ORIGINAL ARTICLE

Korean J Intern Med 2014;29:489-497
http://dx.doi.org/10.3904/kjim.2014.29.4.489

KJIM

Ferritin as a predictor of decline in residual renal function in peritoneal dialysis patients

Soon Mi Hur, Hye Young Ju, Moo Yong Park, Soo Jeong Choi, Jin Kuk Kim, and Seung Duk Hwang

Division of Nephrology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Korea

Received: September 23, 2013
Revised : October 31, 2013
Accepted: November 11, 2013

Correspondence to
Soo Jeong Choi, M.D.
Division of Nephrology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, 170 Jomaru-ro, Wonmi-gu, Bucheon 420-767, Korea
Tel: +82-32-621-5169
Fax: +82-32-621-5015
E-mail: crystal@schmc.ac.kr

Background/Aims: Inflammation is an important factor in renal injury. Ferritin, an inflammatory marker, is considered an independent predictor of rapid renal progression in patients with chronic kidney disease. However, the relationship between ferritin and residual renal function (RRF) in patients undergoing peritoneal dialysis (PD) remains unclear.

Methods: We reviewed the medical records of patients who started PD between June 2001 and March 2012 at Soonchunhyang University Bucheon Hospital, Korea. A total of 123 patients were enrolled in the study. At 1 month after the initiation of PD, RRF was determined by a 24-hour urine collection and measured every 6 months thereafter. Clinical and biochemical data at the time of the initial 24-hour urine collection were considered as baseline.

Results: The RRF reduction rate was significantly greater in patients with high ferritin (ferritin ≥ 250 ng/mL) compared with those with low ferritin (ferritin < 250 ng/mL; –1.71 ± 1.36 mL/min/yr/1.73 m^2 vs. –0.84 ± 1.63 mL/min/yr/1.73 m^2, respectively; $p = 0.007$). Pearson correlation analysis revealed a significant negative correlation between the baseline serum ferritin level and the RRF reduction rate ($r = -0.219$, $p = 0.015$). Using multiple linear regression analysis and adjusting for other risk factors, baseline serum ferritin was an independent factor for the RRF reduction rate ($\beta = -0.002$, $p = 0.002$).

Conclusions: In this study we showed that a higher ferritin level was significantly associated with a more rapid RRF decline in patients undergoing PD.

Keywords: Ferritins; Peritoneal dialysis; Residual renal function

INTRODUCTION

Peritoneal dialysis (PD) is a well-accepted modality for the treatment of end-stage renal disease (ESRD). Preservation of residual renal function (RRF) is a major factor influencing the quality of life and mortality in PD patients [1,2]. Consequently, determining the predictors of RRF decline has become important in the treatment of PD patients. In previous studies, the RRF decline has been associated with several factors, including diabetes mellitus (DM), congestive heart failure (CHF), high body mass index (BMI), episodes of peritonitis, higher baseline RRF, and higher baseline proteinuria [3-5].

Inflammation is common in chronic kidney disease (CKD) and maintenance dialysis patients. Inflammation is a pathogenic factor of poor renal outcome in patients with glomerulosclerosis or tubulointerstitial fibrosis [6] and a predictor of poor clinical outcome, including high mortality in dialysis patients [7,8]. Ferritin, a clinical marker of iron storage, is also an acute-phase reactant and can be increased in chronic inflammatory states. Ferritin induces macrophage accumulation and increas-

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

es reactive oxygen species formation [9]. Several studies have shown that ferritin is a significant risk factor associated with rapid renal progression, morbidity, and mortality in CKD and hemodialysis (HD) patients [10-13]. A trend of poor outcomes was observed in advanced CKD patients with serum ferritin levels > 250 ng/mL [12,14]. However, few reports exist on the relationship between ferritin and renal outcome in PD patients. Thus, we examined whether a high ferritin level was associated with a more rapid RRF decline in PD patients.

METHODS

Patients

We reviewed the medical records of patients who started PD between June 2001 and March 2012 at Soonchunhyang University Bucheon Hospital, Korea. We enrolled patients for whom complete data sets describing changes in RRF over at least a 1-year period were available. Of the 282 patients screened, 159 were excluded for anuria (24-hour urine volume < 100 mL) at the start of PD (n = 66), duration of PD maintenance < 1 year (n = 65), and inadequate data (n = 28), resulting in 123 patients included in the study. The patients were divided into two groups according to the baseline serum ferritin level: low (1st to 75th percentile, n = 89, < 250 ng/mL) and high (75th to 100th percentile, n = 34, ≥ 250 ng/mL) groups.

This study was approved by the Institutional Review Board of Soonchunhyang University Bucheon Hospital.

Data collection

We collected demographic and clinical data, including age, gender, BMI, underlying cause of ESRD, episodes of peritonitis and comorbid conditions such as hypertension, DM and CHF. We recorded medications such as renin-angiotensin system (RAS) blockers, calcium channel blockers, β-blockers, diuretics, intravenous (IV)/oral iron, and erythropoiesis-stimulating agents at baseline. The PD modality was classified as continuous ambulatory PD or automated PD. For the subjective global assessment (SGA), we used a four-item, 7-point Likert-type scale [15], which included weight loss, anorexia, subcutaneous fat, and muscle mass. We performed laboratory tests, 24-hour urine and dialysate effluent collection at 8:00 AM after at least 8-hour nil per os within 1 month of the start of PD (as the baseline) and every 6 months thereafter. Normalized protein nitrogen appearance rate (nPNA), renal Kt/V, and peritoneal Kt/V were calculated using urea clearances from a 24-hour urine and dialysate effluent collection. Total Kt/V was calculated as the sum of renal and peritoneal Kt/V. RRF was calculated as the average of the 24-hour urine urea and creatinine clearances to avoid overestimation errors by creatinine clearance and underestimation by urea clearance [16]. The change in RRF over a 1-year period was determined by calculating the change in RRF from the initiation of PD to 1 year after start of PD. All patients were followed until death, follow-up loss, transfer to HD, transplant, transfer to other hospitals, or the end of the study in March 2013. Patients who had anuria during the study period were eliminated from the study and the mean of the RRF decline was calculated in patients who developed anuria. The mean RRF decline was determined by calculating the change in RRF from the initiation of PD to the time of anuria.

Statistical analyses

Statistical analyses were performed using the SPSS version 18.0 (IBM Co., Armonk, NY, USA). Continuous variables were expressed as means ± SD or medians (25th, 75th percentiles) and categorical variables were expressed as percentages. To evaluate the differences between the two groups, Student *t* test, chi-square test, Mann-Whitney *U* test, and analysis of covariance were used. When comparing time periods, the paired-sample *t* test was used for continuous variables. Pearson correlation analysis was performed to estimate the correlations between the rate of reduction in RRF and other variables. Additionally, univariate and multivariate Cox-regression models were used to identify significant predictors of RRF decline. A Kaplan-Meier survival curve was generated for the descriptive analysis of patient survival. Statistical significance was set at a p value < 0.05.

RESULTS

Baseline characteristics of the study population

We screened 282 patients for eligibility who started PD between June 2001 and March 2012; 123 patients with

http://dx.doi.org/10.3904/kjim.2014.29.4.489

complete data sets followed up for at least 1 year were enrolled. Table 1 shows the baseline demographic, clinical, and laboratory characteristics of the study patients. The mean patient age was 52.7 ± 12.2 years and 57 (46.3%) were males. Diabetes was the most common cause of ESRD in this study (47.1%). The median serum ferritin level was 167 ng/mL (range, 101 to 268).

Comparison of the low- and high-ferritin groups at baseline and 12 months

At baseline, 27.6% of the patients had serum ferritin ≥ 250 ng/dL. Based on serum ferritin concentrations, there was no significant difference between the low- and high-ferritin groups in age, proportion of males, BMI , proportion of patients with a history of CHF, use of RAS blockers, diuretic use, statin, vitamin C, vitamin D analogues, IV/oral iron supplement, dose of erythropoiesis-stimulating agents, serum iron, serum hemoglobin, serum albumin, or serum creatinine. Additionally, serum high-sensitivity C-reactive protein (hs-CRP), total Kt/V, nPNA, SGA, baseline RRF, and 24-hour urine protein were similar between the low- and high-ferritin groups.

However, the proportion of patients with a history of DM was significantly higher in the high-ferritin compared with the low-ferritin group (50.6% vs. 70.6%, respectively, $p = 0.045$; data not shown). No correlation was found between baseline RRF and the serum ferritin level ($r = -0.009$, $p = 0.926$). Additionally, at 12 months after PD initiation, there was no significant difference between the low- and high-ferritin groups in serum hemoglobin, serum albumin, serum hs-CRP, nPNA, SGA, or peritonitis rates. Total Kt/V showed a significantly greater decline in the high-ferritin group compared with the low-ferritin group (Table 2).

Consistency of serum ferritin levels

The serum ferritin level did not change significantly at the 12-month follow-up ($p = 0.352$; data not shown). A positive and statistically significant correlation was found between the baseline and mean serum ferritin levels ($r = 0.700$, $p < 0.001$; data not shown).

Ferritin and change in RRF at the 1-year follow-up

All patients underwent a minimum of two timed urine collections to measure RRF. The RRF decreased signifi-

Table 1. Baseline characteristics of study subjects (n = 223)

Characteristic	Value
Age, yr	52.7 ± 12.2
Male sex	57 (46.3)
Body mass index, kg/m^2	23.4 ± 0.3
Causes of ESRD	
DM	58 (47.1)
Hypertension	30 (24.4)
Hypertension combined with DM	6 (4.9)
Chronic glomerulonephritis	13 (10.6)
Others	16 (13.0)
Comorbid conditions	
Hypertension	112 (91.1)
DM	69 (56.1)
Congestive heart failure	11 (8.9)
Medication	
RAS blockers	81 (65.9)
Calcium channel blockers	100 (81.3)
β-Blockers	72 (58.5)
Diuretics	66 (53.7)
Statin	48 (39.0)
Vitamin C	101 (82.1)
Vitamin D analogues	22 (17.9)
IV/oral iron	71 (57.7)
Erythropoietin, IU/kg/wk	115.1 ± 65.0
PD schedule	
CAPD	64 (52.0)
APD	59 (48.0)
Solute transport and PD adequacy	
Total Kt/V urea	2.75 ± 1.71
nPNA, g/kg/day	1.12 ± 0.88
SGA	26.1 ± 2.2
Laboratory data	
Hemoglobin, g/dL	9.5 ± 1.5
Albumin, g/dL	3.9 (3.5, 4.2)
BUN, mg/dL	52 (40, 65)
Creatinine, mg/dL	9.2 (6.6, 9.8)
Potassium, mg/dL	4 (3.7, 4.5)
Phosphorus, mg/dL	4.12 ± 0.7
Cholesterol, mg/dL	161.4 ± 47.3
Triglyceride, mg/dL	102 (65, 146)
hs-CRP, mg/dL	0.1 (0.1, 0.6)
Ferritin, ng/mL	167 (101, 268)
Fe (iron), μg/dL	52 (31.8, 86.0)
Residual renal function, mL/min/1.73 m^2	2.45 (1.34, 4.01)
24-Hour urine protein, g/day	1.27 (0.68, 2.38)

Values are presented as mean ± SD, number (%), or median (25th, 75th percentile).
ESRD, end-stage renal disease; DM, diabetes mellitus; RAS, renin-angiotensin system; IV, intravenous; PD, peritoneal dialysis; CAPD, ambulatory peritoneal dialysis; APD, automated peritoneal dialysis; nPNA, normalized protein nitrogen appearance rate; SGA, subjective global assessment; BUN, blood urea nitrogen; hs-CRP, high sensitivity C-reactive protein.

Table 2. Comparison of the baseline and 12-month values of factors related to ferritin

Variable	Ferritin < 250 ng/mL (128.2 ± 57.5) (n = 89)	Ferritin ≥ 250 ng/mL (386.9 ± 140.6) (n = 34)	*p* value
Baseline			
Age, yr	52.3 ± 12.4	53.9 ± 12.0	0.520
Male sex	39 (43.8)	18 (52.9)	0.392
Body mass index, kg/m^2	23.3 ± 3.1	23.5 ± 2.8	0.801
History of DM	45 (50.6)	24 (70.6)	0.045
History of CHF	5 (5.6)	6 (17.6)	0.070
RAS blockers	57 (64)	24 (70.6)	0.494
Diuretics	46 (51.7)	20 (58.8)	0.478
Statin	35 (39.3)	13 (38.2)	0.912
Vitamin C	73 (82.0)	28 (82.4)	0.966
Vitamin D analogues	17 (19.1)	5 (14.7)	0.569
IV/oral iron	53 (59.6)	18 (52.9)	0.507
Erythropoietin, IU/kg/wk	110.0 ± 65.2	128.3 ± 63.6	0.165
Fe (iron), μg/dL	62.3 ± 37.6	57.7 ± 32.7	0.614
Hemoglobin, g/dL	9.6 ± 1.5	9.2 ± 1.5	0.144
Albumin, g/dL	3.8 ± 0.5	3.7 ± 0.6	0.531
Creatinine, mg/dL	8.5 ± 2.8	8.6 ± 2.7	0.800
hs-CRP, mg/dL	0.1 (0.1, 0.6)	0.1 (0.1, 0.7)	0.935
Total Kt/V urea	2.8 ± 1.9	2.4 ± 0.8	0.068
nPNA, g/kg/day	1.2 ± 1.0	1.0 ± 0.3	0.350
SGA	26.1 ± 2.3	26.0 ± 2.0	0.784
Baseline RRF, mL/min/1.73 m^2	2.4 (1.2, 4.2)	2.8 (1.8, 3.7)	0.705
24-Hour urine protein, g/day	1.2 (0.6, 2.3)	1.6 (0.9, 2.7)	0.101
At 12 months after PD initiation			
Hemoglobin, g/dL	9.9 ± 1.4	9.9 ± 1.1	0.996
Albumin, g/dL	3.7 ± 0.5	3.6 ± 0.5	0.084
hs-CRP, mg/dL	0.1 (0.1, 0.6)	0.2 (0.1, 0.7)	0.241
Total Kt/V urea	2.4 ± 1.5	1.9 ± 0.6	0.045
nPNA, g/kg/day	1.5 ± 4.3	0.9 ± 0.3	0.437
SGA	26.6 ± 1.8	26.2 ±2.4	0.388
Peritonitis rates, times/patient-yr	0.312 ± 0.932	0.312 ± 0.720	0.981

Values are presented as mean ± SD, number (%), or median (25th, 75th percentile).
DM, diabetes mellitus; CHF, congestive heart failure; RAS, renin-angiotensin system; IV, intravenous; hs-CRP, high sensitivity C-reactive protein; nPNA, normalized protein nitrogen appearance rate; SGA, subjective global assessment; RRF, residual renal function.

cantly at the 1-year follow-up (2.45 mL/min/1.73 m^2 [1.34, 4.01] vs. 1.37 mL/min/1.73 m^2 [0.18, 2.37], $p < 0.001$; data not shown). A significant correlation was found between the baseline serum ferritin level and a negative change in RRF at the 1-year follow-up ($r = -0.219$, $p = 0.015$; data not shown).

When comparing the groups at the 1-year follow-up, the negative change in RRF was significantly greater in the high-ferritin than in the low-ferritin group (–1.67 ± 1.36 mL/min/1.73 m^2 vs. –0.84 ± 1.63 mL/min/1.73 m^2,

http://dx.doi.org/10.3904/kjim.2014.29.4.489

respectively, $p = 0.007$) (Fig. 1). A significant correlation existed between the groups in the model after adjusting for DM, CHF, and total Kt/V ($p = 0.003$).

Ferritin and mean RRF reduction rate

When further subanalyses were performed in the 72 patients who developed anuria during the study period, a significant correlation between the baseline serum ferritin level and the rate of RRF decline was observed ($r = -0.586$, $p < 0.001$; data not shown). The mean follow-up period was 58.6 ± 28.7 months. The mean RRF reduction rate was significantly greater in patients with a high ferritin level than with a low ferritin level (–0.19 ± 0.14 mL/min/mon/1.73 m^2 vs. –0.09 ± 0.07 mL/min/mon/1.73 m^2, respectively, $p = 0.003$) (Fig. 2). A significant correlation was observed between the two groups in the model after adjusting for DM, CHF and total Kt/V ($p < 0.001$). The length of time to anuria onset was 28.6 ± 2.2 months in the low-ferritin group and 19.4 ± 3.0 months in the high-ferritin group ($p = 0.023$) (Fig. 3).

Rate of decline predictors in RRF at the 1-year follow-up

A negative relationship with the RRF reduction rate was found in males, baseline RRF, baseline 24-hour urine protein, and baseline serum ferritin. However, no significant correlation was observed between the RRF reduction rate and age, history of DM, history of CHF, BMI, use of RAS blockers, diuretic use, IV/oral iron supplement, or peritonitis rate. Additionally, the serum hs-CRP was not associated with the rate of RRF decline. Multivariate linear regression analysis showed that baseline RRF, baseline 24-hour urine protein, and baseline serum ferritin were associated with the RRF reduction rate after adjustment for other risk factors (Table 3). Assessment of goodness of fit indicated that the overall model was highly significant ($p < 0.001$, adjusted $R^2 = 0.334$).

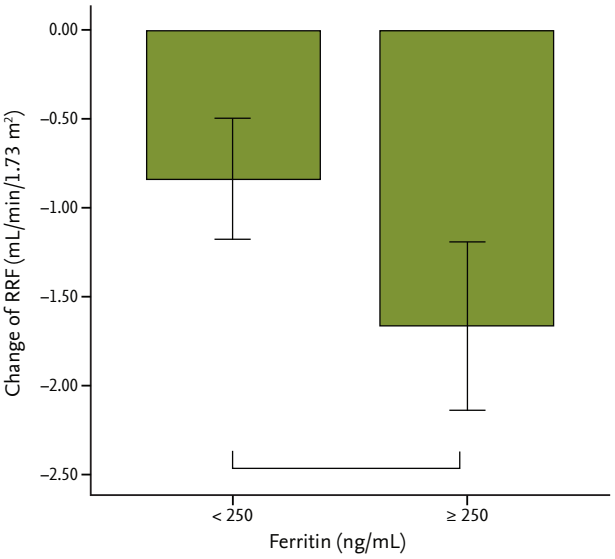

Figure 1. The change in residual renal function (RRF) at the 1-year follow-up was significantly greater in patients with a high ferritin level (ferritin ≥ 250 mg/dL, n = 34) than those with a low ferritin level (ferritin < 250 mg/dL, n = 89) (–1.71 ± 1.36 mL/min/1.73 m^2 vs. –0.84 ± 1.63 mL/min/1.73 m^2, respectively, $p = 0.007$).

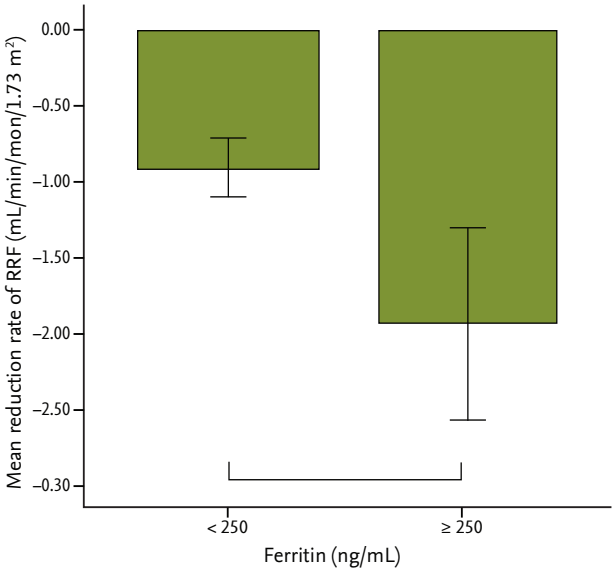

Figure 2. The mean residual renal function (RRF) reduction rate was significantly greater in patients with a high ferritin level (ferritin ≥ 250 mg/dL, n = 22) than those with a low ferritin level (ferritin < 250 mg/dL, n = 50) (–0.19 ± 0.14 mL/min/mon/1.73 m^2 vs. –0.09 ± 0.07 mL/min/mon/1.73 m^2, respectively, $p = 0.003$).

DISCUSSION

In this study a significant correlation was found between the baseline serum ferritin level and the rate of RRF decline, and a higher ferritin level was independently associated with a more rapid RRF decline in

PD patients after adjusting for other risk factors. Preservation of RRF is a clinically important goal in CKD patients, even after starting dialysis [17]. Several studies have shown that PD patients have a lower risk of RRF compared with HD patients and that RRF is independently predictive of morbidity and mortality in PD patients [18,19].

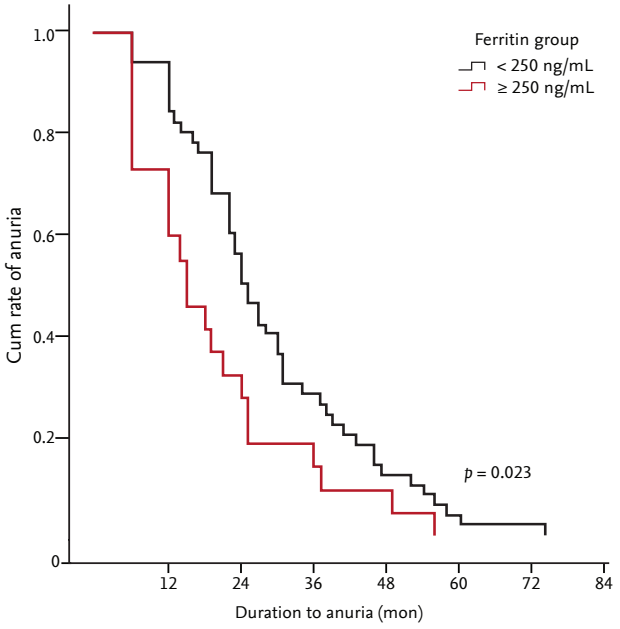

Figure 3. The length of time to anuria onset was 28.6 ± 2.2 months in the low-ferritin group (n = 50) and 19.4 ± 3.0 months in the high-ferritin group (n = 22, $p = 0.023$).

Inflammation influences a poor renal outcome and various markers, such as white blood cell count, hs-CRP, and ferritin, have been used to assess inflammatory status [7-10,12,20].

Serum ferritin can be measured readily with a blood test using an immunoradiometric assay, which has a high specificity for detection of iron storage [21]. However, the clinical importance of serum ferritin in dialysis patients may differ from that in the general population. For example, in dialysis patients, an increased serum ferritin may not reflect increased iron stores [22] but is associated with erythropoietin resistance [23], malnutrition, or inflammatory status [10]. Additionally, in previous studies, hyperferritinemia among dialysis patients was significantly associated with high mortality [11,13,24]. Serum ferritin, which has a molecular weight of ~450 kDa, contains heavy (H) and light (L) subunits that may enter the circulation via cell secretion and leakage from damaged cells [25]. Serum ferritin is slightly different from tissue ferritin and contains little or no iron. Tissue ferritin plays a role in intracellular iron handling but the role of serum ferritin is not clearly understood [25]. Inflammatory cytokines, such as interleukin 1 and

Table 3. Multiple linear regression analysis of the change in residual renal function at the 1-year follow-up and other risk factors

Variable	Univariate		Multivariate	
	β (SE)	*p* value	β (SE)	*p* value
Age, yr	0.015 (0.012)	0.197		
Male	−0.628 (0.284)	0.029	0.181 (0.268)	0.501
History of DM	−0.036 (0.291)	0.903		
History of CHF	−0.390 (0.505)	0.442		
Body mass index, kg/m^2	−0.050 (0.048)	0.294		
Baseline RRF, mL/min/1.73 m^2	−0.360 (0.069)	< 0.001	−0.331 (0.069)	< 0.001
Peritonitis rate, times/patient-yr	0.740 (2.392)	0.757		
Use of RAS blockers	0.049 (0.305)	0.874		
Use of diuretics	−0.167 (0.289)	0.565		
Use of IV/oral Iron	0.033 (0.293)	0.912		
hs-CRP, mg/dL	0.094 (0.079)	0.239		
24-Hour urine protein, g/day	−0.314 (0.064)	< 0.001	−0.279 (0.059)	< 0.001
Ferritin, ng/mL	−0.002 (0.001)	0.015	−0.002 (0.001)	0.002

SE, standard error; DM, diabetes mellitus; CHF, congestive heart failure; RRF, residual renal function; RAS, renin-angiotensin system; IV, intravenous; hs-CRP, high sensitivity C-reactive protein.

http://dx.doi.org/10.3904/kjim.2014.29.4.489

tumor necrosis factor, increase the synthesis of both the H and L subunits of ferritin by inducing ferritin gene expression independently of iron-dependent ferritin gene expression [20,26]. This inflammatory regulation of ferritin requires the presence of cellular iron. In the case of absolute iron deficiency, serum ferritin is almost always low [20,27], but once minimal iron is available, ferritin is controlled by noniron-dependent factors [20]. Thus, hyperferritinemia is considered an indicator of inflammatory status in dialysis patients [9]. Traditionally, hs-CRP has been regarded as an acute-phase protein indicating inflammatory status [9]. However, we found that baseline hs-CRP was not correlated significantly with baseline serum ferritin because of the nonacute inflammatory status of most patients ($p = 0.723$) [9,28,29]. If inflammation is prolonged with a chronic acute-phase reaction, adverse outcomes such as endothelial damage and atherosclerosis [6,30], which are the principal histological features of almost all renal injuries, may occur [31]. One retrospective study documented a significant association between ferritin as a marker of inflammation and poor renal outcome in terms of the beginning of renal replacement therapy and rapid renal progression in CKD patients [12]. Similarly, we also found that RRF declined more rapidly in PD patients with high baseline serum ferritin levels. Our study is the first report regarding ferritin and renal progression in a PD population.

In this study as in previous work, male gender, baseline RRF, and baseline proteinuria were negatively associated with the rate of RRF decline [3-5]. DM is the most significant factor associated with RRF deterioration [1,5]. Similar to previous reports, in our study the mean RRF reduction rate was greater in patients without DM (–0.14 ± 0.12 mL/min/mon/1.73 m^2 vs. –0.09 ± 0.69 mL/min/mon/1.73 m^2, $p = 0.035$; data not shown). However, DM alone may not fully account for the rapid deterioration in RRF in the present study because many diabetic patients were excluded according to the inclusion criteria, such as preservation of RRF and a follow-up period of more than 1 year.

Albumin, nPNA and SGA, regarded as markers of nutrition, did not differ between the two ferritin groups, unlike the IV/oral iron supplement and erythropoiesis-stimulating agents, which are related to iron storage and dosage. Thus, these factors did not influence the ferritin level in our study.

An association between baseline ferritin level and overall survival rate was not confirmed. Although the duration of survival differed between the groups, no statistically significant difference was found (84.9 ± 7.6 months vs. 67.6 ± 7.9 months, $p = 0.779$; data not shown). We hypothesize this may be due to the small proportion of patients (21.9%) followed until death, the cause of death was not analyzed in individual patients, and baseline ferritin levels might not directly represent mean ferritin levels until death. In a previous study, predeath ferritin levels tended to increase compared to baseline levels [11]. Our study had selection bias because patients with a high risk of mortality were excluded and only patients who had RRF at the start of the study and were followed up for more than 1 year were included.

There were several other limitations to the present study. First, this was an observational study conducted at a single center with a relatively small sample size. A considerable number of patients were excluded due to unavailable baseline data and lack of follow-up. Second, single measures of the baseline serum ferritin level could have reflected acute changes in serum ferritin. However, the mean serum ferritin level did not change over a 1-year period, indicating consistency after the start of PD. Lastly, we were unable to measure the mean RRF reduction rate in all patients because the mean RRF decline was considered from the baseline RRF to anuric status during the study period. As a result, only 72 patients (58.5%) had a final date for mean RRF reduction rate. Despite these limitations, the baseline serum ferritin was independently associated with the RRF reduction rate.

In conclusion, our study demonstrated that higher ferritin levels at the start of PD were associated with an increased risk of rapid RRF decline in PD patients. Future studies investigating the pathological role of ferritin with larger study populations are warranted.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

This work was supported by Soonchunhyang University Research.

KEY MESSAGE

1. The higher ferritin level was significantly associated with a more rapid residual renal function (RRF) decline in peritoneal dialysis (PD) patients.
2. The baseline serum ferritin at the start of PD was found to be an independent predictor of RRF reduction rate in PD patients.

REFERENCES

1. Moist LM, Port FK, Orzol SM, et al. Predictors of loss of residual renal function among new dialysis patients. J Am Soc Nephrol 2000;11:556-564.
2. Kim SG, Kim NH. The effect of residual renal function at the initiation of dialysis on patient survival. Korean J Intern Med 2009;24:55-62.
3. Singhal MK, Bhaskaran S, Vidgen E, Bargman JM, Vas SI, Oreopoulos DG. Rate of decline of residual renal function in patients on continuous peritoneal dialysis and factors affecting it. Perit Dial Int 2000;20:429-438.
4. Bargman JM, Golper TA. The importance of residual renal function for patients on dialysis. Nephrol Dial Transplant 2005;20:671-673.
5. Liao CT, Shiao CC, Huang JW, et al. Predictors of faster decline of residual renal function in Taiwanese peritoneal dialysis patients. Perit Dial Int 2008;28 Suppl 3:S191-S195.
6. Rifkin DE, Sarnak MJ. Does inflammation fuel the fire in CKD? Am J Kidney Dis 2009;53:572-575.
7. Qureshi AR, Alvestrand A, Divino-Filho JC, et al. Inflammation, malnutrition, and cardiac disease as predictors of mortality in hemodialysis patients. J Am Soc Nephrol 2002;13 Suppl 1:S28-S36.
8. Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences. Am J Kidney Dis 2003;42:864-881.
9. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med 1999;340:448-454.
10. Kalantar-Zadeh K, Rodriguez RA, Humphreys MH. Association between serum ferritin and measures of inflammation, nutrition and iron in haemodialysis patients. Nephrol Dial Transplant 2004;19:141-149.
11. Kalantar-Zadeh K, Don BR, Rodriguez RA, Humphreys MH. Serum ferritin is a marker of morbidity and mortality in hemodialysis patients. Am J Kidney Dis 2001;37:564-572.
12. Tsai YC, Hung CC, Kuo MC, et al. Association of hsCRP, white blood cell count and ferritin with renal outcome in chronic kidney disease patients. PLoS One 2012;7:e52775.
13. Hasuike Y, Nonoguchi H, Tokuyama M, et al. Serum ferritin predicts prognosis in hemodialysis patients: the Nishinomiya study. Clin Exp Nephrol 2010;14:349-355.
14. Kovesdy CP, Estrada W, Ahmadzadeh S, Kalantar-Zadeh K. Association of markers of iron stores with outcomes in patients with nondialysis-dependent chronic kidney disease. Clin J Am Soc Nephrol 2009;4:435-441.
15. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. J Am Soc Nephrol 1996;7:198-207.
16. II. NKF-K/DOQI Clinical Practice Guidelines for Peritoneal Dialysis Adequacy: update 2000. Am J Kidney Dis 2001;37(1 Suppl 1):S65-S136.
17. Krediet RT. How to preserve residual renal function in patients with chronic kidney disease and on dialysis? Nephrol Dial Transplant 2006;21 Suppl 2:ii42-ii46.
18. Paniagua R, Amato D, Vonesh E, et al. Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. J Am Soc Nephrol 2002;13:1307-1320.
19. Bargman JM, Thorpe KE, Churchill DN; CANUSA Peritoneal Dialysis Study Group. Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. J Am Soc Nephrol 2001;12:2158-2162.
20. Rogers JT, Bridges KR, Durmowicz GP, Glass J, Auron PE, Munro HN. Translational control during the acute phase response: ferritin synthesis in response to interleukin-1. J Biol Chem 1990;265:14572-14578.
21. Cavill I. Iron status as measured by serum ferritin: the marker and its limitations. Am J Kidney Dis 1999;34(4 Suppl 2):S12-S17.
22. Kalantar-Zadeh K, Luft FC, Humphreys MH. Moderately high serum ferritin concentration is not a sign of iron overload in dialysis patients. Kidney Int 1999;56:758-759.
23. Gunnell J, Yeun JY, Depner TA, Kaysen GA. Acute-phase response predicts erythropoietin resistance in hemodialysis and peritoneal dialysis patients. Am J Kidney Dis

http://dx.doi.org/10.3904/kjim.2014.29.4.489

1999;33:63-72.
24. Jenq CC, Hsu CW, Huang WH, Chen KH, Lin JL, Lin-Tan DT. Serum ferritin levels predict all-cause and infection-cause 1-year mortality in diabetic patients on maintenance hemodialysis. Am J Med Sci 2009;337:188-194.
25. Worwood M. Ferritin. Blood Rev 1990;4:259-269.
26. Kwak EL, Larochelle DA, Beaumont C, Torti SV, Torti FM. Role for NF-kappa B in the regulation of ferritin H by tumor necrosis factor-alpha. J Biol Chem 1995;270:15285-15293.
27. Kalantar-Zadeh K, Hoffken B, Wunsch H, Fink H, Kleiner M, Luft FC. Diagnosis of iron deficiency anemia in renal failure patients during the post-erythropoietin era. Am J Kidney Dis 1995;26:292-299.
28. Smith JE, Cipriano JE. Inflammation-induced changes in serum iron analytes and ceruloplasmin of Shetland ponies. Vet Pathol 1987;24:354-356.
29. Rosa NetoI NS, de CarvalhoII JF. The use of inflammatory laboratory tests in rheumatology. Bras J Rheumatol 2009;49:413-430.
30. Avramovski P, Janakievska P, Sotiroski K, Sikole A. Accelerated progression of arterial stiffness in dialysis patients compared with the general population. Korean J Intern Med 2013;28:464-474.
31. Fogo AB. Mechanisms of progression of chronic kidney disease. Pediatr Nephrol 2007;22:2011-2022.