

# LOW LEVELS OF SERUM FERRITIN AND MODERATE TRANSFERRIN SATURATION LEAD TO ADEQUATE HEMOGLOBIN LEVELS IN HEMODIALYSIS PATIENTS

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## Background

The optimal iron levels for patients on hemodialysis (HD) are currently unknown. However, excessive iron intake can lead to oxidative stress or impair the efficiency of its use.

Therefore, it is a high-priority task to identify the optimal iron content for patients on HD.

We investigated the relationship between hemoglobin (Hb) level and iron status in patients on HD receiving recombinant human erythropoietin (rHuEPO) for anemia therapy.

## Methods

① 208 outpatients on maintenance HD were followed up between July 2006 and June 2007 (Tab. 1).

• We measured Hb twice a month, and serum ferritin (s-ft) and TSAT monthly.

• The targeted Hb level was 10-11 g/dL, according to Japanese guidelines.

• Treatment was administered with rHuEPO and low-dose iron preparation.

② Using the mean values for 1-year period, the relationships among Hb, s-ft and TSAT were investigated.

• Receiver operating characteristic curve (ROC) with Hb  $\geq 10$  g/dL as the endpoint (Fig. 1)

• Logistic regression model with Hb  $\geq 10$  g/dL as the endpoint (Tab. 2)

③ Hepcidin was measured by LC-MS/MS assay at baseline.

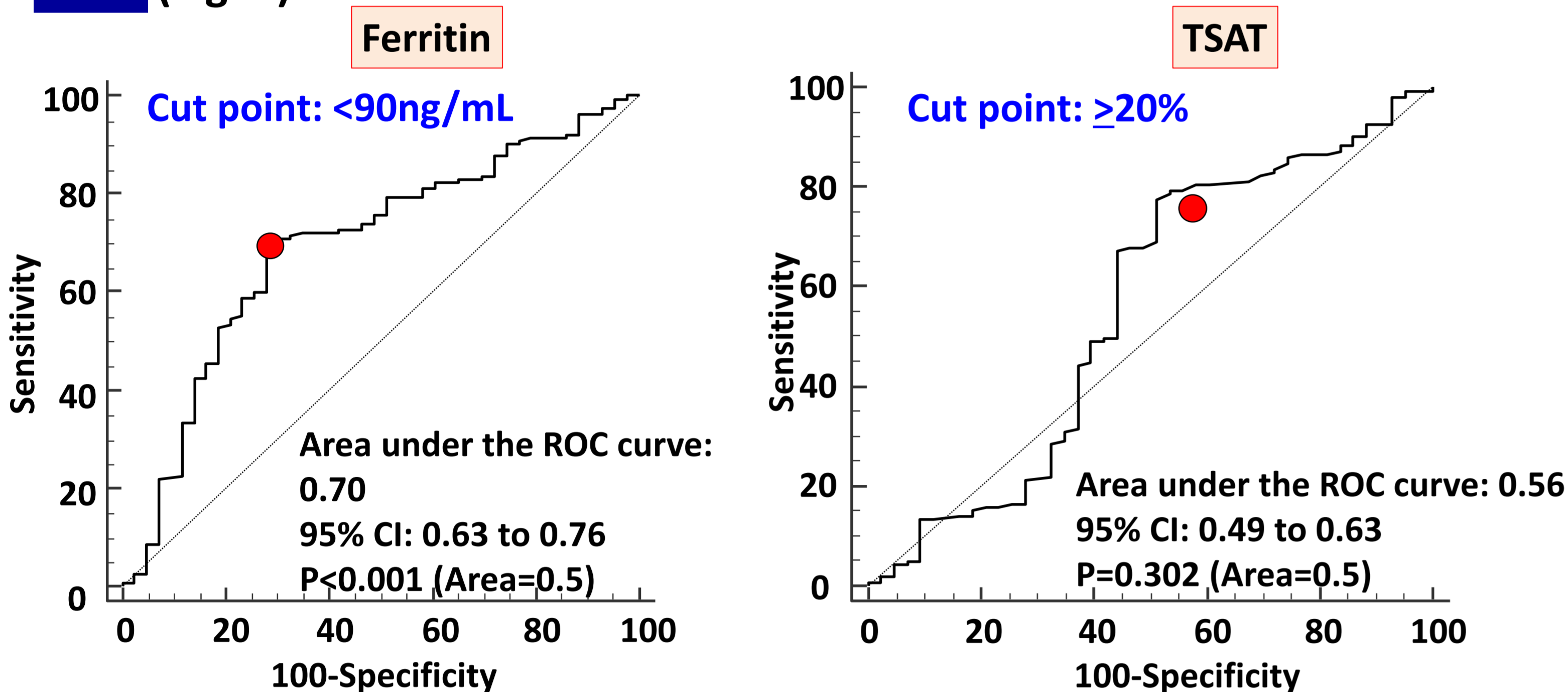
④ The interaction among s-ft, TSAT and Hepcidin was analyzed.

• Pearson product-moment correlation coefficient (Fig. 2)

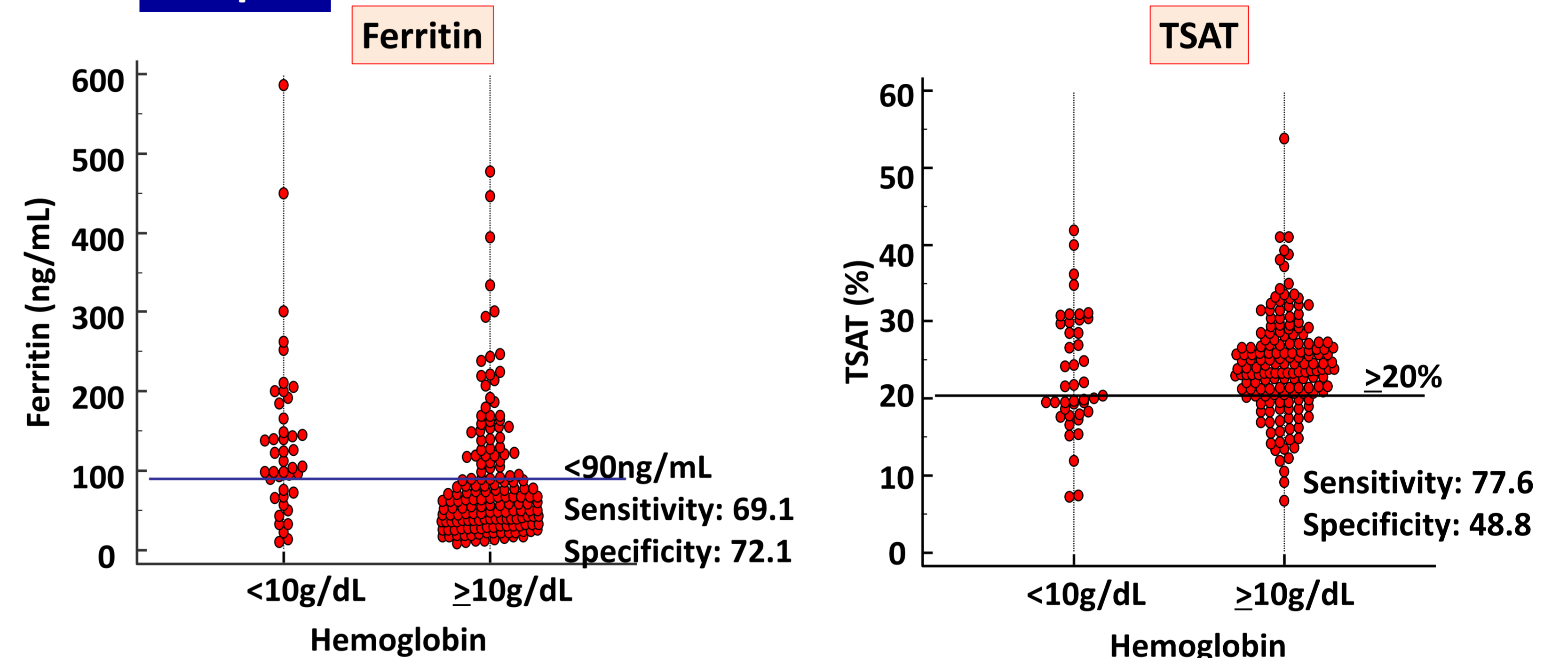
• Linear regression model (Tab. 3)

## ROC

(Fig. 1)



## Dot plot



## Logistic regression model

(Tab. 2)

Variables	No. of Patients	No. of Hb $\geq 10$ g/dL (%)	Univariable analysis			Multivariable analysis		
			Unadjusted Odds ratio	95% CI	P-value	Adjusted Odds ratio	95% CI	P-value
Ferritin(ng/mL)								
$\geq 90$	80	50 (62.5%)	1.00					
$< 90$	128	115 (89.8%)	5.31	(2.56-11.02)	$<.001$	8.13	(3.49-18.90)	$<.001$
TSAT(%)								
$< 20$	53	34 (64.2%)	1.00					
$\geq 20$	155	131 (84.5%)	3.05	(1.5-6.21)	0.002	5.46	(2.3-12.95)	$<.001$
Ferritin(ng/mL), TSAT(%)								
$\geq 90, < 20$	15	4 (26.7%)	1.00					
$\geq 90, \geq 20$	65	46 (70.8%)	6.66	(1.88-23.54)	0.003	-	-	-
$< 90, < 20$	38	30 (78.9%)	10.31	(2.58-41.19)	$<.001$	-	-	-
$< 90, \geq 20$	90	85 (94.4%)	46.75	(10.89-200.70)	$<.001$	-	-	-

## ROC analysis

(Fig. 1) The cutoff point for s-ft was found to be **below 90 ng/mL** (Fig 1), whereas the cutoff point for TSAT was found to be **at least 20%**.

## Logistic model analysis

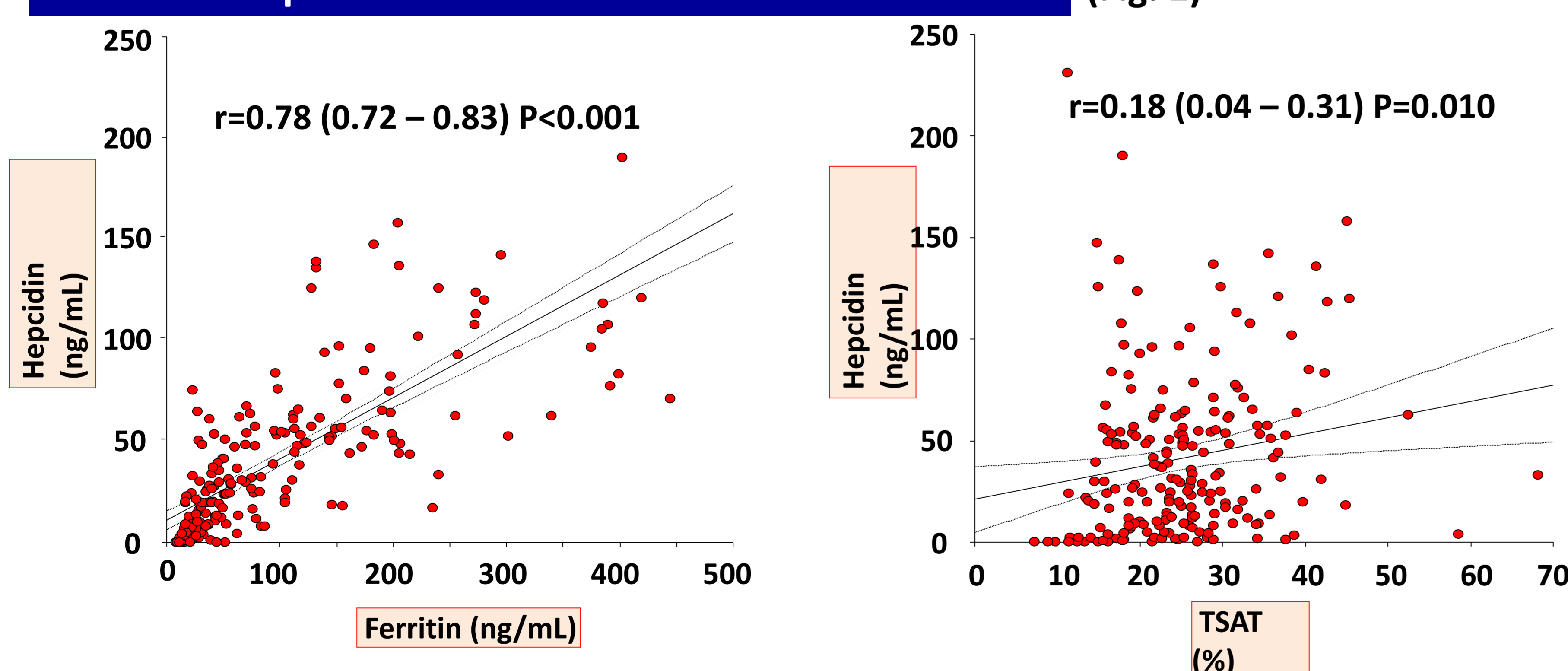
(Tab. 2) The odds ratio of the group with s-ft  $< 90$  ng/mL to the group with s-ft  $\geq 90$  ng/mL was significantly high.

The odds ratio of the group with TSAT  $\geq 20\%$  to the group with TSAT  $< 20\%$  was significantly high.

The odds ratios relative to a group with s-ft  $\geq 90$  ng/mL and TSAT  $< 20\%$  revealed that the group with s-ft  $< 90$  ng/mL and TSAT  $\geq 20\%$  had the highest ratio.

## The Pearson product-moment correlation coefficient

(Fig. 2)



## Pearson product-moment correlation coefficient

(Fig. 2) Hepcidin showed a **strong positive** correlation with s-ft and a **weak positive** correlation with TSAT.

## Linear regression model

(Tab. 3) A **positive relationship** was shown between hepcidin and s-ft. However, **no relationship** was shown with TSAT.

## Linear regression model

(Tab. 3)

Independent variables	No. of Patients	Univariable analysis			Multivariable analysis		
		Unadjusted Regression Coefficient	95%CI	P-value	Adjusted Regression Coefficient	95% CI	P-value
Ferritin (per 1ng/mL increase)	204	0.30	(0.27 to 0.34)	$<.001$	0.30	(0.27 to 0.34)	$<.001$
TSAT (per 1% increase)	204	0.80	(0.19 to 1.41)	0.010	0.09	(-0.31 to 0.49)	0.660

## Conclusion

In this study, the iron status of s-ft  $< 90$  ng/mL and TSAT  $\geq 20\%$  was optimal in HD patients receiving rHuEPO for anemia therapy.

This result indicates that the threshold values for the optimal iron status may be lower than those currently recommended in iron-level management guideline.

Tab. 1 Characteristics

variables	value
Age(years)	58.9 $\pm$ 12.9
Men	135
Duration of dialysis (years)*	7.88 (3.7-14.4)
Primary diagnosis	
Chronic glomerulonephritis	117
Diabetes nephropathy	52
Other	39
Kt/V	1.32 $\pm$ 0.22
Hemoglobin (g/dL)	10.3 $\pm$ 0.9
serum-Ferritin (ng/mL)*	50.6 (22.7-125)
Transferrin saturation (%)	24.7 $\pm$ 9.4
Hepcidin (ng/mL)*	29.8 (9.5-56.9)
Albumin(g/dL)	3.9 $\pm$ 0.3
C-reactive protein (mg/dL)*	0.06 (0.03-0.20)
rHuEPO (IU/week)	3909 $\pm$ 2725

Mean $\pm$ SD, median (interquartile range )\*