Systolic Blood Pressure

Figure 2 showed the distribution of the NYHA functional class indicated that most of the study patients were in the Class II, including 62 participants (60.2%). 41 participants (39.8%) include in the

Class III. Most of the patients were in the Class II, while significant proportion showed Class III functional limitation. No patients were in the NYHA Classes I or IV. Difference was about 21 patients,

with Class II noted with $\frac{1}{2}$ times of the patients in the Class III. The figure suggested that all patients were categorized as NYHA Classes II and III, pro-

vide significant presentation of the functional limitation among the patients.

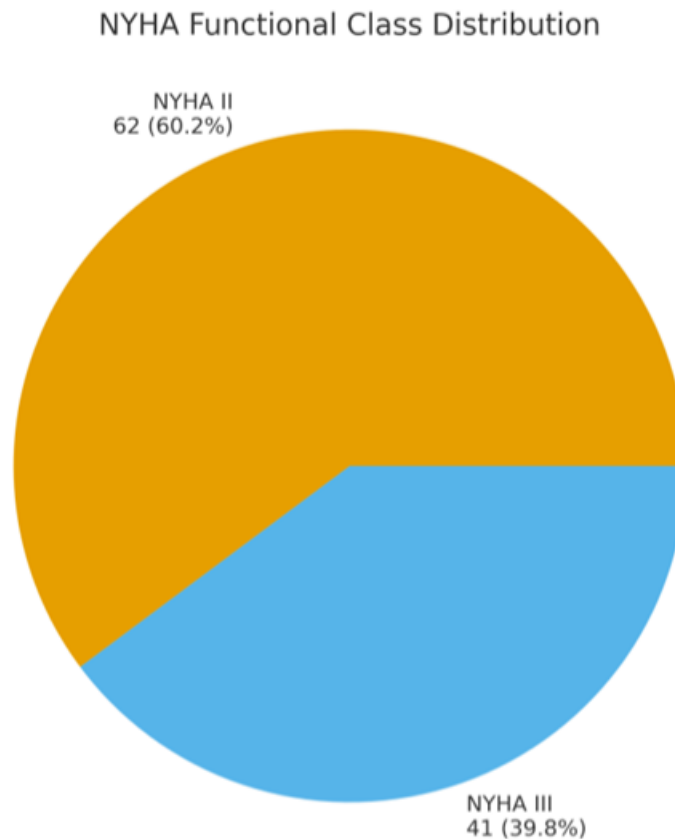


Fig. 2: Distribution of Study Participants According to NYHA Functional Class

howed the evidence of cardiac dysfunction and high prevalence of anaemia among 103 individuals. LVEF was mean $31.7 \pm 4.5\%$, from 18.9% to 39.0% which reflects severe systolic dysfunction. NT-proBNP was high (1905 ± 948.4 pg/mL), median 1632.5 pg/mL which indicated high neuro-hormonal and cardiac load. The mean haemoglobin level was

howed the high prevalence of iron deficiency among the total of 103 subjects of the study. The average value of serum ferritin was reported as 59.4 ng/mL (SD: 41.4). Median and range were recorded as 50.8 ng/mL and 11.9 – 206.2 ng/mL respectively. Functional iron deficiency (ferritin 30-100 ng/mL) was the most common type, occurring in 61 subjects

10.0 ± 1.5 g/dL, ranging from 7.0 to 12.7 g/dL. Mild anaemia was the most common form (44.7%), which was followed by moderate anaemia (35.0%) and severe anaemia (11.7%). Only 8.7% had showed normal haemoglobin level. The baseline data reflect significant systolic dysfunction and mostly mild and moderate anaemia.

(59.2%), while absolute iron deficiency (ferritin <30 ng/mL) occurred in 28 (27.2%) subjects. Only 14 (13.6%) subjects had ferritin in the range of 100-300 ng/mL. Overall, the average TSAT was 17.2% (SD: 6.3) and median TSAT was 17.1%. In 40 (38.8%) subjects, the TSAT was noted as 15-20% while in 37 (35.9%) <15%.

Sustained Haematological and Cardiac Responses Following Intravenous Ferric Carboxymaltose

Table 2. Distribution and Summary of LVEF, NT-proBNP, and Haemoglobin Parameters among Study Participants

Domain	Parameter / Category	Value / Number (n)	Percentage (%)
LVEF (%)	Mean	31.7	—
	Standard Deviation	4.5	—
	Median	31.5	—
	Range	18.9–39.0	—
NT-proBNP (pg/mL)	Mean	1905	—
	Standard Deviation	948.4	—
	Median	1632.5	—
	Interquartile Range	1299.0–2214.5	—
Hemoglobin (g/dL)	Range	428.0–5007.8	—
	Mean	10	—
	Standard Deviation	1.5	—
	Median	10.1	—
Hemoglobin Category	Range	7.0–12.7	—
	Severe Anemia (<8 g/dL)	12	11.7
	Moderate Anemia (8–10 g/dL)	36	35
	Mild Anemia (10–12 g/dL)	46	44.7
Total	Near-Normal Hb (12–13 g/dL)	9	8.7
	Total	103	100

Table 3. Descriptive Statistics and Distribution of SerumFerritin and Transferrin Saturation (TSAT) Among Study Participants

Domain	Parameter / Category	Value / Number (n)	Percentage (%)
Ferritin (ng/mL)	Mean	59.4	—
	Standard Deviation	41.4	—
	Median	50.8	—
	Interquartile Range	26.7–67.4	—
Ferritin Category	Range	11.9–206.2	—
	Absolute Iron Deficiency (<30 ng/mL)	28	27.2
	Functional Iron Deficiency (30–100 ng/mL)	61	59.2
	Ferritin 100–300 ng/mL	14	13.6
TSAT (%)	Total	103	100
	Mean	17.2	—
	Standard Deviation	6.3	—
	Median	17.1	—
TSAT Category	Interquartile Range	11.3–20.0	—
	Range	7.4–32.6	—
	Markedly Low TSAT (<15%)	37	35.9
	Low TSAT (15–20%)	40	38.8
Total	Borderline TSAT (20–30%)	21	20.4
	Near-Normal TSAT (≥30%)	5	4.9
	Total	103	100

tated the marked rise of the haemoglobin and iron parameters after 12 months of FCM therapy. The haemoglobin increased from 10.0 ± 1.5 g/dL initially to 12.2 ± 1.2 g/dL, with an increase of 2.2 g/dL on average (p<0.001). There was also a marked increase in ferritin levels from 59 ± 41 to 293 ± 75 ng/mL and TSAT from 17.2 ± 6.3%

to 30.1 ± 6.5%, both indicated statistical significance (p<0.001). There was also a decrease in TIBC from 349.8 ± 45.2 to 325 ± 36 µg/dL (p=0.002). There were also increases in cardiac parameters, with LVEF increasing from 31.7 ± 4.5% to 41.5 ± 5.8%, while NT-proBNP decreased from 1905 ± 948 to 1620 ± 1010 pg/mL. NYHA III reduced to 15.

4 | DISCUSSION

This is a prospective observational study to assess the longitudinal haematological and cardiac effects

Table 4. Longitudinal Changes in Haematological, Iron, Cardiac, and Renal Parameters Following FCM Therapy

Parameter	Baseline	Post-FCM – 3 Months	Post-FCM – 6 Months	Post-FCM – 12 Months	Mean Change (Baseline → 6m)	p-value
Hemoglobin (g/dL)	10.0 ± 1.5	11.7 ± 1.4	12.0 ± 1.3	12.2 ± 1.2	2.2	<0.001
Ferritin (ng/mL)	59 ± 41	285 ± 92	290 ± 85	293 ± 75	234	<0.001
TSAT (%)	17.2 ± 6.3	27.8 ± 6.2	29.5 ± 6.0	30.1 ± 6.5	12.9	<0.001
TIBC (μg/dL)	349.8 ± 45.2	332 ± 38	320 ± 24	325 ± 36	–29.8	0.002
NT-proBNP (pg/mL)	1905 ± 948	1780 ± 1180	1650 ± 1040	1620 ± 1010	–285	<0.001
LVEF (%)	31.7 ± 4.5	36.4 ± 5.6	39.0 ± 5.5	41.5 ± 5.8	10.2	<0.001
NYHA III patients (n)	41	25	18	15	–26	<0.001
Creatinine (mg/dL)	1.30 ± 0.30	1.31 ± 0.32	1.32 ± 0.30	1.32 ± 0.32	0.02	0.62
eGFR (mL/min/1.73 m ²)	61.4 ± 10.2	57 ± 13	58 ± 12	59 ± 10	–2.4	0.48

of intravenous ferric carboxylates in iron-deficient heart failure with reduced ejection fraction patients over 12 months. This intervention is not just to alleviate anaemia. Iron is essential to mitochondrial oxidative phosphorylation, to the function of myoglobin and to cellular energy metabolism; thus, iron depletion could result in impaired myocardial and skeletal muscle energetics without affecting haemoglobin within the reference range. Current criteria for the diagnosis of HFAD include absolute iron deficiency (Ferritin < 100 mcg/L) or functional iron deficiency (Ferritin 100–299 mcg/L & Transferin saturation (TSAT) < 20%) [1,2].

The haematological effects of FCM are consistent with the pharmacologic effects of intravenous iron, an effect of which is to replenish iron stores rather than through gastrointestinal absorption. In FAIR-HF, the rise in ferritin, related iron availability (RFe) and haemoglobin in FCM was significantly greater than in placebo, especially in those who were anaemic at baseline [6]. Importantly, the improvement of the clinical condition was unrelated to the presence of anaemia, suggesting that Hb is not an adequate marker of the therapeutic importance of iron repletion. If the current cohort does achieve better Hb, ferritin and TSAT at 12 months, then this would support the ongoing restoration of systemic iron availability, rather than just correcting systemic iron parameters.

This is particularly significant compared to

CONFIRM-HF, which was cross-sectional. Patients in the study were ambulatory heart failure patients with symptomatic LVHF and LVEF ≤ 45% and iron deficiency, whose total number was 304, and were followed for 52 weeks in this randomised, double-blinded study. A significant improvement in the 6-minute walk distance was seen with FCM compared to placebo, and was 33 ± 11 m and 36 ± 11 m at week 24 and 52, respectively. Improvements also were noted in NYHA functional class, the patient global assessment, quality of life and fatigue, and the rate of hospitalisation for worsening heart failure [7]. Thus, the 12-month functional and/or cardiac improvement outcomes of the current observational cohort would be consistent with the persistent treatment benefits observed in CONFIRM-HF.

The results should be read in context of the overall evidence, however. In this study, patients with chronic heart failure with or without anaemia who received FCM showed an improvement in symptoms, functional capacity and quality of life compared to those who did not receive FCM [6]. By contrast, patients hospitalised for acute heart failure with LVEF < 50% and IDA in AFFIRM-AHF did not demonstrate significant difference in the primary composite endpoint of total heart-failure hospitalisation or cardiovascular death at 52 weeks, but did show a significant difference in the risk of first heart-failure hospitalisation or cardiovascular death, and in the number of total heart-failure hospitalisations

Sustained Haematological and Cardiac Responses Following Intravenous Ferric Carboxymaltose

[2]. These disparities indicate that the therapeutic benefits of iron IV might be more clearly seen by functional and symptomatic endpoints, rather than in terms of death endpoints.

This is the reason why cardiac responses are important to interpret. LVEF, NYHA class, exercise capacity and natriuretic peptides have to be evaluated after iron repletion; they are not determinants of favourable reverse-remodelling and/or improvement in myocardial efficiency [9-11]. Cardiac recovery can be significantly facilitated by guideline-directed medical therapy such as the use of beta-blockers, renin-angiotensin system inhibitors, angiotensin receptor-neprilysin inhibitors, mineralocorticoid receptor antagonist, and sodium-glucose cotransport-2 inhibitors. Therefore, the temporality of FCM administration and improvement of cardiac parameters can only be considered as a positing association and not as a definite causal association [12,13].

The 12-month period also allows for a look at the persistence of iron repletion or the development of further iron deficiency. This is clinically relevant as iron status may fluctuate in heart failure and current practice also includes several ferritin and TSAT measurements. The ESC 2023 focused update guidelines recommend that all patients with symptomatic HFrEF and HFmrEF with ID should be monitored for iron levels routinely and that iron should be given via IV to help reduce symptoms and improve quality of life [2,3]. Normalisation of iron indices, even though the clinical response has been favourable in the present cohort, would support sustainability of the treatment response; biochemical iron deficiency despite clinical improvement may indicate greater need for more structured follow-up in the long-term and repeat doses as needed.

The new HEART-FID results provide a welcome counterpoint. This large randomised trial of ambulatory HFrEF patients with IDA was not able to prove a significant improvement at the prespecified composite endpoint (death or HF hospitalisation), or at the primary significance level [8] at the 6MWD endpoint. The result shows that the improvements in haematological indices do not necessarily suggest a decrease in the mortality or hospitalisation rates. These seemingly paradoxical findings from functional benefit in previous trials to neu-

tral outcomes with regard to a broader spectrum of clinical outcomes may be associated with baseline risk, intensity of therapy, hierarchy of outcomes, iron-deficiency phenotype, and contemporary background heart-failure therapy.

Overall, the current 12-month observational study has the benefit of being able to integrate haematological and cardiac trajectories, not only iron indices. With time, improvements in Hb levels and Fe stores, along with improvements in cardiac function or functional status, would provide proof of concept for continual monitoring and treatment of IDA as a key component of HFrEF [10]. The results need, however, to be interpreted as longitudinal associations because of the design of the study and the absence of randomisation and concurrent heart failure therapy that might have caused confounding. Despite the encouraging clinical trial results, further larger, more controlled, and more standardised studies are required to elucidate the long-term effects of ongoing biological iron replacement on heart failure outcomes and endpoints, and clinical-event adjudication.

5 | CONCLUSION

The study has concluded that intravenous ferric carboxymaltose therapy may be an effective therapeutic approach for patients with iron-deficient heart failure with reduced ejection fraction. Its use appears to provide sustained correction of iron deficiency and anaemia while supporting improvement in cardiac functional status over prolonged follow-up. The findings also suggest that appropriate management of iron deficiency may have an important role as an adjunct to conventional heart failure treatment. Furthermore, the overall therapeutic response indicates the potential clinical value of intravenous iron supplementation in patients with concomitant iron deficiency and systolic heart failure. Long-term management should therefore incorporate systematic assessment of iron status and consideration of intravenous iron therapy where clinically appropriate. Further prospective studies with larger populations and longer follow-up are warranted to establish its long-term efficacy, safety, and impact on major cardiovascular outcomes.

References

Reference

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baum-bach A, Böhm M, et al. 2021 ESC Guide-lines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42(36):3599-3726.
 2. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023; 44 (37) :3627-3639.
 3. American College of Cardiology. 2023 Focused Update of the 2021 ESC Guidelines for Acute and Chronic Heart Failure: Key Points. 2023.
 4. Jankowska EA, von Haehling S, Anker SD, Macdougall IC. Iron deficiency and heart failure: diagnostic dilemmas and therapeutic perspectives.*Eur Heart J*. 2013;34(11):816-829.
 5. Lewis GD, Malhotra R, Hernandez AF, McNulty SE, Smith A, Felker GM, et al. Effect of oral iron repletion on exer-cise capacity in patients with heart failure with reduced ejection fraction and iron defi-ciency: the IRONOUT HF randomised clin-ical trial. *JAMA*. 2017;317(19):1958-1966.
 6. Anker SD, Comin Colet J, Filippatos G, Wil-lenheimer R, Dickstein K, Drexler H, et al. Ferric carboxymaltose in patients with heart failure and iron deficiency. *N Engl J Med*. 2009;361(25):2436-2448.
 7. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, Ertl G, Koma-jda M, Mareev V, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron defi-ciency : CONFIRM-HF. *Eur Heart J*. 2015;36 (11):657-668.
 8. Mentz RJ, Garg J, Rockhold FW, et al. Ferric carboxymaltose in heart failure with iron defi-ciency. *N Engl J Med*. 2023;389:975-986.
 9. Graham FJ, Pellicori P, Kalra PR, Ford I, Cleland JGF, Jhund PS, et al. Intravenous iron in patients with heart failure and iron deficiency: an individual patient data meta-analysis. *Lancet*. 2023;402:204-213.
 10. Cheema B, Chokshi A, Orimoloye O, Ardehali H. Intra-venous iron repletion for patients with heart failure and iron deficiency: JACC state-of-the-art review. *J Am Coll Cardiol*. 2024;83:2674-2689.
 11. Yadav I, Waqas R, Mohammad A, Lashari UG, Sabra M, Dwayat A, Rajput J. Heart rate variability as a predictor of mortality in heart failure: a systematic review and meta-analysis. *Cureus*. 2025 Dec 13;17(12).
 12. Dalal J, Chandra P, Ray S, Hazra PK, Hiremath J, Kumar V, Shah MK, Abdullakutty J, Ghosh D, Vasudevan K, Sahoo P. Practical recommen-dations for the use of angiotensin receptor-neprilysin inhibitors (ARNI) in heart failure: insights from Indian cardiologists. *Cardiology and Therapy*. 2023 Sep;12(3):445-71.
 13. Jadhav U, Nair T, Mohanan P, Chopra V, Kerkar P, Biswas AD, Hazra PK, Zalte N, Sugumaran A, Mohanasundaram S, Mohanan PP. Impact of mineralocorticoid receptor antagonists in the treatment of heart failure: targeting the heart failure cascade. *Cureus*. 2023 Sep 14;15(9).
- How to cite this article:** Verma D.P., Shukla A., Venkatesh P.S., Kanodia N. Sustained Haematological and Cardiac Responses Follow-ing Intravenous Ferric Carboxymaltose in Iron-Deficient Heart Failure with Reduced Ejection Fraction: A 12-Month Prospective Observational Study. *Current Clinical and Medical Education*. 2026;515–523.