Clinical significance of evaluation of collateral circulation in short-term prognosis of wake-up stroke patients

Haijing Sui[1,A,B,F], Chenggong Yan[2,B,C,F], Juan Yang[3,B,C,F], Xiaohui Zhao[3,A,D–F]

[1] Department of Radiology, Pudong New Area People's Hospital, Shanghai, China
[2] Department of Radiology, Shanghai Pudong New Area Hospital of Traditional Chinese Medicine, China
[3] Department of Neurology, Pudong New Area People's Hospital, Shanghai, China

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online) *Adv Clin Exp Med*. 2021;30(2):183–188

Address for correspondence
Xiaohui Zhao
E-mail: zxh191029@sina.com

Funding sources
Pudong New Area Health System Academic Leaders Training Program (No. PWRd2018-15); Pudong New Area Health System Academic Leader Training Program (grant No. PWRd2020-02); Science and Technology Development Fund of Shanghai (grant No. PW2018B-58); Key Specialty of Shanghai Pudong New Area (grant No. PWZy2020-01).

Conflict of interest
None declared

Received on February 19, 2020
Reviewed on February 27, 2020
Accepted on May 1, 2020

Published online on February 26, 2021

Abstract

Background. In recent years, the clinical significance of collateral circulation in vascular embolism has been gradually found.

Objectives. To investigate the relationship between collateral circulation and short-term prognosis of wake-up stroke patients.

Materials and methods. The present observational study enrolled 269 cases of wake-up ischemic stroke patients. All patients presented with mismatched low perfusion volume/main infraction volume and received thrombolytic therapy after admission. The hemorrhagic transformation rate was recorded. The American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grading was used for evaluation of collateral circulation. The stroke condition was determined using the National Institutes of Health Stroke Scale (NIHSS). The Barthel Index (BI) score was used for measurement of quality of life. The Modified Rankin Scale (mRS) was used for measurement of prognosis.

Results. The hypertension, diabetes and current smoker rates were significantly higher. The baseline NHISS scores and NIHSS scores after 24 h were remarkably lower. The NIHSS scores were markedly lower in ASITN/SIR grade 2–3 patients compared with ASITN/SIR grade 0–1 patients at 1 week, 2 weeks, 4 weeks, and 3 months after treatment. Patients with ASITN/SIR grade 2–3 had lower mRS score and higher BI scores. The ASITN/SIR grade was an independent risk factor for bad prognosis of wake-up ischemic stroke patients in 3 months.

Conclusions. Collateral circulation condition may be associated with short-term prognosis of wake-up stroke patients. Patients with worse collateral circulation may present higher risk for bad short-term prognosis.

Key words: outcomes, coronary collateral circulation, NHISS, wake-up stroke

Cite as
Sui H, Yan C, Yang J, Zhao X. Clinical significance of evaluation of collateral circulation in short-term prognosis of wake-up stroke patients. *Adv Clin Exp Med*. 2021;30(2):183–188. doi:10.17219/acem/121927

DOI
10.17219/acem/121927

Background

Despite the development of treatment methods and molecular mechanisms, the incidence of stroke is still high, with almost 7 million of ischemic stroke patients and 3 million of hemorrhagic stroke patients worldwide in 2013 among 20–64 years-old adults.[1–3] It is also reported that about 1.5~2.0 million of new stroke cases are diagnosed every year in China.[4,5] Among the stroke patients, about 20–25% ischemic stroke patients are healthy before sleep and wake up with neurological deficits.[6–8] Since the accurate time of stroke onset is difficult to determine for wake-up stroke patients, the application of thrombolysis treatment for these patients is still controversial.[9,10]

In recent years, the clinical significance of collateral circulation in vascular embolism has been gradually noticed.[11] It is thought that collateral circulation is associated with intravenous thrombolysis,[12] coronary chronic total occlusion[13] and also ischemic stroke.[14] However, up to now, few studies focused on role of collateral circulation in wake-up stroke.

Objectives

In the present study, we demonstrated for the first time that collateral circulation was associated with short-term prognosis of wake-up stroke patients. The worse collateral circulation predicted higher risk for bad short-term prognosis. This research might provide more clinical evidence for collateral circulation in wake-up stroke patients.

Materials and methods

Subjects

The present observational study enrolled 269 cases of wake-up ischemic stroke patients who reported to our hospital from January 2017 to June 2019. All patients were healthy before sleep and were found to show typical stroke symptoms after waking up, including a side face, arm or leg numbness or sudden onset of deviation, hemiplegia, confusion, difficulty in speaking or understanding, difficulty in single or binocular vision, difficulty in walking, dizziness, and loss of balance or coordination. The diagnosis of ischemic stroke was confirmed with computed tomography (CT) or magnetic resonance imaging (MRI) methods according to the guidelines of Chinese Medical Association.[15] All patients were consecutively enrolled. The following patients were excluded: patients with hemorrhagic stroke, patients who received anticoagulation therapy within 1 month before the study, patients who received intracranial or spinal surgeries within 3 months before the study, patients who had stroke or brain trauma within 3 months before the study, and patients with severe dysfunction of liver, kidney or heart. Written informed consent was obtained from all study participants. The present study was approved by the Ethic Committee of Shanghai Pudong New Area Hospital of Traditional Chinese Medicine, China.

Thrombolytic therapy

All patients included in this research received thrombolytic therapy after admission. The computed tomography perfusion (CTP) was conducted using a Dual Source Imaging System (Siemens, Munich, Germany). The multimode MRI was performed using a General Electric Corporation 3.0T Magnetic Resonance Instrument (Signa Excite HD; General Electric Medical Systems, Chicago, USA). The image reconstruction was then conducted using MIStar® software (Apollo Medical Imaging Technology Ltd., Melbourne, Australia). The peak time picture of cerebral blood flow (T_{max}) was obtained and the area with $T_{max} > 6$ s was defined as low perfusion volume.[16] The diffusion-weighted imaging (DWI) high-signal volume or a volume of lesion side which reduced more than 30% of the normal side on the cerebral blood flow (CBF) picture was regarded as the main infraction volume. The thrombolytic therapy was only conducted for patients with low perfusion volume/main infraction volume ≥120% and ≥10 mL.[17–19]

The thrombolytic therapy was conducted using the recombinant tissue plasminogen activator (rt-PA) with a dose of 0.9 mg/kg. The first 10% of the drug was intravenously injected at once, and the rest of the dose was injected using a venous micropump within 60 min. The hemorrhagic transformation was evaluated using CT or MRI after 24 h of treatment.

Evaluation of collateral circulation

For evaluation of collateral circulation, the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grading was used after digital subtraction angiography (DSA).[20] The ASITN/SIR grade 0–1 was defined as bad collateral circulation compensatory, ASITN/SIR grade 2 was defined as moderate compensatory and ASITN/SIR grade 3–4 was considered as good compensatory.

The study population was then divided into 2 groups: ASITN/SIR grade 0–1 patients and ASITN/SIR grade 2–3 patients.

Data measurement

Demographic data such as age and gender, and clinical information including complications and medication condition were also recorded. The stroke condition was determined using the National Institutes of Health Stroke Scale (NIHSS). The Barthel Index (BI) score was used for measurement of quality of life after 3 months of treatment. The Modified Rankin Scale (mRS) was used for

measurement of prognosis after 3 months of treatment. The mRS score ≤2 was defined as good prognosis while mRS score >2 was a bad prognosis. The NIHSS scores were measured before treatment, 24 h after treatment, and 1 week, 2 weeks, 4 weeks and 3 months after treatment. The follow-up lasted for 3 months.

Statistical analysis

Continuous data was expressed using mean ± standard deviation (SD). The χ^2 test was used to compare the counting materials and rates. Comparison between the 2 groups was performed using the Student t-test. The Kaplan–Meier (K–M) curve was used to determine the relationship between NHISS scores and three-month mortality. Logical regression was used to analyze risk factors for three-month prognosis using a binary logistic regression model with step-back method. A value of $p < 0.05$ was considered statistically significant. All calculations were made using SPSS v. 22.0 (IBM Corp., Armonk, USA).

Results

Basic characteristics for all patients

The basic characteristics of all patients were shown in Table 1. Among the 269 patients, 142 cases had the ASITN/SIR grade 0–1 and 127 cases had the ASITN/SIR grade 2–3. The hypertension, diabetes and current smoker rates were found significantly higher in ASITN/SIR grade 0–1 patients ($p < 0.05$). Besides, the baseline NHISS scores were remarkably lower in ASITN/SIR grade 2–3 patients ($p < 0.05$). Moreover, NIHSS scores after 24 h were also lower in ASITN/SIR grade 2–3 patients ($p < 0.05$). No significant differences were found in other indices.

Dynamic changes of NIHSS scores and its relationship with ASITN/SIR grading

To further investigate the relationship between ASITN/SIR grading and clinical outcomes of wake-up stroke, NIHSS scores were evaluated before treatment, 24 h after treatment, and 1 week, 2 weeks, 4 weeks and 3 months after treatment. As shown in Fig. 1, at all timepoints, the NIHSS scores were remarkably lower in ASITN/SIR grade 2–3 patients compared with ASITN/SIR grade 0–1 patients ($p < 0.05$), indicating that the ASITN/SIR grade at admission might be associated with the treatment outcomes.

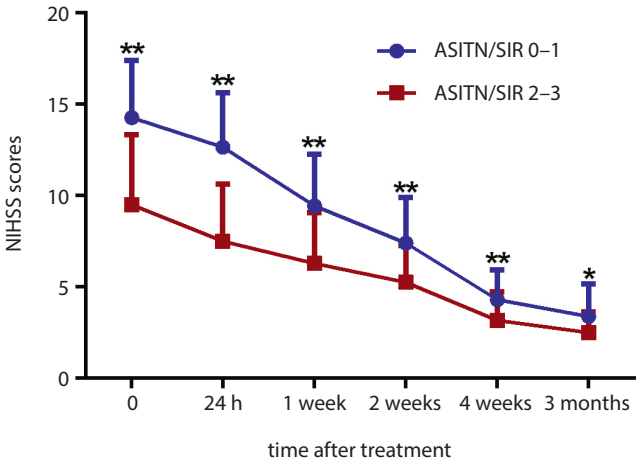

Fig. 1. Dynamic changes of NIHSS and their relationship with ASITN/SIR grading

Table 1. Basic characteristics for all patients

Variables	All patients (n = 269)	ASITN/SIR 0–1 (n = 142)	ASITN/SIR 2–3 (n = 127)	p-value*
Age [years]	56.64 ±10.09	56.44 ±10.07	56.85 ±10.15	0.742
Gender (male:female)	153 (56.9): 116 (43.1)	78 (54.9): 64 (45.1)	75 (59.1): 52 (40.9)	0.668
Complications, n (%)				
Hypertension	126 (46.8)	78 (54.9)	48 (37.8)	0.023
Diabetes	74 (27.5)	49 (34.5)	25 (19.7)	0.026
Current smoker	139 (51.7)	85 (59.9)	54 (42.5)	0.016
Atrial fibrillation	21 (7.8)	11 (7.7)	10 (7.9)	0.602
Stroke family history	54 (20.1)	29 (20.4)	25 (19.7)	0.570
TOAST type, n (%) cardiogenic embolism large-artery atherosclerosis small-artery occlusion others	 81 (30.1) 76 (28.3) 79 (29.4) 33 (12.3)	 45 (31.7) 37 (26.1) 33 (23.2) 20 (14.1)	 36 (28.3) 39 (30.7) 36 (28.3) 13 (10.2)	0.644
Baseline NIHSS	12.02 ±4.20	14.28 ±3.12	9.50 ±3.82	<0.001
NIHSS after 24 h	10.22 ±4.00	12.66 ±2.98	7.50 ±3.15	<0.001
Hemorrhagic transformation, n (%)	71 (26.4)	39 (27.5)	32 (25.2)	0.749

* ASITN/SIR 0–1 compared with ASITN/SIR 2–3. The χ^2 test was used to compare the counting materials and rates. Comparison between the 2 groups was performed using the Student's t-test. ASITN/SIR – the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; NIHSS – the National Institutes of Health Stroke Scale; N/A – not applicable.

Prediction value of ASITN/SIR grading for three-month prognosis of wake-up ischemic stroke patients

Finally, we analyzed the relationship between ASITN/SIR grading and three-month prognosis of wake-up ischemic stroke patients. Both mRS and BI scores were measured 3 months after treatment. Results showed that patients with ASITN/SIR grade 2–3 had lower mRS score and higher BI scores than patients with ASITN/SIR grade 0–1 (Table 2). However, the three-month mortality rate did not show significant difference. Then, we defined mRS score >2 as bad prognosis and analyzed risk factors for three-month prognosis. Results showed that the ASITN/SIR grade was the independent risk factor for bad prognosis of wake-up ischemic stroke patients in 3 months (Table 3). The K–M curve showed patients with ASITN/SIR grade 2–3 might have longer survival in 3 months; however, the difference was not statistically significant (Fig. 2, p = 0.116).

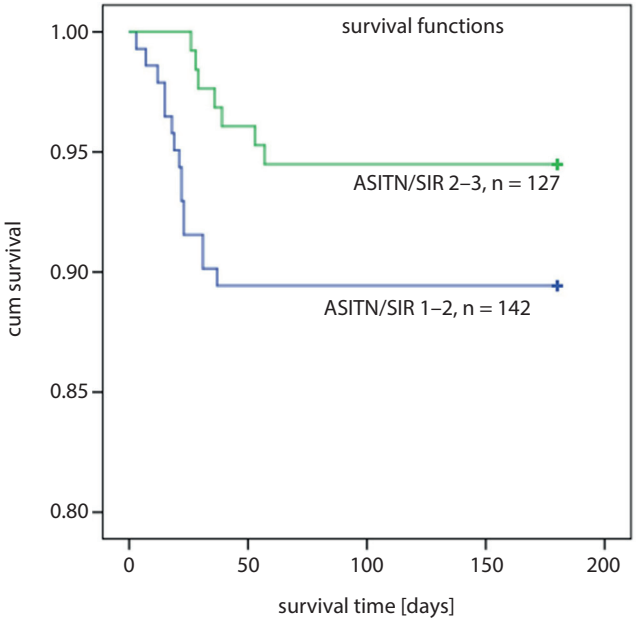

Fig. 2. Kaplan–Meier curve for three-month mortality

Discussion

Despite numerous studies on ischemic stroke, the wake-up stroke is still a clinical problem, especially due to the difficulty to determine the accurate time of onset. In recent years, the importance of collateral circulation has been noticed in embolism diseases. In a clinical trial, it was found that the coronary collateral circulation could be increased by intensive exercise for coronary artery disease patients.[21] In patients with celiac artery compression syndrome, the authors also found that different types of collateral circulation were also observed in patients with celiac artery compression syndrome.[22] However, up to now, no research reported the relationship between collateral circulation and wake-up stroke. In the present research, we demonstrated that collateral circulation condition was associated with short-term clinical outcomes of wake-up stroke patients after thrombolytic therapy. Better collateral circulation condition predicted better clinical outcomes, and collateral circulation was also an independent risk factor for bad short-term prognosis of wake-up stroke patients.

The treatment of wake-up stroke is still a clinical challenge and the application of thrombolytic therapy shows different outcomes in different studies. Kurz et al. considered that stroke onset occurred close to wake-up and not during earlier sleep phases in the wake-up stroke patients, and thus the proper use of MRI could select patients who would benefit from thrombolysis.[23] Another clinical research also demonstrated that the wake-up stroke and normal stroke within therapeutic window had similar clinical severity, imaging characteristics and clinical outcome.[24] Odland et al. also stated that current diffusion-weighted imaging-fluid-attenuated inversion recovery (DWI-FLAIR) mismatch concept might exclude lager amount of wake-up stroke patients who might benefit from thrombolysis.[25] In our research, we also used thrombolytic therapy only in patients with mismatched low perfusion volume and main infraction volume. Results showed the application of thrombolytic therapy could achieve good clinical outcomes. Meanwhile, the treatment outcomes were associated with collateral circulation.

Table 2. The mRS and BI scores after 3 months of treatment

Variables	ASITN/SIR 0–1 (n = 142)	ASITN/SIR 2–3 (n = 127)	p-value*
mRS	2.19 ±1.41	1.49 ±1.14	<0.001
BI	71.81 ±7.61	79.41 ±8.67	<0.001
Mortality, n (%)	15 (10.6)	7 (5.5)	0.216

mRS – Modified Rankin Scale; BI – Barthel Index; ASITN/SIR – the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology.

Table 3. Relationship between ASITN/SIR grade and mRS score >2 as bad prognosis

Variable	Wald	OR	95% CI	p-value
ASITN/SIR grade 0–1	15.750	0.313	0.731 (0.627~0.853)	<0.001

OR – odds ratio; 95% CI – 95% confidence interval; ASITN/SIR – the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology; mRS – Modified Rankin Scale.

Studies on collateral circulation in stroke have also been reported. It was considered that the premature rarefaction of the collateral circulation might be associated with ischemic tissue injury, and cardiovascular risk factors might enhance the risk.[26] In a review, Iwasawa et al. demonstrated the development of collateral circulation in ischemic stroke and pointed that good collateral circulation was associated with better neurological outcomes and smaller infarct volume in stroke patients.[27] Seyman et al. demonstrated in a clinical research that collateral circulation determined cortical infarct volume in anterior circulation ischemic stroke.[28] A meta-analysis also showed that good collateral circulation predicted favorable outcomes in intravenous thrombolysis in stroke patients.[12] In this study, we demonstrated for the first time that better collateral circulation condition was associated with better clinical outcomes of wake-up stroke patients.

Limitations

The present study has also some limitations. Firstly, the study only included a small sample size. Secondly, we mainly showed the relationship between ASITN/SIR grading, NIHSS score and prognosis. The relationship between ASITN/SIR grading and other laboratory indices requires further studies to confirm.

Conclusions

We conducted a prospective observational study and found that collateral circulation condition was associated with short-term prognosis of wake-up stroke patients. Patients with worse collateral circulation might present a higher risk for bad short-term prognosis. This study might give more clinical evidence for the use of collateral circulation measurement in prediction of prognosis of stroke patients.

ORCID iDs

Haijing Sui https://orcid.org/0000-0002-5594-2201
Chenggong Yan https://orcid.org/0000-0002-1792-7625
Juan Yang https://orcid.org/0000-0002-6269-8534
Xiaohui Zhao https://orcid.org/0000-0001-5378-0934

References

1. Wen LT, Abdin E, Vaingankar JA, et al. Prevalence of stroke, risk factors, disability and care needs in older adults in Singapore: Results from the WiSE study. *BMJ Open*. 2018;8(3):e020285. doi:10.1136/bmjopen-2017-020285
2. Rofes L, Muriana D, Palomeras E, et al. Prevalence, risk factors and complications of oropharyngeal dysphagia in stroke patients: A cohort study. *Neurogastroenterol Motil*. 2018;30(8):e13338. doi:10.1111/nmo.13338
3. Krishnamurthi RV, Moran AE, Feigin VL, et al. Stroke prevalence, mortality and disability-adjusted life years in adults aged 20–64 years in 1990–2013: Data from the global burden of disease 2013 study. *Neuroepidemiology*. 2015;45(3):190–202. doi:10.1159/000441098
4. Wang W, Jiang B, Sun H, et al. Prevalence, incidence and mortality of stroke in China: Results from a nationwide population-based survey of 480,687 adults. *Circulation*. 2017;135(8):759. doi:10.1161/CIRCULATIONAHA.116.025250
5. Gelin X, Minmin M, Xinfeng L, Hankey GJ. Is there a stroke belt in China and why? *Stroke*. 2013;44(7):1775–1783. doi:10.1161/STROKEAHA.113.001238
6. Thomalla G, Gerloff G. Treatment concepts for wake-up stroke and stroke with unknown time of symptom onset. *Stroke*. 2015;46(9):2707–2713. doi:10.1161/STROKEAHA.115.009701
7. Silva GS, Lima FO, Camargo ECS, et al. Wake-up stroke: Clinical and neuroimaging characteristics. *Cerebrovasc Dis*. 2010;29(4):336–342. doi:10.1159/000278929
8. Peter-Derex L, Derex L. Wake-up stroke: From pathophysiology to management. *Sleep Med Rev*. 2019;48:101212. doi:10.1016/j.smrv.2019.101212
9. Dankbaar JW, Bienfait HP, Van Den Berg C, et al. Wake-up stroke versus stroke with known onset time: Clinical and multimodality CT imaging characteristics. *Cerebrovasc Dis*. 2018;45(5–6):236–244. doi:10.1159/000489566
10. Bücke P, Pérez MA, Hellstern V, AlMatter M, Bäzner H, Henkes H. Endovascular thrombectomy in wake-up stroke and stroke with unknown symptom onset. *Am J Neuroradiol*. 2018;39(3):494–499. doi:10.3174/ajnr.A5540
11. Moutinho M, Silvestre L, Silva E, Pedro LM. Coarctation of the aorta and the nature of collateral circulation. *J Vasc Surg Cases Innov Tech*. 2018;4(4):339–340. doi:10.1016/j.jvscit.2018.08.006
12. Leng X, Lan L, Liu L, Leung TW, Wong KS. Good collateral circulation predicts favorable outcomes in intravenous thrombolysis: A systematic review and meta-analysis. *Eur J Neurol*. 2016;23(12):1738–1749. doi:10.1111/ene.13111
13. Ying S, Feng HD, Yang D, et al. Reduced coronary collateralization in type 2 diabetic patients with chronic total occlusion. *Cardiovasc Diabetol*. 2018;17(1):26. doi:10.1186/s12933-018-0671-6
14. Iwasawa E, Ichijo M, Ishibashi S, Yokota T. Acute development of collateral circulation and therapeutic prospects in ischemic stroke. *Neural Regen Res*. 2016;11(3):368–371. doi:10.4103/1673-5374.179033
15. W. L. The fourth cerebrovascular diseases academic meeting of the Chinese Medical Association: Diagnostic points of various cerebrovascular diseases. *Chinese J Neurol*. 1996;29:379–380.
16. Lou M, Chen Z, Wan J, et al. Susceptibility-diffusion mismatch predicts thrombolytic outcomes: A retrospective cohort study. *AJNR*. 2015;35(11):2061–2067. doi:10.3174/ajnr.A4017
17. Yue-Han L, Min L, Ren-Yang Z, Yu-Qing Y, Zhi-Cai Z, Mei-Ping D. Multimode MRI-based intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) reduces hemorrhagic transformation in ischemic stroke patients [in Chinese]. *Zhejiang Da Xue Xue Bao Yi Xue Ban*. 2012;41(6):665–671.
18. Shih LC, Saver JL, Alger JR, et al. Perfusion-weighted magnetic resonance imaging thresholds identifying core, irreversibly infarcted tissue. *Stroke*. 2003;34(6):1425–1430. doi:10.1161/01.STR.0000072998.70087.E9
19. Carrera E, Simon Jones P, Iglesias S, et al. The vascular mean transit time: A surrogate for the penumbra flow threshold? *J Cereb Blood Flow Metab*. 2011;31(4):1027–1035. doi:10.1038/jcbfm.2010.197
20. Wufuer A, Mijiti P, Abudusalamu R, et al. Blood pressure and collateral circulation in acute ischemic stroke. *Herz*. 2019;44(5):455–459. doi:10.1007/s00059-018-4691-5
21. Möbiuswinkler S, Uhlemann M, Adams V, et al. Coronary collateral growth induced by physical exercise: Results of the impact of intensive exercise training on coronary collateral circulation in Patients With Stable Coronary Artery Disease (EXCITE) Trial. *Circulation*. 2016;133(15):1438–1448; discussion 1448. doi:10.1161/CIRCULATIONAHA.115.016442
22. van Petersen AS, Kolkman JJ, Gerrits DG, Van dPJ, Zeebregts CJ, Geelkerken RH. Clinical significance of mesenteric arterial collateral circulation in patients with celiac artery compression syndrome. *J Vasc Surg*. 2017;65(5):1366–1374. doi:10.1016/j.jvs.2016.11.052
23. Kurz MW, Advani R, Behzadi GN, Eldøen G, Farbu E, Kurz KD. Wake-up stroke: Amendable for thrombolysis-like stroke with known onset time? *Acta Neurol Scand*. 2017;136(1):4–10. doi:10.1111/ane.12686

24. Costa R, Pinho J, Alves JN, Amorim JM, Ribeiro M, Ferreira C. Wake-up stroke and stroke within the therapeutic window for thrombolysis have similar clinical severity, imaging characteristics and outcome. *J Stroke Cerebrovasc Dis*. 2016;25(3):511–514. doi:10.1016/j.jstrokecerebrovasdis.2015.10.032
25. Odland A, Særvoll P, Advani R, Kurz MW, Kurz KD. Are the current MRI criteria using the DWI-FLAIR mismatch concept for selection of patients with wake-up stroke to thrombolysis excluding too many patients? *Scand J Trauma Resusc Emerg Med*. 2015;23(1):22. doi:10.1186/s13049-015-0101-7
26. Moore SM, Zhang H, Maeda N, Doerschuk CM, Faber JE. Cardiovascular risk factors cause premature rarefaction of the collateral circulation and greater ischemic tissue injury. *Angiogenesis*. 2015;18(3):265–281. doi:10.1007/s10456-015-9465-6
27. Iwasawa E, Ichijo M, Ishibashi S, Yokota T. Acute development of collateral circulation and therapeutic prospects in ischemic stroke. *Neural Regen Res*. 2016;11(3):368–371. doi:10.4103/1673-5374.179033
28. Seyman E, Shaim H, Shenhar-Tsarfaty S, Jonash-Kimchi T, Bornstein NM, Hallevi H. The collateral circulation determines cortical infarct volume in anterior circulation ischemic stroke. *BMC Neurol*. 2016;16(1):206. doi:10.1186/s12883-016-0722-0