

Original Paper

International Survey on the Management of Wake-Up Stroke

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Key Words

Wake-up stroke · Brain imaging · Intravenous thrombolysis · Mechanical thrombectomy · Intra-arterial thrombolysis · Endovascular treatment

Abstract

Background: Patients who wake up having experienced a stroke while asleep represent around 20% of acute stroke admissions. According to international guidelines for the management of acute stroke, patients presenting with wake-up stroke are not currently eligible to receive revascularization treatments. In this study, we aimed to assess the opinions of stroke experts about the management of patients with wake-up stroke by using an international multicenter electronic survey. **Method:** This study consisted of 8 questions on wake-up stroke treatment. **Results:** Two hundred invitations to participate in the survey were sent by e-mail. Fifty-nine participants started the survey, 4 dropped out before completing it, and 55 completed the full questionnaire. We had 55 participants from 22 countries. **Conclusions:** In this study, most stroke experts recommended a recanalization treatment for wake-up stroke. However, there was considerable disagreement among experts regarding the best brain imaging method and the best recanalization treatment. The results of ongoing randomized trials on wake-up stroke are urgently needed.

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Introduction

Stroke is one of the primary causes of neurologic disability and death worldwide. Intravenous thrombolysis using a recombinant tissue plasminogen activator (rTPA) and, more recently, endovascular mechanical thrombectomy has been shown to improve the clinical

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Table 1. List of countries and rate of participants per country

Country (n = 22)	Participants per country, % (total = 55)
FR	14.75
US	13.11
BR	13.11
IT	8.20
DE	6.56
CA	6.56
IN	6.56
ES	4.92
AU	3.28
CH	3.28
PY	1.64
JO	1.64
IL	1.64
AT	1.64
NO	1.64
JP	1.64
NZ	1.64
GB	1.64
CL	1.64
SE	1.64
FI	1.64
DK	1.64
Total	100.00

outcomes of patients presenting acute ischemic stroke when it is used within the first 4.5–6 h after the onset of the symptoms [1, 2]. However, stroke trials did not include patients with either non-witnessed strokes or wake-up strokes.

Patients presenting stroke with symptoms that began at an unknown time represent around 30% of patients with acute stroke, while around 20% of stroke admissions are for wake-up stroke [3–5]. Although acute reperfusion treatment has not yet been proven effective and safe for wake-up stroke, a large proportion of these patients share similarities with patients admitted within 3–6 h of stroke onset when judged by baseline clinical and brain imaging data [3–5]. Some patients with wake-up stroke may thus benefit from recanalization treatments [6, 7]. However, it is not known how patients with wake-up stroke should best be managed. In this study, we aimed to assess the opinions of stroke experts about the management of patients with wake-up stroke using an international multicenter electronic survey.

Method

Study Design and Selection of Participants

This study was an international electronic survey on the treatment of wake-up stroke. The questions were elaborated using the QuestionPro electronic platform (<http://www.questionpro.com>). We identified 200 stroke experts as potential participants in PubMed and Embase. The experts selected included equal portions of stroke neurologists and interventional neuroradiologists who had at least one publication on the acute treatment of ischemic stroke between 2012 and 2015. First authors, corresponding authors, authors who had publications in journals with higher impact factors, or authors who had published the most recently

were given priority for invitation to participate in the survey. Descriptive statistical analyses were conducted using statistics software (SPSS version 20.0, IBM, Chicago, Ill., USA). Variables were reported as means, confidence intervals at the 95% confidence level, standard deviations, and standard errors.

Results

Two hundred invitations to participate in the survey were sent by e-mail. Fifty-nine invitees started the survey, 4 dropped out of the survey before completing it, and 55 completed the full questionnaire. To complete the 8 questions, participants spent a mean of 3 min. Table 1 summarizes the participation rate per country. The 8 questions of the survey and the rates of various responses are listed in table 2.

Discussion

Around 20% of acute stroke admissions are for patients who wake up with a stroke, and according to international guidelines for the management of acute stroke, patients presenting with wake-up stroke are not eligible to receive revascularization treatments [8, 9]. There are currently 8 prospective trials enrolling patients to receive recanalization treatments who present with a stroke at an unknown time after the onset of their symptoms or after a stroke where symptoms began more than 4.5 h earlier. In a recent review, Thomalla and Gerloff [10] described these ongoing trials in detail and discussed emerging perspectives about this subject.

In the present study, we designed a simple questionnaire about the management of wake-up stroke and invited stroke experts, including stroke neurologists and interventional neurologists in equal proportions, to respond. Our survey was initiated after publication of the MrCLEAN trial [3]. The positive results obtained in that study for stentriever and intravenous rTPA for treating large blood vessel occlusions were thus already known to our participants.

In the first question, we found that around 70% of participants would recommend a revascularization treatment for patients presenting with wake-up stroke outside a clinical trial. This finding invites discussion of whether we should recommend nonstandard treatments in our daily practice. A high level of evidence is not always available to guide decisions during daily clinical practice, but doctors must still make these decisions. Although 70% of our survey participants would treat a patient presenting with wake-up stroke outside a trial, this survey did not assess the reasons for this response.

In the second, third, and fourth questions, stroke experts were asked about the best treatment strategies and brain imaging methods for use with wake-up stroke patients. There were discrepancies among their responses. In questions 5 and 6, we described a common clinical case; a patient presenting with wake-up stroke due to a distal blood vessel occlusion. This example represents a patient who would benefit from intravenous treatment with rTPA from the time of the onset of their symptoms up to 4.5 h afterwards. As for the first question of this survey, around 65% of participants would treat the patient. In questions 7 and 8, we described a case of a patient presenting with wake-up stroke due to a large blood vessel occlusion (left M1). In this case, around 83% recommended a revascularization treatment.

In this study, the fact that stroke experts agreed in their responses to questions 1, 5 and 7 indicates that most of them are inclined to treat patients with wake-up strokes. However, the considerable disagreement among experts in their responses to questions 2, 3, 4, 6, and 8 showed that stroke experts have not reached consensus on the best brain imaging method and on the best treatment strategy for patients with wake-up stroke.

Table 2. Questionnaire with results

Questions	Responses
1 For the treatment of wake-up stroke outside clinical trials, are you generally inclined to recommend a recanalization treatment?	a Yes (68.52%) b No (31.48%)
2 In general, would you recommend intravenous thrombolysis (rTPA) for a patient presenting with a wake-up stroke?	a Yes (51.85%) b No (48.15%)
3 In general, which revascularization treatment method would you recommend for a patient presenting with a wake-up stroke?	a Intravenous thrombolysis-rTPA (5.56%) b Mechanical thrombectomy-stentriever (42.59%) c Intravenous rTPA and stentriever (38.89%) d No revascularization treatment (12.96%)
4 Suppose that you are inclined to recommend a revascularization treatment for a patient presenting with a wake-up stroke, outside a clinical trial. What brain imaging technique would you recommend at hospital admission?	a Brain CT non-contrast-enhanced (5.66%) b Brain CT with perfusion and angio-CT (37.74%) c Brain CT with perfusion, angio-CT, magnetic resonance (5.66%) d Magnetic resonance (50.94%)
5 A 65-year-old male patient presenting with a wake-up stroke was admitted with complete aphasia. A computed tomography (CT) angiogram scan performed at admission showed that an M3 segment of the left middle cerebral artery was occluded, and the patient's ASPECTS score was 10. For this specific case, would you recommend a revascularization treatment?	a Yes (64.81%) b No (35.19%)
6 If you recommended a revascularization treatment, which would be your preferred method of revascularization for the case described above?	a Intravenous thrombolysis-rTPA (49.06%) b Intra-arterial thrombolysis-rTPA (7.55%) c Mechanical thrombectomy-stentriever (13.21%) d Intravenous rTPA and stentriever (1.89%) e No revascularization treatment (28.30%)
7 A 65-year-old male patient presenting with a wake-up stroke was admitted with complete right hemiplegia and aphasia (NIHSS score of 23). A CT angiogram scan performed at admission showed an occlusion of the M1 segment of the left middle cerebral artery and an ASPECTS score of 8. For this specific case, would you recommend a revascularization treatment?	a Yes (83.33%) b No (16.67%)
8 If you recommended a revascularization treatment, which would be your preferred revascularization treatment method for the case described above?	c Intravenous thrombolysis-rTPA (1.82%) d Mechanical thrombectomy-stentriever (52.73%) e Intravenous rTPA and stentriever (32.73%) f No revascularization treatment (12.73%)

The limitations of the study are the small size of the sample of experts and the limited number of questions asked. The questions did not cover all aspects of the treatment of patients with stroke. Moreover, most of the experts (72.5%) who were invited to participate in the survey did not respond. The low rate of response obtained on this survey might be due to e-mail spam blockers, because the first 100 invitations were sent collectively and not individually.

Conclusion

In this study, most of stroke experts recommended a recanalization treatment for wake-up stroke. However, there was considerable disagreement among experts regarding the best brain imaging method and the best recanalization treatment. The results of ongoing randomized trials on wake-up stroke are urgently needed.

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References

- 1 Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, et al: Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008;359:1317–1329.
- 2 Berkhemer OA, Fransen PS, Beumer D, et al: MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015;372:11–20.
- 3 Mackey J, Kleindorfer D, Sucharew H, Moomaw CJ, Kissela BM, Alwell K, et al: Population-based study of wake-up strokes. *Neurology* 2011;76:1662–1667.
- 4 Moradiya Y, Janjua N: Presentation and outcomes of ‘wake-up strokes’ in a large randomized stroke trial: analysis of data from the International Stroke Trial. *J Stroke Cerebrovasc Dis* 2013;22:e286–e292.
- 5 Roveri L, La Gioia S, Ghidinelli C, et al: Wake-up stroke within 3 hours of symptom awareness: imaging and clinical features compared to standard recombinant tissue plasminogen activator treated stroke. *J Stroke Cerebrovasc Dis* 2013;22:703–708.
- 6 Buck D, Shaw LC, Price CI, Ford GA: Reperfusion therapies for wake-up stroke: systematic review. *Stroke* 2014;45:1869–1875.
- 7 Stampfl S, Ringleb PA, Haehnel S, et al: Recanalization with stent-retriever devices in patients with wake-up stroke. *AJNR Am J Neuroradiol* 2013;34:1040–1043.
- 8 Kern R, Nagayama M, Toyoda K, Steiner T, Hennerici MG, Shinohara Y: Comparison of the European and Japanese guidelines for the management of ischemic stroke. *Cerebrovasc Dis* 2013;35:402–418.
- 9 Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, Johnston KC, Johnston SC, Khalessi AA, Kidwell CS, Meschia JF, Ovbiagele B, Yavagal DR; American Heart Association Stroke Council: 2015 AHA/ASA focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46:3020–3035.
- 10 Thomalla G, Gerloff C: Treatment concepts for wake-up stroke and stroke with unknown time of symptom onset. *Stroke* 2015;46:2707–2713.