Original article

Restless legs syndrome and its variants in acute ischemic stroke

Tomohiko Shiina, MD; Keisuke Suzuki, MD, PhD; Madoka Okamura, MD, PhD; Takeo Matsubara, MD; Koichi Hirata, MD, PhD

Department of Neurology, Dokkyo Medical University, Tochigi, Japan

*Corresponding author:
Keisuke Suzuki, MD, PhD
Department of Neurology, Dokkyo Medical University
880 Kitakobayashi, Mibu, Shimotsuga
Tochigi 321-0293, Japan
Tel.: +81-282-86-1111; Fax: +81-282-86-5884
Email: keisuke@dokkyomed.ac.jp

Word counts: Abstract, 249 words; text, 2,990 words; 2 table; 4 figures; 33 references.
Running title: RLS in acute ischemic stroke
Keywords: Restless legs syndrome, restless legs syndrome variants, acute ischemic stroke, magnetic resonance imaging

Conflict of interest: The authors declare that they have no potential conflicts of interest in relation to this article.

Abstract

Background: The clinical–radiological correlation between restless legs syndrome (RLS) or its variants and acute ischemic stroke remains unclear.

Methods: This study prospectively included 104 consecutive patients with acute ischemic stroke, confirmed by diffusion-weighted imaging. The frequency and clinical characteristics of RLS or RLS variants were evaluated according to the International RLS Study Group criteria, as was the topography of the associated lesions.

Results: Among 104 patients with acute ischemic stroke, 6 (5.8%) and 2 patients (1.9%) had RLS and RLS variants, respectively, for a total of 8 patients (7.7%). Three (3.3%) had poststroke RLS/RLS variants: 2 (66.7%) had bilateral symptoms, and 1 (33.3%) had unilateral symptoms contralateral to the lesion. RLS symptoms developed within 2 days after the onset of stroke. Forty percent of prestroke RLS/RLS variant patients experienced exacerbation of their symptoms after stroke onset, and two-thirds of poststroke RLS/RLS variant patients required treatment for their RLS/RLS variants. Patients positive for RLS/RLS variants tended to have difficulty falling asleep, but there was no difference in daytime sleepiness, sleep quality, depressive symptoms, stroke subtypes, comorbid diseases, laboratory data or modified Rankin Scale scores at admission or discharge between patients with and without RLS/RLS variants. RLS/RLS variants were most frequently observed to accompany lesions in the medulla (25%), followed by the pons (15.4%), the corona radiata (14.8%), the basal ganglia (3.8%) and the cortex (3.8%).

Conclusion: RLS/RLS variants were found in 8% of acute ischemic stroke patients. Adequate screening and management are needed to improve patients' quality of life.

Introduction

Restless legs syndrome (RLS) is a neurological disorder that significantly impacts patients' sleep, mood, and work as well as their partner's sleep and the relationship between the partner and the patient (1). The prevalence of RLS in a rural community in Japan was reported to be 1.8% (2), which is lower than the rates in Europe and the USA (7-10%) (3). More than 50% of Japanese patients with RLS show periodic limb movements during sleep (PLMS), which also disrupt sleep (4). A recent systematic review on RLS and major diseases provided insufficient evidence for a relation between RLS and stroke (5). By contrast, previous studies have observed the emergence of RLS/PLMS following ischemic stroke in the medulla, pons, corona radiata, basal ganglia and thalamus (6-9), helping to clarify the neuroanatomical substrates of sleep-related movement disorders. Thus far, the clinical correlates of RLS in Japanese patients with acute ischemic stroke have never been studied. RLS variants, in which abnormal sensations in regions other than the legs fulfill the four essential features of RLS when applied to the involved body parts, have been reported (10). However, the correlation of RLS variants with acute ischemic stroke is unknown. We aimed to investigate the prevalence, lesion topography and clinical correlations of RLS and its variants in Japanese patients with acute ischemic stroke.

Methods

We prospectively evaluated patients with acute ischemic infarction who were admitted to

our university hospital between April 2016 and March 2018. Patients who were unable to answer the clinical interview or questionnaires due to disturbance of consciousness, aphasia, dementia or cognitive impairment were excluded from the study. A total of 104 patients were included in our study. Case 7, in which the abnormal sensation was restricted to the shoulder (an RLS variant) following stroke, has been reported previously (11).

All patients were evaluated by diffusion-weighted brain magnetic resonance imaging (DWI) at 1.5 teslas (Symphony, Sonata, Siemens Japan Company, Tokyo, Japan) within 3 days after admission to confirm acute ischemic stroke. Patients with cerebral hemorrhage, hemorrhagic infarction or negative DWI findings for infarction were excluded from the study. The etiology of ischemic stroke was classified according to the Trial of Org 10172 in Acute Stroke Treatment classification (12).

The topography of acute ischemic lesions was classified according to a study by Lee et al., (7) as follows: 1) cortical lesions with or without subcortical involvement; 2) basal ganglia and/or corona radiata; 3) internal capsule; 4) thalamus; 5) midbrain; 6) pons; 7) medulla; 8) cerebellum; and 9) multiple subcortical lesions.

Within 7 days after stroke onset, the participants received questionnaires regarding their habits and sleep status and underwent clinical interviews on RLS/RLS variants. Daytime sleepiness was measured using the Japanese version of the Epworth sleepiness scale (ESS) (13). Any patient who scored ≥10 on the ESS was defined as having excessive daytime sleepiness (EDS). Sleep disturbance was assessed using the Pittsburgh Sleep Quality Index (PSQI). The PSQI includes 7 component scores (C1, sleep quality; C2, sleep latency; C3, sleep duration; C4, habitual sleep efficiency; C5, sleep disturbances; C6, use of sleeping medications; and C7, daytime dysfunction). Sleep

99 disturbance was defined as a global PSQI score >5 (14). Depressive symptoms were
100 assessed with the Beck Depression Inventory-II (BDI-II) (15).
101 RLS was diagnosed according to the International RLS Study Group (IRLS)
102 criteria (16) in a clinical interview by neurologists (TS or MO) to confirm the presence
103 of the four essential features: 1) the patient has an urge to move the legs, usually
104 accompanied by or caused by uncomfortable and unpleasant sensations in the legs; 2)
105 the urge to move the legs and any accompanying unpleasant sensations begin or worsen
106 during periods of rest or inactivity; 3) the urge to move the legs and any accompanying
107 unpleasant sensations are partially or totally relieved by movement; and 4) the urge to
108 move the legs and any accompanying unpleasant sensations occur only during the
109 evening or night or are worse at those times than during the day. RLS mimics such as
110 positional discomfort, muscle cramp, venous stasis, vascular claudication and peripheral
111 neuropathy were excluded by TS or MO. We also assessed RLS variants (symptoms in
112 the arms, hips, trunk or face without leg involvement), in which uncomfortable
113 sensations fulfill the four essential features of RLS when applied to the involved body
114 parts (3). Leg motor restlessness, in which the urge to move the legs exists but does not
115 fulfill the RLS criteria, was also evaluated (17).

116 Blood samples were collected to determine following parameters using
117 standard clinical methods: urea nitrogen (UN), calcium (Ca), phosphorus (P), creatinine
118 (Cre), iron, ferritin, total cholesterol (T-C), triglyceride (TG), high-density lipoprotein
119 cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), glucose, glycated
120 hemoglobin (HbA1C), ferritin and hemoglobin. Functional disability was assessed using
121 a modified Rankin Scale (mRS) twice: once at admission and once at discharge (18).

The study was approved by the Institutional Review Board of Dokkyo Medical University Hospital, and written informed consent was obtained from all participants enrolled in the study.

Statistical analysis

In this study, a chi-squared test or Fisher's exact test was used to compare the categorical variables, and a Mann-Whitney U test or an unpaired t-test was used as appropriate to compare the continuous variables. A two-tailed p-value of <0.05 was considered statistically significant. IBM SPSS Statistics 25.0 (IBM SPSS, Tokyo, Japan) was used for the statistical analysis.

Representative case presentation of 3 ischemic stroke patients with RLS/RLS variants

Case 5 (prestroke RLS)

A 48-year-old man developed numbness and weakness of the right hand upon awakening after a nap. The man’s past medical history included bronchial asthma, chronic sinusitis and untreated hypertension. On admission, the patient’s blood pressure was 220/150 mmHg, and his pulse rate was 76/min with a regular rhythm. Neurological examination revealed right hemiparesis and hypesthesia. Brain magnetic resonance imaging (MRI) showed acute infarctions extending from the left basal ganglia to the corona radiata (Figure 1). Upon laboratory examination, hemoglobin was 14.0 g/dl,

creatinine was 1.01 mg/dl, ferritin was 199 ng/ml and iron was 75 μg/dl. The patient complained of leg restlessness 3 days after the onset of stroke, but a detailed history-taking revealed that he had had untreated RLS since the age of 6 years. After the onset of stroke, the patient's RLS symptoms worsened compared with before. Administration of rotigotine at 2.25 mg/day markedly improved RLS symptoms from 32 points to 11 points on the IRLS Study Group rating scale (19). The patient had habitual snoring, obesity and an oxygen desaturation index of 13.2/h on the pulse oximeters, suggesting obstructive sleep apnea. However, the patient refused to undergo polysomnography for further investigation.

Case 6 (poststroke RLS)

A 70-year-old man with diabetes mellitus and hypertension presented with sudden-onset weakness of the left upper and lower extremities. The man's blood pressure was 163/91 mmHg, and his pulse rate was 72/min with a regular rhythm. Neurological examinations revealed left hemiparesis, including the left side of the face, and paresthesia of the left upper and lower limbs. Brain MRI showed fresh infarcts (Figure 2). The patient's blood test results, including hemoglobin, creatinine, ferritin and iron levels, were unremarkable. Uncomfortable, abnormal sensations in both legs developed just after the onset of stroke. RLS was diagnosed, but the symptoms were mild and did not require treatment.

Case 7 (poststroke RLS variants)

A 70-year-old woman presented with speech difficulty and weakness of the left upper and lower limbs upon awakening. On neurological examination, dysarthria and left hemiparesis were noted. The sensory systems were intact. Brain MRI showed acute infarction in the right posterior limb of the internal capsule (Figure 3). On Day 1, the patient developed an RLS variant, in which the abnormal sensations were restricted to the bilateral shoulders, resulting in insomnia. Laboratory data were unremarkable. The patient was treated with pramipexole 0.25 mg/day 1 hour before bed time, which significantly ameliorated the abnormal sensation in her shoulders.

Results

In our study, the classification of stroke was as follows: large-artery atherosclerosis, n=55 (52.9%); cardioembolism, n=24 (23.1%); small-vessel occlusion, n=10 (9.6%); stroke of other determined etiology, n=7 (6.7%); stroke of undetermined etiology, n=8 (7.7%). Among 104 ischemic stroke patients, 8 of them (7.7%) (6 men and 2 women, aged 43-74 years) had either RLS or RLS variants: 6 (5.8%) and 2 patients (1.9%) showed RLS and RLS variants, respectively (Table 1). Six patients had an urge to move the legs but did not meet the criteria for RLS or RLS variants; those patients were considered to have leg motor restlessness. One patient had leg restlessness with unpleasant and uncomfortable sensations, characteristics similar to RLS, but had no urge to move. In five patients (4.8%), RLS/RLS variants preceded the onset of ischemic stroke, and in 3 (2.9%), RLS/RLS variants followed the onset of ischemic stroke. Among the 5 patients with RLS/RLS variants preceding stroke, all patients had bilateral RLS symptoms, one of whom had an RLS variant involving the lower back. In case 2,

RLS symptoms in the right leg were exacerbated after the onset of stroke. Forty percent (2/5) of patients with RLS preceding stroke experienced worsening of RLS symptoms after the onset of stroke. Among the 3 patients with RLS/RLS variants following stroke, 2 (66.7%) had bilateral symptoms (one had RLS variants involving the shoulder), and 1 (33.3%) had unilateral symptoms contralateral to the brain lesion. Two of the three (66.7%) patients with RLS/RLS variants following stroke required treatment. Case 1, which showed a low serum ferritin level (4.3 μg/L), was treated with oral iron. Dopamine agonists (pramipexole or rotigotine) were used in Cases 5, 6, and 7. RLS symptoms developed 1-2 days after the onset of stroke.

In Table 2, there was no significant difference in PSQI, BDI-II or ESS scores between patients with and without RLS. No significant differences in clinical subtypes of ischemic stroke, comorbid diseases including hypertension and diabetes, or mRS at admission or discharge were found between the patients with and without RLS. The laboratory findings of patients with and without RLS are shown in Supplementary Table 1. We found no differences in the laboratory data, including the ferritin, UN, creatinine, hemoglobin, electrolytes, fasted blood glucose and HbA1C values.

Figure 4 shows the frequency of ischemic stroke related to RLS/RLS variants for different lesion sites among all patients. RLS/RLS variants were most frequently observed in the medulla (25%), followed by the pons (15.4%), the corona radiata (14.8%), the basal ganglia (3.8%) and the cortex (3.7%).

Discussion

In this study, we evaluated RLS and its variants among patients with DWI-confirmed

211 acute ischemic stroke. We found that 7.7% of patients had RLS or RLS variants. The
212 frequency of poststroke RLS/RLS variants was 2.9%, which was lower than the 10-12%
213 reported in previous studies of poststroke RLS (7, 20). However, a study by Ruppert et al.
214 (8) including 30 patients with brainstem stroke reported a similar frequency to our study,
215 with 1 patient (3.3%) showing poststroke RLS and 2 (6.7%) showing exacerbation of pre-
216 existing RLS symptoms following stroke. In our study, 2 patients with RLS variants, in
217 which abnormal sensation restricted to a restless lower back (prestroke RLS variants) or
218 shoulder (poststroke RLS variants), were found. To the best of our knowledge, this study
219 is the first to evaluate RLS variants in patients with acute ischemic stroke. On detailed
220 assessment, we found no difference in daytime sleepiness, sleep quality, depressive
221 symptoms, laboratory data (including ferritin, hemoglobin, creatinine, fasted blood
222 glucose and HbA1C), stroke subtypes or mRS scores on admission or discharge between
223 patients with and without RLS/RLS variants. Regarding comorbid diseases, our study
224 found no difference in hypertension, dyslipidemia, diabetes mellitus or atrial fibrillation
225 between patients with and without RLS/RLS variants. By contrast, Schlesinger et al. (21)
226 showed that hypertension and dyslipidemia were more prevalent in the RLS-positive
227 group than in the RLS-negative group among patients with stroke and transient ischemic
228 attack. A systematic review and meta-analysis also showed RLS patients had higher
229 prevalences of hypertension, diabetes and hyperlipidemia compared with healthy controls,
230 but no evidence of a significant risk of cerebrovascular and cardiovascular events was
231 observed in RLS patients after adjusting for potential confounders (22). However, the
232 observation that 40% of prestroke RLS/RLS variant patients showed exacerbation of their
233 symptoms and required treatment for RLS/RLS variants and that 66.7% of poststroke
234 RLS/RLS variant patients needed dopaminergic treatment for RLS/RLS variant

symptoms suggests importance in the assessment of RLS/RLS variants in patients with acute ischemic stroke. In addition, there was a nonsignificant trend toward increased difficulty in initiating asleep in the RLS/RLS variant group compared with the no RLS/RLS variant group. Therefore, early diagnosis and treatment of RLS/RLS variants in the setting of acute stroke can improve patients' quality of life.

Brain iron insufficiency, as well as dopamine and other neurotransmitters such as opioids, adenosine, orexin and glutamine, participate in the pathophysiology of RLS (23, 24). A functional MRI study showed bilateral activation of the cerebellum and contralateral activation of the thalamus during RLS (25). In the central nervous system, the motor and somatosensory cortex, striatum, anterior cingulate gyrus, thalamus, A11 hypothalamic region, substantia nigra, red nucleus, cerebellum and inferior olive of the medulla have been implicated in RLS (26).

Poststroke RLS patients showed lesions in the basal ganglia, brainstem, thalamus, corona radiata, and internal capsules (6, 7, 27). Among 3 patients in our study with poststroke RLS/RLS variants, lesions were present in the medial pons, the posterior internal capsule, or the region of the cerebral hemisphere within the middle cerebral artery territory. Additionally, RLS/RLS variant-related lesions were most frequently found in the medulla (25%), followed by the pons (15.4%), the corona radiata (14.8%), the basal ganglia (3.8%) and the cortex (3.7%). All of those regions have already been reported to cause RLS (26). The onset of RLS after stroke was rapid (within 2 days), in agreement with a previous study (mean 1.8 days; range 1-4 days) (7).

Our patients with RLS/RLS variants were treated with oral iron and dopamine agonists (pramipexole and rotigotine). A low serum ferritin level (< 50 μg/L) was related to increased severity and the occurrence of RLS, even in patients with normal hemoglobin

levels (16). Therefore, an iron supplement is recommended in RLS patients with low ferritin levels. Dopamine agonists (pramipexole, rotigotine, cabergoline) and gabapentin enacarbil are recommended for the treatment of RLS patients (Level A) (28). A favorable response to dopaminergic drugs is included as supportive criterion for RLS (16), and in our study, dopamine agonists were chosen rather than gabapentin enacarbil to further enhance the accuracy of RLS diagnosis. Because stroke-related symptoms such as sensory symptoms and hemiparesis sometimes mimic RLS symptoms, which have to be differentiated from true RLS. Gabapentin enacarbil can be effective for both RLS and sensory symptoms related to stroke, whereas dopamine agonists respond well to RLS but not sensory symptoms due to other causes.

The basal ganglia–brainstem system has been involved in rhythmic limb movements, postural muscle tone control and regulation of awake-sleep states (29). It is possible that involvement of the corticospinal tract and basal ganglia–brainstem axis directly causes unilateral RLS contralateral to the lesion. However, another consideration is needed for bilateral presentation of RLS following stroke. In a study by Lee et al., (7) 5 of 17 (29.4%) poststroke RLS patients showed unilateral symptoms contralateral to the brain lesion, while 12 of 17 (70.6%) poststroke RLS patients showed bilateral symptoms involving the brainstem, corona radiata and internal capsule. Similarly, in our study, 1 of 3 (33.3%) patients with poststroke RLS/RLS variants showed unilateral symptoms contralateral to the hemispheric infarction, and 2 of 3 (66.7%) patients with poststroke RLS/RLS variants showed bilateral symptoms. Furthermore, all prestroke RLS/RLS variants had bilateral symptoms, and 40% of those patients' bilateral symptoms worsened after stroke. Activation of the contralateral motor cortex resulting from dysfunctions of interhemispheric inhibition has been suggested to play a role in bilateral occurrence of

RLS (6, 7). Woo et al. (9) suggested that additional involvement of basal ganglia may play a role in bilateral occurrence of poststroke RLS.

Schlesinger et al. (21) reported that RLS was observed more frequently in patients with stroke and transient ischemic attack (15%) than in controls (3%), and a multivariate logistic regression model showed that only stroke and transient ischemic attack predicted RLS. In all patients with stroke and transient ischemic attack, RLS preceded those conditions, suggesting RLS as a possible risk factor for subsequent cerebrovascular events; however, periodic limb movements in sleep, which are known to increase cerebrovascular events through changes in blood pressure (30), were not evaluated. Gupta et al. (31) conducted a 3-year prospective study and reported that unilateral or grossly asymmetrical RLS was a predictor of subsequent subcortical stroke. In their study, the mean duration of RLS was 5 years. In contrast, our study showed that all prestroke RLS/RLS variant groups had bilateral symptoms with an RLS duration ranging from 2 days to 32 years. Longstanding RLS (>10 years) accompanied by periodic limb movements in sleep has been associated with increased small-vessel diseases (32).

As a limitation of this study, we did not perform polysomnography to detect PLMS, which are included in the supportive criteria for RLS (3). We did not have the appropriate control group to compare the frequency of RLS and its variants among patients with ischemic stroke. Sensory neuropathy in patients with diabetes, which could impact the diagnosis of RLS, was not assessed in this study. Thyroid hormone levels were also not evaluated. Although a relationship between RLS and thyroid disease was not confirmed (5), one study indicated an increased frequency of RLS-like symptoms in thyroid disease compared with healthy controls (8.2% vs. 0.9%) (33). Because of the cross-sectional nature of our study, we followed patients with RLS/RLS variants for a

short period, and thus the clinical course and clinical efficacy of RLS treatment over time in patients with RLS/RLS variants were unclear. Finally, causative lesions for RLS/RLS variants were difficult to determine because a few patients exhibited poststroke RLS/RLS variants.

In conclusion, RLS/RLS variants were found in 8% of acute ischemic stroke patients. Newly developed RLS/RLS variants should be screened, especially within a few days after ischemic stroke, and worsening of symptoms of pre-existing RLS/RLS variants should be considered after ischemic stroke. Adequate screening and management for RLS/RLS variants are needed to improve patients' quality of life.

Financial disclosures

This work was supported by Grants-in the Explanation of a Role of the Central Sensitization in the Refractory Disease Patients with Various Type of Symptoms and an Improvement of the Patients Care to Follow it, Research on Policy Planning and Evaluation for Rare and Intractable Diseases, Health, Labour and Welfare Sciences Research Grants, the Ministry of Health, Labour and Welfare, Japan. This study was partly supported by a Dokkyo Medical University Young Investigator Award (No. 2016-08).

Conflict of interest statement

None declared.

Acknowledgments

The authors would like to thank Drs. Hidehiro Takekawa, Akio Iwasaki and Hirotaka

331 Sakuramoto, Department of Neurology, Dokkyo Medical University; Prof. Masayuki
332 Miyamoto, Department of Clinical Medicine for Nursing, Dokkyo Medical University
333 School of Nursing; and all of the medical staff members for their assistance with this
334 study.

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Figure legends

Figure 1: Brain MRI findings from case 5 (prestroke RLS)

Figure 2: Brain MRI findings from case 6 (poststroke RLS)

Figure 3: Brain MRI findings from case 7 (poststroke RLS variant)

Figure 4: Frequency of ischemic stroke related to RLS/RLS variants classified by different ischemic lesions.

Table 1: Clinical characteristics and MRI findings of acute ischemic stroke patients with RLS and RLS variants

No.	Age/sex	Stroke location	Neurological symptoms/signs	Risk factors	RLS/RLS variants	RLS/RLS variant onset: pre/poststroke	RLS/RLS variant location, laterality	RLS/RLS variant treatment	F/U period for RLS/RLS variants (days)	PSQI	ESS
1	43/F	Right corona radiata	Left hemiparesis	HT, DLP, Basedow disease	RLS variants	Prestroke (at age 41 y)	Bilateral lower back	Iron supplement	12*	5	6
2	62/M	Left medial medulla	Dysarthria, right hemiparesis	DM, Af, dilated cardiomyopathy	RLS	Prestroke (2 days before stroke onset)	Bilateral legs. Right leg symptoms worsened after stroke	None	22	1	8
3	74/M	Right corona radiata	Left hemiparesis	HT, Af	RLS	Prestroke (at age 30 s)	Bilateral legs	None	22	2	11
4	69/M	Ventral part of pons	Diplopia, left facial hypesthesia	HT	RLS	Prestroke (at age 65 y)	Bilateral legs	None	16	9	6
5	48/M	Left basal ganglia, corona radiata	Right hemiparesis and paresthesia of right U/L limbs	HT	RLS	Prestroke (at age 6 y)	Bilateral legs	Rotigotine 2.25 mg/day	25*	13	14
6	70/M	Right medial pons	Left hemiparesis and paresthesia of left U/L limbs	HT, DM	RLS	Poststroke (Day 2)	Bilateral legs	Pramipexole 0.125 mg	14*	2	5

7	70/F	Right posterior internal capsule	Dysarthria, left hemiparesis	HT, DLP	RLS variants	Poststroke (Day 1)	Bilateral shoulder	Pramipexiole 0.125 mg→0.25 mg	18*	4	6
8	65/M	Right MCA territories (posterior M2)	Left hemiparesis	DM, Af	RLS	Poststroke (Day 2)	Left leg	None	16	5	9

M=male, F=female, RLS=restless legs syndrome, HT=hypertension, DLP=dyslipidemia, Af=atrial fibrillation, MCA=middle cerebral artery, U/L=upper and lower, PSQI=Pittsburgh Sleep Quality Index, ESS=Epworth Sleepiness Scale; F/U=follow-up; a period between the initial examination or * the initiation of RLS treatment and the last follow-up

Table 2: Comparison of demographic and characteristics between patients with and without RLS/RLS variants

	No RLS/RLS variants	RLS/RLS variants	p-value
Age (years)	65.4±12.3	62.3±13.2	0.61
Sex (M/F)	65/31	6/2	0.60
BMI (kg/m^2)	23.9±3.5	24.0±1.9	0.39
Classification of stroke subtypes			
Large-artery atherosclerosis	50 (52.1)	5 (62.5)	0.72
Cardioembolism	23 (24.0)	1 (12.5)	0.68
Small-vessel occlusion	8 (8.3)	2 (25.0)	0.17
Stroke of other determined etiology	7 (7.3)	0 (0.0)	1.0
Stroke of undetermined etiology	8 (8.3)	0 (0.0)	1.0
Caffeine, n (%)	91 (94.8%)	6 (75.0%)	0.35
Smoking, n (%)	61 (63.5%)	7 (87.5%)	0.49
Alcohol, n (%)	56 (58.3%)	4 (50.0%)	0.62
Hypertension, n (%)	61 (63.5%)	6 (75.0%)	0.41
Diabetes, n (%)	33 (34.4%)	3 (37.5%)	0.57
Dyslipidemia, n (%)	55 (57.2%)	2 (25.0%)	0.082
Atrial fibrillation, n (%)	20 (20.8%)	3 (37.5%)	0.25
PSQI global score	3.96±2.67	5.13±4.05	0.258
PSQI component score			
C1, sleep quality	1.08±0.74	1.38±0.52	0.22
C2, sleep latency	0.79±0.80	1.63±1.30	0.058
C3, sleep duration	0.74±0.96	0.38±0.52	0.42
C4, habitual sleep efficiency	0.34±0.74	0.50±0.76	0.35
C5, sleep disturbances	0.44±0.60	0.38±0.59	0.85
C6, use of sleeping medications	0.20±0.67	0.38±1.06	0.74
C7, daytime dysfunctions	0.40±0.63	0.50±0.76	0.73

PSQI>5, n (%)	24 (25.5%)	2 (25.0%)	0.36
BDI-II	8.97±6.58	11.57±8.26	0.323
ESS	6.78±4.06	8.13±3.09	0.363
ESS≥10, n (%)	20 (21.1%)	2 (25.0%)	0.54
mRS at admission	1.86±0.69	2.01±1.04	0.52
mRS at discharge	1.40±1.07	1.14±0.69	0.17

M=male; F=female; BMI=body mass index; PSQI=Pittsburgh Sleep Quality Index; BDI-II=Beck Depression Inventory, second edition; ESS=Epworth Sleepiness Scale; mRS=-modified Rankin scale