

Original Article

Circadian Variation of Acute Stroke -Hospital Based Study-

Sang-Pil Yun, Woo-Sang Jung, Sang-Kwan Moon, Ki-Ho Cho,
Young-Suk Kim Hyung-Sup Bae

Department of Cardiovascular and Neurologic Diseases (Stroke Center)
College of Oriental Medicine, Kyung-Hee University, Seoul, Korea

Objectives : This study aimed to investigate the circadian variation in stroke types, ischemic stroke subtypes, and *Sasang* constitutions.

Methods : 295 patients with acute stroke within 14 days onset were included, who were admitted to Kyunghee Oriental Medical Center from October 2005 to May 2007. The stroke onset time was subdivided into four groups of 6-hour intervals in a day. Stroke types, ischemic stroke subtypes, and *Sasang* constitutions in four groups were examined.

Results : Most ischemic stroke occurred between 6:01-12:00 hours (30.2%). For ischemic stroke subtypes, the peak period of small-vessel occlusion was between 6:01-12:00 hours (33.2%), large-artery atherosclerosis was most common between 12:01-18:00 hours (39.5%), and cardiac embolism was most frequent between 18:01-24:00 hours (50%). In terms of *Sasang* constitution, *Soyeumin* and *Taeyeumin* were most common between 6:01-12:00 hours (36.4% versus 41.5%, respectively), but the peak time of *Soyangin* was between 12:01-18:00 hours (35.2%).

Conclusion : Most ischemic stroke events occurred in the mid-to-late morning hours in the present study and there was a circadian variation of onset in ischemic stroke subtypes and *Sasang* constitution.

Key Words : Stroke, circadian variation, stroke type, *Sasang* constitution

Introduction

Several studies have described a circadian pattern for the onset of stroke. A higher frequency in the morning was identified¹⁻⁶⁾. This tendency of higher morning incidence of stroke was confirmed by a recent meta-analysis⁷⁾. However, there has been no data yet examined

from oriental medical hospitals, although many Koreans with stroke prefer to being treated by an oriental medical therapeutic method⁸⁾.

To investigate the possibility that stroke occurs more often at certain times of the day and that different types of stroke may have different circadian variations, we examined data from the Kyunghee stroke registry.

The aim of this study was to determine whether there is a circadian pattern of stroke onset according to the stroke subtypes, ischemic stroke subtypes and *Sasang* constitutions.

Subjects and Methods

We included consecutive patients admitted to

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- Correspondence to : Sang-Pil Yun
Kyunghee Oriental Medical Center, Hoegi-dong 1, Dongdaemungu, Seoul, Korea.
(Tel : +82-2-958-9129 / Fax : +82-2-958-9132
E-mail : yunpaul@yahoo.co.kr)
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Kyunghee Oriental Medical Center with first-ever stroke within 14 days of onset from October 2005 to May 2007. The diagnosis of stroke was based on the clinical features and neuroradiologic images (brain computed tomography (CT) scan and/or magnetic resonance imaging (MRI)), which was confirmed by at least two neurologists. Stroke onset time was defined as the earliest time patient or witness noticed neurological deficits. The time was obtained from history taking. For patients who first noticed their stroke symptoms on awakening, it was presumed that stroke had occurred during sleep. For patients who first noticed their stroke symptoms on awakening from sleep, the time of awakening was used as the time of onset. The stroke onset time was subdivided into four groups of 6-hour intervals in a day. These were 0:00-6:00 hours, 6:01- 12:00 hours, 12:01-18:00 hours, and 18:01-24:00 hours. Patients' characteristics and variables were distributed among these four groups. All patients fulfilled clinical protocol, which included stroke types, ischemic stroke subtypes, and *Sasang* constitutions.

For each patient, the following data were analyzed. (1) age; (2) *Sasang* constitution (*Soyeumin*, *Soyangin*, *Taeyeumin*, *Taeyangin*, and unidentified), which was diagnosed using the Questionnaire for *Sasang* Constitution Classification II (QSCC II); (3) stroke subtypes: cerebral infarction and cerebral hemorrhage; (4) ischemic stroke subtype classifications, which were based on the modified TOAST classification^{9,10}: large-artery atherosclerosis (LAA) - these patients have clinical and brain imaging findings of either significant (> 50 %) stenosis or occlusion of a major brain artery owing to atherosclerosis, small-vessel occlusion (SVO) - these patients have lacunar syndrome, cardiac

embolism (CE) - these patients have arterial occlusion due to an embolus arising in the heart, stroke of other determined etiologies (SOD) - these patients have rare causes of stroke, such as nonatherosclerotic vasculopathy, hypercoagulable states, or hematologic disorder, and stroke of undetermined etiologies (SUE) - these patients have no likely etiology determined in spite of an extensive evaluation. For statistical analysis, Windows SPSS package was used. Independent t-test was used for the comparison of continuous variables. The Pearson chi-square test was used for analysis of noncontinuous variables. A p value less than 0.05 was considered statistically significant.

Results

During the 19-month period, 307 consecutive patients with first ever stroke were admitted to Kyunghee Oriental Medical Center. The exact time of stroke onset was uncertain in 12 patients, so these were excluded from the analysis. The remaining 295 patients were included in this study.

The mean age of the 295 patients was 63.14±11.02 years. The age and sex distribution was not significantly different among the four groups.

274 patients (92.9 %) were diagnosed as ischemic stroke while 21 patients (7.1 %) had hemorrhagic stroke. The circadian variation of ischemic and hemorrhagic stroke onset among the 295 patients is depicted in Fig. 1.

The peak time of ischemic stroke occurring was between 6:01 and 12:00 hours (89 patients, 30.2 %) and the lowest risk of ischemic stroke onset occurred between 18:01 and 24:00 hours (48 patients, 16.3 %).

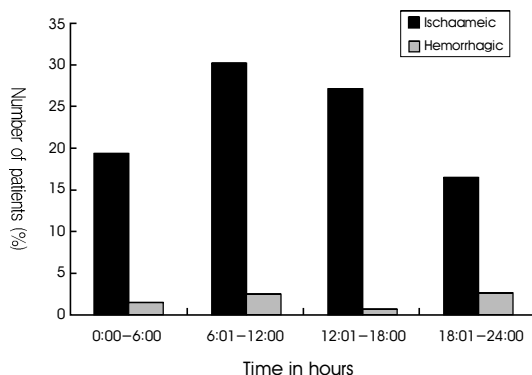


Fig. 1. Circadian variation of ischemic and hemorrhagic stroke onset

As indicated in Table 1, the peak time of stroke occurrence was between 6:01 and 12:00 hours for the SVO and SUE (33.2 % versus 71.4 %, respectively). The great proportion of LAA was present between 12:01 and 18:00 hours (39.5 %) and the peak period of CE was between 18:01

and 24:00 hours (50 %). There was no significant difference in ischemic stroke subtypes.

As analyzed according to the *Sasang* constitution, 28 patients could not get a QSCC II test and 89 patients were not identified by *Sasang* constitution because they were mixed among the

Table 1. Circadian Frequency According to Stroke Subtype

Subtype	00:00-6:00 h	6:01-12:00 h	12:01-18:00 h	18:01-24:00 h
LAA				
n (%)	9 (20.9)	10 (23.3)	17 (39.5)	7 (16.3)
Frequency	15.8 %	11.2 %	21.3 %	14.6 %
CE				
n (%)	1 (16.7)	2 (33.3)	0 (0)	3 (50)
Frequency	1.8 %	2.2 %	0 %	6.3 %
SVO				
n (%)	47 (21.7)	72 (33.2)	61 (28.1)	37 (17.1)
Frequency	82.5 %	80.9 %	76.3 %	77.1 %
SOE				
n (%)	0 (0)	0 (0)	1 (100)	0 (0)
Frequency	0 %	0 %	1.3 %	0 %
SUE				
n (%)	0 (0)	5 (71.4)	1 (14.3)	1 (14.3)
Frequency	0 %	5.6 %	1.3 %	2.1 %
Total, n (%)	57 (20.8)	89 (32.5)	80 (29.2)	48 (17.5)

LAA: Large-artery atherosclerosis; SVO: Small-vessel occlusion; CE: Cardiac embolism; SOE: Stroke of other determined etiologies; SUE: Stroke of undetermined etiologies.

Table 2. Circadian Frequency According to *Sasang* Constitution

Subtype	00:00-6:00 h	6:01-12:00 h	12:01-18:00 h	18:01-24:00 h
<i>Soyeumin</i>				
n (%)	6 (18.2)	12 (36.4)	11 (33.3)	4 (12.1)
Frequency	16.2 %	20.0 %	19.6 %	16.0 %
<i>Taeyeumin</i>				
n (%)	10 (18.9)	22 (41.5)	12 (22.6)	9 (17.0)
Frequency	27.0 %	36.7 %	21.4 %	36.0 %
<i>Soyangin</i>				
n (%)	21 (23.1)	26 (28.6)	32 (35.2)	12 (13.2)
Frequency	56.8.2 %	43.3 %	57.1 %	48.0.0 %
<i>Taeyangin</i>				
n (%)	0 (0)	0 (0)	1 (100)	0(0)
Frequency	0 %	0 %	1.8 %	0 %
Total, n (%)	37 (20.8)	60 (33.7)	56 (31.5)	25 (14.0)

4 constitutions. Thus, the remaining 178 patients were analyzed.

Table 2 shows that stroke occurrence of *Soyeumin* and *Taeyeumin* peaked between 6:01 and 12:00 hours (36.4 % versus 41.5 %, respectively). The peak time of stroke attack in *Soyangin* was between 12:01 and 18:00 hours (35.2 %). No significant difference was observed in *Sasang* constitution.

Discussion

Current study shows that ischemic stroke has a circadian rhythm, with a higher frequency during early morning (between 6:01-12:00 hours) and a lower frequency during night (18:01-24:00 hours). These results were similar to other reports¹⁻⁷⁾.

Although the cause of this diurnal variation is uncertain, it has been related to the circadian rhythm of fibrinolysis, platelet aggregability, and, mainly, arterial blood pressure, with its minimum value during sleep and maximum value in the early hours in the morning, in both normotensive and hypertensive patients¹¹⁻¹³⁾ and it has been suggested that an increase in morning

stroke onset could be due to patients awakening with neurological deficits as a result of a stroke that could have occurred during the night^{14,15)}.

In contrast to ischemic stroke, there was less certainty of data of circadian variation in patients with hemorrhagic stroke due to the shortage of hemorrhagic stroke patients in the present study.

In terms of ischemic stroke subtypes, this study had a different distribution - the peak time of SVO was between 6:01-12:00 hours, LAA was most common between 12:01-18:00 hours, and CE was most frequent between 18:01-24:00 hours-though all ischemic stroke subtypes occurrence in other studies were most common between 6:01-12:00 hours¹⁶⁾. These results may be because SVO was too many and other stroke subtypes were too few to generalize circadian variation of stroke subtypes.

In the analysis of circadian patterns according to the *Sasang* constitution, *Soyeumin* and *Taeyeumin* were most common between 6:01-12:00 hours in accordance with the onset of stroke occurrence, but *Soyangin* was between 12:01-18:00 hours. This is associated with the personality of *Soyangin* which is active, hot

tempered, extroverted and interested in the outside world¹⁷⁾.

In conclusion, most ischemic stroke events occurred in the mid-to-late morning hours in the current study and there was a circadian variation of onset in ischemic stroke subtypes and *Sasang* constitution. Further studies will be required to reveal the pathophysiological mechanism of this circadian variation of onset.

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