Serum Ferritin Level is an Independent Risk Factor for All-Cause Mortality in Incident Hemodialysis Patients

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INTRODUCTION

Serum ferritin has been regarded as an indicator of inflammation as well as a marker of body iron storage in patients with end-stage renal disease (ESRD). In addition, high serum ferritin levels were significantly associated with poor clinical outcomes in prevalent dialysis patients.

AIM

The aim of this study was to investigate prognostic value of serum ferritin levels on patient outcomes in incident hemodialysis (HD) patients.

PATIENTS AND METHODS

A prospective cohort of 939 incident HD patients from 36 dialysis centers of the Clinical Research Center for ESRD in Korea was selected for this study. Serum ferritin levels were measured at the time of HD initiation. Patients were divided into tertiles according to log ferritin concentrations; <2.17, 2.17-2.50, and >2.50 ng/mL.
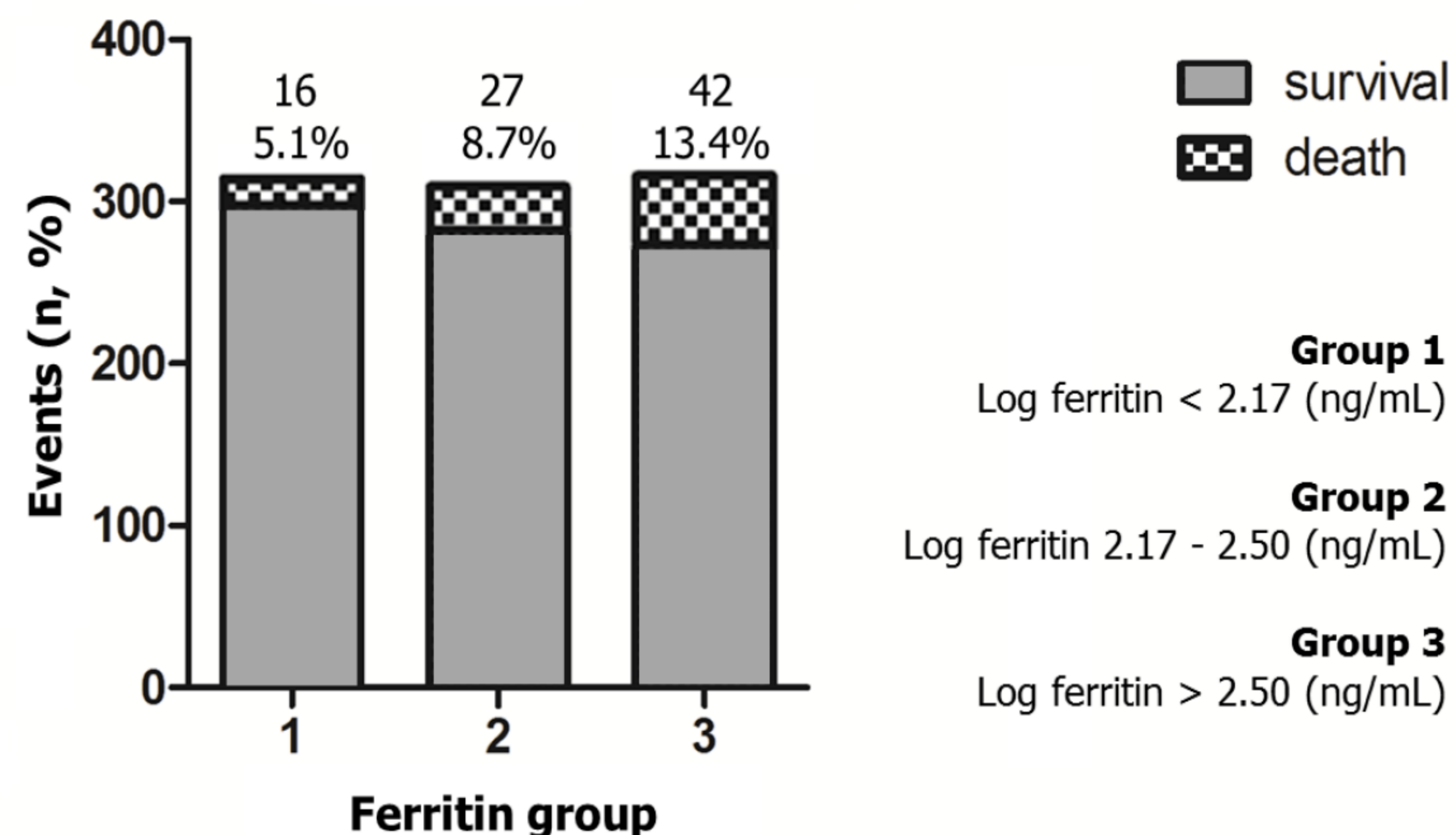
RESULTS

Table 1. Baseline characteristics according to the ferritin groups

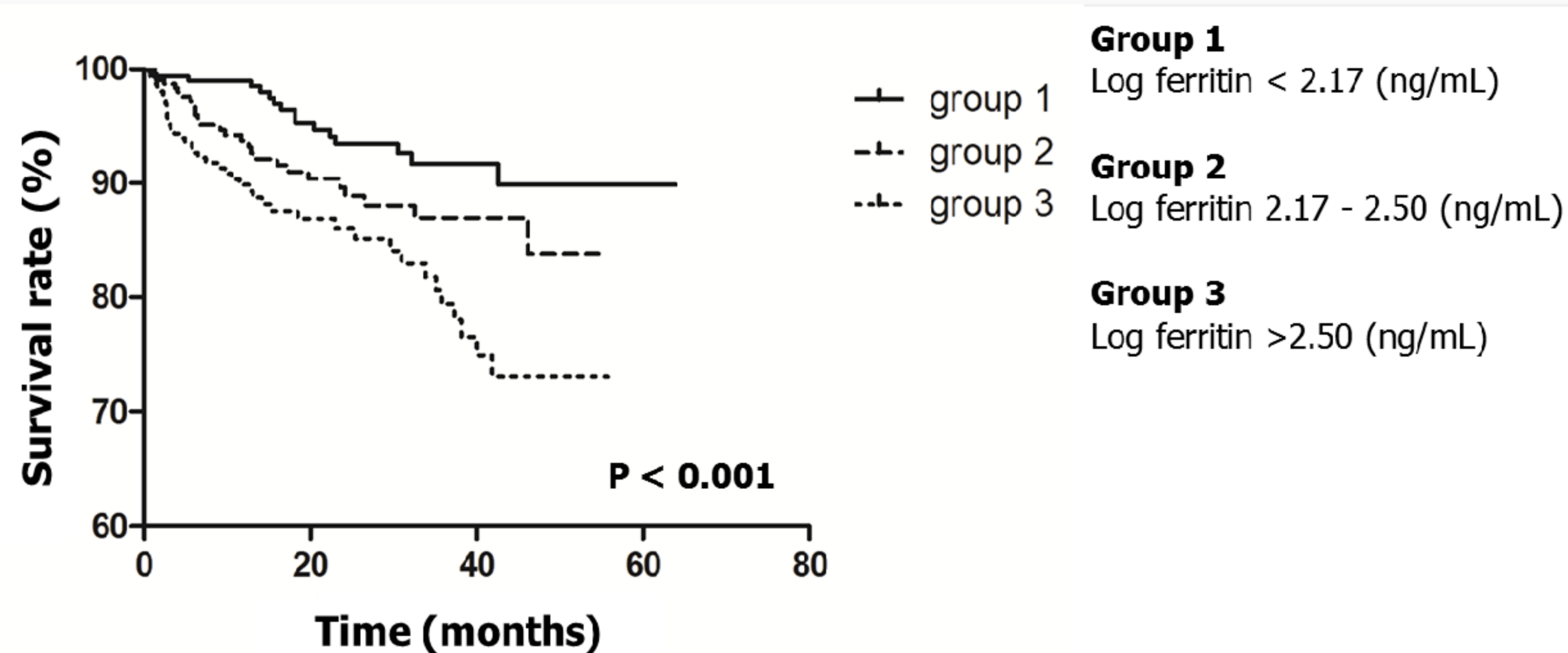|	All patients (n=939)	Group 1 log ferritin < 2.17 (n=314)	Group 2 log ferritin 2.17- 2.50 (n=311)	Group 3 log ferritin > 2.50 (n=314)	P
Male (%)	573 (61.0%)	194 (61.8%)	184 (59.2%)	195 (62.1%)	0.711
Age (yr)	63 (52-71)	61 (50-70)	64 (52-72)	63 (53-73)	0.060
DM (%)	551 (58.7%)	183 (58.3%)	185 (59.5%)	183 (58.3%)	0.940
BMI (kg/m^2)	22.6 (20.7-25.0)	22.9 (20.9-25.1)	22.6 (20.6-25.4)	22.4 (20.6-24.8)	0.319
CAD	127 (13.6%)	48 (15.3%)	34 (11.0%)	45 (14.4%)	0.528
PAD	85 (9.1%)	27 (8.6%)	27 (8.7%)	31 (9.9%)	0.669
CVD	92 (9.8%)	26 (8.3%)	30 (9.6%)	36 (11.5%)	0.591
CHF	119 (12.7%)	40 (12.7%)	34 (10.9%)	45 (14.4%)	0.613
Hemoglobin (g/dL)	8.7 (±1.7)	8.8 (±1.5)	8.6 (±1.5)	8.6 (±1.9)	0.436
BUN (mg/dL)	82.5 (60.0-107.5)	78.1 (59.3-100.4)	82.5 (60.5-107.5)	87.6 (60.0-116.5)	0.002
Creatinine (mg/dL)	7.9 (6.2-7.9)	7.9 (6.2-9.9)	8.0 (6.3-10.3)	7.7 (5.8-10.8)	0.161
Albumin (g/dL)	3.3 (2.9-3.7)	3.4 (3.0-3.8)	3.4 (3.0-3.8)	3.2 (2.8-3.7)	0.001
Calcium (mg/dL)	7.8 (7.2-8.3)	7.8 (7.3-8.3)	7.9 (7.2-8.4)	7.7 (7.2-8.4)	0.716
Phosphate (mg/dL)	5.4 (4.4-6.7)	5.3 (4.4-6.5)	5.4 (4.5-6.8)	5.4 (4.3-6.9)	0.166
PTH (pg/mL)	210.7 (121.0-342.3)	225.6 (126.5-374.2)	214.6 (128.7-352.0)	184.3 (102.8-313.5)	0.066
Hs-CRP (mg/L)	0.35 (0.08-1.60)	0.20 (0.06-0.87)	0.31 (0.06-1.32)	0.74 (0.14-2.78)	<0.001
Log ferritin (ng/mL)	2.33 (2.07-2.58)	1.94 (1.71-2.08)	2.34 (2.25-2.41)	2.68 (2.58-2.86)	<0.001
Serum iron (µg/dL)	54.0 (35.0-80.3)	46.7 (32.0-68.0)	58.0 (39.0-82.0)	60.0 (36.0-91.4)	<0.001
TIBC (mg/dL)	207.0 (177.9-241.3)	228.0 (201.0-262.2)	203.0 (177.0-234.0)	188.0 (160.0-219.0)	<0.001
Iron use (n, %)	343 (70.6%)	132 (72.1%)	124 (74.7%)	87 (63.5%)	0.088
ESA use (n, %)	379 (78.1%)	137 (74.9%)	133 (80.6%)	109 (79.6%)	0.387

Table 2. Correlation between log ferritin and laboratory parameters representing inflammation

		Age	DM	Hb	Albumin	Iron	TIBC	WBC	Log hs-CRP
Log ferritin	r	0.094	-0.007	-0.051	-0.116	0.179	-0.342	0.108	0.151
	P	0.004	0.834	0.119	<0.001	<0.001	<0.001	0.001	<0.001
Age	r	1	-0.144	0.146	-0.021	-0.138	-0.147	0.000	0.165
	P		<0.001	<0.001	0.530	<0.001	<0.001	0.993	<0.001
DM	r		1	0.058	-0.274	-0.088	-0.066	-0.103	0.008
	P			0.076	<0.001	0.007	0.043	0.002	0.805
Hb	r			1	0.173	-0.014	0.164	0.088	-0.113
	P				<0.001	0.659	<0.001	0.007	0.001
Albumin	r				1	0.193	0.397	-0.108	-0.227
	P					<0.001	<0.001	0.001	<0.001
Serum iron	r					1	0.187	-0.132	-0.208
	P						<0.001	<0.001	<0.001
TIBC	r						1	-0.131	-0.232
	P							<0.001	<0.001
WBC	r							1	0.190
	P								<0.001
Log hs-CRP	r								1
	P								

Figure 1. Ferritin and proportional death-event according to ferritin level

Group 1
Log ferritin < 2.17 (ng/mL)

Group 2
Log ferritin 2.17 - 2.50 (ng/mL)

Group 3
Log ferritin > 2.50 (ng/mL)

Figure 2. Kaplan-Meier plots for all-cause mortality

Group 1
Log ferritin < 2.17 (ng/mL)

Group 2
Log ferritin 2.17 - 2.50 (ng/mL)

Group 3
Log ferritin >2.50 (ng/mL)

Table 3. Univariate Cox`s proportional hazard models of baseline parameters for all-cause mortality

Variables	Univariate	
	HR (95% CI)	P
Age (year)	1.048 (1.029-1.067)	<0.001
Female (vs. male)	1.172 (0.754-1.824)	0.481
DM (vs. non-DM)	1.839 (1.140-2.968)	0.013
WBC (per 100/uL)	1.005 (1.000-1.010)	0.041
Hb (per 1 g/dL)	0.978 (0.860-1.112)	0.734
Albumin (per 1g/dL)	0.719 (0.508-1.017)	0.063
Log ferritin (per 1 ng/mL)	3.189 (1.823-5.578)	<0.001
TIBC (per 1 mg/dL)	0.995 (0.991-1.000)	0.031
Serum iron (per 1 µg/dL)	0.994 (0.988-1.000)	0.070
Log hs-CRP (per 1 mg/L)	1.559 (1.192-2.039)	0.001

Table 4. Multivariate Cox`s proportional hazard model for all-cause mortality

Variables	Multivariate	
	HR (95% CI)	P
Age (year)	1.046 (1.025-1.066)	<0.001
DM (vs. non-DM)	1.786 (1.094-2.917)	0.02
Log ferritin (per 1 ng/mL)	2.623 (1.454-4.732)	0.001
Log hs-CRP (per 1 mg/L)	1.317 (1.000-1.735)	0.05

SUMMARY & CONCLUSION

Serum ferritin concentration was a significant independent predictor of all-cause mortality in incident HD patients.

References

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