Causes of preoperative anaemia in Cardiothoracic patients

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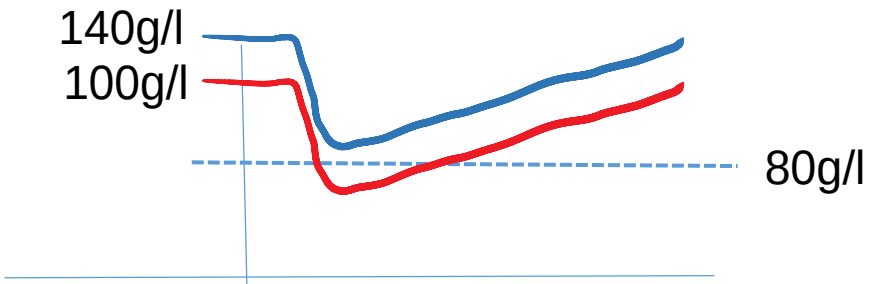
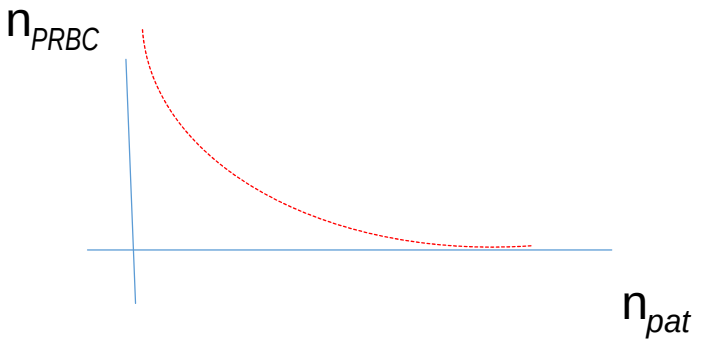
Preoperative Anaemia – BCSH 2015 guidelines – Common sense

Important modifiable risk factor for morbidity and mortality in all forms of surgery (Australian PBM guidelines)





Patients should be counselled about the relationship between anaemia, morbidity and mortality, and should be given the opportunity to defer non-urgent surgery until anaemia is investigated and treated (Grade 1C)

BUT: No RCT evidence that anaemia correction alters this risk

BUT: Best timing for intervention not known – delay should be avoided, earlier, likely better

It's more complicated than we think

Fe Deficiency often defined as Ferritin <25 in males and <13 ug/l in females

In anaemic patients accepted therapy is to push Ferritin >100 by iron supplementation

= grey zone 15-100 ug/l

Ferritin <100ug/l will deplete if 1200ml of blood are lost (165mg of Fe for every 10g of Hb loss)

Best mode of iron replacement unknown

Published evidence

- 4 small trials of IV Iron in cardiac surgery – 'perioperatively'
- Anaemia = Higher morbidity and mortality , higher transfusion rate
- Cardiac Surgery :
  - Preop Hct predicted mortality, renal failure and sternal wound infection
  - Cochrane review: IV vs oral Iron: 4745 participants in 21 trials
    - Heterogenous evidence but better chance of response with IV iron

Preoperative anaemia in Papworth

- Highly prevalent
- Associated with perioperative mortality, complication and length of stay

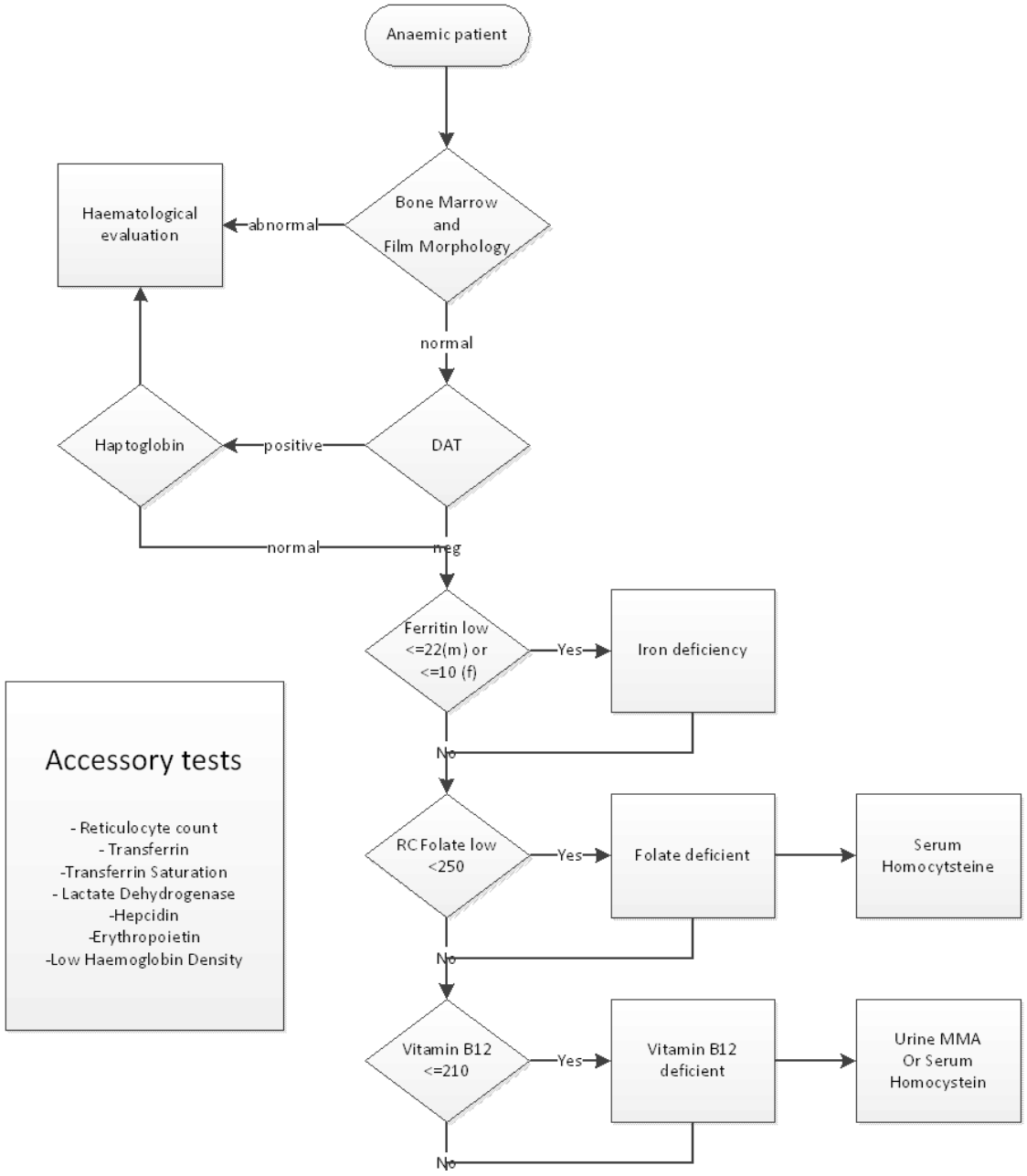
- Retrospective study - N=2688
- Prevalence 54.5%

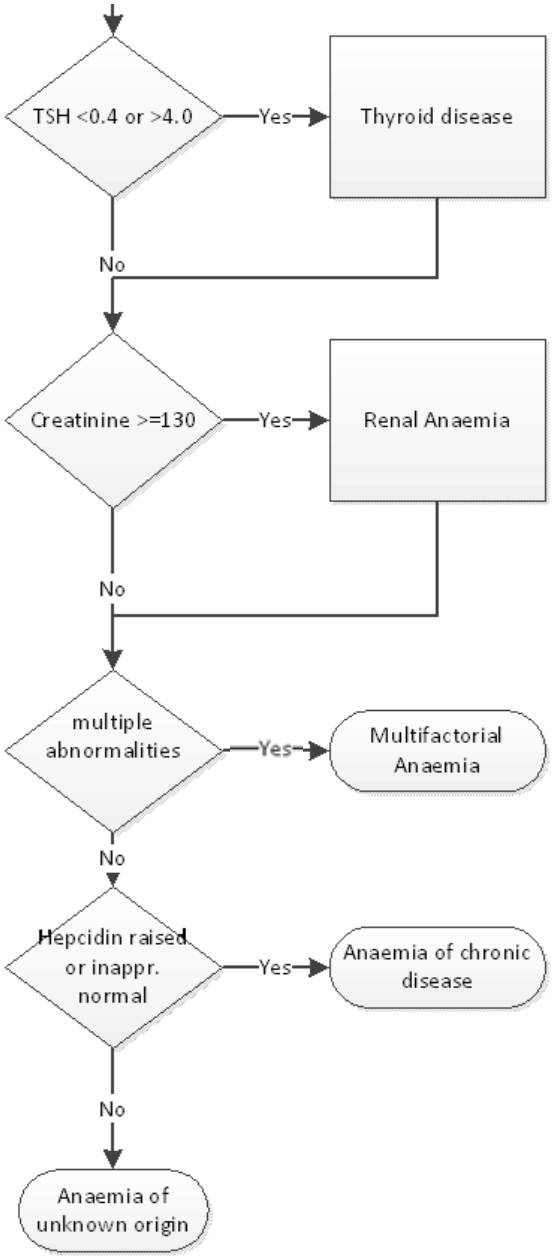
	Non-anaemic (n = 1225)	Anaemic (n = 1463)	p value*
Transfusion	275 (22.4%)	791 (54.1%)	< 0.0001
Total units of RBC transfused	0 (0–1 [0–20])	0 (0–2 [0–34])	< 0.0001
Units of RBC if transfused	2 (1–3 [1–20])	2 (1–3 [1–24])	< 0.0001
Transfusion > 6 units RBC	25 (2%)	102 (7%)	0.098
Postoperative haemoglobin	10.5 (3.1)	9.2 (3.4)	< 0.001
In-hospital deaths	13 (1.1%)	45 (3.1%)	0.0005
ICU stay; days	1 (0–2 [0–81])	1 (0–2) [0–69]	< 0.0001
ICU stay > 2 days	168 (13.7%)	287 (19.6%)	< 0.0001
Transfusion cost per patient; £	133 (0–410 [0–4205]	362 (0–795 [0–4205]	< 0.0001

RBC, red blood cells. *p value refers to the Wilcoxon signed-rank test or Pearson's chi-squared test for contingency tables.

Anaesthesia, 2011, **66**, pages 812–818

M. Hung et al.





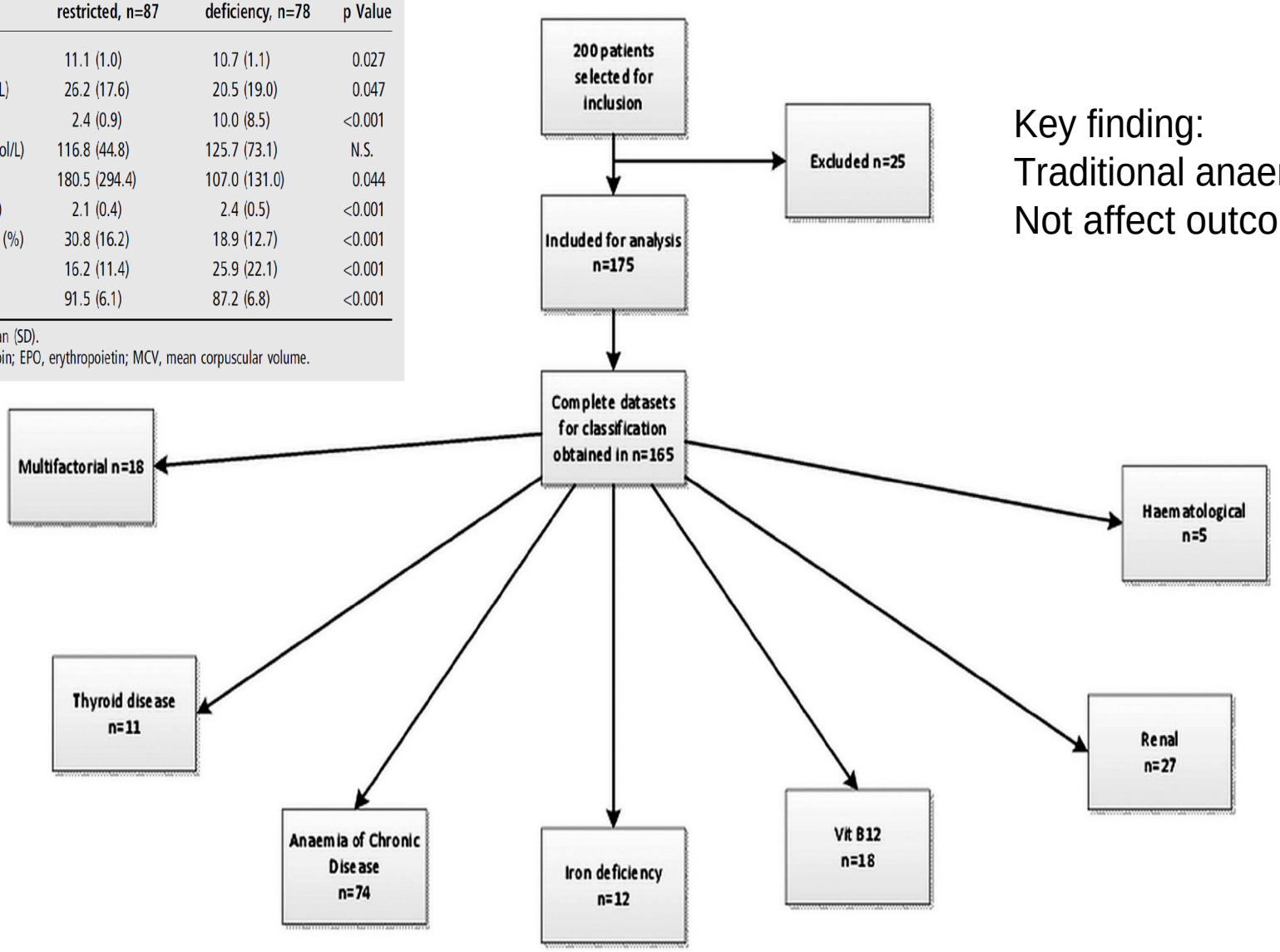
Hung M, *et al*. *Heart* 2014;**0**:1–6. doi:10.1136/heartjnl-2014

Pap60: Observed Transfusion rate: 83%

Table 3 Haematological parameters for patients with and without functional iron deficiency, defined as low haemoglobin density (LHD) >4%

	Anaemia, not iron restricted, n=87	Functional iron deficiency, n=78	p Value
Hb (g/L)	11.1 (1.0)	10.7 (1.1)	0.027
Hepcidin (ng/mL)	26.2 (17.6)	20.5 (19.0)	0.047
LHD (%)	2.4 (0.9)	10.0 (8.5)	<0.001
Creatinine (mmol/L)	116.8 (44.8)	125.7 (73.1)	N.S.
Ferritin (µg/L)	180.5 (294.4)	107.0 (131.0)	0.044
Transferrin (g/L)	2.1 (0.4)	2.4 (0.5)	<0.001
Transferrin sats (%)	30.8 (16.2)	18.9 (12.7)	<0.001
EPO (mU/mL)	16.2 (11.4)	25.9 (22.1)	<0.001
MCV	91.5 (6.1)	87.2 (6.8)	<0.001

Values are mean (SD).
Hb, haemoglobin; EPO, erythropoietin; MCV, mean corpuscular volume.



Key finding:
Traditional anaemia categories did
Not affect outcome

29/74 iron restricted

Hung M, *et al*. *Heart* 2014;**0**:1–6. doi:10.1136/heartjnl-2014-305

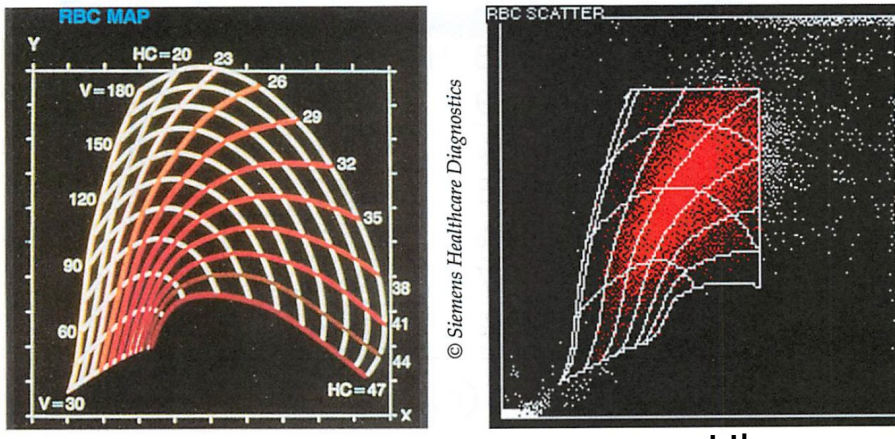
Functional iron deficiency (British Journal of Haematology, 2013, 161, 639–648)

Haemogram parameters

- Entire Red cell mass – ie last 120 days
  - Siemens: %HRC >=6% (best evidence)
  - Sysmex : Hypo-He (MCH<17 cells)
  - Coulter: LHD

- Reticulocyte fraction only:
  - Siemens: CHr <29pg,
  - Sysmex: RetHe

volume



Hb conce

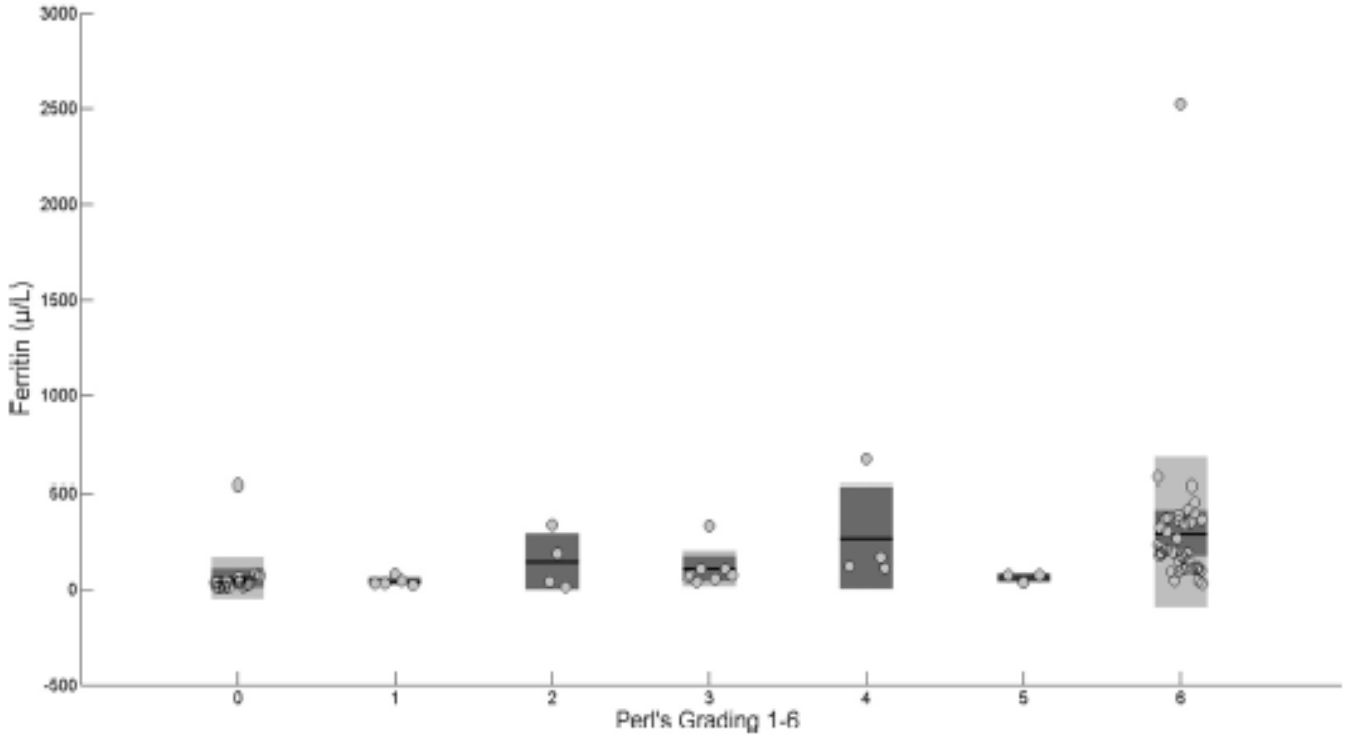
Figure 42: (A) An annotated representation of the Mie Map showing the relationship between volume (V) in fL a haemoglobin concentration (HC) in g/dL; (B) The Mie Map shown superimposed over the red cells with haemogl concentration (HC) shown on the x-axis against volume (V) on the y-axis. Platelets can be seen in the far lower l corner.

Plasma and bone marrow tests

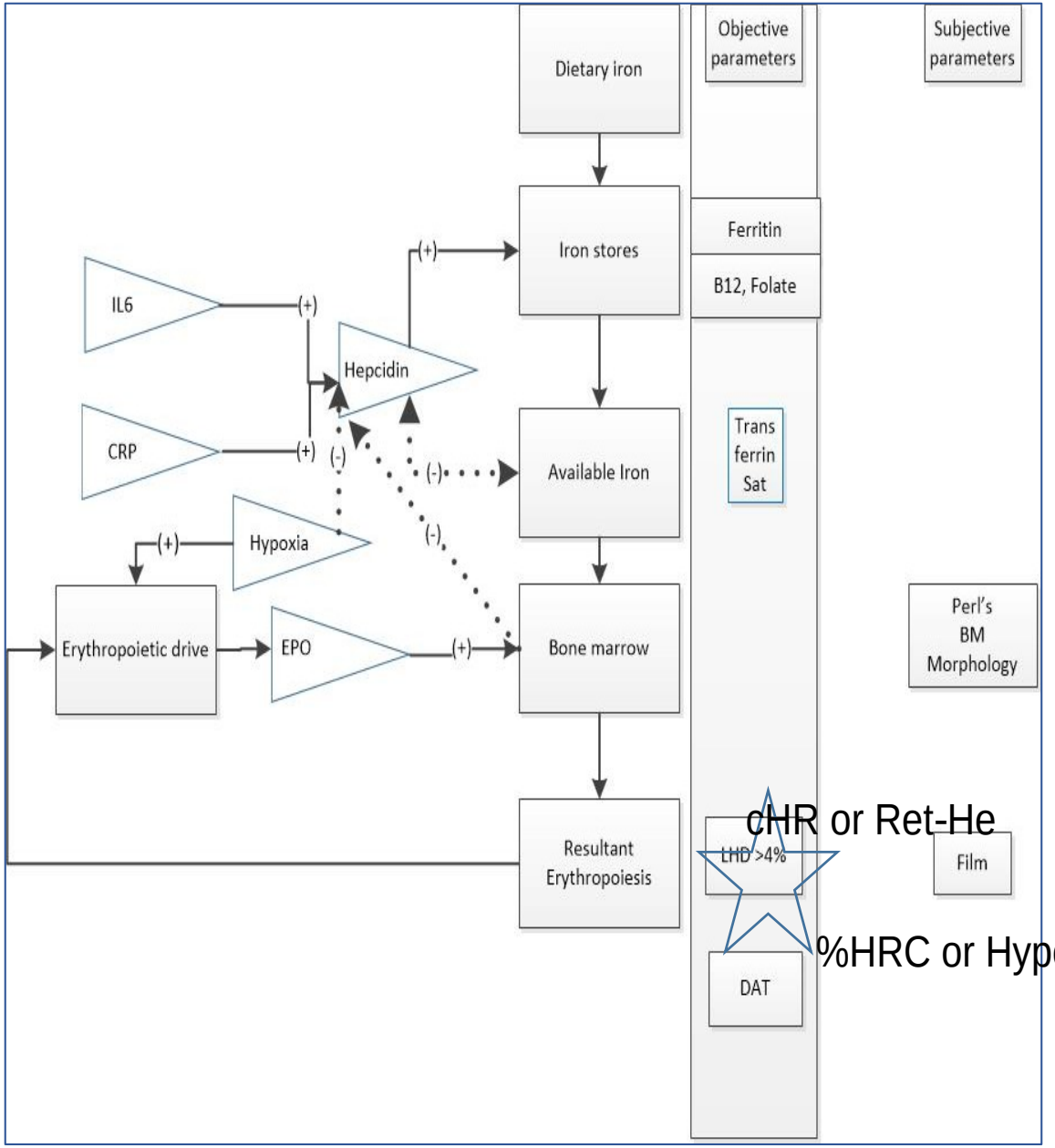
- sTfr insufficient experience and availability, can be replaced with the hemogram values above.
- Tf Sat in isolation not recommended to assess responsiveness to IV Iron
- Zinc protoporphyrine – washed red cells
- EPO, Retics and Hepcidin not useful
- BM stain rarely justified maybe if suspected that Ferritin >1200 does not reflect iron storage

Is Perl the answer? Stainable iron and ACD

Figure 2 Perl's grade evaluable patients (x-axis) and respective ferritin concentration in these patients. Data points are plotted as dots and the box represents median and first and third quartiles.



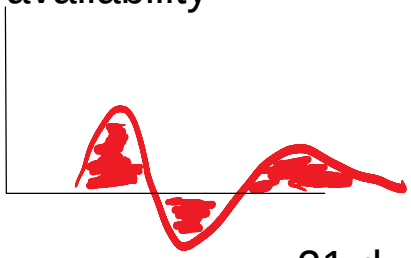
DID NOT AFFECT LHD as opposed to EPO, and TF SAT – ie static – not dynamic
Martin-Cabrera et al 2015



cHR or Ret-He

%HRC or Hypo-He

Fe availability



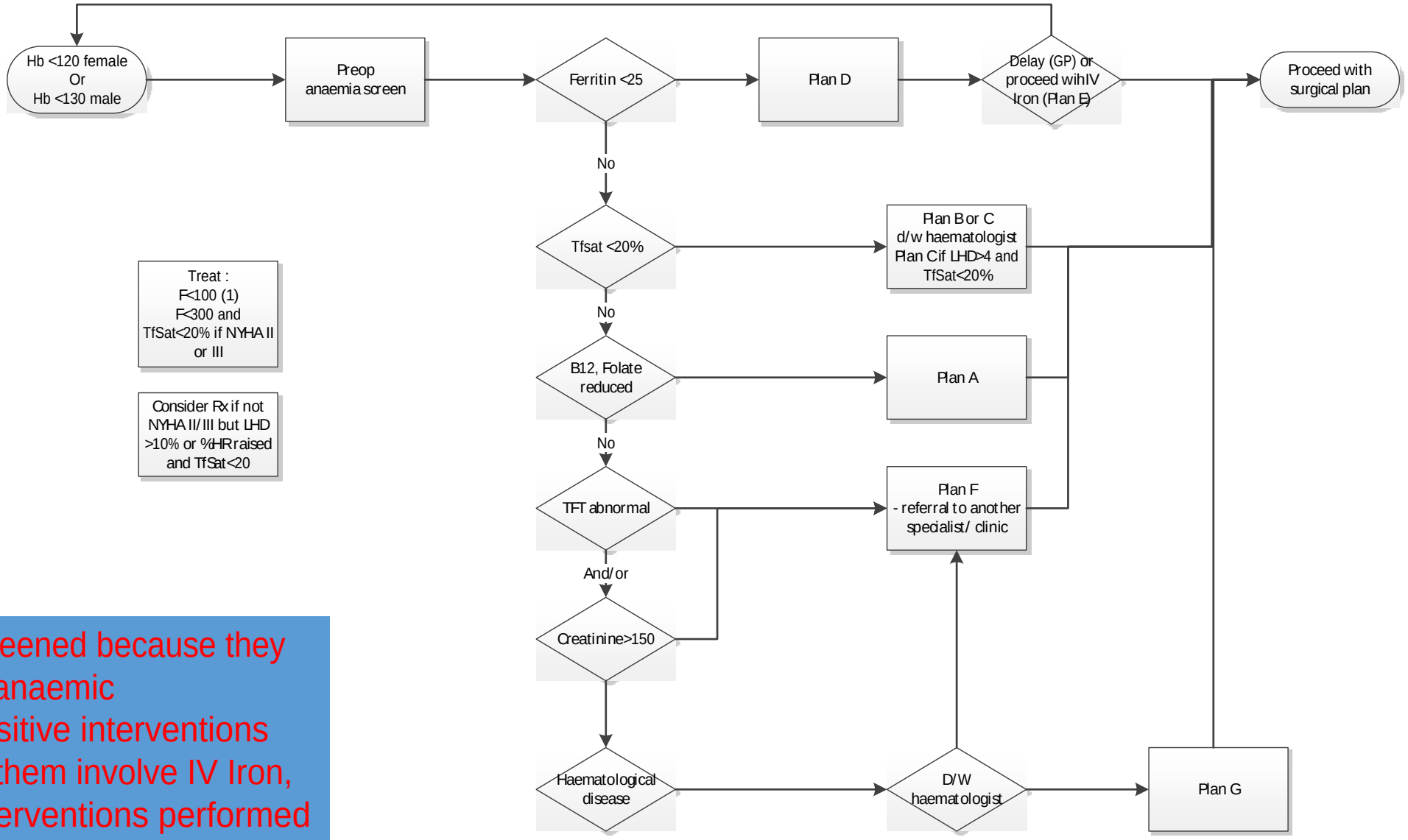
21 d

Epo and Tf Sat determines the LHD

Martin Cabrera et al. 201

MB1 **serum iron concentration flls withij hours pf inflammation but TIBC staus up Thomas 2013**

M Besser, 05/10/2015



96 screened because they were anaemic
65 positive interventions
43 of them involve IV Iron,
28 interventions performed
1: no IV Iron but B12, one failed screening due to lab

Treat with iron

- Patients with absolute or functional IDA (?? Definition)
- Patients scheduled for surgery who have a Ferritin<100 and TfSat<20% even if not anaemic (caution) if predicted loss >30g (1200ml)
- IV Iron for functional FeDef and if rapid response required (2B)

What could go wrong ?

- 15% cancer incidence in FeDef anaemia
- Low Ferritin in men and PMP women 0.9% cancer incidence
- GFR<45ml/min in diabetics and GFR 30 ml/min in non diabetic – likely renal
- Considered the domain of the endoscopist
- Giving 6 months of IV iron supply could significantly delay the diagnosis of the above if gastroenterology guidelines are subsequently applied by the letter

AIR HF trial - Anker et al. NEJM 2009

Ferritin <100,

TfSat<20% and Ferritin <300

Hb does not rise if not anaemic

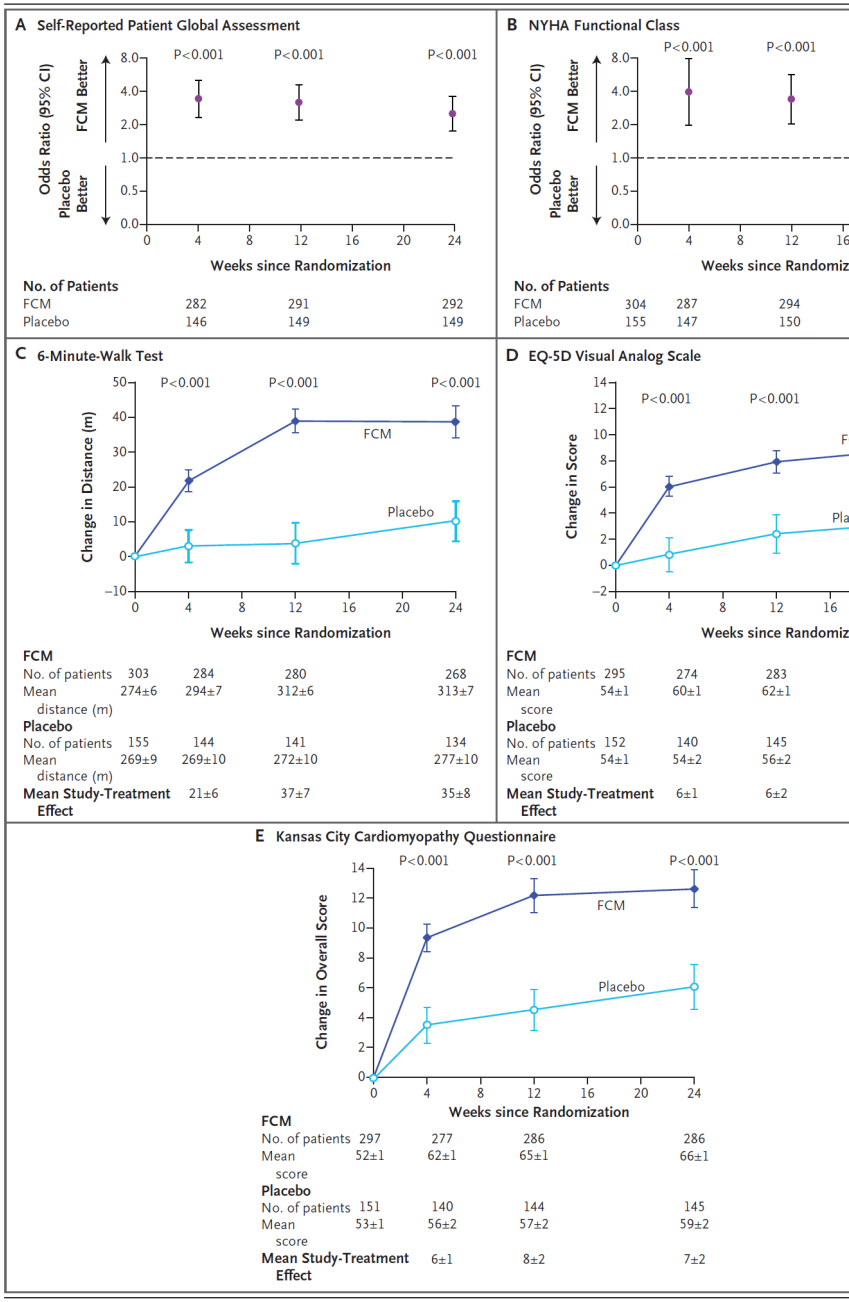
Dosing was stopped if Ferritin >800

- or 500-800 if TfSat > 50%

until Ferritin dropped to <400 and Hb <160

- and TfSat <45%

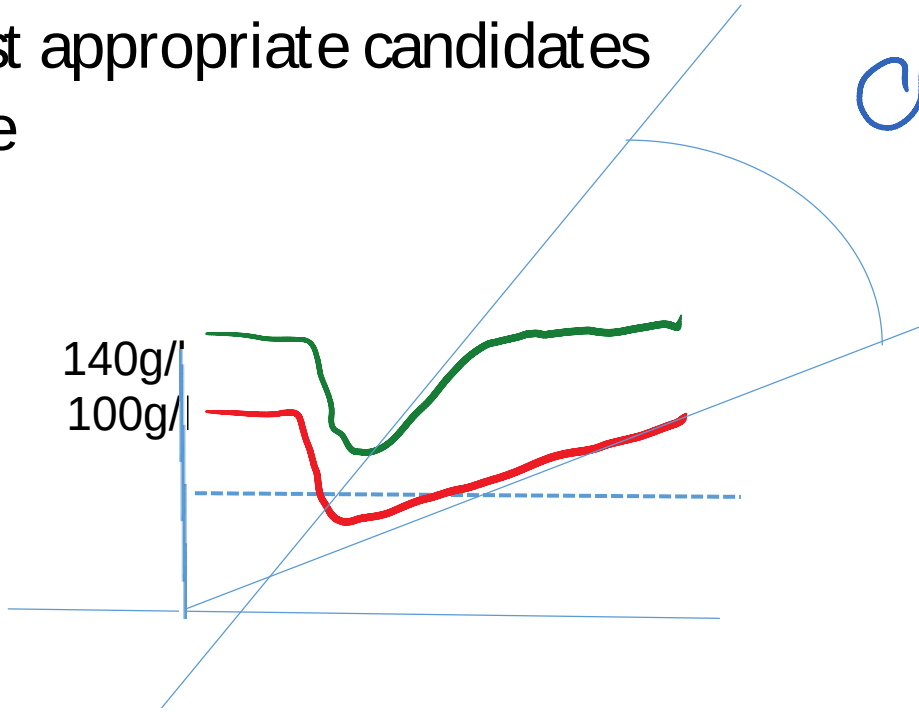
200mg Fe Carboxymaltose per week



N ENGL J MED 361;25

Sorted ?

- Pro: automatic enrolment if surgeon requests right blood test
- Con:
  - Complicated
  - Grey zone in patients with TfSat<20% and Ferritin >100 but <400
  - Could use %HRC to prescreen earlier most appropriate candidates
  - No information on postop recovery phase



Simplified protocol

Aspirations

- Prospectively prove the improved outcomes
- Improve coverage
- Include platelet function