

Iron Deficiency and Heart Failure in General Practice



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1

Iron Deficiency - General Principles

- Easy to identify , crucial numbers:
 - Absolute ID, Ferritin 30
 - T sat 20 (functional ID , ferritin 100-300)
 - Hb 130 (male), 120 (female)
- Absolute and Functional ID
- A cause must be ascribed when ID is found - may need further investigation
- Most cases can be managed safely and effectively in general practice

2

Key Messages

- Iron deficiency in heart failure is common
- Associated with poor outcomes independent of anaemia
- Definition differs from standard criteria
- Treatment of choice is intravenous iron
- Effectively managed in general practice
- Finding Iron deficiency (regardless of HB) in heart failure is an indication for treatment

3

Prevalence – Heart Failure

- 10-20 patients per FTE GP ¹
- More common in
 - Elderly (*3)
 - Female (*2)
 - Indigenous persons (*1.7)
 - Rural and remote communities
- Likely to increase
 - Ageing population
 - Better survival form coronary artery disease
 - Increasing obesity and diabetes
- Economic Burden
 - 1-3% of all healthcare spending

1. Sahle et al 2016

4

Iron Deficiency is common in Heart Failure

- Prevalence (HF and ID without anaemia) 30-60 % (variable definitions)
- Increased risk in
 - Women
 - Non Caucasian
 - Elderly (<75 yrs)
- Severity of heart failure (NYHA class 3 & 4 , 2/3 men and 3/4 of women)
- Anaemia as comorbidity
- Poor prognosis 25-30 % mortality after first hospitalisation, *"a more ominous finding than anaemia"*

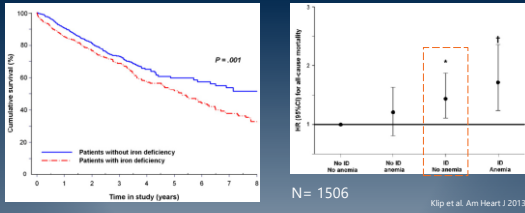
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Heart Failure & Iron Deficiency

- Independent of any co-existent anaemia
- Higher mortality – 2 fold greater risk
- Poor Quality of Life
- Reduced exercise capacity and endurance

6

Iron deficiency is independently associated with poor outcome



Mortality increases when ID is present

ID is a negative prognostic factor, **stronger** than anemia

7

Why is Iron Important in Heart Failure

- Uptake, transport, storage and metabolism of oxygen
- Erythropoiesis
- Cellular immune response
- Important for enzymatic activity within Krebs cycle and mitochondrial respiratory chain. Important in tissues with high energy demands (cardiac and skeletal muscle)

8

Causes of iron deficiency in heart failure

Reduced iron storage:
Absolute iron deficiency

- Malnutrition**
- Loss of appetite: <math><50\%</math> intake
- Malabsorption:**
- GI mucosal oedema
 - Delayed gastric emptying, altered intestinal motility
 - PPI, PO_4 binders
 - Reduced iron transport in duodenum. Altered villous blood flow
- GI blood losses**
- Gastritis/peptic ulcer
 - Medications - Anti-coagulants, NSAIDs, antiplatelet
 - Mucosal integrity
- Blood Loss** menstrual, blood sampling

Reduced iron mobilization:
Functional iron deficiency

- Inflammation**
- Cytokines, IL-6, IL-1, TNF- α
- Blunted responses to EPO
 - Apoptosis of erythroid progenitors
 - Hepcidin-mediated malabsorption and RES pooling

Modified from Janikowska et al. Eur Heart J 2013

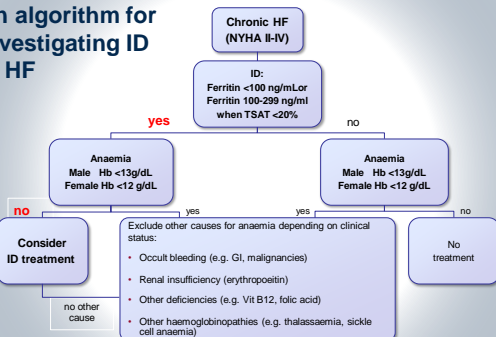
9

Diagnostic criteria for iron deficiency in heart failure

- **Ferritin <math><100</math>**
- OR
- **Ferritin 100-300 and Tsat <math><20</math>**

10

An algorithm for investigating ID in HF



McDonagh T, Eur J Heart Fail 2015;17:248-62
McMurray JJ, et al. Eur Heart J 2012;33:1787-847.

11

Heart Failure & Iron Deficiency - Treatment

- IV iron is preferable
- Oral – poorly tolerated (GI) and not as effective
- Fe Carboxymaltose is preferred agent (other preparations not as well studied)
- Check levels at 6w and give further dose if low
- Review – clinical, functional assessment 6 min walk test
- Once optimised monitor 6-12 monthly₂

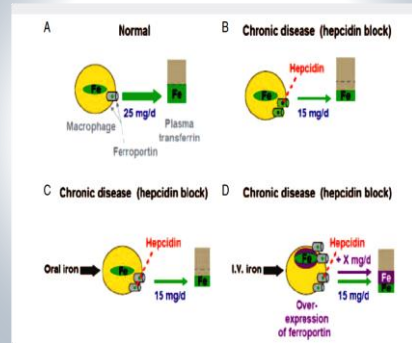


Oral therapy is not so effective

- Poorly tolerated
- GI absorption impaired, standard doses often insufficient
- Drug interactions
- Hepcidin issues

13

Hepcidin, IV iron and oral iron



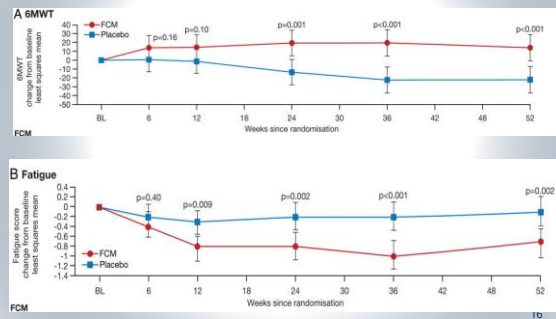
14

Heart Failure & Iron Deficiency- Outcomes of treatment

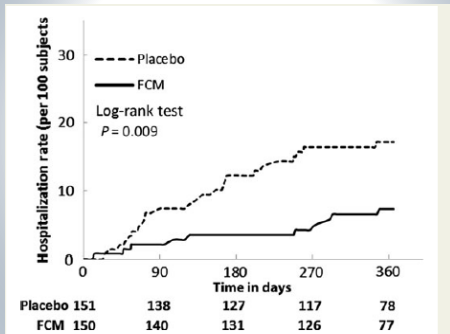
- Improved QoL
- Better exercise capacity and endurance
- Reduced hospitalisation (disease progression)
- Ejection fraction
- Improvement in NYHA Class
- Reduced mortality ??

15

Confirm HF study - Functional outcomes

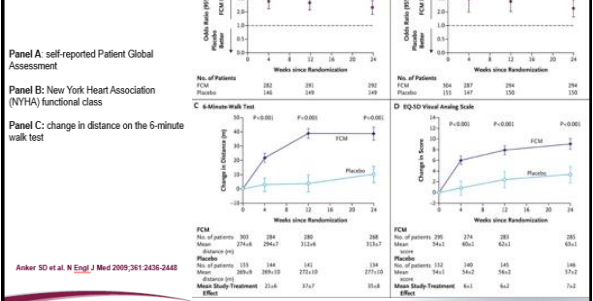


Confirm HF study - Hospitalisation Rates



17

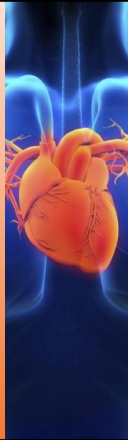
Main Secondary Outcomes during the Study, According to Assigned Study Treatment



Anker SD et al. *N Engl J Med* 2009;361:2436-2448

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18



Heart Failure & Iron Deficiency-Recommendations

- European Society of Cardiology(ESC) HF Guidelines 2016, which recommend screening for ID in HF patients (recommendation IC)
- Consider using i.v. FCM in symptomatic systolic HF patients with ID (recommendation IIaA)

19

Managing ID in HF patients in general practice – A summary

- **Identify**
 - Opportunistic, symptoms
 - FBP, CRP, Iron studies, (6 -12 monthly)
- **Investigate**
 - Identify cause , consider GI investigation
 - Renal function
 - Correct causes where possible
- **Assess**
 - Echo/functional
- **Treat**
 - iv carboxymaltose
 - Dosage calculation
- **Monitor**
 - FBP and iron studies at 6 weeks
 - Objective and subjective measures
 - Further dose 500 mg if necessary
 - Recall for next test 6-12 months

20

Summary

- Iron deficiency in heart failure is common
- Associated with poor outcomes independent of anaemia
- Definition:
 - Ferritin <100 or
 - Ferritin 100-300 and T sat <20
- Finding Iron deficiency (regardless of HB) in heart failure is an indication to consider treatment
- Treatment of choice is intravenous iron
- Effectively and safely managed in general practice

21

Reading

- **Anker, SD et al.** Effects of ferric carboxymaltose on hospitalisations and mortality rates in iron deficient heart failure patients : An individual patient data meta analysis. *European Journal of Heart Failure* 2017
- **Drozid, M et al.** Iron Therapy in Patients with Heart Failure and Iron Deficiency: Review if iron preparations for practitioners, *Am J Cardiovasc Drugs* 2016
- **McDonagh T & Macdougall IC.** Iron therapy for the treatment of iron deficiency in chronic heart failure: intravenous or oral? *European Journal of Heart Failure* 2015
- **Ponikowski, P et al:** Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency. *European Heart Journal* 2015

22