

Low levels of serum ferritin are associated with good prognosis in patients on haemodialysis.

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Background: Control of iron storage is an important therapeutic measure for anaemia in haemodialysis (HD) patients. Oxidative stress due to excessive iron (Fe) supplementation has been associated with atherosclerosis, infection, myocardial infarction, and malignancy. As such, taking particular care to avoid high serum ferritin (s-ft) levels in the setting of anaemia is an important part of care for those on HD, though optimal levels remain unclear. In order to clarify the appropriate level of s-ft, we investigated the relationships between s-ft level, haemoglobin (Hb), and mortality in HD patients.

Methods: 147 outpatients on stable HD, excluding those with acute cardiovascular disease, active infection, and malignancy, were followed from May 2002 to April 2012. We measured Hb twice a month, and s-ft, serum Fe, and transferrin saturation (TSAT) monthly. An erythropoiesis-stimulating agent (ESA) and low-dose Fe supplement were administered to maintain an Hb level of 10-11 g/dL recommended by Japanese guidelines. Patients were categorized into five groups by mean s-ft and TSAT for observed term (Tab. 1). We assessed survival rates and Hb levels by group. Taking into account that Fe/s-ft ($\mu\text{g/dL}$ per ng/mL) reflects the efficiency of iron utilization, we further divided mean Hb (<9.5, 9.5-9.9, 10-10.4, 10.5-10.9, ≥ 11.0 g/dL), s-ft level (<60, 60-99, 100-199, ≥ 200 ng/mL), and Fe/s-ft (<0.5, 0.5-0.9, 1.0-1.9, 2.0-2.9, ≥ 3.0), evaluating the relationship of each with prognosis.

Kaplan-Meier, logrank testing, and generalized Wilcoxon statistics were used for analyses.

Tab. 1. The iron groups

Group	s-ft (ng/mL)	TSAT (%)
G1	$100 \leq$	$20 \leq$
G2	$60 \leq$	<20
G3	60-99	$20 \leq$
G4	<60	$20 \leq$
G5	<60	<20

Tab. 2. Baseline characteristics in G1-5 at starting study (means \pm SD)

	G1	G2	G3	G4	G5
Number	22	27	25	39	34
Age (yrs)	61.8 ± 9.2	56.5 ± 10.8	56.5 ± 13.5	54.7 ± 10.8	53.2 ± 11.0
Diabetes (%)	21.7	30.8	28.0	20.5	17.6
HD Duration (yrs)	5.8 ± 6.1	7.6 ± 5.3	7.6 ± 5.3	8.4 ± 7.4	9.1 ± 7.0
SBP (mmHg)	160.9 ± 23.6	162.7 ± 26.2	156.2 ± 17.4	156.3 ± 19.6	150.1 ± 21.3
Kt/V	1.27 ± 0.20	1.27 ± 0.16	1.33 ± 0.21	1.37 ± 0.25	1.25 ± 0.19
s-Alb (g/dL)	3.8 ± 0.3	3.9 ± 0.3	3.8 ± 0.3	3.8 ± 0.3	3.8 ± 0.3

Tab.3 10 years averaged palameters in G1-5 (means \pm SD)

	G1	G2	G3	G4	G5
Hb(g/dL)	10.0 ± 0.6	10.2 ± 0.5	10.2 ± 0.4	10.4 ± 0.4	10.5 ± 0.5
s-ft (ng/mL)	180.2 ± 125.9	110.8 ± 46.7	81.4 ± 12.3	33.4 ± 11.9	33.8 ± 13.5
TSAT (%)	25.8 ± 4.0	17.0 ± 1.9	25.6 ± 3.5	24.1 ± 3.1	16.6 ± 2.4
Ret (%)	14.2 ± 6.4	12.2 ± 4.8	11.6 ± 3.9	15.1 ± 3.7	16.5 ± 4.6
TIBC ($\mu\text{g/dL}$)	2272 ± 29.0	255.1 ± 29.5	240.8 ± 24.4	271.6 ± 31.2	299.5 ± 29.7
Fe (mg/dL)	57.9 ± 9.5	42.3 ± 6.6	60.6 ± 9.4	64.2 ± 8.2	48.8 ± 8.8
Fe/s-ft	0.42 ± 0.24	0.45 ± 0.18	0.76 ± 0.16	2.25 ± 1.21	1.68 ± 0.69
CRP (mg/dL)	0.56 ± 0.6	0.62 ± 0.52	0.38 ± 0.50	0.20 ± 0.18	0.40 ± 0.48
ESA (IU/W)	4565 ± 2041	4060 ± 3261	3841 ± 1964	4418 ± 2356	3240 ± 2538
Iv-Fe (mg/W)	6.5 ± 3.6	8.8 ± 7.5	6.3 ± 3.3	5.2 ± 2.7	6.9 ± 4.7

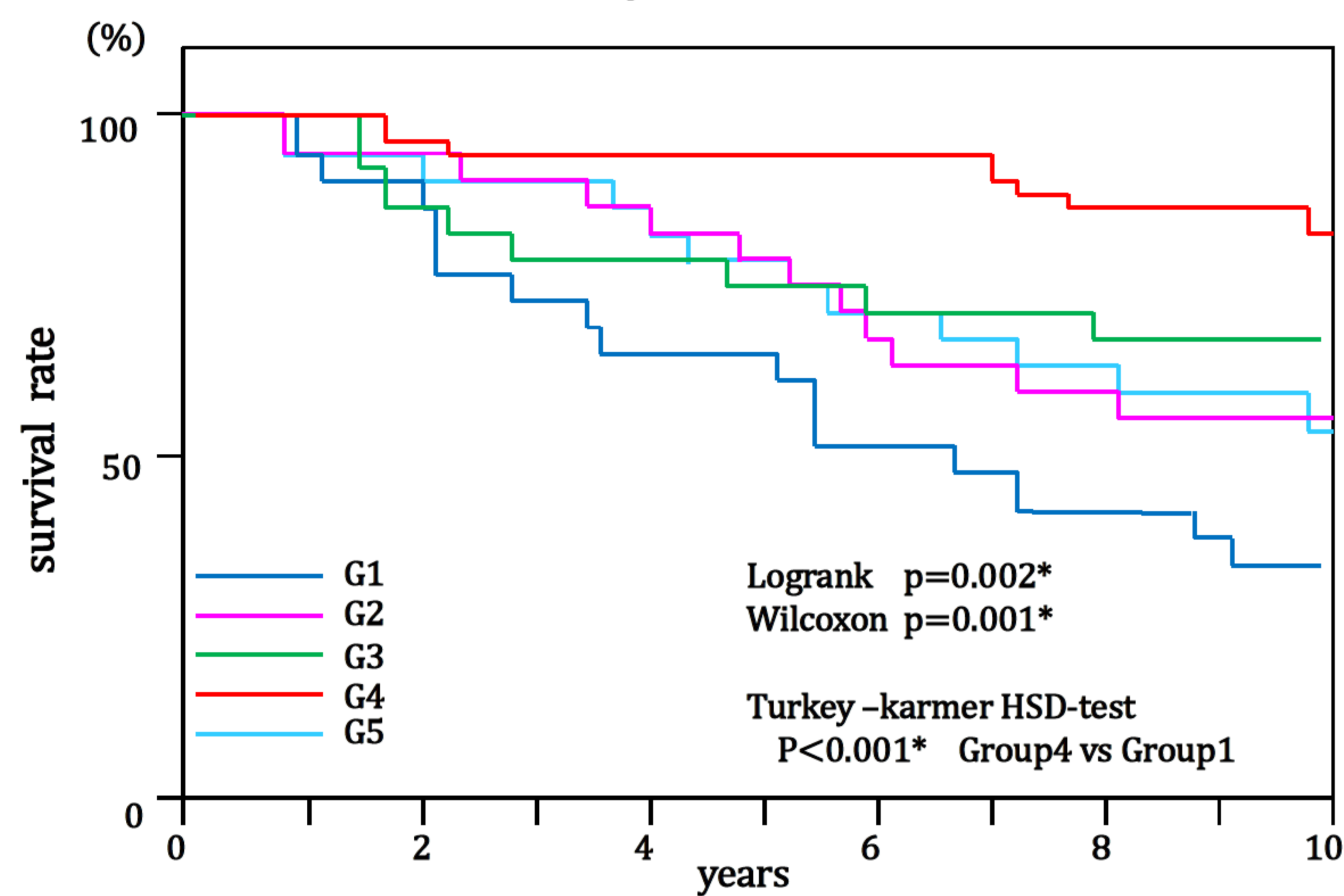


Fig. 1. 10-year survival by groups

10-year survival rate was 36.4, 55.6, 68.0, 84.6, and 61.8% respectively in G1 to 5. Survival in G4 was noted to be substantially high.

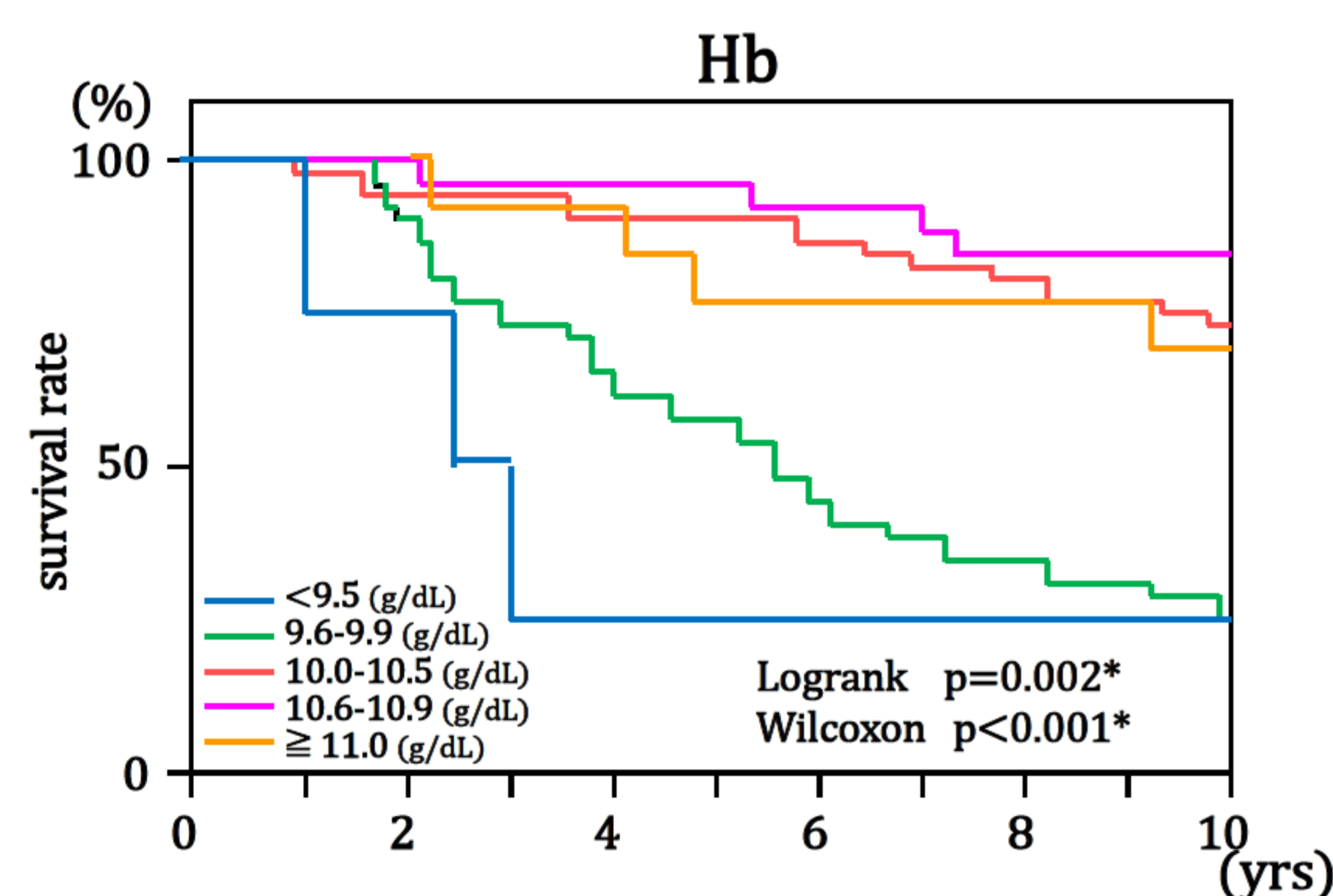


Fig. 2 Survival by mean Hb

Survival was highest in 10.5-10.9 g/dL group and lower in <10.0 g/dL groups.

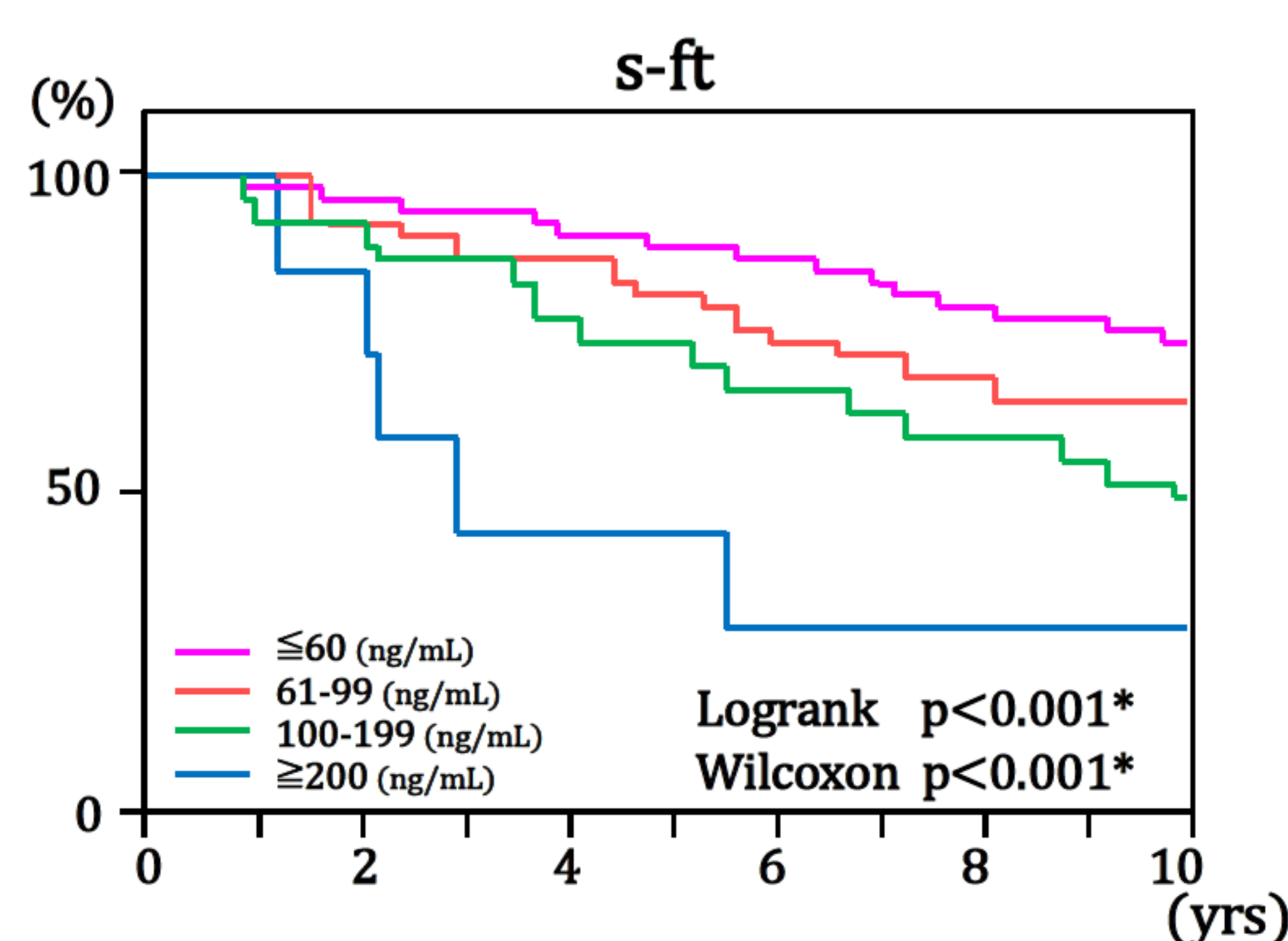


Fig. 3 Survival by mean s-ft

Survival rate was highest in the low s-ft (<60ng/mL) group, decreasing with increasing ferritin levels.

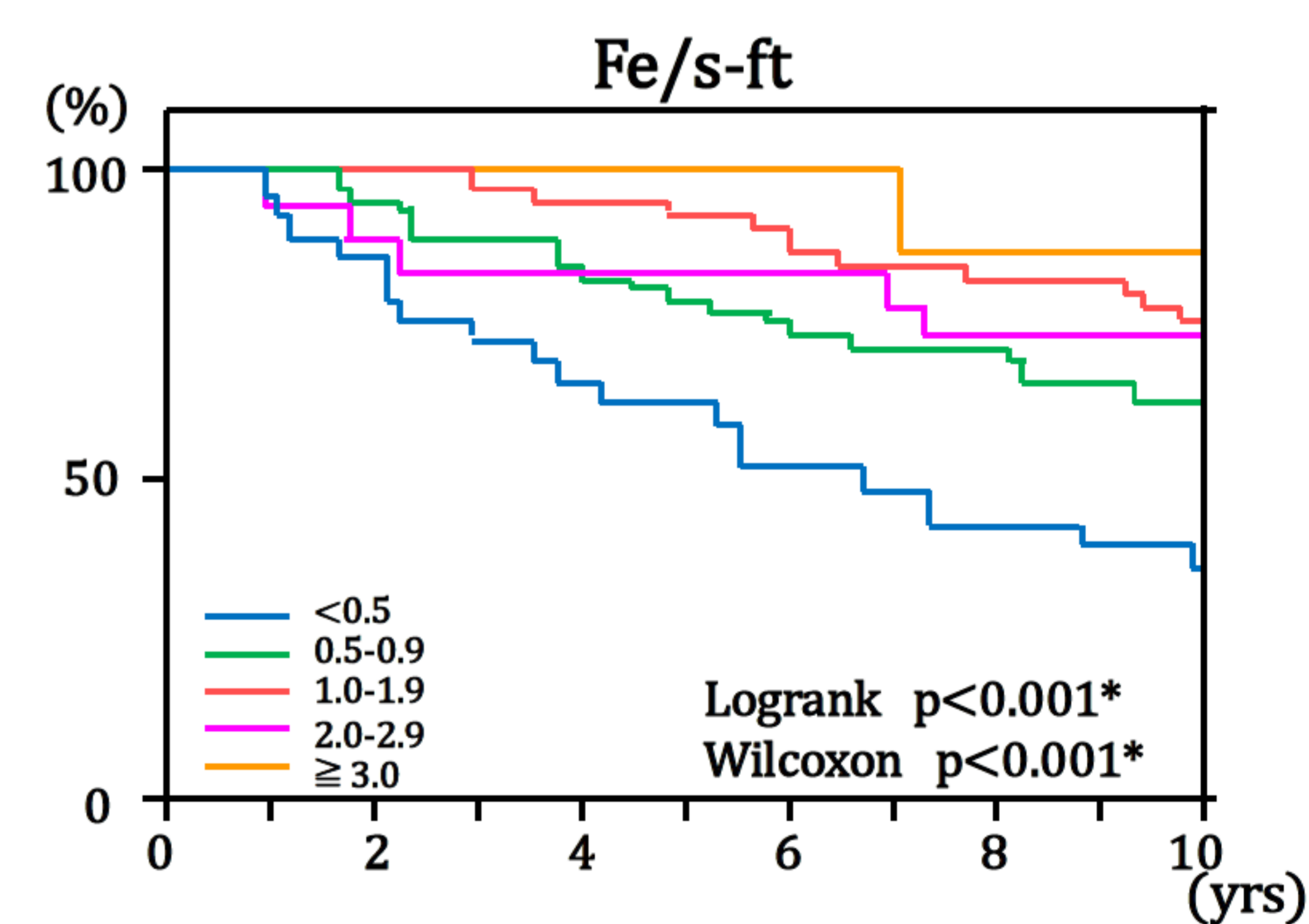


Fig. 4 Survival by mean Fe/s-ft

Survival rate was 87.5% in the highest group (≥ 3), while only, 36.7% in lowest group (<0.5).

Conclusion

Our data indicate that low serum ferritin is associated with adequate Hb levels. Furthermore, low levels of serum ferritin with moderate Fe levels, 10-11g/dL Hb and well efficiency of iron utilization are robustly associated with better prognosis among patients on HD.

