

# FACTORS ASSOCIATED WITH THE MRI-ESTIMATED LIVER CONCENTRATION IN LONG-TERM HEMODIALYSIS PATIENTS RECEIVING INTRAVENOUS IRON SUPPLEMENTATION

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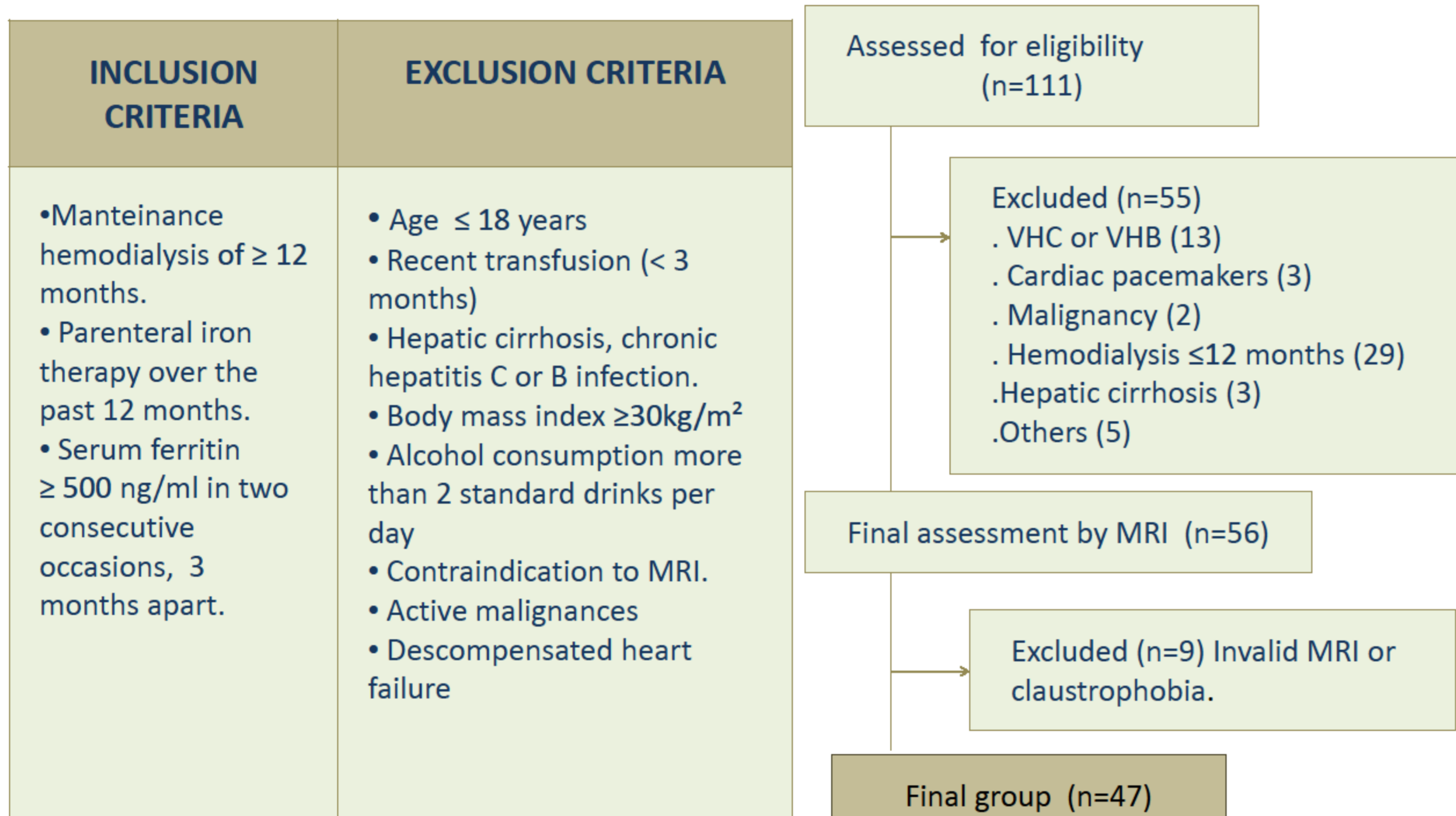
## INTRODUCTION

Several studies using Magnetic Resonance Imaging (MRI) T<sup>2</sup> and T<sup>2</sup>\* techniques have shown hepatic iron overload in hemodialysis (HD) patients treated with intravenous iron. Predictors of iron overload in these patients are not well defined:  
-Results regarding serum ferritin levels and transferrin saturation (TSAT) as a markers of liver iron stores are conflicting.  
- Some but not all studies have found that cumulative iron dose and duration of dialysis correlate with hepatic iron content.

## AIMS

The aim of this study was to identify factors affecting liver iron concentration (LIC) in this setting

## CHRONIC HEMODIALYSIS PATIENTS – CHARACTERISTICS



## METHODS

Liver iron concentration (LIC) was measured using MRI, as established by Gandon et al at Rennes University. The upper limit of normal LIC was set at 50 μmol/g. Patients were classified as: Mild iron overload: LIC 51-100 μmol/g. Moderate iron overload: LIC 101-200 μmol/g. Severe iron overload: > 201 μmol/g.

## SPECIFIC MEASUREMENTS

- Biological markers of iron metabolism: ferritin and hepcidin levels, TSAT.
- Oxidative stress markers: F2-isoprostanes methionine sulfoxide.
- Inflammatory markers: RCPus, TWEAK.
- Macrophage activation markers: CD163.
- Insulin resistance (HOMA).
- Hemochromatosis gene

## RESULTS

### Clinical parameters according to MRI -LIC

Characteristics	Overall (n=47)	Mild iron overload (n=25)	Moderate or severe iron overload (n= 18)
Age, years	70.6(13)	71.4(13.8)	69.3(11.9)
Female sex (n)	16	8	8
Body mass index (kg/m <sup>2</sup> )	24.7(3.2)	25.1(3.3)	24.1(2.9)
Time on dialysis (months)	75(42.3)	70.2(40.7)	82.8(44.7)
Cumulative iron dose last 6 years (gr)	7.4(3.3)	6.9(3)	8.2(3.6)
Diabetes (n)	14	8	6
Hepatic iron content at MRI (μmol/g)	121.9(67.7)	73.4(20.2)	200(35.9)*
Statin therapy (n)	21	16	5 **
Hemochromatosis gene (n)	1	1	0

\* P: < 0.0001

\*\* P: 0.08

### Bibliography.

- Ferrari P, Kulkarni H, Dheda S. et al. Serum iron markers are inadequate for guiding iron repletion in chronic kidney disease. Clin J Am Soc Nephrol 2011; 6:77-83.
- Rostoker G, Griuncelli M, Loridon. C et al. Hemodialysis-associated hemosiderosis in the era of erythropoiesis-stimulating agents. A MRI study. Am J Med 2012; 125:991-999.
- Rostoker G, Griuncelli M, Loridon. C et al. Reassessment of iron biomarkers for prediction of dialysis iron overload: an MRI study. Plos One 2015; 10(7):e0132006.

## Biochemical Parameters according to MRI - LIC

Parameter	Overall (n=47)	Mild iron overload (n=25)	Moderate or severe iron overload (n= 18)
Hemoglobin (g/dL)	11.6 (1.6)	12 (1.7)	10.9 (1)
TSAT (%)	32.9 (13)	32 (13.9)	34.3 (11.7)
Serum ferritin (ng/mL)	574.2 (242.5)	556.2 (255.3)	603.2 (224.4)
Serum Hepcidin (nM)	7.5 (2.8)	7.3 (3)	7.8 ( 2.6)
HOMA	7.5 (11.8)	9.3 ( 14.7)	4.8 ( 3.5)
PCRus (mg/dL)	14.8 (25.4)	14.8 (19.8)	16.1 (33.1)
TWEAK (pg/mL)	1174 (425.5)	1212.1 (499.6)	1114.4 (278)
CD163 (ng/mL)	211.1 (54.2)	212.6 (57.4)	208.5 (50.1)
8-iso-PGF2α (nM)	1.46 (0.53)	1.56 (0.58)	1.31 (0.4)
Methionine sulfoxide (nM)	1.71 (0.45)	1.69 (0.45)	1.73 (0.47)
Methionine sulfoxide (oxidized %)	18.1 (4.7)	18.3 (4.9)	17.8 (4.5)

## Correlation between demographic, clinical variables biochemical markers and LIC at MRI

Parameter	r	P
Serum ferritin	0.33	0.02
Serum Hepcidin	0.27	0.05
Serum Hemoglobin	-0.30	0.04
Cumulative iron dose (last 6 years)	0.25	0.08

## LIC at MRI according to gender and statin therapy

LIC	Statin Therapy		P
	Yes	No	
	100.7(57.6)	139 (71.5)	0.04
LIC	Gender		P
	Male	Female	
	106.6(58.2)	151 (76.6)	0.02

## Múltiple Lineal regression analysis for LIC

Parameter	OR	CI 95%	P
Gender ( female)	2.34	0.51-10.6	NS
Statin therapy	4.12	1.4-16.75	0.04
Serum Ferritin	0.99	0.99-1.00	NS
Serum Hepcidin	0.42	0.82-1.57	NS
Cumulative iron dose (last 6 years)	1.00	1.00-1.00	0.07

## CONCLUSIONS

- ✓ The majority of hemodialysis patients receiving intravenous iron have hepatic iron overload on MRI.
- ✓ TSAT, ferritin and hepcidin levels are poor indicators of liver iron deposits.
- ✓ Inflammation and oxidative stress markers are not related to hepatic iron overload in these patients
- ✓ Statin therapy may have a protective effect on hepatic iron overload associated with iron therapy in this population.