RELATIONSHIP BETWEEN DECLINE OF RESIDUAL RENAL FUNCTION AND HYPORESPONSIVENESS TO ERYTHROPOIESIS-STIMULATING AGENTS IN PERITONEAL DIALYSIS

Authors Ken Mizuguchi, Chiharu Ito, Satoru Kominato, Atsushi Ogawa, Tomomi Kimura, Yuji Sasakawa, Masashi Mizuno, Katsushi Koyama

Hospital Department of Nephrology and Rheumatology
Kariya Toyota General Hospital, Aichi, Japan

OBJECTIVES

Residual renal function (RRF) is an important risk factor that affects the prognosis of peritoneal dialysis (PD) patients[1]. Hyporesponsiveness to erythropoiesis-stimulating agents is an also important prognostic factor in PD patients[2]. However, Relationship between RRF and hyporesponsiveness to ESA has not been reported. We conducted a retrospective study assessing the relationship between the decline speed of RRF and clinical characteristics including ESA resistance index (ERI).

METHODS

From 123 patients who initiated PD between March 2006 and December 2014 at our hospital, 55 patients were recruited. We excluded patients who were not PD first, drop out from PD or peritonitis within a year from PD initiation.
The baseline characteristics and laboratory data were collected at the PD initiation. The baseline ESA resistance index(ERI) was calculated using the averaged value of weekly ESA dosage administered during three months from the PD initiation. Creatinine clearance(Ccr) was evaluated by the 24 hour urine collection. RRF decline speed was estimated as the slope of regression line based on time-course Ccr's change. All statistical analysis were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). The correlation between the baseline parameters including ERI and the RRF decline speed were tested by using Spearman's rank correlation coefficient.

Table 1. Baseline characterristics and laboratory data

		R	p value
Patients (N)	55		
Sex (M : F)	35 : 20		0.965#
PD initiation age (years)	54.8 ± 14.0	0.356	0.009$
PD duration (months)	45.5 ± 22.9	0.012	0.930$
Body weight (kg)	62.9 ± 16.1	-0.241	0.076$
Systolic BP (mmHg)	141 ± 26	-0.042	0.753$
Diastolic BP (mmHg)	80 ± 14	-0.169	0.211$
Diabetes (%)	59		0.086#
CAD/CVD (%)	36		0.173#
ACEI/ARB (%)	79		0.289#
Diuretics (%)	64		0.196#
Cause of renal failure (%)			
Diabetic nephropathy	56		
Glomerulonephritis	18		P >0.05
Nephrosclerosis	13		
Others	13		

		R$	p value$
Creatinine (mg/dl)	8.7±3.6	0.150	0.271
Blood urea nitrogen (mg/dl)	92.6±125.0	0.137	0.314
β2- microglobulin (mg/dl)	19.3±6.7	-0.193	0.160
Albumin (g/dl)	3.4±0.55	0.327	0.016
Hemoglobin (g/dl)	9.0±1.2	0.029	0.831
Ferritin (ng/ml)	206.9±255.7	0.063	0.646
Reticulocyte (%)	10.9±6.4	0.000	0.999
C-reactive protein (mg/dl)	0.44±0.95	-0.136	0.323
Hemoglobin A1c (%)	6.0±1.0	0.343	0.032
Proteinuria (g/g•cr)	4.9±3.6	-0.034	0.815
IVST (mm)	0.90±0.17	-0.150	0.270
IMT (mm)	0.73±0.24	0.034	0.813
Pulse wave velocity (cm/s)	1693.8±704.4	0.315	0.035
Ankle-brachial index	1.16±0.31	0.244	0.090
ERI (μg/g/dl/kg/week)	0.03±0.01	-0.591	0.00001

IVST: Interventricular septum thickness, IMT: Intima-media thickness, CAD: Cardiovascular disease, CVD: Cerebralvascular disease, ACEI: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin II receptor blocker, BP: Blood pressure. Continuous values are expressed as mean ± SD. #: Mann-Whitney U test, $: Spearman's rank correlation coefficient.

Figure 2. RRF decline speed was defined as simple linear regression's slope.
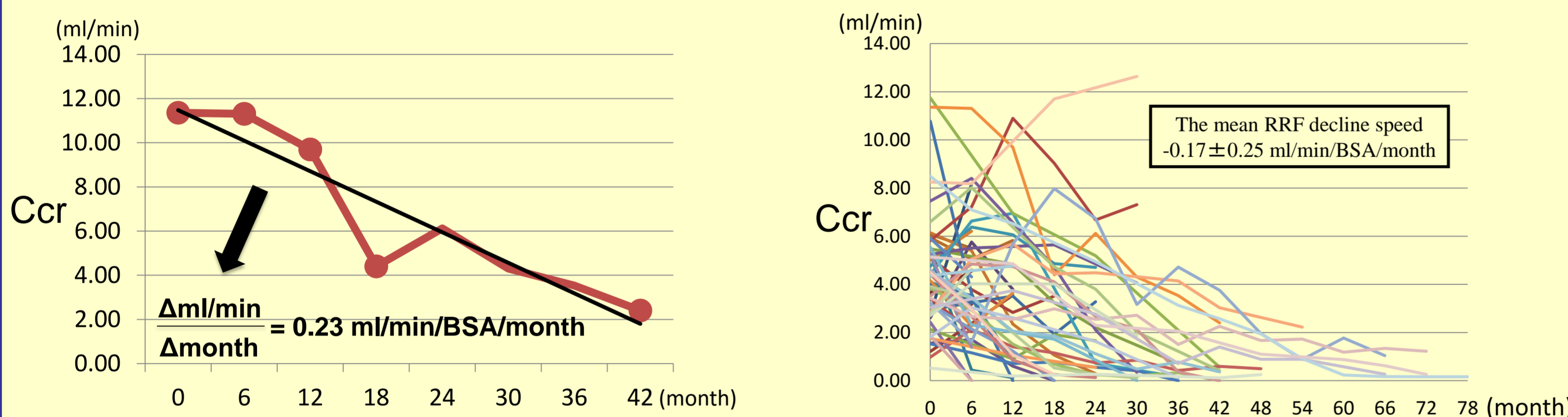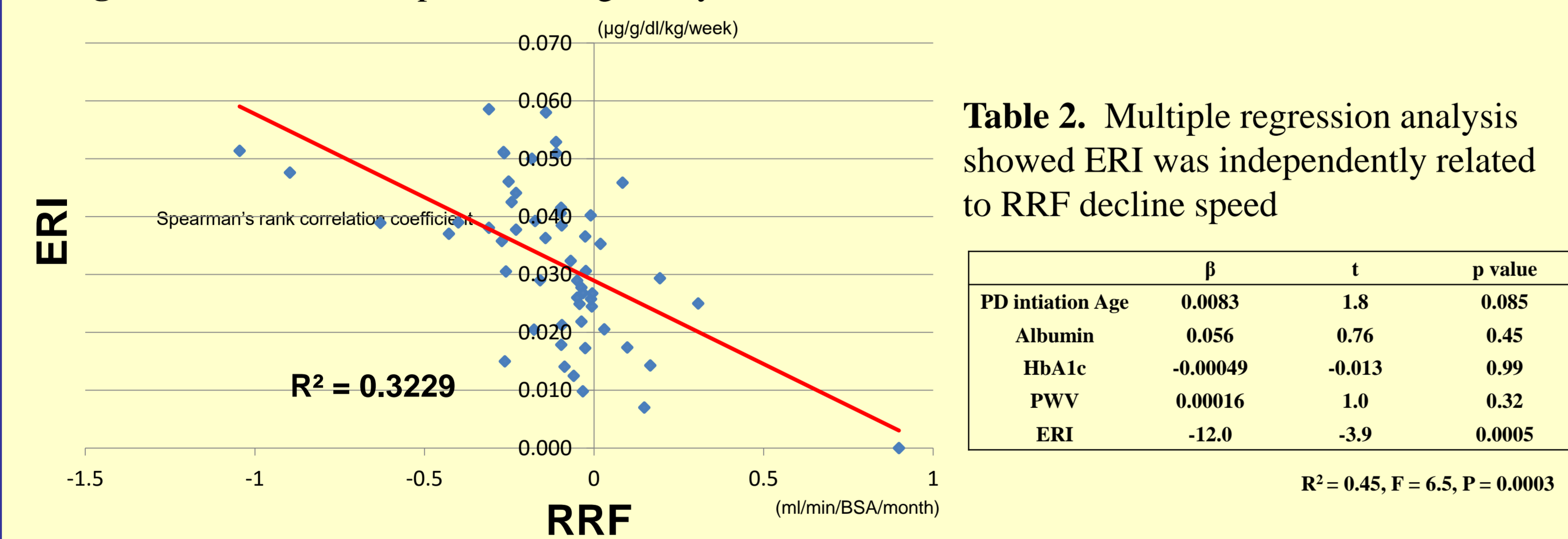

$\dfrac{\Delta ml/min}{\Delta month}$ = 0.23 ml/min/BSA/month

The mean RRF decline speed -0.17±0.25 ml/min/BSA/month

Figure 3. RRF decline speed was negatively correlated with ERI

Spearman's rank correlation coefficient

$R^2 = 0.3229$

Table 2. Multiple regression analysis showed ERI was independently related to RRF decline speed

	β	t	p value
PD intiation Age	0.0083	1.8	0.085
Albumin	0.056	0.76	0.45
HbA1c	-0.00049	-0.013	0.99
PWV	0.00016	1.0	0.32
ERI	-12.0	-3.9	0.0005

$R^2 = 0.45$, F = 6.5, P = 0.0003

RESULTS

The mean PD initiation age was 54.8 ± 14.0 years. 63% of the patients were male. The mean PD duration was 45.5 ± 22.9 months. The mean BP was 141/80 mmHg, and body weight was 62.9 ± 16.1 kg. The mean ERI was 0.03 ± 0.01 μg/g/dl/kg/week (Table 1). The main cause of renal failure was diabetic nephropathy (56%), glomerulonephritis (18%) and nephrosclerosis (12%). The mean RRF decline speed was 0.17 ± 0.25 ml/min/BSA/month (Figure 2). In simple regression analysis of baseline data, the PD initiation age, albumin, hemoglobin A1c, pulse wave velocity and ERI were correlated with RRF decline speed (R = 0.356, 0.327, 0.343, 0.315 and -0.591 respectively). In multiple regression analysis, only ERI was independently related to RRF decline speed ($R^2 = 0.45$, β = -12.0) (Figure 3 & Table 2).

CONCLUSIONS

Our study showed that the baseline ERI, which was evaluated at PD intiation, was independently related to decline speed of RRF after PD initiation. In conclusion, our result suggests that some pathological causes of hyporesponsiveness to ESA could affect the decline of RRF in PD patients. Further studies are needed to clarify that mechanism.

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