Outcomes of Wake-Up Stroke in the Mechanical Thrombectomy Era

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Abstract

A substantial portion of stroke patients wake up with stroke, and they are likely excluded from intravenous alteplase treatment due to unknown time of onset. Currently, mechanical thrombectomy (MT) is approved to treat selected patients with large vessel occlusion (LVO) within 24 hours. This may change outcomes in these patients.

Objective: The aim of the study was to evaluate the causes and outcomes in patients with non-wake-up stroke compared to wake-up stroke.

Methods: Patients with acute ischemic stroke during September, 2022 to March, 2023 were studied. All patients were investigated and treated according to the standard stroke protocol in the certified stroke unit. Causes and outcomes were compared in patients between non-wake-up and wake-up stroke.

Results: A total of 693 patients were included, with 138 patients (19.9%) presenting as wake-up stroke. The etiologies of stroke were nonsignificantly different between non-wake-up and wake-up stroke. MT was performed in 18% of patients in each group. Intravenous alteplase alone was given to 14.2% of patients with non-wake-up stroke, but none in the wake-up group. Favorable outcome at 3 months revealed a nonsignificant difference (non-wake-up: 54% vs wake-up:55%, p=0.83). A slightly higher death rate (6.8% vs 2.2%, p=0.037) and symptomatic intracerebral hemorrhage (5.4% vs 1.4%, p=0.188) were found in patients with non-wake-up compared to wake-up stroke.

Conclusion: In the MT era, the rate of favorable outcome in wake-up stroke patients did not significantly differ from that observed in non-wake-up stroke cases, despite none of the wake-up stroke patients being treated with intravenous alteplase alone.

Keywords: stroke, wake-up, thrombolysis, mechanical thrombectomy (J Thai Stroke Soc. 2025;24(2): 5-13)

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ผลการรักษาผู้ป่วยโรคหลอดเลือดสมองที่มีอาการขณะตื่นนอนในยุคที่มีการรักษาด้วยวิธีลากลิ่มเลือด

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บทคัดย่อ

ผู้ป่วยโรคหลอดเลือดสมองที่มีอาการผิดปกติทางระบบประสาทภายหลังตื่นนอนมีแนวโน้มที่จะไม่ได้รับการรักษาด้วยยาละลายลิ่มเลือดทางหลอดเลือดดำ เนื่องจากไม่ทราบเวลาที่เกิดอาการอย่างชัดเจน ปัจจุบันมีการรักษาผู้ป่วยโรคหลอดเลือดสมองอุดตันที่เข้าเกณฑ์ที่จะได้รับการรักษา และมีอาการภายใน 24 ชั่วโมงด้วยการลากลิ่มเลือด การรักษาดังกล่าวอาจเปลี่ยนผลการรักษาผู้ป่วยโรคหลอดเลือดสมองที่พบว่ามีอาการขณะตื่นนอน

วัตถุประสงค์การวิจัย: เพื่อศึกษาเปรียบเทียบสาเหตุและผลการรักษาผู้ป่วยโรคหลอดเลือดสมองในกลุ่มที่ไม่มีและมีอาการขณะตื่นนอน

วิธีวิจัย: ศึกษาในผู้ป่วยโรคหลอดเลือดสมองตีบตันที่มารับการรักษาในช่วงเดือนกันยายน พ.ศ. 2565 ถึงมีนาคม พ.ศ.2566 ผู้ป่วยทุกรายจะได้รับการตรวจเพิ่มเติมและรักษาตามมาตรฐานการรักษาที่หอผู้ป่วยโรคหลอดเลือดสมอง ข้อมูลสาเหตุและผลการรักษาผู้ป่วยโรคหลอดเลือดสมองในกลุ่มที่ไม่มีและมีอาการขณะตื่นนอนจะได้รับการวิเคราะห์เปรียบเทียบ

ผลการวิจัย: จากผู้ป่วยทั้งสิ้น 693 คน มีผู้ป่วย 138 คน (ร้อยละ 19.9) พบอาการโรคหลอดเลือดสมองขณะตื่นนอน สาเหตุของโรคหลอดเลือดสมองในกลุ่มที่ไม่มีและมีอาการขณะตื่นนอนไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ ผู้ป่วยร้อยละ18 ของแต่ละกลุ่มได้รับการรักษาด้วยการลากลิ่มเลือด ผู้ป่วยร้อยละ 14.2 ของกลุ่มที่ไม่มีอาการขณะตื่นนอนได้รับยาละลายลิ่มเลือดทางหลอดเลือดดำเพียงอย่างเดียว แต่ไม่มีผู้ป่วยในกลุ่มที่มีอาการขณะตื่นนอนได้รับยาละลายลิ่มเลือด ผลการฟื้นตัวดีที่ 3 เดือนของทั้ง 2 กลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ (ไม่มีอาการขณะตื่นนอน: ร้อยละ 54 เทียบกับ มีอาการขณะตื่นนอน: ร้อยละ 55, ค่า p=0.83) พบอัตราการเสียชีวิต(ร้อยละ 6.8 เทียบกับร้อยละ 2.2,ค่า p=0.037) และการเกิดเลือดออกในสมอง (ร้อยละ 5.4 เทียบกับร้อยละ 1.4,ค่า p=0.188) ที่ทำให้อาการแย่ลงในกลุ่มที่ไม่มีอาการขณะตื่นนอนสูงกว่า

บทสรุป: ในยุคที่มีการรักษาด้วยการลากลิ่มเลือด อัตราการฟื้นตัวดีในกลุ่มผู้ป่วยโรคหลอดเลือดสมองที่มีและไม่มีอาการขณะตื่นนอนไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ ทั้งที่ไม่มีผู้ป่วยที่มีอาการขณะตื่นนอนได้รับยาละลายลิ่มเลือดเลย

คำสำคัญ: โรคหลอดเลือดสมอง, ตื่นนอน, ยาละลายลิ่มเลือด, ลากลิ่มเลือด (J Thai Stroke Soc. 2025;24(2): 5–13)

Introduction

Wake-up stroke accounts for approximately 20% (14-24%) of all ischemic strokes.[1-3] A large proportion of wake-up strokes occur in the second part of the night, according to the interaction between circadian fluctuation and the sleep-wake cycle.[2] The circadian pattern of blood pressure, characterized by a mid-morning peak, and concurrent morning hypercoagulability may explain the increased risk of acute ischemic stroke in the morning.[4, 5] A study also reported that new atrial fibrillation was diagnosed 3-times more frequently in patients with wake-up stroke than in non-wake up stroke patients.[6]

Acute reperfusion therapy, especially intravenous thrombolysis, depends on time window from stroke onset to the treatment. Intravenous alteplase is recommended to treat eligible patients with acute ischemic stroke within 4.5 hours. The earlier the treatment begins, the higher the chance of having favorable outcome. However, a substantial portion of patients did not know the time of stroke onset, particularly in wake-up stroke, which represents around one-fifth of all ischemic strokes.[1-3] DWI (diffusion-weighted imaging) -FLAIR (fluid-attenuated inversion recovery) mismatch has been applied to identify patients with recent stroke onset who may be eligible for intravenous thrombolytic treatment, especially in those with wake-up stroke.[7] The EXTEND trial included patients who woke up with stroke within 9 hours from the midpoint of sleep, using computed tomography (CT) or magnetic resonance imaging (MRI) core/perfusion mismatch to choose patients for intravenous alteplase.[8] The American Stroke Association recommends to treat patients with intravenous alteplase in those who awaken with stroke within 4.5 hours of symptom recognition and have DWI-FLAIR mismatch by the MRI, with a class IIa recommendation.[9] While the European Stroke Organization, besides using DWI-FLAIR mismatch as a guide to select those who will benefit from intravenous alteplase, suggests that CT or MRI core/perfusion mismatch within 9 hours from the midpoint of sleep can be used to select eligible patients for whom mechanical thrombectomy is not indicated or not planned, to be treated with intravenous alteplase, with moderate quality of evidence and stroke recommendation.[3] In Thailand, due to limitation of resources, only a small portion of patients with wake-up stroke are treated with intravenous alteplase

After publication of the DAWN and DEFUSE3 trials, mechanical thrombectomy is recommended to treat selected patients with acute ischemic stroke from acute large vessel occlusion (LVO) within 6 to 16 hours of last known well.[9] This provides a significant improvement of the outcomes for eligible patients after mechanical thrombectomy (MT) (modified Rankin Scale (mRS) score 0-2; 45-49% (MT) versus 13-17% (medical treatment alone)).[10, 11] The timeframe covers most wake-up stroke cases. Our hypothesis was that after MT was introduced into clinical practice, the outcomes of patients with wake-up and non-wake-up stroke would not differ significantly. The purpose of the study was to evaluate the baseline characteristics, causes and the outcomes of patients with non-wake-up stroke compared to those with wake-up stroke.

Methods

Patients with acute ischemic stroke who were treated during September, 2022 to March, 2023 were studied. All patients were investigated and treated according to the standard stroke protocol in the certified stroke unit. Wake-up stroke was defined in patients who woke up with stroke

symptoms. All patients had non-contrast CT. Multiphase computed tomography angiography (CTA) brain was performed to evaluate the status of major arteries and assess collateralization in all patients with the last known well within 16 hours and a National Institute of Health Stroke Scale (NIHSS) score of at least 6 and a Field Assessment Stroke Triage for Emergency Destination (FAST-ED) scale score of at least 4. FAST-ED scale was developed to identify large vessel occlusion strokes; with a higher score, there is a higher likelihood of having large vessel occlusion.[12] The Alberta Stroke Program Early CT score (ASPECTS) was used to assess early ischemic changes in brain parenchyma supplied by the MCA territory, with a score of 0-10; the higher the score, the less early ischemic changes. For patients who had stroke onset between 6-24 hours and an NIHSS score of at least 6, computed tomography perfusion (CTP) was performed to evaluate the volume of infarct core and penumbra. They were eligible for mechanical thrombectomy if they had a small infarct core and a significant volume of penumbra per DAWN or DEFUSE3 inclusion criteria.[10, 11]

Data on baseline characteristics, stroke severity, causes of stroke, ASPECT score, treatment and stroke outcomes were collected. Causes of stroke were classified by TOAST (Trial of ORG 10172 in Acute Stroke Treatment); large-artery atherosclerosis (LAA), small-artery occlusion (SAO), stroke of other determined cause (OC), or stroke of undetermined cause (UND). Outcomes of interest were assessed by the Modified Rankin Scale (MRS) at 3 months after stroke onset. Favorable outcomes were defined as having MRS 0-1. Symptomatic intracerebral hemorrhage was defined according to ECASS study criteria; i.e. if there was intracerebral hemorrhage and there had subsequently been neurological deterioration with an increase in NIHSS score at least 4 from baseline. Baseline characteristics and the outcomes of the patients were compared between non-wake-up and wake-up stroke using chi-square test (for dichotomous data) and student t-test (for continuous variables). The research protocol was approved by the Human Ethic Committee of Thammasat University no. 1, Faculty of Medicine (Project No: MTU-EC-IM-0-014/66).

Results

There were 693 patients treated during the study period. One hundred and thirty-eight patients woke up with stroke symptoms, accounting for 19.9% of all ischemic strokes. **[Table 1]** represented baseline characteristics of the patients. The mean age was 65 years and the mean NIHSS score was 8.79. Small artery occlusion (43%) was the most common stroke subtype in the study. Patients with wake-up stroke had a slightly lower proportion of bedridden individuals and independence in their previous status, and less diabetes mellitus compared to those with non-wake-up stroke in our study. For other baseline characteristics and the causes of stroke, there was a nonsignificant difference between non-wake-up versus wake-up stroke; such as atrial fibrillation (20.6% vs 22.5%), LAA (26.1% vs 21%), CE (26.1% vs 22.5%).

Table 1. *Baseline characteristics in patients with non wake-up and wake-up stroke*

Baseline Characteristics	Non-wake-up stroke N=555	Wake-up stroke N=138	p-value
Mean age (years)	64.49	67.49	0.678
Male sex n (%)	307 (55.3%)	69 (50%)	0.262
Mean NIHSS*	8.89	8.37	0.539
NIHSS*			
- 0-5	267 (48%)	75 (54%)	
- ≥ 6	288 (52%)	63 (46%)	0.190
Previous Status n			
-Independent (mRS† 0-1)	488 (87.9%)	115 (83.3%)	
-Walk with instruments/dependent	49 (8.8%)	22 (15.9%)	0.016
- Bedridden	18 (3.2%)	1 (0.7%)	
Hypertension n (%)	320 (57.7%)	77 (55.8%)	0.809
Diabetes mellitus n (%)	212 (38.2%)	40 (29%)	0.044
Hyperlipidemia n (%)	262 (47.2%)	66 (47.8%)	0.896
Coronary artery disease n (%)	55 (9.9%)	15 (10.9%)	0.738
History of ischemic stroke n (%)	90 (16.2%)	22 (15.9%)	0.938
Old intracerebral hemorrhage	14 (2.5%)	2 (1.4%)	0.452
History of transient ischemic attack n (%)	7 (1.3%)	2 (1.4%)	0.863
Atrial fibrillation n (%)	114 (20.6%)	31 (22.5%)	0.788
Smoking n (%)	52 (9.4%)	16 (11.6%)	0.432
Valvular heart diseases n (%)	7 (1.3%)	1 (0.7%)	0.597
Alcohol drinking n (%)	42 (7.6%)	12 (8.7%)	0.658
Stroke Subtypes n (%)			
- LAA‡	145 (26.1%)	29 (21%)	
- SAO§	232 (41.8%)	68 (49.3%)	
- CE‖	145 (26.1%)	31 (22.5%)	
- UND¶	21 (3.8%)	4 (2.9%)	
- OC**	12 (2.2%)	6 (4.3%)	0.482
Mean ASPECTs†† scores	8.36	8.31	0.098

Location of large vessel occlusion n (%)			
– Internal carotid artery	50/180 (28%)	5/37 (14%)	
– M1 segment of MCA‡‡	70/180 (39%)	18/37 (49%)	
– M2 segment of MCA‡‡	21/180 (12%)	4/37 (11%)	
– M3 segment of MCA‡‡	1/180 (0.6%)	–	
– Basilar artery	11 (6%)	2/37 (5%)	
– Others: vertebral artery, anterior cerebral artery	2(1%)	1/37 (3%)	0.805

(*NIHSS = National Institute of Health Stroke Scale, †mRS = modified Rankin Scale, ‡Large-artery atherosclerosis (LAA), §small artery occlusion (SAO), ||Cardioembolism (CE), ¶Undetermined cause (UND), **Other defined cause (OC), †† ASPECT = Alberta Stroke Program Early CT Score, ‡‡MCA= middle cerebral artery)

For patients who came to the hospital within 24 hours from last known well (LKW), mean time from LKW-to-door was longer in wake-up stroke (339 minutes vs 721 minutes, p-value < 0.001). In patients with wake-up stroke, who had significant deficit and would have been eligible for intravenous thrombolysis except for the time window (80/138 patients), less than half of the patients (46.3%, 37/80 patients) came to the hospital within 4.5 hours after waking up.

CTA was performed in all patients with acute ischemic stroke who came within 16 hours of LKW and had NIHSS of at least 6 and FAST-ED score of at least 4; with a total number of CTAs of 180 in non-wake-up stroke and 37 in wake-up stroke cases. CTA revealed large vessel occlusion in 86% (155/180) and 81% (30/37) of patients with non-wake-up and wake-up stroke, respectively. Intravenous alteplase alone was given to 79 patients with non-wake-up stroke (14.2%), but none in the wake-up stroke group received intravenous alteplase alone. MT was performed in 17.8% (99/555) of non-wake-up stroke patients, of which 57 patients received a combination of intravenous alteplase and MT. Twenty-five patients (18.1%) with wake-up stroke had MT. Although there was a significant difference in the treatment between non-wake-up and wake-up groups, the proportion of favorable outcome (mRS 0-1) at 3 months was comparable (54.1% vs 55.1%, p-value= 0.83). **[Table 2, Figure 1]**

Figure 1. *Distribution of modified Rankin Scale scores at 3 months in non-wake-up and wake-up stroke*

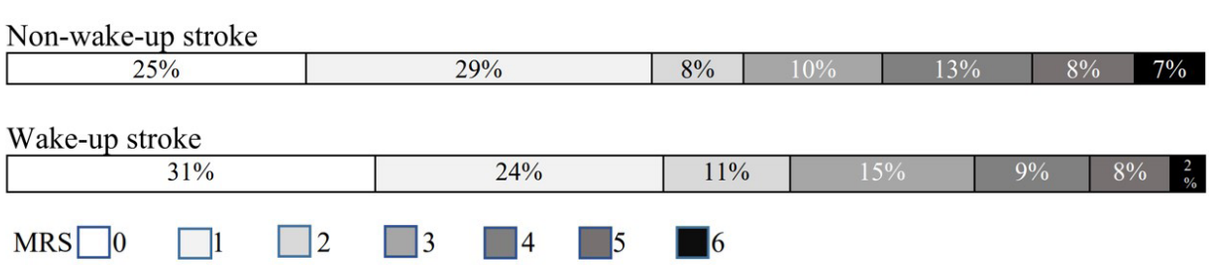

Table 2. *Outcomes of the patients with non-wake-up and wake-up stroke*

Outcomes	Non-wake-up stroke N=555	Wake-up stroke N=138	p-value
Favorable outcome at 3 months n (%)	300 (54.1%)	76 (55.1%)	0.83
Mean mRS at 3 months	2.1	1.79	0.017
Complication during admission n (%)	172 (31.1%)	31 (22.6%)	0.051
Death within 3 months n (%)	38 (6.8%)	3 (2.2%)	0.037
Hemorrhagic transformation n (%)			
- Asymptomatic	42 (7.5%)	8 (5.7%)	0.188
- Symptomatic	30 (5.4%)	2 (1.4%)	
Hemorrhagic transformation classification n(%)			
- Hemorrhagic infarct type1	14 (2.5%)	4 (2.8%)	
- Hemorrhagic infarct type2	24 (4.3%)	3 (2.2%)	
- Parenchymal hematoma type1	15 (2.7%)	1 (0.7%)	
- Parenchymal hematoma type2	18 (3.2%)	2 (1.4%)	0.51
Recurrent stroke in 3 months n (%)	20 (5%)	5 (4.2%)	0.738

The rate of symptomatic hemorrhagic transformation was higher in the non-wake-up stroke group (5.4% vs 1.4%, p-value=0.188). Death rate at 3 months was significantly higher in the non-wake-up stroke group (6.8% vs 2.2%, p-value=0.037).

Discussion

The prevalence of wake-up stroke in our study (20%) was comparable to previous studies. Early morning stroke risk is raised due to circadian change in several vascular risk factors.[2] The last sleep cycles contain more rapid eye movement (REM) sleep, which is a state of autonomic instability toward sympathetic influences and is characterized by a transient increase in muscular tone and bursts of sympathetic activity. This may explain the morning peak of vascular events.[2, 13] A prospective study in 356 patients with acute ischemic stroke, of which 82 (23%) were wake-up stroke, reported an association between newly diagnosed atrial fibrillation and wake-up stroke compared to non-wake-up stroke (OR 3.6, 95%CI 1.2-7.7, p-value=0.019).[6] However, a large population-based study in 1,854 ischemic stroke patients did not find a significant difference in vascular risk factors, including atrial fibrillation between non-wake-up stroke (1,581 patients) and wake-up stroke (273 patients).[1] A recently published meta-analysis, which included 29 studies (12,790 patients), examined the relationship between the incidence of atrial fibrillation, circadian fluctuation in blood pressure, and oxygen desaturation, and wake-up stroke. Only atrial fibrillation was identified as an independent risk factor (OR 1.28, 95%CI 1.06-1.55, p-value = 0.01).[14]

Our study showed less diabetes mellitus in wake-up stroke (38.2% vs 29%, p-value =0.044), but comparable atrial fibrillation (20.6% vs 22.5%, p-value =0.788). There was no significant difference between non-wake-up and wake-up stroke in stroke subtypes.

Time from the stroke onset to intravenous alteplase treatment is crucial in defining who may benefit from the treatment. However, in patients who wake up with a stroke, the onset of stroke symptoms cannot be identified. DWI-FLAIR mismatch by MRI or a small infarct core and a significant amount of penumbra per protocol by CTP are used to select patients with wake-up stroke to receive intravenous alteplase. [3, 9] However, in this study only 46% of patients came to hospital within 4.5 hours after waking up and would be deemed to benefit from having an imaging screen to see whether they were eligible for intravenous alteplase. Also, performing MRI in an emergency setting was not practical in many hospitals, and because the class of recommendation for intravenous alteplase in patients with wake-up stroke is Class II, intravenous alteplase has rarely been given to patients with wake-up stroke in Thailand. No patients with wake-up stroke received intravenous alteplase alone in our study.

On the other hand, since 2018, MT has been recommended for patients who have experienced acute ischemic stroke from LVO in the anterior circulation within 6 to 16 hours of their last known well and who also meet other eligibility requirements for DAWN or DEFUSE3 studies.[9] This indication was recommended in the Thai stroke guideline since 2019. CTA was done in 217 patients with stroke onset within 16 hours who had NIHSS of at least 6 and FAST-ED of at least 4, which was able to detect LVO in 86% in non-wake-up and 81% in wake-up stroke cases. MT was performed in 17.8% and 18.1% of patients with non-wake-up and wake-up stroke, respectively. Although there was a significant difference in the treatment between non-wake-up and wake-up groups, as none of the wake-up group received intravenous alteplase alone, the proportion of favorable outcome (mRS 0-1) at 3 months was comparable (54.1%vs 55.1%, p-value= 0.83). This might be explained by the almost equivalent rate of MT performed in both groups. The rate of symptomatic hemorrhagic transformation was higher in the non-wake-up stroke patients (5.4% vs 1.4%, p-value=0.188). The death rate within 3 months was significantly higher in the non-wake-up stroke group (6.8% vs 2.2%, p-value=0.037), which might be partly due to the factors of higher proportion in bedridden status prior to the current stroke, slightly higher stroke severity, and a higher proportion of LAA, CE in the non-wake-up stroke group.

Conclusion

About one-fifth of patients woke up with stroke. Despite the unknown time of stroke onset, this will not preclude the patients from MT. A comparable rate of favorable outcome was found in patients with wake-up as compared to non-wake-up stroke.

องค์ความรู้ใหม่

ผู้ป่วยโรคหลอดเลือดสมองที่พบว่ามีอาการขณะตื่นนอนมีจำนวนถึงร้อยละ 20 สาเหตุของการเกิดโรคหลอดเลือดสมองไม่แตกต่างกับผู้ป่วยในกลุ่มที่ไม่มีอาการขณะตื่นนอน ในการให้ยาละลายลิ่มเลือดทางหลอดเลือดดำในผู้ป่วยกลุ่มนี้จำเป็นต้องได้รับการคัดเลือกด้วยการตรวจภาพเอ็มอาร์หรือการตรวจ CT Perfusion ซึ่งจำนวนผู้ป่วยไทยเข้าถึงการตรวจดังกล่าวได้น้อย การศึกษานี้พบว่าถึงแม้ว่าผู้ป่วยมีอาการขณะตื่นนอนไม่ได้รับยาละลายลิ่มเลือดทางหลอดเลือดดำ แต่ถ้าเข้าเกณฑ์และได้รับการรักษาด้วยการลากลิ่มเลือดผู้ป่วยกลุ่มนี้ก็มีผลการรักษาฟื้นตัวดีไม่แตกต่างจากกลุ่มที่ไม่มีอาการขณะตื่นนอน

References

1. Mackey J, Kleindorfer D, Sucharew H, Moomaw CJ, Kissela BM, Alwell K, et al. Population-based study of wake-up strokes. Neurology. 2011;76(19):1662-7
2. Peter-Derex L, Derex L. Wake-up stroke: from pathophysiology to management. Sleep Med Rev. 2019;48:101212.
3. Berge E, Whiteley W, Audebert H, De Marchis GM, Forseca AC, Padiglioni C, et al. European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischemic stroke. Eur Stroke J. 2021;6(1):I-LXII.
4. Andreotti F, Davies GJ, Hackett DR, Khan MI, De Bart AC, Aber VR, et al. Major circadian fluctuations in fibrinolytic factors and possible relevance to time of onset of myocardial infarction, sudden cardiac death and stroke. Am J Cardiol. 1988;62(9):635-7.
5. Millar-Craig ME, Bishop CN, Raftery EB. Circadian variation of blood pressure. Lancet. 1978;1(8068):795-7.
6. Riccio PM, Klein FR, Pagani Cassara F, Munoz Giacomelli F, Gonzalez Toledo ME, Racosta JM, et al. Newly diagnosed atrial fibrillation linked to wake-up stroke and TIA: hypothetical implications. Neurology. 2013;80(20):1834-40.
7. Thomalla G, Cheng B, Ebinger M, Hao Q, Tourdias T, Wu O, et al. DWI-FLAIR mismatch for the identification of patients with acute ischemic stroke within 4.5 h of symptom onset (PRE-FLAIR): a multicenter observational study. Lancet Neurol. 2011;10(11):978-86.
8. Ma H, Campbell BCV, Parsons WM, Churilov L, Levi CR, Hsu C, et al. EXTEND Investigators. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. N Engl J Med. 2019;380(19):1795-803.
9. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke. Stroke. 2019;50(12):e344-e418.
10. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med. 2018;378(1):11-21.
11. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for stroke at 6 and 16 hours with selection by perfusion imaging. N Engl J Med. 2018;378(8):708-18.
12. Lima FO, Silva GS, Furie KL, Frankel MR, Lev MH, Camargo EC, et al. Field Assessment Stroke Triage for Emergency Destination, a simple and accurate prehospital scale to detect large vessel occlusion strokes. Stroke. 2016;47(8):1997-2002.
13. Cabiddu R, Ceruttin S, Viardot G, Werner S, Bianchi AM. Modulation of the sympatho-vagal balance during sleep: frequency domain study of heart rate variability and respiration. Front Physiol. 2012;3:45.
14. Zhou J, Xu J, Cheng A, Kadier Y, Liang X, Mutailipu M, et al. Meta-analysis of the association between atrial fibrillation, hypertension, sleep-disordered breathing, and wake-up stroke. Tex Heart Inst J. 2023;50(3):e217698.