RELATIONSHIP BETWEEN RESTLESS LEGS SYNDROME AND MORTALITY IN HEMODIALYSIS PATIENTS

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Introduction

Restless legs syndrome (RLS) is a sensorimotor neurological disorder characterized by paraesthesia, dysaesthesia and the irresistible urge to move the legs especially at night [1]. Its prevalence is much higher among dialysis patients compared to the general population [2]. RLS is known to associate with depression and quality of life [3]. Recently, the association between the severity of RLS and the risk of new cardiovascular events in hemodialysis patients was also reported [4]. In this study, we examined the relationship between RLS and mortality in hemodialysis patients.

Subjects and Methods

A total of 67 patients receiving maintenance hemodialysis at Sangenjaya Hospital were enrolled in this study. Clinical data, including age, gender, duration of hemodialysis therapy and cause of end-stage kidney disease were collected. The clinical follow-up data were obtained from the hospital records. A peripheral blood sample was obtained before hemodialysis on a Monday or a Tuesday, and standard biological data were measured. RLS was diagnosed according to the four diagnostic criteria established by the International RLS Study Group [1].

The clinical endpoints were defined as death from any cause. Cox proportional hazards model for the predictor of survival was examined. We divided patients according to the presence or absent of RLS and compared the survival rate between the groups. The survival curves were estimated using the Kaplan-Meier method followed by a log-rank test.

Results

RLS affected 14.9 % of the study population. The mean observation period was 2.8 ± 0.8 years. During the follow-up period, 16 deaths were recorded. In the univariate regression analysis, the hazard ratio (HR) of patients with RLS was 2.16 (95% CI, 1.25 - 3.61, P=0.008). A multivariate Cox analysis which include age, albumin, creatinine and presence of diabetic nephropathy identified RLS as an independent predictor of mortality (HR 2.19 (95% CI 1.21 - 3.93), P=0.011). The survival curves showed a statistically significant difference between patients with and without RLS (P=0.010). Patient survival rate at 2 years was 70.0 % in the patients with RLS group and 91.0 % in the patients without RLS.

Discussion

Our study conformed the high prevalence of RLS (14.9 %) in hemodialysis patients. In CHOICE study, RLS in hemodialysis patients were associated with lower quality of life and shorter survival [5]. In Italy, severe RLS was reported to be independently associated with the risk of new cardiovascular events and with higher mortality [4]. We conformed RLS was a risk factor for mortality and acted independently of other risk factors, including age, albumin, creatinine and presence of diabetic nephropathy.

Strong correlation between RLS and dysfunction of the cardiovascular system in the general population was reported [6, 7]. There are well established connections among RLS, periodic limb movement during sleep (PLMS), transient rises of heart rate [8, 9] and arterial blood pressure [10, 11] probably mediated by sympathetic overactivity. Based on this and the strong detrimental effect of nocturnal hypertension on the cardiovascular system, some authors recently hypothesized that nocturnal hypertension may contribute to increased cardiovascular risk in dialysis patients with RLS [12]. Association between low level of serum albumin and RLS was observed in this study, that was same as previous report [4]. Malnutrition is another risk factor for mortality in hemodialysis patients.

Conclusion

RLS was a risk factor for mortality and acted independently of other risk factors, including age, albumin, creatinine and presence of diabetic nephropathy.

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Background characteristics of the study participants 1.

	RLS (Y, n=10)	RLS (N, n=57)	P value
Gender (M/F)	7 / 3	37 / 20	NS
Age (year)	65.6 ± 12.6	65.3 ± 12.4	NS
Duration of HD (year)	16.5 ± 14.8	15.6 ± 13.3	NS
Death n (%)	6 (60.0)	9 (15.8)	0.006
Primary Cause of ESKD, n (%)			
Chronic glomerulonephritis	5 (50.0)	32 (56.1)	
Diabetic Nephropathy	4 (40.0)	13 (22.8)	
Nephrosclerosis	0 (0.0)	4 (0.7)	
Unknown and others	1 (10.0)	8 (14.0)	

Observation period 2.8 ± 0.8 years

Background characteristics of the study participants 2.

	RLS (Y, n=10)	RLS (N, n=57)	P value
Total protein (g/dl)	6.8 ± 0.6	6.9 ± 0.4	NS
Albumin (g/dl)	3.8 ± 0.3	4.0 ± 0.2	0.015
Creatinine (mg/dl)	9.72 ± 1.82	10.83 ± 2.77	NS
Calcium (mg/dl)	9.0 ± 0.5	9.3 ± 0.5	NS
Phosphate (mg/dl)	5.5 ± 1.1	5.6 ± 1.1	NS
Iron (μg/dl)	68 ± 27	52 ± 17	NS
Total iron-binding capacity (μg/dl)	269 ± 33	270 ± 46	NS
Transferrin saturation	0.20 ± 0.08	0.26 ± 0.12	NS
Total-Cholesterol (mg/dl)	174 ± 47	160 ± 33	NS
Triglyceride (mg/dl)	127 ± 99	110 ± 69	NS
Ferritine (ng/ml)	148 ± 114	148 ± 111	NS
I-PTH (pg/dl)	217 ± 157	249 ± 158	NS
C-reactive protein (mg/dl)	0.21 ± 0.13	0.21 ± 0.21	NS
White blood cell count (/μl)	5840 ± 2511	5842 ± 1805	NS
Hemoglobin (g/dl)	10.6 ± 1.6	10.6 ± 1.0	NS
Platelet count (x10⁴/μl)	16.5 ± 7.6	18.8 ± 6.2	NS

Cause of death among the study participants

	Number
Cardiovascular disease	6
Infection	8
Tumor	1
Unknown	1

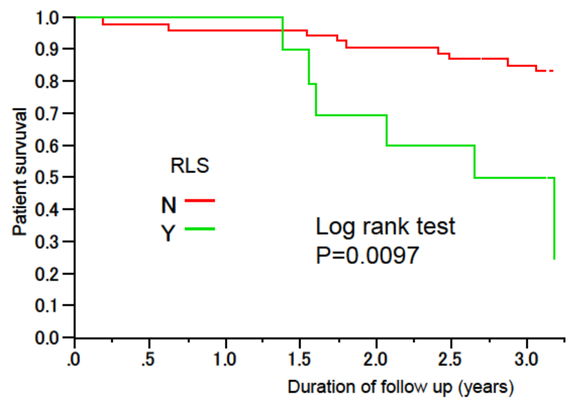
Cox proportional hazards analysis of the covariates for all cause of death (simple analysis)

	Hazard Ratio (95% CI)	P value
Age (per year)	1.02 (0.98 - 1.07)	0.383
HD duration (per year)	1.01 (0.97 - 1.05)	0.671
Total protein (per g/dl)	0.69 (0.21 - 2.24)	0.544
Albumin (per g/dl)	0.44 (0.06 - 3.24)	0.424
Creatinine (per mg/dl)	0.88 (0.73 - 1.07)	0.207
Calcium (per mg/dl)	0.71 (0.28 - 1.85)	0.471
Phosphate (per mg/dl)	1.14 (0.71 - 1.73)	0.571
Fe (per μg/dl)	1.00 (0.97 - 1.02)	0.775
TSAT (per 1)	2.24 (0.02 - 121.08)	0.727
Ferritine (per ng/ml)	1.00 (1.00 - 1.01)	0.57
Total-Cholesterol (per mg/dl)	1.00 (0.99 - 1.02)	0.593
Triglyceride (per mg/dl)	1.00 (0.99 - 1.01)	0.827
i-PTH (per pg/dl)	1.00 (1.00 - 1.00)	0.708
C-reactive protein (per mg/dl)	1.43 (0.09 - 9.05)	0.758
Hemoglobin (per g/dl)	0.97 (0.58 - 1.50)	0.888
Diabetic Nephropathy (Y)	1.25 (0.70 -2.10)	0.428
RLS (Y/N) [Y]	2.16 (1.25 - 3.61)	0.008

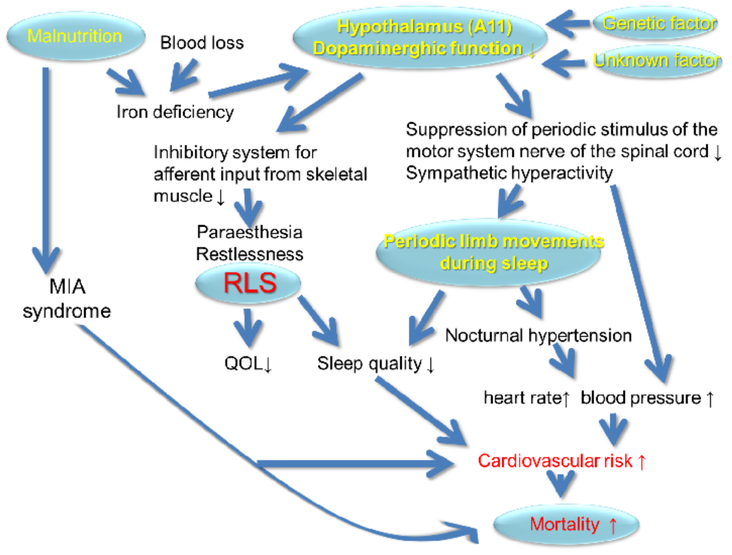
Cox proportional hazards analysis of the covariates for all cause of death (Multiple analysis)

	Hazard Ratio (95% CI)	P value
Age (per year)	1.01 (0.97 - 1.07)	0.586
Albumin (per g/dl)	1.98 (0.20 - 20.60)	0.56
Creatinine (per mg/dl)	0.92 (0.72 - 1.16)	0.456
Diabetic Nephropathy (Y)	1.11 (0.61 - 1.89)	0.704
RLS (Y/N) [Y]	2.19 (1.21 - 3.93)	0.011

Comparison of survival probabilities between RLS (Y) group and RLS (N) group



Relationship between RLS and mortality



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