BMC Neurology

RESEARCH Open Access

# Sex differences in the risk of excessive daytime sleepiness in mild and moderate ischaemic stroke patients: a retrospective database study

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## Abstract

**Background** Excessive daytime sleepiness (EDS) is a common complication of stroke that has a detrimental effect on patients' daily life and functional recovery. The clinical characteristics and risk factors for poststroke EDS may differ between males and females.

**Methods** A retrospective study based on hospital medical records was conducted on patients with a diagnosis of stroke who participated in polysomnographic monitoring at the Affiliated Hospital of Yangzhou University from February 2022 to May 2024. Baseline data, laboratory test data, polysomnographic data, and related scale scores were retrospectively collected. The Epworth Sleepiness Scale (ESS) score was used to assess EDS after stroke. Binary logistic regression was used to determine the risk factors for daytime sleepiness. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Statistical analysis was performed via IBM SPSS 26.0.

**Results** ESS scores were higher in males than in females, whereas females had higher Pittsburgh Sleep Quality Index (PSQI) scores and Hospital Anxiety and Depression Scale (HADS) scores. Male sex and higher depression scores were risk factors for EDS; among male patients, higher anxiety scores were a risk factor for EDS, whereas smoking was a protective factor. Depression, a higher arousal index and a reduced proportion of N3 sleep periods were risk factors for EDS in females.

**Conclusions** The characteristics and influencing factors of EDS differ between the sexes in patients with mild and moderate ischaemic stroke. Our study may provide evidence and guidance for clinical diagnosis and treatment. Interventional studies are needed to assess the impact of treating these risk factors in the future.

**Keywords** Stroke, Sex differences, Excessive daytime sleepiness, Polysomnography

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## Background

Excessive daytime sleepiness (EDS) refers to uncontrollable drowsiness or even sudden sleepiness during the main part of the day when wakefulness is supposed to be maintained [1]. Sleepiness after stroke is a common complication and refers to the aggravation of sleepiness tendency, excessive daytime sleepiness, and increased napping. The prevalence of sleepiness in stroke patients ranges from 1.1 to 27% [2]. Poststroke EDS is a pathognomonic condition that has a detrimental effect on patients' daily life and functional recovery. In addition to reducing quality of life and increasing occupational risks and accident rates, which may result from the drowsiness itself, EDS may affect cognitive function and learning ability and reduce overall well-being in stroke patients [3, 4]. It has also been shown that higher Epworth Sleepiness Scale (ESS) scores are independently associated with stroke [5] and that EDS can lead to worsening of acute stroke, with adverse effects on subsequent stroke prognosis and recurrence [6].

The mechanism of EDS production after a stroke involves multiple factors. After stroke, changes in blood flow, ischaemia and hypoxia, excitatory amino acids and other toxic effects occur in the ascending reticular activation system (RAS), nucleus tractus solitaris, raphe nucleus, thalamic reticular nucleus and other areas of the brain that may interfere with the sleep–wake mechanism [7] and lead to sleep disorders. Lesions affecting the reticular activating system often lead to drowsiness. These lesions include the subcortical (caudate, putamen), bilateral thalami, thalamo-midbrain, supramedullary and medial pontine regions where RAS fibres are highly concentrated [8]. Damage to neuroanatomical sites after stroke leads to the destruction of neurotransmitter pathways, which in turn leads to an abnormal increase or decrease in sleep-related transmitter synthesis, resulting in sleep disorders. Abnormalities in acetylcholine, norepinephrine, 5-hydroxytryptophane and other transmitters usually lead to EDS [9]. Poststroke sleep-disbreathing is another factor that causes EDS, as it is associated with sleep disruption and nocturnal hypoxemia caused by frequent awakenings. The hypoxic index during sleep has been shown to be an independent risk factor for daytime sleepiness [10]. Anxiety, depression and other psychological factors also cannot be ignored.

There have been several previous studies on poststroke sleep disorders and sex. Previous evidence suggests that there is no correlation between poor sleep and sex after stroke [11]. A study on stroke survivors revealed that sleep disorders, including EDS, are associated with sex and that sex is an important correlate of ESS scores in stroke patients [12]. Another study showed that male sex is an independent predictor of EDS [13]. However, few studies have explored sex differences in the clinical characteristics and influencing factors of poststroke EDS. We suggest that daytime sleepiness in stroke patients may differ between men and women. The purpose of this study was to explore and analyse the characteristics and risk factors for daytime sleepiness in stroke patients of different sexes to provide new insights in this field, which will help promote more targeted clinical interventions for stroke patients.

## Methods

### Study design

This was a retrospective study based on hospital medical records. The database was constructed by the Department of Neurology, Affiliated Hospital of Yangzhou University. Patients with a diagnosis of ischaemic stroke who attended the Affiliated Hospital of Yangzhou University and participated in polysomnography from 2022 to 2024 were identified. The diagnosis of ischaemic stroke was performed according to the International Classification of Diseases, 10th Edition (ICD-10: I60 ~ I64), and the diagnosis of various cerebrovascular diseases was performed according to the fourth Chinese Conference on Cerebrovascular Diseases [14], which is based on the patient's medical history, physical examination, and head magnetic resonance with diffusion-weighted imaging or head CT imaging results. The Department of Neurology of the Affiliated Hospital of Yangzhou University has 2 general wards and 1 neurological intensive care and neurological rehabilitation ward, with a total of 96 beds. It currently provides diagnosis and treatment services for stroke patients in Yangzhou city and the surrounding areas.

The study was approved by the Medical Ethics Committee of Yangzhou University Hospital (Ethics No. 2023-YKL09).

### Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Chinese male and female adults aged 18–90 years; (2) patients with a first stroke attack or patients with new-onset stroke and a previous history of stroke; and (3) patients with a National Institutes of Stroke Scale (NIHSS) score less than 15 points [15]. All the patients who were identified were assessed via the NIHSS and Barthel Index on the day of admission. The exclusion criteria were as follows: (1) patients with an NIHSS score of 15 or above or with disorders of consciousness; (2) patients who are currently taking or have taken antipsychotics (sedative-hypnotic, anxiolytic-depressant drugs, etc.) in the last three months; (3) patients with alcoholism and long-term caffeine intake; (4) patients with severe sleep disorders that existed before their stroke; (5) patients with dementia or severe cognitive disorders; and (6) patients with incomplete or missing information on some of the scales or

clinical data. The following patients were excluded from the study after the exclusion criteria were applied: 18 patients with severe stroke (NIHSS score ≥ 15), 5 patients with long-term use of psychotropic drugs, and 3 patients with data loss. We ultimately enrolled 281 patients from February 2022 to May 2024.

### Demographic and clinical data

Demographic information; height and weight data; smoking status; alcohol consumption; and concomitant medical history, such as a history of hypertension and diabetes, were collected from the electronic medical records of all patients. Laboratory biochemical parameters, including white blood cell counts, neutrophil counts, triglyceride levels, total cholesterol levels, creatinine levels, and glycosylated haemoglobin levels, were also collected.

### Questionnaire assessment and outcome measures

#### *ESS*

The participants completed the relevant questionnaires on the day they underwent polysomnography. The Epworth sleepiness scale (ESS) score was the primary outcome measure. This scale is used to assess daytime sleepiness and consists of 8 items to assess the tendency to fall asleep in different situations in daily life. A total score of less than or equal to 10 is considered normal, whereas a score higher than 10 indicates drowsiness; the higher the score is, the greater the degree of daytime sleepiness [16]. We used an ESS score > 10 to distinguish EDS patients from normal controls. The ESS is the most commonly used subjective method for assessing EDS after stroke [3].

#### *PSQI*

Patients' subjective self-assessment of sleep quality were collected through the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a 7-part self-assessment scale comprised of 18 questions. A total score greater than or equal to 5 was used to indicate poor sleep quality and a total score less than 5 was used to indicate good sleep quality [17].

#### *RBDSQ*

The sleep behaviour data of the patients were obtained through the REM Sleep Behaviour Disorder Screening Questionnaire (RBDSQ). The RBDSQ is a self-report scale containing 10 items, with a total possible score of 13 [18].

#### *HADS*

The degree of anxiety and depression was assessed by the Hospital Anxiety and Depression Scale (HADS), which is a 4-point scale based on the frequency of symptoms in the last January, with a score ranging from 0 to 3 for each item. The HADS contains two subscales, the HADS-A and the HADS-D, both of which have 7 items and a total score that ranges from 0 to 21, with higher scores indicating more severe anxiety or depressive symptoms and scores between 0 and 7 on either subscale indicating that the patient falls within the normal range [19].

### Polysomnography

Systematic screening for sleep disorders such as sleep apnoea, insomnia, and periodic limb movements is critical to stroke prognosis [20], leading us to routinely monitor polysomnography (PSG) in stroke patients who meet the criteria. PSG (SOMNOscreenPlusPSG+, medics GmbH, Germany) was performed within one week of the patient's admission to the hospital via a sleep monitor with sleep variables obtained from electroencephalography (F3-O2), electrooculography, and electromyography and sleep respiration variables obtained from nasal airflow, thermography, chest and abdominal belts, and finger pulse oximetry. We monitored both types of snoring with an electrocardiogram. Nocturnal sleep-related data, including the respiratory effort-related arousal index (RERAI), oxygen desaturation index (ODI), apnoea-hypopnea index (AHI), total sleep time (TST), sleep efficiency, wake-time after sleep onset (WASO), sleep onset latency, REM latency, N1/N2/N3/REM period percentage, minimum pulse oxygen saturation, arousal index (Arl), and periodic limb movements syndrome index (PLMS), were continuously collected from the subjects. Sleep parameters and the classification of sleep stages (N1/N2/N3/REM) were assessed by professional PSG technicians, and the assessment criteria and the calculation of the AHI, ODI and other indices were based on the standards of the American Academy of Sleep Medicine (AASM) [21].

### Statistical analysis

Our study was conducted and the data were analysed according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [22]. The statistical analyses were performed via the Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.). First, we conducted descriptive analyses between the male group and the female group. Data that met normality were assessed via chi-square tests and are expressed as the mean ± standard deviation. Comparisons between groups were made via the Student's t test. Data that did not conform to a normal distribution or could not be analysed via a chi-square test are expressed as medians (interquartile ranges) [M(Q1,Q3)], and comparisons between groups were made via a nonparametric test (Mann–Whitney test). The K-S test was used to analyse

**Table 1** Comparison of the population and baseline characteristics

| Characteristic | Males (*N* = 189) | Females (*N* = 92) | *P* value |
|---|---|---|---|
| Age (years) | 64.93 ± 11.97 | 67.03 ± 9.61 | 0.142 |
| BMI (kg/m$^2$) | 25.41 ± 3.25 | 25.45 ± 4.24 | 0.798 |
| Smoking status (%) | 67 (35.4) | 5 (5.4) | <0.001* |
| Drinking status (%) | 43 (22.8) | 6 (6.5) | <0.001* |
| Hypertension status (%) | 137 (72.3) | 61 (66.3) | 0.373 |
| Diabetes status (%) | 53 (28.0) | 29 (31.5) | 0.449 |
| Triglyceride level | 1.49 (0.98,2.19) | 1.22 (0.89,1.74) | 0.041* |
| Total cholesterol level | 4.07 ± 1.07 | 4.45 ± 1.09 | 0.011* |
| Creatinine level | 75.15 (62.23,86.58) | 54.80 (46.90, 65.80) | <0.001* |
| HbA1C level | 6.58 ± 1.65 | 6.71 ± 1.59 | 0.569 |
| Leukocyte count | 6.54 ± 1.97 | 6.42 ± 1.70 | 0.613 |
| Neutrophile granulocyte count | 4.14 (3.23, 5.32) | 4.33 (3.07, 5.28) | 0.911 |
| NIHSS score | 0.00 (0.00, 2.00) | 0.00 (0.00, 1.00) | 0.026* |
| Barthel index | 72.85 ± 22.98 | 79.10 ± 18.05 | 0.922 |

(*$P$ < 0.05; continuous variables in the table are expressed as x ± s or M (P25, P75); categorical variables are expressed as cases (%)). Abbreviations: *BMI*, *body mass index; NIHSS*, National Institutes of Stroke Scale

**Table 2** Comparison of the ESS, PSQI, RBD and HADS scores

| Characteristic | Males (*N* = 189) | Females (*N* = 92) | *P* value |
|---|---|---|---|
| ESS | 8.00 (3.00, 15.00) | 5.00 (2.00, 12.00) | 0.010* |
| PSQI | 8.00 (5.00, 12.00) | 10.00 (6.00, 14.00) | 0.011* |
| RBDSQ | 3.00 (1.00, 4.00) | 3.00 (1.00, 4.00) | 0.583 |
| HADS-A | 1.00 (0.00, 4.00) | 2.00 (1.00, 5.00) | 0.034* |
| HADS-D | 2.00 (0.00, 4.00) | 4.00 (1.00, 7.00) | 0.010* |

(*$P$ < 0.05; the data in the table are expressed as x ± s, or M (P25, P75)). Abbreviations: *ESS*, Epworth Sleepiness Scale; *PSQI*, Pittsburgh Sleep Quality Index; *RBD*, REM Sleep Behaviour Disorder Screening Questionnaire; *HADS*, Hospital Anxiety and Depression Scale

the normally distributed data. Count data are expressed as the number of cases (%). Comparisons between groups were performed via the χ2 test. An ESS = 10 was defined as the category boundary, and the ESS score was transformed from a continuous variable to a binary variable. The risk factors for daytime sleepiness were investigated via binary logistic regression, which explored the impact of multiple independent variables on the binary outcome. A p value less than 0.05 was considered to indicate statistical significance.

## Results

### Baseline characteristics

A total of 281 patients with ischaemic stroke were included in the study. There were 189 male patients, with a mean age of 64.93 ± 11.97 years, accounting for 67.3% of all the patients. There were 92 female patients, accounting for 32.7%, with a mean age of 67.03 ± 9.61 years. The baseline characteristics of the patients are shown in Table 1. The proportion of smokers and drinkers was significantly greater among males than among females ($p$ < 0.001). The triglyceride (1.49 (0.98, 2.19) vs. 1.22 (0.89, 1.74), $p$ = 0.041) and creatinine (75.15 (62.23, 86.58) vs. 54.80 (46.90, 65.80), $p$ < 0.001) levels and National Institutes of Health Stroke Scale (NIHSS) scores (0.00 (0.00, 2.00) vs. 0.00 (0.00, 1.00), $p$ = 0.026) were higher in male patients than in female patients; the total cholesterol level was higher in females than in males (4.07 ± 1.07 vs. 4.45 ± 1.09, $p$ = 0.011). No sex differences were found in the other indicators.

### Sleep, anxiety and depression scales

Table 2 shows the comparisons of the ESS, PSQI, RBD and HADS scores between males and females. The ESS score of male patients was significantly greater than that of female patients (8.00 (3.00, 15.00) vs. 5.00 (2.00, 12.00), $p$ = 0.010). Females had higher PSQI scores (8.00 (5.00, 12.00) vs. 10.00 (6.00, 14.00), $p$ = 0.011), HDS-A scores (1.00 (0.00, 4.00) vs. 2.00 (1.00, 5.00), $p$ = 0.034) and HADS-D scores (2.00 (0.00, 4.00) vs. 4.00 (1.00, 7.00), $p$ = 0.010).

### Polysomnography data

We compared the sleep structure and sleep apnoea-related polysomnography data in the EDS vs. no EDS groups of male vs. female patients according to sex (Table 3). Males had fewer N3 sleep periods (7.60 (2.35, 14.03) vs. 10.70 (3.90, 17.30), $p$ = 0.039), longer longest apnoea durations (53.50 (34.00, 91.25) vs. 40.00 (18.00, 80.00), $p$ = 0.002), and higher ArI (29.00 (20.85, 39.75) vs. 23.00 (16.30, 36.60), $p$ = 0.014) and RERAI (5.00 (2.50, 10.40) vs. 3.90 (1.80, 7.60), $p$ = 0.019) values. Females had a longer sleep latency (6.90 (2.98, 14.73) vs. 11.80 (4.50, 21.80), $p$ = 0.004).

### Risk factors for EDS in patients according to sex

Factors related to the ESS score were included as independent variables, and patients with ESS scores ≥ 10 were defined as having EDS when an ESS score = 10 was used as the boundary. Binary logistic regression analysis in Table 4 revealed that male sex and higher depression

**Table 3** Comparison of the polysomnographic data

| Parameter | Males (*N* = 189) | Females (*N* = 92) | *P* value |
|---|---|---|---|
| TST (min) | 374.34 ± 132.58 | 371.22 ± 132.00 | 0.854 |
| S-efficiency (%) | 74.21 ± 17.06 | 73.41 ± 15.50 | 0.705 |
| WASO (min) | 85.75 (44.73, 142.65) | 93.30 (41.50, 148.00) | 0.769 |
| N1 (%TST) | 6.25 (3.00, 13.33) | 5.60 (2.40, 13.30) | 0.324 |
| N2 (%TST) | 59.62 ± 15.33 | 55.67 ± 18.02 | 0.058 |
| N3 (%TST) | 7.60 (2.35, 14.03) | 10.70 (3.90, 17.30) | 0.039* |
| REM (%TST) | 18.30 (11.35, 26.13) | 19.50 (13.20, 27.80) | 0.364 |
| SOL (min) | 6.90 (2.98, 14.73) | 11.80 (4.50, 21.80) | 0.004* |
| REM latency (min) | 67.00 (25.25, 115.13) | 64.50 (23.25, 132.25) | 0.927 |
| AHI | 24.35 (13.95, 45.13) | 20.90 (18.00, 80.00) | 0.081 |
| ODI | 24.85 (11.38, 43.65) | 25.65 (8.78, 38.15) | 0.866 |
| Longest apnoea (sec) | 53.50 (34.00, 91.25) | 40.00 (18.00, 80.00) | 0.002* |
| Longest hypoventilation (sec) | 96.88 ± 24.27 | 95.82 ± 28.02 | 0.749 |
| Min-$SpO_2$ (%) | 93.60 ± 7.55 | 85.10 ± 6.79 | 0.806 |
| ArI | 29.00 (20.85, 39.75) | 23.00 (16.30, 36.60) | 0.014* |
| RERAI | 5.00 (2.50, 10.40) | 3.90 (1.80, 7.60) | 0.019* |
| PLMS index | 12.95 (3.23, 28.38) | 8.70 (2.60, 21.30) | 0.254 |

(*$P < 0.05$; the data in the table are expressed as x ± s, or M (P25, P75)). Abbreviations: *TST*, total sleep time; *WASO*, wake time after sleep onset; *REM*, rapid eye movement sleep; *SOL*, sleep onset latency; *AHI*, apnoea–hypopnea index; *ODI*, oxygen desaturation index; *Min-$SpO_2$*, minimum pulse oxygen saturation; *ArI*, arousal index; *RERAI*, respiratory effort-related arousal index; *PLMS*, periodic limb movement syndrome

**Table 4** Binary logistic regression analysis of the ESS score in stroke patients according to sex

| Variables | OR (95% confidence interval) | *P* value |
|---|---|---|
| **Overall model** | | |
| Sex (male) | 3.245 (1.084–9.712) | 0.035* |
| HADS-A | 1.199 (0.978–1.469) | 0.080 |
| HADS-D | 1.151 (1.002–1.321) | 0.046* |
| Barthel index | 1.012 (0.990–1.034) | 0.292 |
| AHI | 0.992 (0.944–1.042) | 0.737 |
| ODI | 1.024 (0.977–1.073) | 0.321 |
| SOL | 0.982 (0.956–1.008) | 0.164 |
| ArI | 1.012 (0.986–1.038) | 0.376 |
| **Male model** | | |
| HADS-A | 1.407 (1.021–1.940) | 0.037* |
| HADS-D | 1.065 (0.834–1.359) | 0.615 |
| Creatinine level | 1.001 (0.993–1.009) | 0.751 |
| Smoking status | 0.154 (0.040–0.592) | 0.006* |
| AHI | 0.964 (0.901–1.030) | 0.276 |
| ODI | 1.054 (0.990–1.122) | 0.099 |
| SOL | 0.944 (0.891–0.999) | 0.048 |
| **Female model** | | |
| HADS-A | 0.986 (0.760–1.280) | 0.915 |
| HADS-D | 1.686 (1.200-2.368) | 0.003* |
| N3% | 0.855 (0.765–0.956) | 0.006* |
| REM latency (min) | 0.991 (0.981-1.000) | 0.058 |
| ArI | 1.036 (1.004–1.069) | 0.027* |
| NIHSS | 0.567 (0.275–1.168) | 0.567 |

Abbreviations: *HADS*, Hospital Anxiety and Depression Scale; *AHI*, apnoea–hypopnea index; *ODI*, oxygen desaturation index; *SOL*, sleep onset latency; *ArI*, arousal index; *REM*, rapid eye movement sleep; *NIHSS*, National Institutes of Stroke Scale

scores were risk factors for EDS in all patients. In male patients, higher anxiety status was a risk factor for EDS, whereas smoking was a protective factor; in women, higher levels of depression, a greater arousal index, and a reduced proportion of N3 sleep periods were risk factors for EDS.

## Discussion

Poststroke drowsiness is a common complication that seriously affects the quality of life and functional rehabilitation of stroke patients. This study investigated sex differences in clinical and sleep characteristics and the risk factors for daytime sleepiness in patients with mild to moderate ischaemic stroke. In our retrospective database study, the main risk factors associated with incident EDS were male sex and depression symptoms. Stratified analysis according to sex revealed that anxiety symptoms were a risk factor for EDS in males, whereas smoking was a protective factor. Depression symptoms, the arousal index, and a reduced proportion of N3 sleep periods were risk factors for EDS in females.

Previous studies have investigated the influence of sex on blood lipid levels. A study of elderly Chinese patients with ischaemic stroke revealed that the levels of TC, TG and LDL-C in female patients were greater than those in male patients [23]. Our study revealed that the TC level in female stroke patients was greater than that in male stroke patients, whereas male stroke patients presented higher TG levels, which was not completely consistent with the findings of previous studies. This may be related to the influence of age and sex hormones as well as the differences in populations in different regions. At present,

there is no conclusive reason for the differences in blood lipid levels between different sexes; therefore, further research and sex-based stroke prevention are meaningful. Additionally, we found that blood creatinine values were greater in male patients than in female patients. Blood creatinine is a marker of renal impairment, and the lower the creatinine clearance is, the higher the blood creatinine concentration and the risk of atherosclerosis and cardiovascular disease [24]. A study in a middle-aged and elderly individuals revealed that men had higher creatinine levels than women did and were at greater risk for kidney damage and stroke development [25]. In addition, nicotine can increase the severity of kidney damage [26]. The higher prevalence of smoking among men may account for this difference.

A previous multivariate regression analysis of excessive daytime sleepiness revealed that male sex, depression, and poor sleep quality were risk factors for EDS [13]. In our study, males had higher ESS scores, which means more severe drowsiness, than females did and male sex was a risk factor for EDS, similar to previous results. Furthermore, males had a lower proportion of slow-wave sleep and more severe sleep breathing problems than females did. Women had worse subjective sleep quality and higher levels of anxiety and depression. Previous studies using the PSQI as a subjective sleep assessment tool confirmed that female sex is more significantly associated with self-rated sleep disturbances [27, 28]. Women are more likely to complain of sleep problems than men are, although objective PSG monitoring may not detect a large sex difference. The results of this study are consistent with previous findings. Females' perceptions of subjective sleep may differ from those of males, which suggests that there is a need to pay attention to the impact of sex on sleep assessments in clinical practice and that sleep disorders in male patients may be underestimated.

EDS has been associated with depression in several previous studies, which have shown that EDS is independently associated with depressive symptoms and that the relationship may be bidirectional, with depression being an important factor in the development of EDS and that EDS increases the risk of subsequent depression in patients [29]. In stroke patients, depression has likewise been proposed to be a factor in EDS, while the risk of depressive symptoms in stroke patients may increase after stroke [30]. In our study, higher depression scores were a risk factor for EDS in all patients. The same finding was also observed in female patients. This finding is similar to those of previous studies. From the perspective of social psychology, stroke patients are more prone to depression, pessimism, anxiety and other negative emotions due to disturbances in their psychological balance caused by their own neurological impairment, decreased self-care ability and social and family status gap compared with prior to the stroke. From a biological perspective, abnormal secretion of neurotransmitters such as serotonin and cytokines such as TNF-α after stroke can cause poststroke depression (PSD) [31]. Sleep deprivation, decreased productivity and sleep fragmentation due to depression can be precursors to EDS [32]. Owing to the effects of stress, social status, oestrogen, and serotonin, females are at greater risk of depression. A study has shown that women are more likely to suffer from poststroke depression than men are [33]. Although women are more prone to mental problems such as anxiety and depression than men are, we found that a higher anxiety score was a risk factor for EDS only in male patients. The specific reason is not clear, but the anxiety of male patients cannot be ignored. Clinical attention should be given to the mood changes of patients, and the prevention and treatment of stroke can be facilitated by timely identification and intervention for anxiety, depression and other psychosomatic problems, which can reduce sleep disorders. In addition to depression, decreased slow-wave sleep and an increased arousal index were risk factors for EDS in females. Sleep fragmentation and disturbances in sleep structure may be more likely to affect sleepiness in women.

However, we found that smoking was a protective factor for EDS in males. It is generally believed that sleep disorders are more common in smokers than in never smokers. The exciting effects of nicotine and smokers' cravings for smoking often lead to insomnia at night and daytime dysfunction, but one study reported that smokers who smoke more often have better sleep quality [34]. Another study reported that the sleep of former smokers who have quit smoking is more affected than that of never smokers and current smokers [35]. In this study, patients were defined as current smokers, which may have affected the study results. We further speculate that smoking cessation behaviour has a greater impact on insomnia and sleepiness than smoking amount does, which requires more comprehensive research.

Additionally, respiratory disorders during sleep (SDB) have been shown to be strongly associated with daytime sleepiness in the general population, and ESS scores increase with the severity of obstructive sleep apnoea hypopnea syndrome (OSHAS) [36]. This study revealed that males had more severe sleep breathing problems, such as longer sleep apnoea durations and higher respiratory effort-related arousal indices, than females did. However, when the AHI and other sleep breathing parameters were included in the correlation and regression analyses, no correlation was found between them and EDS. A study revealed no general correlation between SDB and EDS in patients with cardiovascular diseases such as atrial fibrillation who had comorbid

SDB [29, 37]; similar findings were reported in stroke patients, and a study involving stroke patients with OSA [38] revealed that stroke patients with comorbid OSA were less likely than the general population to suffer from EDS and that subjective somnolence was not significantly correlated with sleep apnoea in stroke patients compared with the general population. Owing to the lack of a significant association between subjective drowsiness and sleep disorders in stroke patients, the mechanism of sleepiness in stroke patients with SDB is more complex than that in the general population. There are more factors influencing the occurrence of sleepiness, such as a lack of exercise and the use of stroke medications such as statins and antiplatelet drugs. The decline in cognition in response to subjective sleepiness caused by stroke is also a possibility. The prediction of SDB in stroke patients on the basis of subjective sleepiness scores alone might not be highly efficient.

The limitation of our study is that we did not include the location of the stroke. Stroke in the thalamus may be more likely to cause EDS symptoms [39]. This results in a lack of control for these unobserved confounding variables in this study. Although the ESS is a more commonly used method for assessing sleepiness, it relies on the patient's subjective perception, and the multiple sleep latency test (MSLT) is a method to objectively evaluate the degree of drowsiness and is the gold standard for measuring EDS; however, owing to the limitations of the test site and the number of researchers, our study lacked relevant MSLT data, which may lead to bias in the assessment of EDS.

In addition, although some patients with NIHSS scores greater than 10 were included, most of the included patients had NIHSS scores of 2 or even lower. One study showed that NIHSS scale mainly focuses on the signs caused by anterior circulation infarction [40]. Another study revealed that an NIHSS score of 0 was more common in patients with postcirculation infarction than in patients with anterior circulation infarction [41]. A portion of postcirculation stroke patients in this study presented with dizziness and walking instability without typical stroke symptoms such as hemiplegia and aphasia, resulting in lower overall NHISS scores and reflecting the selection bias of our included population.

Finally, unstable factors such as nervous system deterioration or mental disorders may affect PSG examination results in the early stage of stroke, which cannot be excluded in this study because of objective conditions. Further unified management of the PSG examination time point is necessary.

## Conclusions

The results of this study suggest that male sex and depression are risk factors for EDS in all patients with mild to moderate ischaemic stroke. Depression symptoms, fragmented sleep, and reduced slow-wave sleep are risk factors for EDS in women. Anxiety symptoms aggravate EDS in men. An understanding of these predictors is necessary, especially when evaluating a patient's psychological state. The results of our study may provide evidence and guidance for clinical diagnosis and treatment. Interventional studies are needed to assess the impact of treating these risk factors in the future.

### Abbreviations

| | |
|---|---|
| EDS | Excessive daytime sleepiness |
| ESS | Epworth Sleepiness Scale |
| NIHSS | National Institutes of Health Stroke Scale |
| BMI | Body mass index |
| RBDSQ | REM Sleep Behaviour Disorder Screening Questionnaire |
| HADS | Hospital Anxiety and Depression Scale |
| PSQI | Pittsburgh Sleep Quality Index |
| TST | Total sleep time |
| WASO | Wake-time after sleep onset |
| SOL | Sleep onset latency |
| REM | Rapid eye movement sleep |
| AHI | Apnoea-hypopnea index |
| ODI | Oxygen desaturation index |
| Min-$SpO_2$ | Minimum pulse oxygen saturation |
| ArI | Arousal index |
| RERAI | Respiratory effort-related arousal index |
| PLMS | Periodic limb movement syndrome |

### Acknowledgements

We acknowledge the support and contribution of all the study participants and their relatives, and the nurses and staff of the clinical team of the Department of Neurology, Affiliated Hospital of Yangzhou University.

### Author contributions

Yi-Xi Zheng and Shu-Tong Sun collected the data, analyzed the data, and drafted the manuscript. Wen-Yi Yu, Li-Wen Xu and Ruo-Nan Liu collected the data.Cheng Chu designed the study and revised the manuscript.

### Funding

This research was funded by the Yangzhou Natural Science Foundation-Youth Fund Project (YZ2017111).

### Data availability

No datasets were generated or analysed during the current study.

## Declarations

### Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of Yangzhou University Hospital (Ethics No. 2023-YKL09). Informed consent was obtained from all the patients. All methods were performed in accordance with the relevant guidelines and regulations.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

Received: 28 March 2024 / Accepted: 2 October 2024
Published online: 14 October 2024

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