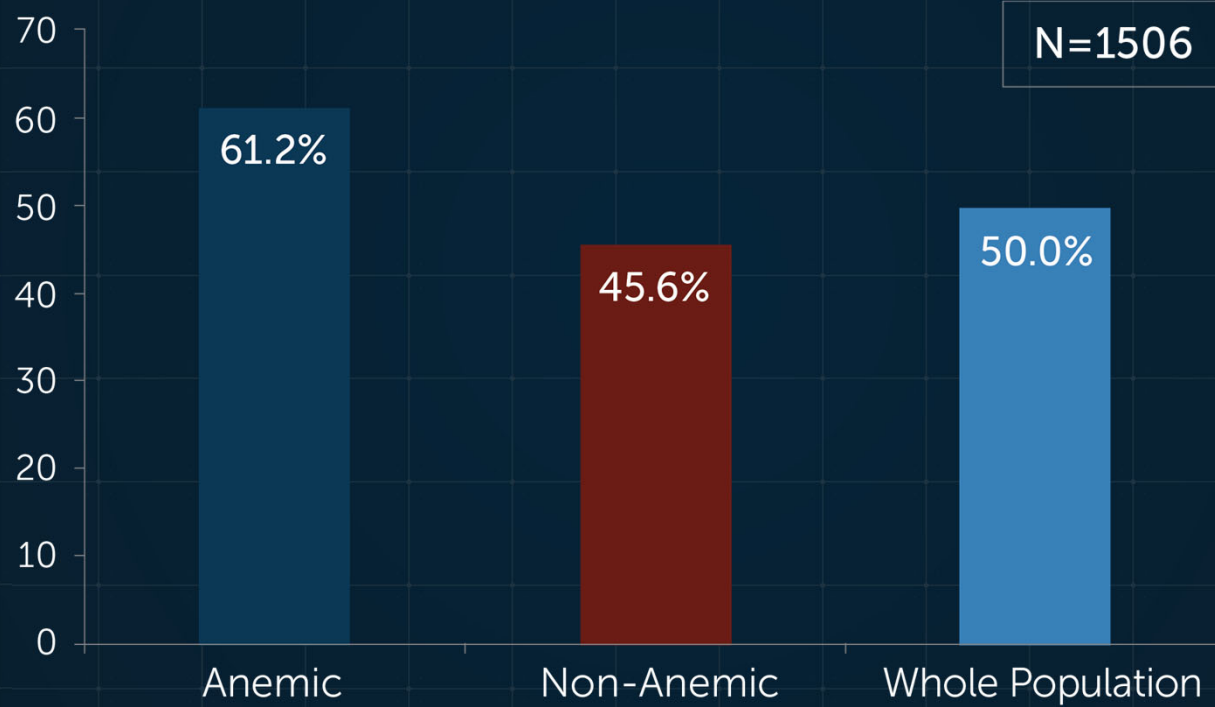


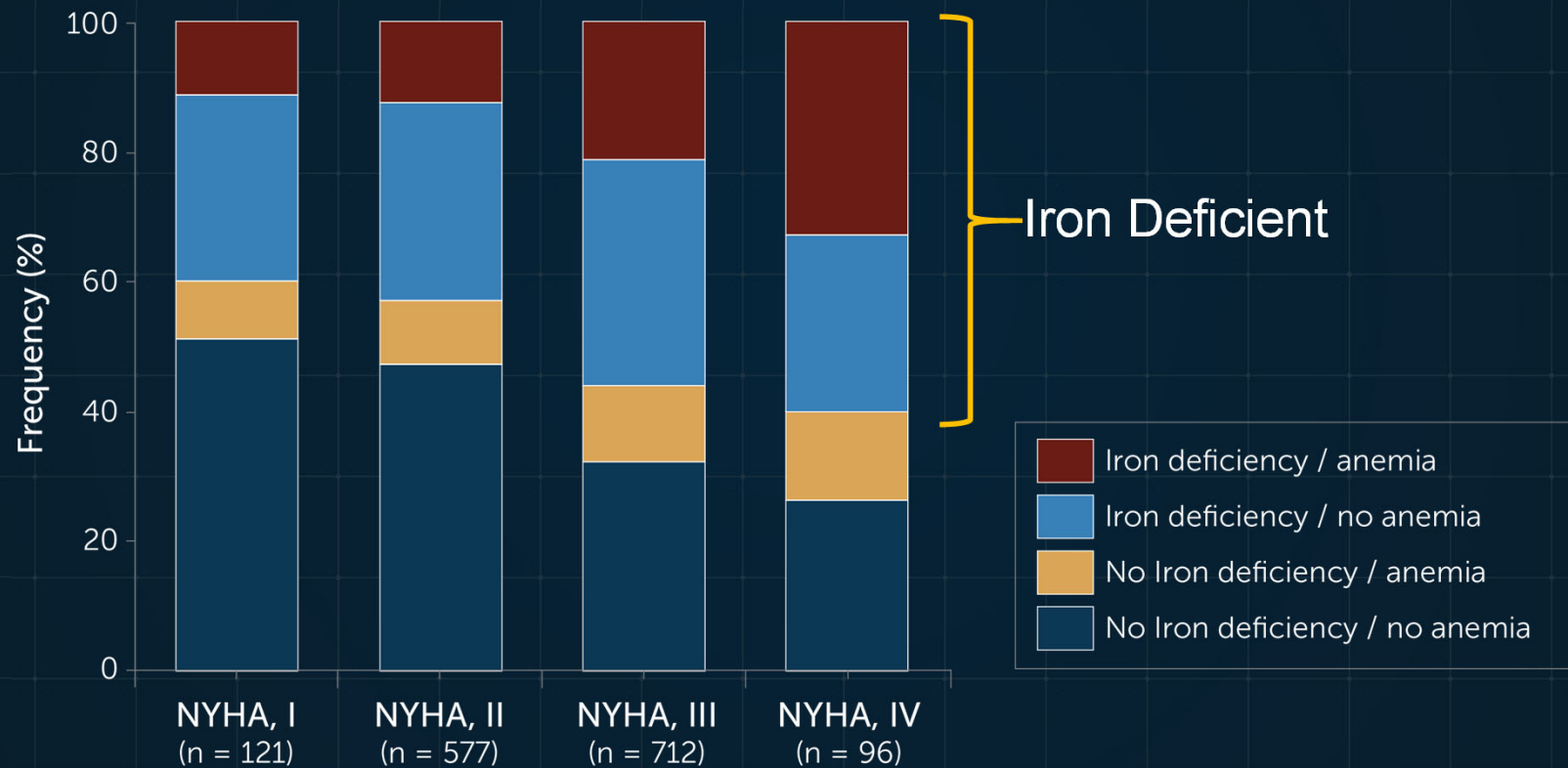
Don't Be Fooled:  
It's Not Just Anemia,  
It's Iron Deficiency

Iron deficiency can be a comorbidity and complication of heart failure **regardless** of hemoglobin level.

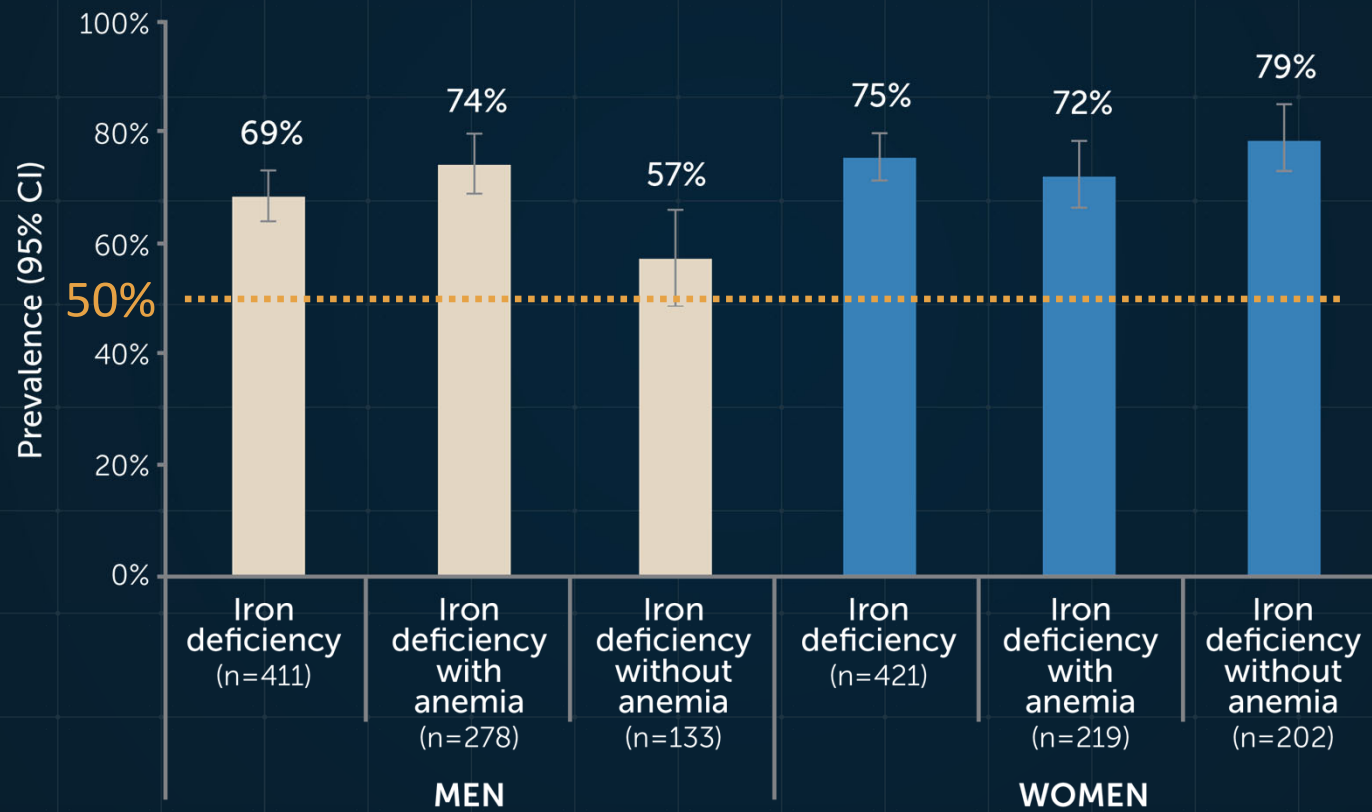
# Iron Deficiency in HFrEF



# Iron Deficiency is Common in All NYHA Classes



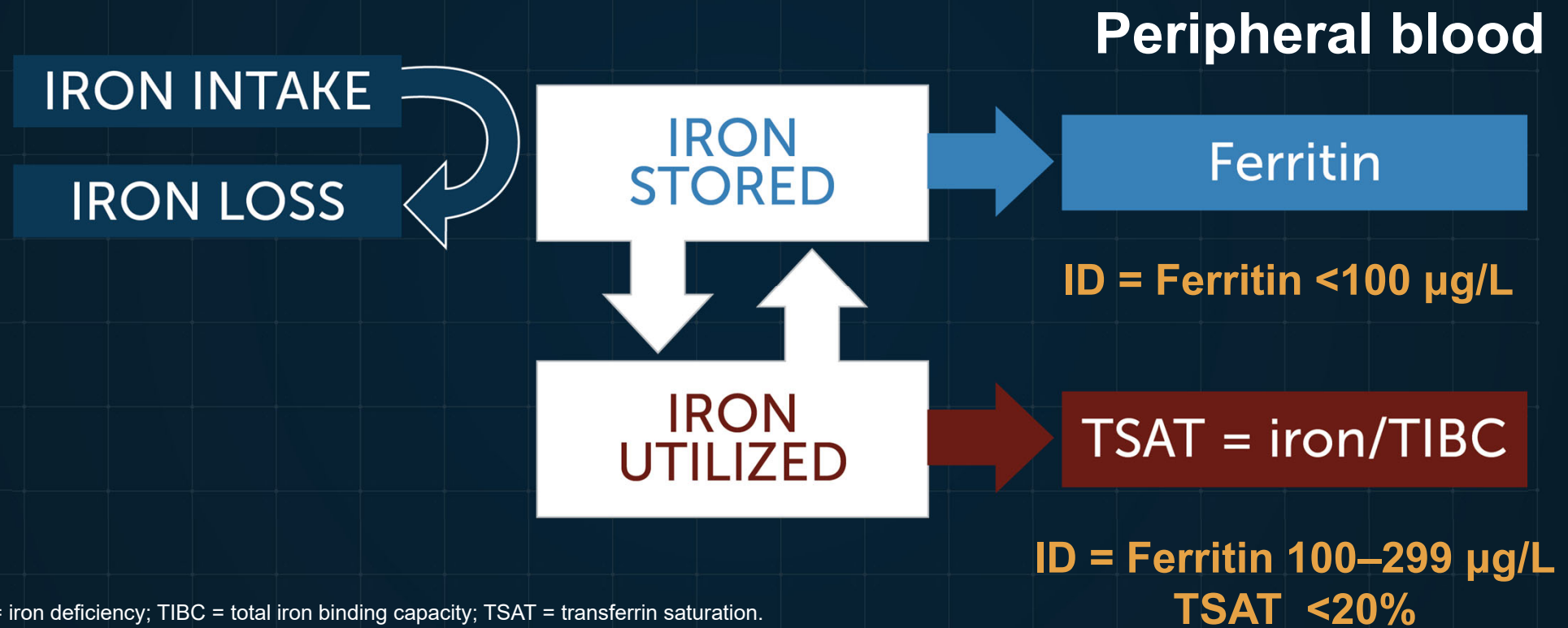
# Iron Deficiency is Prevalent in Acute Heart Failure



# Iron Deficiency in HF

- Can be present regardless of:
  - Ejection fraction
  - Anemia status
  - Severity of HF

# Iron Deficiency: Biomarkers of Iron Storage and Utilization



ID = iron deficiency; TIBC = total iron binding capacity; TSAT = transferrin saturation.

Jankowska EA et al. *Eur Heart J*. 2013;34(11):827-834.  
Ponikowski P, et al. *Eur Heart J*. 2016;18(8):891-975.

Ferritin and TSAT should be performed simultaneously  
and evaluated together.



# Iron Deficiency in HF: Rationale for Testing

- High prevalence in HF
- Affects quality of life and exercise tolerance
- Can lead to poor HF outcomes

# Effect of FCM in Chronic Heart Failure: Meta-analysis

**Table 3** Recurrent event outcomes

Data from FER-CARS-01, FAIR-HF, EFFICACY-HF (NCT00821717) and CONFIRM-HF

Outcomes	RR (95% CI)	P-value
CV hospitalizations and CV mortality	0.59 (0.40–0.88)	0.009
HF hospitalizations and CV mortality	0.53 (0.33–0.86)	0.011
CV hospitalizations and all-cause mortality	0.60 (0.41–0.88)	0.009
HF hospitalizations and all-cause mortality	0.54 (0.34–0.87)	0.011
All-cause hospitalizations and all-cause mortality	0.73 (0.52–1.01)	0.060
HF hospitalizations	0.41 (0.23–0.73)	0.003
CV hospitalizations	0.54 (0.36–0.83)	0.004
All-cause hospitalizations	0.71 (0.50–1.01)	0.056

FCM = ferric carboxymaltose

# IV Iron Study Results

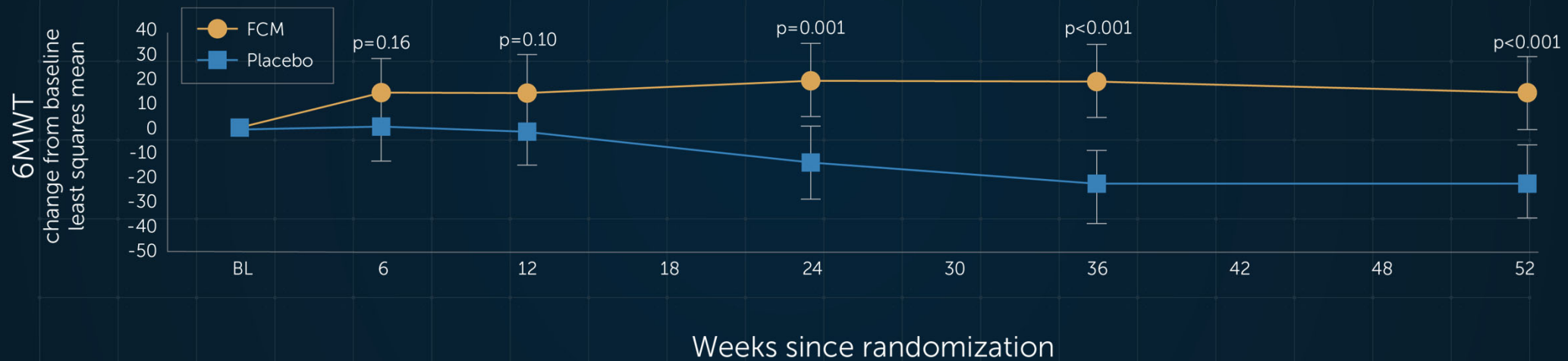
Trial	Patients	Time (weeks)	Primary endpoint
FAIR-HF	459	24	Global assessment score
CONFIRM-HF	304	52	6MWD
EFFECT-HF	172	24	Peak VO <sub>2</sub>

Improvements in:

- Functional status (6MWD, peak VO<sub>2</sub>, NYHA Class)
- Biomarkers (BNP)
- Patient global assessment

6MWD = 6-minute walk test distance; BNP = brain natriuretic peptide; NYHA = New York Heart Association.

# CONFIRM-HF: IV Iron Improves Exercise Capacity in HFrEF



FCM = ferric carboxymaltose

6MWT = 6-minute walk test

# Select Ongoing Large HFrEF Trials

Study Name	FAIR-HF-2	AFFIRM-AHF	HEART-FID	IRONMAN
# of Patients	1,200	1,100	3,014	1,300
Diagnosis	Chronic HF EF≤45%	<b>Acute HF</b> EF<50%	Chronic HF EF≤40%	Chronic HF <45%
Blinding	Double blind	Double blind	Double blind	<b>Open label</b>
Study Arm	FCM	FCM	FCM	<b>Iron (III) isomaltoside</b>
Duration	Event driven + at least 12 mos f/u	52 weeks	Event driven + 12 mos last patient	120 weeks
Primary Endpoint	HF hosp + CVD	HF hosp + CVD	All-cause mortality + total HF hosp through 12 mos and 6-month 6MWD	CVD or HF hosp

# Guideline Recommendations

## 2016 ESC Guidelines

Class	Level	Recommendation
IIa	A	Intravenous FCM should be considered in symptomatic patients with HFrEF and iron deficiency (serum ferritin <100 µg/L, or ferritin between 100–299 µg/L and transferrin saturation <20%) in order to alleviate HF symptoms, and improve exercise capacity and quality of life.

## 2017 AHA/ACC/HFSA Guideline Update

Recommendation for Anemia		
COR	LOE	Recommendation
IIb	B-R	In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and QoL (173, 174).

# Case Study

## 76-year-old woman with NYHA III HF

- History of dyslipidemia, hypertension, and prior MI
- Diagnosed with HF 4 years ago
- EF 35%
- Shortness of breath with moderate exertion
  - Can only walk 330 meters during 6MWT
  - Denies angina

# Case Study

76-year-old woman with NYHA III HF

- Current treatment
  - Spironolactone 50 mg qd
  - Sacubitril/valsartan 97/103 mg bid
  - Carvedilol 25 mg bid
  - Furosemide 120 mg bid

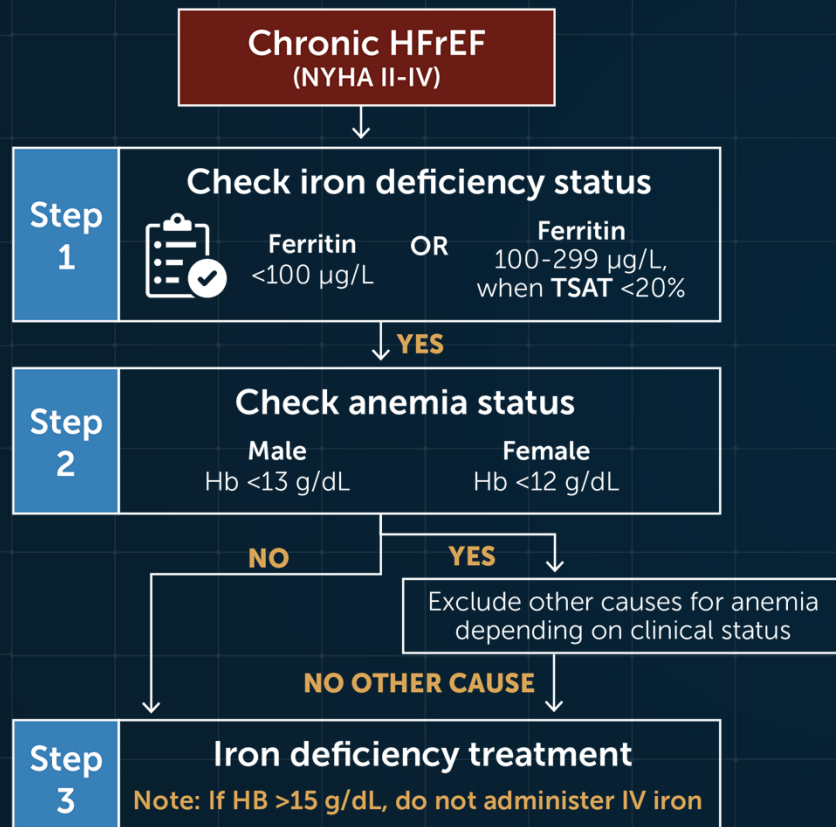


# Case Study

76-year-old woman with NYHA III HF

- Physical examination
  - HR: 75 bpm
  - BP: 120/85 mm Hg
  - RR: 23 breaths per minute
  - No peripheral edema
  - No congestion

# Dosing IV Ferric Carboxymaltose



Consider ferric carboxymaltose as 500-1000 mg single doses of iron to correct iron deficiency

**DOSING CALCULATIONS ACCORDING TO HEMOGLOBIN LEVELS AND BODY WEIGHT**

Hemoglobin		Patient Body Weight		
g/dL	mmol/L	<35 kg	35 kg - <70 kg	≥70 kg
<10	<6.2	500 mg	1500 mg	2000 mg
10-14	6.2-8.7	500 mg	1000 mg	1500 mg
>14	>8.7	500 mg	500 mg	500 mg

↓

**Step 4** **Check ferritin + TSAT**  
 at next scheduled visit (preferable at 3 months)

↓

**Step 5** **Check ferritin + TSAT**  
 1-2 times per year or if change in clinical picture or if hemoglobin decreases

# Practice Pearls

- Be proactive in screening newly diagnosed and established patients with heart failure for iron deficiency, regardless of anemia
- Treat patients with IV iron formulations