RELATIONSHIP BETWEEN RESTLESS LEGS SYNDROME AND CARDIOVASCULAR DISEASE IN HEMODIALYSIS PATIENTS

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Introduction

Restless legs syndrome (RLS) is a neurological disorder characterized by sensorimotor symptoms such as paraesthesia and restlessness that mainly affected the lower limbs, occurring during rest in the evenings or overnight [1]. Recently, the association between the severity of RLS and the risk of new cardiovascular events in hemodialysis patients was reported [2]. In this study, we examined the relationship between RLS and cardiovascular mortality in hemodialysis patients.

Subjects and Methods

A total of 67 patients receiving maintenance hemodialysis at Sangenjaya Hospital were enrolled in this study. The clinical endpoints were defined as death from any cause and cardiovascular death. Cox proportional hazards model for the predictor of survival was examined.

Results

RLS affected 14.9 % of the study population. The mean observation period was 3.4 ± 1.2 years. The complication of cardiovascular disease tends to be higher in the patients with RLS group (70.0 %) than in the patients without RLS group (45.6 %, P=0.155). In the univariate regression analysis, the hazard ratio (HR) of patients with RLS was 1.94 (95% CI 1.19 - 3.02, P=0.009) for all cause of death and 2.70 (95% CI 1.31 – 5.56, P=0.009) for cardiovascular death. A multivariate Cox analysis which include age and presence of diabetic nephropathy identified RLS as an independent predictor of cardiovascular death (HR 1.88 (95% CI 1.15 – 2.94, P=0.014)).

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 [3]. In Italy, severe RLS was reported to be independently associated with the risk of new cardiovascular events and with higher mortality [2]. We conformed RLS was a risk factor for cardiovascular death and acted independently of other risk factors, including age and presence of diabetic nephropathy. There are well established connections among RLS, periodic limb movement during sleep (PLMS), transient rises of heart rate [4, 5] and arterial blood pressure [6, 7] 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 [8].

Conclusion

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

Background characteristics of the study participants

	with RLS (n=10)	without RLS (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
Cardiovascular disease n (%)	7 (70.0)	26 (45.6)	NS
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)	
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 (mg/dL)	68 ± 27	52 ± 17	NS
Total iron-binding capacity (mg/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
Ferritin (ng/mL)	148 ± 114	148 ± 111	NS
Intact parathyroid hormone (pg/dL)	217 ± 157	249 ± 158	NS
c-reactive protein (mg/dL)	0.21 ± 0.13	0.21 ± 0.21	NS
White blood cells count (/mL)	5840 ± 2511	5842 ± 1805	NS
Hemoglobin (g/dL)	10.6 ± 1.6	10.6 ± 1.0	NS
Platelet count (x10^4/mL)	16.5 ± 7.6	18.8 ± 6.2	NS
KT/V	1.30 ± 0.35	1.39 ± 0.23	NS
nPCR (g/kg/day)	0.96 ±0.14	1.06 ± 0.18	NS
Death n (%)	7 (70.0)	14 (24.6)	0.004
Cardiovascular related death n (%)	4 (40.0)	4 (7.0)	0.003

Observation period 3.4 ± 1.2 years

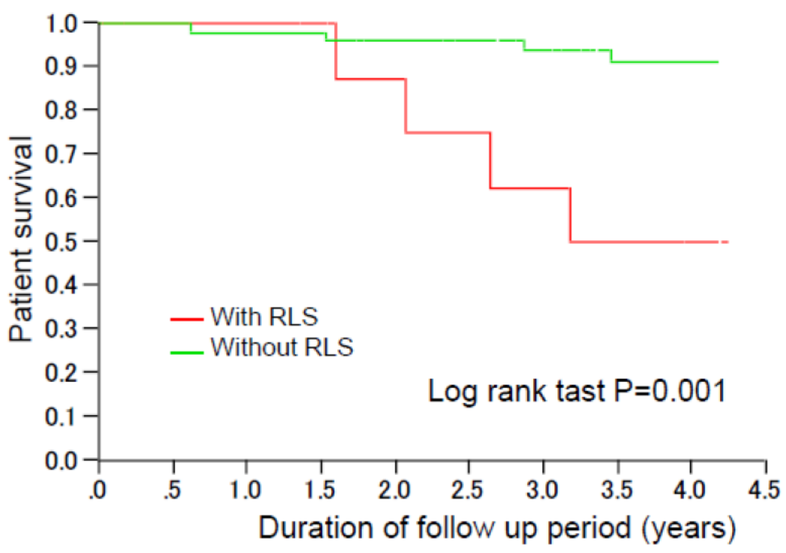
Cause of death among the study participants

	with RLS	without RLS
Cardiovascular disease	4	4
Heart failure	2	2
Myocardial Infarction	1	2
Cerebrovascular disease	1	0
Infection	2	10
Tumor	1	0

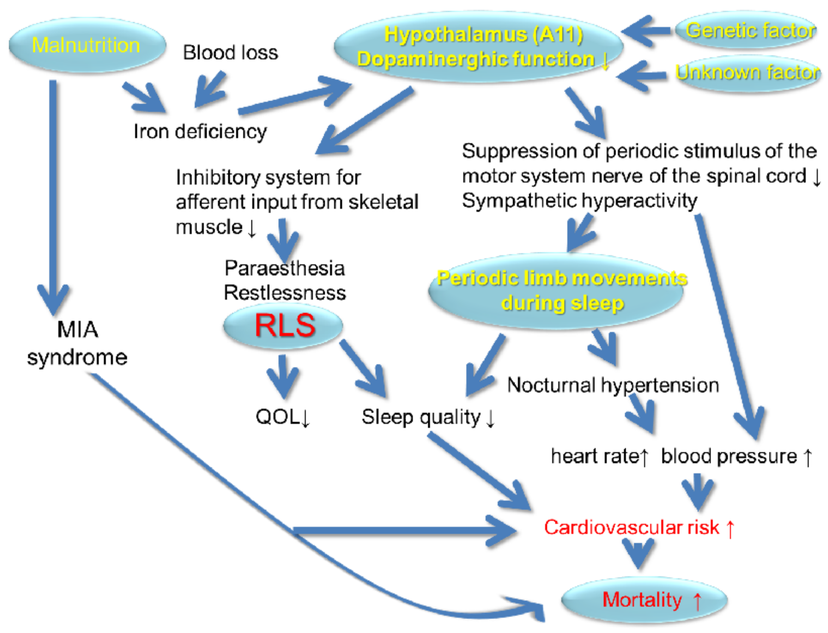
Cox proportional hazards analysis of the covariates for cardiovascular death (simple analysis)

	Hazard Ratio (95% CI)	P value
Age (per year)	1.06 (1.00 - 1.14)	0.063
HD duration (per year)	0.95 (0.86 - 1.01)	0.088
Total protein (per g/dL)	2.86 (0.61 – 12.09)	0.179
Albumin (per g/dL)	1.52 (0.10 – 22.17)	0.760
Creatinine (per mg/dL)	0.85 (0.67 - 1.11)	0.241
Calcium (per mg/dL)	0.34 (0.10 - 1.16)	0.085
Phosphate (per mg/dL)	1.42 (0.76 – 2.40)	0.256
Iron (per μg/dL)	1.00 (0.99 - 1.01)	0.610
Transferrin saturation (per 1)	2.92 (0.00 - 797.22)	0.746
Ferritin (per ng/mL)	1.00 (1.00 - 1.01)	0.167
Total-Cholesterol (per mg/dL)	1.01 (0.99 - 1.03)	0.309
Triglyceride (per mg/dL)	1.01 (1.00 - 1.01)	0.116
Intact parathyroid hormone (per pg/dL)	1.00 (1.00 - 1.00)	0.763
C-reactive protein (per mg/dL)	5.12 (0.32 – 34.66)	0.208
Hemoglobin (per g/dL)	1.21 (0.62 – 2.06)	0.543
nPCR (per g/kg/day)	1.48 (0.03 – 57.08)	0.841
Diabetic nephropathy (Y)	3.01 (1.45 – 7.87)	0.003
Restless legs syndrome (Y)	2.70 (1.31 – 5.56)	0.009

Comparison of survival probabilities for cardiovascular death between with RLS group and without RLS group



Possible relationship between RLS and cardiovascular disease



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

	Hazard Ratio (95% CI)	P value
Age (per year)	1.01 (0.98 – 1.05)	0.574
Diabetic Nephropathy (Y)	1.16 (0.71 – 1.81)	0.530
Restless legs syndrome (Y)	1.88 (1.15 – 2.94)	0.014

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