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Sleep Status Changes and Prognostic Factors in Patients with Acute Posterior Circulation Ischemic Stroke (Postprint)

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Abstract

Background Stroke patients often present with disrupted and imbalanced sleep states, which are easily overlooked in clinical practice, and current research on whether sleep status affects prognosis in this disease category remains limited.

Objective To investigate the factors associated with sleep state changes and their impact on prognosis in patients with acute posterior circulation ischemic stroke.

Methods Sixty patients with acute posterior circulation ischemic stroke admitted to Kailuan General Hospital affiliated with North China University of Science and Technology between December 2019 and December 2023 were selected as the case group. Based on the modified Rankin Scale (mRS) score at discharge, the case group was subdivided into a good prognosis subgroup (45 cases) and a poor prognosis subgroup (15 cases). Fifty-two patients without cerebrovascular stenosis and without acute ischemic stroke during the same period were selected as the control group. General and clinical data were collected, and differences in circadian sleep-wake rhythm, daytime sleep-wake rhythm, and nocturnal sleep-wake rhythm indicators between the case and control groups were compared, as well as differences in infarct brain region distribution between the good and poor prognosis subgroups. Multivariate Logistic regression analysis was employed to identify prognostic influencing factors in patients with acute posterior circulation ischemic stroke.

Results The apnea-hypopnea index (AHI) was significantly higher in the case group compared to the control group ($P<0.05$). The proportions of reversed sleep cycle, increased daytime sleep, and difficulty initiating sleep were significantly higher in the case group than in the control group ($P<0.05$). The case group exhibited significantly higher daytime total sleep time, wake time after

sleep onset, light sleep stage, deep sleep stage, NREM sleep stage, REM sleep stage, REM sleep stage proportion, and deep sleep stage proportion compared to the control group, while the NREM sleep stage proportion and light sleep stage proportion were significantly lower (P<0.05). The case group also showed significantly higher nocturnal total sleep time, light sleep stage, and NREM sleep stage compared to the control group (P<0.05). The proportion of pontine infarction was significantly higher in the poor prognosis subgroup than in the good prognosis subgroup (P<0.05). Multivariate Logistic regression analysis revealed that daytime deep sleep stage (OR=1.203, 95%CI=1.032~1.401) and pontine infarction (OR=16.497, 95%CI=1.142~238.391) were influencing factors for prognosis in acute posterior circulation ischemic stroke (P<0.05).

Conclusion Patients with acute posterior circulation ischemic stroke exhibit increased apnea-hypopnea index, characterized by reversed sleep cycle, increased daytime sleep, and nocturnal difficulty initiating sleep. Furthermore, daytime deep sleep stage and pontine infarction are influencing factors for poor prognosis in these patients.

Full Text

Study on Sleep Status Changes and Prognostic Factors in Patients with Acute Posterior Circulation Ischemic Stroke

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Abstract

Background: Stroke patients often experience sleep disturbances and imbalances that are easily overlooked in clinical practice. Moreover, research on whether sleep status affects the prognosis of such diseases remains limited.

Objective: To investigate factors influencing sleep state changes and prognosis in patients with acute posterior circulation ischemic stroke.

Methods: Sixty patients with acute posterior circulation ischemic stroke admitted to Kailuan General Hospital Affiliated to North China University of Science and Technology between December 2019 and December 2023 were selected as the case group. Based on modified Rankin Scale (mRS) scores at discharge, the

case group was divided into a good prognosis subgroup (45 cases) and a poor prognosis subgroup (15 cases). Additionally, 52 patients without cerebrovascular stenosis or acute ischemic stroke during the same period were selected as the control group. General and clinical data were collected to compare circadian sleep-wake rhythms, daytime sleep-wake rhythms, nighttime sleep-wake rhythms, and differences in infarct brain region distribution between the good and poor prognosis subgroups. Multivariate logistic regression analysis was used to identify prognostic factors in acute posterior circulation ischemic stroke patients.

Results: The apnea-hypopnea index (AHI) was significantly higher in the case group than in the control group ($P<0.05$). The case group also showed significantly higher proportions of reversed sleep cycles, increased daytime sleep, and difficulty falling asleep compared to the control group ($P<0.05$). Daytime total sleep time, wake time after sleep onset, light sleep duration, deep sleep duration, NREM sleep duration, REM sleep duration, REM sleep proportion, and deep sleep proportion were all significantly higher in the case group, while NREM sleep proportion and light sleep proportion were significantly lower ($P<0.05$). The case group exhibited significantly longer nighttime total sleep time, light sleep duration, and NREM sleep duration than the control group ($P<0.05$). The proportion of pontine infarction was significantly higher in the poor prognosis subgroup than in the good prognosis subgroup ($P<0.05$). Multivariate logistic regression analysis revealed that daytime deep sleep duration (OR=1.203, 95%CI=1.032~1.401) and pontine infarction (OR=16.497, 95%CI=1.142~238.391) were independent influencing factors for prognosis in acute posterior circulation ischemic stroke ($P<0.05$).

Conclusion: Patients with acute posterior circulation ischemic stroke exhibit increased apnea-hypopnea index and characteristic sleep disturbances including reversed sleep cycles, increased daytime sleep, and difficulty falling asleep at night. Daytime deep sleep duration and pontine infarction are factors that adversely affect patient prognosis.

Keywords: Stroke; Brain infarction, posterior circulation; Sleep state; Prognosis; Case-control studies; Root cause analysis

Introduction

Acute posterior circulation ischemic stroke is an ischemic cerebrovascular disease primarily caused by stenosis, embolism, or in-situ thrombosis formation in the bilateral vertebral arteries, basilar artery, and posterior cerebral arteries. Patients typically present with vertigo as the main feature, accompanied by nausea, vomiting, limb sensory disturbances, and balance disorders [1-2]. The incidence of acute posterior circulation ischemic stroke accounts for 20% of all ischemic strokes, with a fatality rate reaching 5%, significantly impacting the health index of Chinese residents [3]. Research has shown that sleep du-

ration, sleep rhythm, and apnea-hypopnea index (AHI) all undergo significant changes after stroke [4]. Currently, there is limited research on changes in daytime and nighttime sleep-wake rhythms after stroke, particularly regarding how daytime sleep-wake rhythms affect disease prognosis, and whether the distribution of ischemic brain regions influences stroke outcomes remains inconclusive. This study further investigates how AHI, changes in daytime and nighttime sleep-wake rhythms, and differences in infarct brain region distribution affect prognosis in acute posterior circulation ischemic stroke patients.

Methods

1.1 Study Subjects Patients with acute ischemic stroke diagnosed and treated in the Department of Neurology at Kailuan General Hospital Affiliated to North China University of Science and Technology between December 2019 and December 2023 were selected as the case group.

Inclusion criteria: (1) All selected patients met the diagnostic criteria of the *Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke 2018* [5]; (2) Cranial magnetic resonance imaging (MRI, GE Discovery MR750W) confirmed that lesions were mainly distributed in the posterior circulation 供血区 such as the thalamus, pons, medulla, cerebellum, and corpus callosum, and magnetic resonance angiography (MRA, GE Discovery MR750W) showed stenosis or occlusion of the vertebral artery, basilar artery, and posterior cerebral artery; (3) No disturbance of consciousness; (4) Total daytime and nighttime sleep monitoring time $\geq$ 5 days.

Exclusion criteria: (1) Prior history of psychiatric disorders; (2) Severe functional impairment of vital organs including heart, lung, liver, and kidney; (3) Use of sedative or sleep-aid medications.

Control group: Volunteers from the same hospital period confirmed by MRI and MRA to have no cerebrovascular stenosis or acute ischemic stroke, with good compliance and total daytime and nighttime sleep monitoring time $\geq$ 5 days. Exclusion criteria were the same as for the case group.

This study included 60 cases in the case group and 52 cases in the control group. The study was approved by the Medical Ethics Committee of Kailuan General Hospital Affiliated to North China University of Science and Technology (approval number 2023005), and all participants or their legal representatives signed informed consent forms.

1.2 Data Collection **1.2.1 Clinical data collection:** Included gender, age, BMI, history of hypertension, diabetes, hyperhomocysteinemia, hyperlipidemia, smoking history, alcohol consumption history, and AHI. Diagnostic criteria were as follows: Hypertension: systolic blood pressure $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg, or use of antihypertensive medication; Diabetes:

fasting blood glucose $\geq$ 7.0 mmol/L or use of hypoglycemic medication; Hyperhomocysteinemia: homocysteine $>$ 15 mol/L; Hyperlipidemia: total cholesterol $>$ 5.72 mmol/L and/or triglycerides $>$ 1.70 mmol/L, or use of lipid-lowering medication; Smoking history: $\geq$ 1 cigarette/day for $\geq$ 1 year; Alcohol consumption: $\geq$ 100 mL/day for $\geq$ 1 year.

1.2.2 Sleep parameters and AHI monitoring: Sleep parameters and AHI were monitored using the SC-500 sleep monitor (Nanjing Bochuang Haiyun Electronic Technology Co., Ltd.). Sleep indicators were recorded from 6:00-18:00 and 18:00 to 6:00 the next day, including daytime total sleep time, sleep latency, rapid eye movement (REM) sleep latency, wake time after sleep onset, light sleep duration (N1, N2 stages), deep sleep duration (N3 stage), non-rapid eye movement (NREM) sleep duration, REM sleep duration, NREM sleep proportion, REM sleep proportion, light sleep proportion, deep sleep proportion, and sleep efficiency. The mean value of each parameter over 5 days was calculated, and recordings with $<$ 8 hours per 24-hour period were excluded.

1.2.3 Circadian sleep-wake rhythm indicators: Included increased circadian sleep, reversed sleep cycles, increased daytime sleep, nighttime sleep maintenance disorders, difficulty falling asleep at night, and low sleep efficiency. Specific criteria were based on references [6-7].

1.2.4 Modified Rankin Scale (mRS) scoring: Based on mRS scores at discharge, the case group was divided into a good prognosis subgroup (mRS score $\leq$ 2 points, 45 cases) and a poor prognosis subgroup (mRS score $>$ 2 points, 15 cases).

1.3 Statistical Methods Statistical analysis was performed using SPSS 26.0 software. Normally distributed measurement data were expressed as mean $\pm$ standard deviation ($\bar{x}\pm s$) and compared between groups using independent samples t-test. Non-normally distributed data were expressed as median (P25, P75) and compared using non-parametric tests. Count data were expressed as percentages and compared using ^{2} test. Multivariate logistic regression analysis was used to explore stroke prognosis influencing factors. P$<$0.05 was considered statistically significant.

Results

2.1 Comparison of Clinical Data Between Groups There were no significant differences in BMI, smoking history, or hyperlipidemia history between the two groups (P$>$0.05). The case group had significantly higher proportions of male patients, older age, hypertension history, diabetes history, hyperhomocysteinemia history, alcohol consumption history, and AHI compared to the control group (P$<$0.05) .

2.2 Comparison of Circadian Sleep-Wake Rhythm Between Groups No significant differences were observed between groups in the proportions of increased circadian sleep, sleep maintenance disorders, difficulty falling asleep, or low sleep efficiency (P>0.05). However, the case group showed significantly higher proportions of reversed sleep cycles, increased daytime sleep, and difficulty falling asleep compared to the control group (P<0.05) .

2.3 Comparison of Daytime Sleep-Wake Rhythm Between Groups No significant differences were found in sleep latency, REM sleep latency, or sleep efficiency between groups (P>0.05). The case group exhibited significantly higher daytime total sleep time, wake time after sleep onset, light sleep duration, deep sleep duration, NREM sleep duration, REM sleep duration, REM sleep proportion, and deep sleep proportion compared to the control group, while NREM sleep proportion and light sleep proportion were significantly lower (P<0.05) .

2.4 Comparison of Nighttime Sleep-Wake Rhythm Between Groups No significant differences were observed in sleep latency, REM sleep latency, wake time after sleep onset, deep sleep duration, REM sleep duration, NREM sleep proportion, REM sleep proportion, light sleep proportion, deep sleep proportion, or sleep efficiency (P>0.05). However, the case group had significantly longer nighttime total sleep time, light sleep duration, and NREM sleep duration than the control group (P<0.05) .

2.5 Comparison of Infarct Brain Region Distribution in Acute Posterior Circulation Ischemic Stroke Group No significant differences were found between the good and poor prognosis subgroups in the proportions of thalamic, medullary, cerebellar, or corpus callosum infarctions (P>0.05). However, the proportion of pontine infarction was significantly higher in the poor prognosis subgroup than in the good prognosis subgroup (P<0.05) .

2.6 Prognostic Factors for Acute Posterior Circulation Ischemic Stroke Using patient prognosis as the dependent variable (good prognosis=0, poor prognosis=1), multivariate logistic regression analysis was performed with variables showing significant associations in univariate analysis and without collinearity as independent variables. These included gender (female=0, male=1), age, hypertension (no=0, yes=1), diabetes (no=0, yes=1), hyperhomocysteinemia (no=0, yes=1), alcohol consumption history (no=0, yes=1), AHI (actual value), increased daytime sleep (no=0, yes=1), reversed sleep cycle (no=0, yes=1), difficulty falling asleep (no=0, yes=1), daytime total sleep time (actual value), daytime wake time after sleep onset (actual value), daytime light sleep (actual value), daytime deep sleep (actual value), daytime REM sleep duration, nighttime total sleep time (actual value), nighttime light sleep duration (actual value), and pontine infarction (no=0, yes=1). The results showed that daytime deep sleep duration (OR=1.203, 95%CI=1.032~1.401) and pontine infarction (OR=16.497, 95%CI=1.142~238.391) were independent

influencing factors for prognosis in acute posterior circulation ischemic stroke ($P<0.05$) .

Discussion

The posterior circulation of the brain, composed of the vertebro-basilar arterial system, primarily supplies blood to the brainstem, thalamus, cerebellum, posterior occipital lobe of the cerebral hemisphere, and upper spinal cord, making it a high-incidence site for ischemic stroke [8]. The prognosis of acute posterior circulation ischemic stroke patients is poor, with mortality and disability rates reaching up to 80% in patients with moderate to severe basilar artery occlusion [9]. Traditional risk factors for stroke prognosis include age, cholesterol, and low-density lipoprotein [10], while novel factors encompass C-reactive protein levels, atrial fibrillation, and uric acid levels [11]. Currently, domestic and international research on the correlation between post-stroke sleep status indicators and prognosis is limited. This study explores the relationship between AHI, changes in circadian sleep-wake indicators, and differences in infarct brain region location with stroke prognosis in acute posterior circulation ischemic stroke patients.

Our results show that the case group had higher proportions of male patients, older age, and higher rates of hypertension, diabetes, hyperhomocysteinemia, alcohol consumption history, and AHI compared to the control group. Stroke combined with high-risk factors increases its incidence, and obstructive sleep apnea-hypopnea syndrome (OSAHS) is an independent influencing factor for stroke and affects neurological function rehabilitation and prognosis. The baseline data and elevated AHI in this study are consistent with previous research [12-13]. OSAHS can cause nocturnal paroxysmal hypoxia and carbon dioxide retention in stroke patients, increase micro-arousals, activate the sympathetic nervous system, elevate sleep-related inflammatory mediators and neurotransmitter levels (such as cortisol), and alter sleep-wake rhythms. These changes are characterized by increased light sleep duration, elevated arousal index, and reduced deep sleep and REM sleep duration, leading to sleep fragmentation and disruption of normal sleep cycles [14]. Additionally, during sleep in OSAHS patients, repeated intermittent hypoxia exacerbates brain tissue hypoxia, increases oxidative stress, causes hippocampal neuronal apoptosis, accumulation of neuropathological proteins, reduced mitochondrial efficiency in neuronal cells, decreased synaptic numbers, and impaired synaptic plasticity, which interferes with neuronal transmission and affects recovery processes including motor function, learning, and memory [15].

Research has shown that the bimodal onset pattern of ischemic stroke is closely related to changes in the circadian rhythm system. The circadian rhythm system is a self-regulating system characterized by 24-hour rhythmic oscillations, influenced by multiple circadian genes (primarily clock and BMAL1 genes) and

their protein products. Its central pacemaker is located in the suprachiasmatic nucleus and includes numerous organ- and tissue-specific cells [16]. Our study on circadian sleep-wake rhythms in acute posterior circulation ischemic stroke patients revealed increased sleep cycle reversal, increased daytime sleep, and higher proportions of difficulty falling asleep. Daytime sleep-wake rhythm analysis showed increased daytime total sleep time, wake time after sleep onset, light sleep duration, deep sleep duration, NREM sleep duration, and REM sleep duration, with elevated REM sleep proportion and deep sleep proportion, while NREM sleep proportion and light sleep proportion decreased. Nighttime sleep-wake rhythm analysis revealed prolonged nighttime total sleep time, light sleep duration, and NREM sleep duration. These findings indicate that acute posterior circulation ischemic stroke patients experience altered daytime and nighttime sleep-wake rhythms, with more prominent changes in daytime sleep-wake patterns—a topic rarely addressed in domestic and international research. Studies have shown [17] that neurotransmitter levels related to post-stroke sleep-wake rhythms change, with sleep-promoting neurotransmitters (such as gamma-aminobutyric acid and acetylcholine) and wake-promoting neurotransmitters (such as dopamine, serotonin, and norepinephrine) varying with circadian cycles and brain regions, leading to varying degrees of disturbance. Additionally, the ascending arousal system is located in the posterior circulation brainstem 供血区 and serves as the switch for sleep-wake states. When brainstem infarction occurs, sleep-wake rhythm regulation becomes imbalanced [18], consistent with our findings.

Our multivariate analysis identified daytime deep sleep duration as a prognostic factor for acute posterior circulation ischemic stroke. Stable sleep status is related to metabolism and thermoregulation, plays an important role in regulating inflammation and apoptosis, enhances neuroprotective mechanisms, and promotes neural plasticity, forming the basis for post-stroke neurological recovery [19]. Research has shown that deep sleep duration (slow-wave sleep) may play a key role in post-stroke neural circuit plasticity, neuroprotection, brain waste clearance, and sensorimotor function [13]. Furthermore, FACCHIN et al. [20] found in animal studies that deep sleep duration directly promotes anatomical and functional plasticity of neural circuits during sleep and can serve as an intervention window for stroke prognosis recovery. Studies have shown that compared with anterior circulation infarction patients, posterior circulation infarction patients have prolonged deep sleep and increased awakenings [21]. In the posterior circulation 供血区, the thalamus is an important regulatory center for the arousal system. Once thalamic infarction occurs, sleep quality declines, sleep disorder incidence increases, sleep-wake rhythms are disrupted, and daytime total sleep time significantly increases [22-23]. Different infarct locations can cause varying degrees of sleep-wake system disturbance.

Our multivariate analysis also found that pontine infarction is a prognostic factor for acute posterior circulation ischemic stroke. Pontine infarction accounts for the highest proportion of brainstem infarctions. The pons contains the ascending reticular activating system with numerous intersecting nerve fibers and

serves as a relay station for cerebral cortex information transmission [24]. The pons has many nerve nuclei with relatively greater blood supply demand and is relatively more sensitive to ischemia. When pontine infarction occurs, neural activity weakens, brain network connectivity function declines, cerebral arousal threshold increases, and both the default functional network maintaining brain arousal and the frontoparietal network affecting human cognition are altered. This causes Wallerian degeneration of nerve fibers in remote areas, subsequently worsening limb motor dysfunction and language disorders [25-26]. In summary, pontine infarction activates multiple repair pathways, primarily involving tissue repair and neural network reconstruction, which can cause varying degrees of functional impairment and is an important factor affecting stroke prognosis.

Acute posterior circulation ischemic stroke patients exhibit increased apnea-hypopnea index and characteristic sleep disturbances including reversed sleep cycles, increased daytime sleep, and difficulty falling asleep at night. Daytime deep sleep duration and pontine infarction are factors that adversely affect patient prognosis.

This study has certain limitations, including a small sample size and lack of comparison with anterior circulation ischemic stroke cases. Therefore, comprehensive evaluation combined with clinical disease progression and outcomes is still needed. Future studies should expand sample sizes to further validate our conclusions.

Author Contributions

ZHANG Pingshu was responsible for study conception, design, and feasibility analysis, statistical processing, and results analysis and interpretation. XUE Jing was responsible for data analysis, chart preparation, literature review, and drafting the manuscript. XING Aijun was responsible for manuscript guidance and revision. WANG Lianhui, MA Qian, and FU Yongshan were responsible for data collection. YUAN Xiaodong was responsible for overall quality control and final approval of the manuscript.

This article has no conflicts of interest.

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