Original Research

A Feasibility Study Involving Recruitment and Screening for Aphasia in Acute Stroke: Emerging Viability of the English Adaptation of the Language Screening Test (LASTen)

Heather L. Flowers, PhD a,b, Leanne K. Casaubon, MD, MSc b,c, Charmaine Arulvarathan, MN b,*, Anne Cayley, MN b,*, Sherry Darling, MSc b,d,*, Nesanet Girma, MSc b,d,*, Louise Pothier, MCommPath b,d,*, Tim Stewart, MN b,*, Janice Williams, MN b,e,*, Frank L. Silver, MD b,c

a School of Rehabilitation Sciences, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
b University Health Network, Toronto Western Hospital, Toronto, Ontario, Canada
c Department of Medicine — Neurology, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
d Department of Speech-Language Pathology, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
e Lawrence S. Bloomberg Faculty of Nursing, University of Toronto, Toronto, Ontario, Canada

List of abbreviations: C-SLP, coordinating speech-language pathologist; LAST, Language Screening Test; LASTen, Language Screening Test, English; NVU, Neurovascular Unit; SLP, speech-language pathologist; TAMS, Transient Ischemic Attack and Minor Stroke.

H.L. Flowers received funding from the University of Ottawa, Faculty of Health Sciences, Ottawa, Ontario, Canada.

Disclosures: H.L. Flowers does not perceive a conflict of interest directly with the work for this study. However, after completing the data collection, she provided consultation services to Transperfect (June 2018) as a paid expert, providing suggestions to change items from an existing language tool for application to Canadian English. None of her proposed modifications reflected the content of LASTen. The other authors have nothing to disclose.

Presented to the Clinical Outreach Seminar, School of Communication Sciences and Disorders, February 26, 2018, McGill University, Montreal, Québec, Canada; the Canadian Partnership for Stroke Recovery, Stroke Program in Neurorecovery, June 14, 2018, University of Ottawa, Ottawa, Ontario, Canada; the Summer School, Rehabilitation Department, Laval University, June 27, 2018, Québec, Québec, Canada; and the Ottawa Stroke Summit, Champlain Stroke Network, November 2, 2018, Ottawa, Ontario, Canada.

Cite this article as: Arch Rehabil Res Clin Transl. 2020;2:100062.

https://doi.org/10.1016/j.arrct.2020.100062
2590-1095/© 2020 The Authors. Published by Elsevier Inc. on behalf of the American Congress of Rehabilitation Medicine. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Aphasia occurs in one-third of stroke patients, often incurring a longer hospital stay\(^1\) and an increased need for rehabilitation services.\(^1\) Accurate screening has the potential to enhance early aphasia detection and management, especially in complex patients with multiple co-occurring impairments. In fact, nearly one-third of patients with acute aphasia have concomitant dysarthria or dysphagia,\(^3\) and 1 in 10 stroke patients has all 3 impairments.\(^3\) Without routine referral processes, patients with aphasia requiring management by speech-language pathologists may remain unidentified by front-line health care professionals, especially in the context of confounding co-occurring impairments.\(^5\) Accordingly, stroke guidelines recommend aphasia screening and assessment in the acute stage and at transition points in care. Screening is important for rapid identification of potential disease sequelae. Routine implementation of screening protocols may foster improved management involving timely assessment by specialists and comprehensive attention to multiple facets of patient care by the entire health care team.

A recently validated tool, the Language Screening Test (LAST), initially developed in French, addresses the current need for a rapid accurate bedside aphasia screening tool.\(^6\) The LAST has 2 parallel versions, permitting repeated testing in the acute stage and beyond.\(^6\) More specifically, the LAST has excellent psychometric properties,\(^6\)\(^,\)\(^7\) proven construct validity,\(^6\) and is practical for routine use.\(^6\) The constructs of the LAST include mental processing specific to language (therefore minimizing demands on memory or executive functions) in oral language modalities (ie, excluding reading or writing tasks).\(^6\)

There are 5 subtests in the LAST within expressive (production) and receptive oral language (comprehension) indices.\(^6\) The expressive index includes 3 subtests: picture naming (5 items), word and sentence repetition (2 items), and automatic speech (1 item).\(^6\) The receptive index includes 2 subtests: picture identification (4 items) and verbal commands (3 items of increasing complexity).\(^6\) Each correct item is accorded 1 point, for a total of 15 points per version (8 from the expressive and 7 from the receptive index).\(^6\) However, there are 29 different items across the 2 versions, because the automatic speech item (expressive index) is identical in each.\(^1\) Consequently, a maximum of 29 points are possible if the 2 versions are administered in rapid sequence (whereby only the first production of the automatic speech item is counted).

The LAST is practical, rapid, and easy to administer, requiring approximately 2 minutes per version.\(^6\) The test is administered from a single sheet of paper with the expressive index on 1 side and the receptive index on the other.\(^6\) The instructions and scoring are on the bottom third of each side of the paper, which is folded for examiner viewing only.\(^6\) Other than a single sheet of paper, the examiner uses a pen and cup (LAST-A) and another piece of paper and a key (LAST-B) for the verbal commands subtest.\(^6\) The LAST is limited to oral language and is, therefore,
Language screening in acute stroke

appropriate for patients with visual impairments and for those with poor literacy. Overall, the LAST meets recent guidelines for developing routing screenings and aphasia tests in any language.9

We recently adapted and harmonized the LAST for multiple English dialects (LASTen)^10 by conducting normative testing in 109 healthy adults in 4 countries: Australia, Canada, England, and the United States.10 Testing demonstrated equivalent performance across dialects and comparable results on the LASTen-A and LASTen-B.10 Nevertheless, participants with high school education (or less) made more errors than those who had completed community college or university programs.10

The LASTen still requires validation in acute stroke survivors to establish its psychometric properties and to determine appropriate cutoff scores according to education level. The purpose of the current study was to lay the groundwork for a future diagnostic accuracy trial by: (1) determining recruitment potential in acute stroke patients, (2) associating individual profiles with test performance according to aphasia status (presence vs absence), and (3) investigating parallel form reliability. Therefore, our overarching objectives were to ensure recruitment viability and to elucidate psychometric features of the LASTen that would support a future diagnostic accuracy trial in acute stroke patients.

Methods

We prospectively tracked eligibility and recruited patients admitted to the acute stroke units of a tertiary care hospital. The hospital’s research ethics board approved the study protocol for the enrollment of 12 patients. We included patients who were at least 18 years of age, had a clinically or radiologically confirmed stroke, spoke English as a first and primary language, and who were alert for 30 minutes at a time or longer. We excluded patients with subarachnoid hemorrhage, history of neurologic disease other than stroke, premorbid dementia, medical instability, severe psychiatric disorders, or severe vision or hearing disturbance. We sampled factors of interest, including varied age, sex, and stroke types. That is, we sought equal sex representation, a mean age of 65 years, varied stroke etiologies (involving an approximate 25% to 75% split for intracerebral hemorrhage and ischemic stroke, respectively), and a range of education levels (from incomplete high school education to university graduation). We also desired comparable characteristics within groups dichotomized for the presence (ranging in severity) or absence of aphasia.

We conducted our study in the Neurovascular Unit (NVU) and the Transient Ischemic Attack and Minor Stroke (TAMS) Unit. The NVU provides tertiary level acute care to stroke patients requiring specialized care such as endovascular therapy. The TAMS Unit provides specialized care in an ambulatory day area where patients with transient ischemic attack or minor stroke receive comprehensive evaluations by a nurse practitioner. Early diagnosis and treatment are paramount for patients admitted to the TAMS Unit. The nurse practitioner conducts a detailed assessment including urgent brain imaging, reviews cases with a stroke neurologist, and makes referrals to the interprofessional health team. Ensuing investigations may include same-day swallowing and communication evaluations by a speech-language pathologist.

We dedicated a full month to eligibility tracking within a year-long recruitment period (June 2017-May 2018) in the NVU and TAMS Unit. Eligibility tracking was important to determine potential numbers of patients for a future diagnostic accuracy trial. It involved significant time resources and close daily communication within the research team and members of the circle of care. In particular, confirming the criterion that patients speak English as a first and primary language often necessitated an informal bedside visit and interview by a speech-language pathologist (SLP). The 1-month period for eligibility tracking also permitted interprofessional discussion and promotion of study awareness among front-line hospital staff. When feasible, we attempted recruitment during the eligibility tracking period. However, we still required a full year for recruitment to permit careful consideration of predetermined characteristics of interest that would ensure the most representative sample of patients with and without aphasia.

Recruitment practices required the study team and attending care personnel to identify new English-speaking stroke patients admitted to the NVU or TAMS Unit, while providing the coordinating SLP (C-SLP [H.L.F.]) with minimal clinical information. That is, the team indicated suspected aphasia status and severity, if necessary, to achieve the desired sample based on factors of interest. The C-SLP remained blind to results of previous or ongoing testing and neuroimaging results. After a member of the circle of care determined patient willingness to discuss the study, the C-SLP presented the study purpose and obtained written consent from the patients. She used supported communication strategies with patients who had difficulty communicating to enable them to sign on their own behalf. The C-SLP also requested consent to video recording from select patients to facilitate development of future training materials. She only initiated video recording sessions when patient care constraints were minimal and when there was adequate time for equipment set up and secure storage procedures.

Before test administration, the C-SLP recorded patient reports of hearing and vision status and noted deviations to their usual use of aids (eg, patient not wearing hearing aids, because they were not at the hospital). She then administered both versions of the LASTen in sequence, reversing the presentation order across patients to ensure counterbalancing. Subsequently, she asked patients about their level of education in the following categories: final grade obtained (if no high school diploma), high school diploma, and college or university degree.

After the LASTen testing, we conducted a chart review to record patient demographics, in-hospital stroke interventions, neuroimaging results, evaluation of aphasia by an SLP, and evaluation of other poststroke impairments by the health care team. Lesion localization was determined from the neuroimaging reports by stroke radiologists and through consultation with the staff stroke neurologist as needed. Medical records identifying the presence of aphasia and other co-occurring impairments included
information from usual practice. The presence of aphasia was established based on bedside evaluation by an SLP. Such assessments often involved partial or complete administration of test batteries, such as the Western Aphasia Battery.

The co-occurring impairments of interest were dysphagia, communication impairments other than aphasia, and cognitive deficits. The attending SLP conducted dysphagia assessments based on physician referral. However, the SLP could initiate evaluation of any communication impairments, including dysarthria, apraxia of speech, and cognitive communication dysfunction. Additionally, the attending occupational therapist conducted more comprehensive evaluations of cognition, using standardized tests such as the Montreal Cognitive Assessment.

Data analysis involved summarizing patient characteristics, hospital course, and stroke-related interventions. We described individual profiles according to aphasia status, along with other co-occurring impairments from usual care reports. The LASTen scores were tabulated and depicted to describe patient performance according to aphasia status and brain lesion localization. To evaluate the LASTen-A and LASTen-B total score reliability, we computed a Pearson correlation coefficient.

### Results

Our study demonstrated feasible recruitment practices in the acute stroke setting. We established an eligibility rate
of 25 patients per month. In addition, all 12 patients recruited provided written consent, even those requiring additional communication support owing to cognitive impairments or aphasia. Two of 3 patients solicited for video recording provided consent, 1 without aphasia and 1 with moderate aphasia. The sample included 7 men and 5 women aged 29 to 85 years (Table 1). Three had intracerebral hemorrhage, and 10 had sustained a first stroke. The education level ranged from grade 10 to university degree completion.

Timing from stroke onset to the LASTen testing covered the hyperacute to early subacute stages. Median scores in patients with and without aphasia were 10 and 15, respectively (fig 1). Patients without aphasia performed comparably to the healthy participants in a previous normalization study, making occasional isolated errors (table 2). The most likely explanations for errors included lower education level, poor hearing with background noise despite corrective aids, or fatigue on the second version. All but 1 patient with aphasia achieved a maximum of 12 points on both versions, demonstrating complete score dissociation between those with and without aphasia. The patient with aphasia who achieved higher scores had a unique and potentially explanatory profile, being left-handed and having incurred a mild middle cerebral artery borderzone infarction.

There was a strong positive correlation across the LASTen versions, confirming parallel functioning ($r = 0.95$). Discrepant scores on the 2 LASTen versions involved a 1-point difference in all but 1 case. One patient had a 5-point difference between the 2 versions. The patient in question had fluent aphasia, spontaneously producing semantically-loaded circumlocutions relating to the LASTen items. This presumed practice effect facilitated naming, automatic speech, and picture identification on the second version, conceivably linked to therapeutic stimulability from inadvertent self-cueing.

**Discussion**

Our study demonstrated that it is feasible to recruit patients with various characteristics and stroke time course for aphasia screening in the acute setting. Our results have provided evidence for routine screening in stroke patients with aphasia who may have other common co-occurring impairments and an early debilitating recovery course. Implementing the LASTen will be possible once it is validated against a criterion standard. Currently, few rapid and accurate screening tools exist for aphasia early after stroke. Nevertheless, a previous review and systematic review identified 10 aphasia screening tools with psychometric evaluation in the acute stage. They include the Sheffield Screening Test, the Frenchay Aphasia Screening Test, the Mississippi Screening Test, the Acute Aphasia Screening Protocol, the Aphasia Screening Test, the Screeling, the Ulleval Aphasia Screening, the Mobile Aphasia Screening Test, the Semantic Verbal Fluency Test, and the Language Screening Test. Moreover, we have identified an additional tool, also developed and validated for the acute setting, the Aphasia Rapid Test. The recent systematic review identified the LAST and the Screeling as the most accurate screening tools for acute stroke.

Our review of the 11 tools supports the determination that the LAST is the most accurate and practical tool for the acute setting. Six of the 11 tools lacked validation against standardized test batteries, 2 involved a lengthy administration, and 7 included items that require use of executive functions (mental organization and planning) for

---

**Fig 1** Histogram showing individual patient performance on the 2 LASTen versions according to order of administration by aphasia status. A ceiling score of 15 indicates perfect performance.
| Patients | LASTen Testing | Stroke Onset to Testing | First-Second Scores (maximum, 15) | Expressive-Receptive Indices (maximum, 29) | Subtest Errors | Related Deficits | Lesion Side | Stroke Factors | Lesion Localization |
|----------|----------------|-------------------------|-----------------------------------|---------------------------------------------|---------------|-----------------|-------------|---------------|-------------------|
| No Aphasia | | | | | | | | | |
| 1* | | <5 days | 15-14 | 15-13 (28) | PI | Cognitive | Right | Temporoparietal region |
| 2* | | <3 weeks | 15-15 | 15-14 (29) | — | — | Right | Cerebellum |
| 3 | | <48 hours | 14-15 | 14-14 (28) | NM | — | Right | Posterior putamen |
| 4 | | <48 hours | 15-15 | 15-14 (29) | — | — | Right | Pars triangularis |
| 5* | | <24 hours | 15-15 | 15-14 (29) | — | — | Left | Inferior frontal lobe |
| 6 | | <4 days | 15-14 | 15-13 (28) | VC | — | Left | Medial occipital lobe |
| Aphasias | | | | | | | | | |
| 7 | | <5 days | 12-12 | 9-14 (23) | NM, RP, AS | AOS | Left | Parietal cortex |
| 8* | | <11 days | 13-14 | 13-13 (26) | RP, PI | Dysarthria | Left | MCA border zone |
| 9* | | <24 days | 12-11 | 10-12 (22) | NM, RP, PI, VC | Cognitive | Left | Deep white matter |
| 10 | | <4 days | 3-8 | 2-8 (11) | All | Cognitive | Left | Basal ganglia |
| 11 | | <16 days | 8-8 | 4-12 (16) | NM, RP, VC | Cognitive | Left | Anterior, superior, posterior temporal lobe |
| 12* | | <23 days | 1-1 | 0-2 (2) | All | Cognitive | Left | High frontoparietal region |

Abbreviations: AOS, apraxia of speech; AS, automatic speech; NM, naming; PI, picture identification; RP, repetition; VC, verbal commands.

* Wearing glasses (otherwise not required).
* Wearing hearing aids.
1 Lower than high school diploma.
1 Tested supine (postprocedural restrictions).
1 Intracerebral hemorrhage.
1 Hearing aids required but not available.
1 Moderate impairment (otherwise mild).
their language tasks. Like the LAST, 5 other tools were developed in languages other than English, including French, Norwegian, Dutch, and Korean. The French-language development and validation of the LAST addressed the current need for a rapid accurate bedside aphasia screening tool. It has the unique advantage of having 2 parallel versions with excellent reliability in the original version demonstrated by an intraclass correlation coefficient of 0.95. To our knowledge, there are 2 recent original version demonstrated by an intraclass correlation coefficient of 0.91 and 0.99 for the German and Chinese tests, respectively. Even our small sample size demonstrated a very strong correlation across the 2 LASTen versions, confirming the robustness of their parallel functioning.

Study limitations

One limitation of this study was that testing was performed by the C-SLP, who was aware of the study objectives. However, we sought to understand whether the psychometric properties of the LASTen were confirmatory for future validation or problematic, requiring potential modifications. Also, testing was not in keeping with anticipated routine administration by front-line care providers. However, having an SLP conduct testing permitted the consideration of potentially confounding linguistic and communication factors. A future validation will require not only comparison of LASTen scores with a criterion standard, but also measures of inter-rater reliability. Our request to video record patients in the current study served to determine its usefulness for inter-rater reliability procedures and to provide training materials for future routine implementation of the LASTen. We can now consider the possibility that video recordings could supplement online bedside scoring of test administration by multiple raters. That is, video recording could circumvent demands on multiple health care professionals to attend test administration sessions at the bedside. It could provide an alternate or exclusive means to document inter-rater reliability, ensuring independent and blinded scoring.

Another unanticipated limitation was that there were longer latencies between time of stroke onset to LASTen testing for patients with aphasia compared with those without. Our careful documentation of patient characteristics has provided a window into possible reasons. Patients with aphasia had more stroke-related interventions (eg, reperfusion treatments) and more co-occurring deficits than those without. Some patients who had already been admitted to their local hospital required rerouting to the study hospital for specialized treatment, such as endovascular therapy or neurosurgical intervention. Such care transitions inevitably lengthened the timeframe between stroke onset and arrival at our facility for LASTen testing. Also, we awaited patients’ capability to attend to a 30-minute assessment session and their capacity to consent, likely delaying testing for some patients with aphasia and co-occurring deficits.

Our study involved a small sample size, but it was sufficient for our purposes. That is, we demonstrated good potential for recruiting stroke patients even in the hyperacute stage. Our focus on individual patient profiles was helpful to show divergence in scores for patients with and without aphasia despite comparable education levels, age, and stroke type. Our sample confirmed desirable functioning of the LASTen, particularly its parallel version reliability. Given that the LASTen is feasible to administer in the acute stage of stroke and that it shows emerging psychometric viability, we will commence a large-scale validation in acute stroke patients.

Conclusions

Currently, a rapid and repeatable screening tool for stroke patients at risk of aphasia is sorely lacking in the English-speaking world. The current study demonstrated feasible recruitment of acute stroke patients and desirable psychometric properties of the LASTen. There were ceiling effects for patients without aphasia and heterogeneity of scores in those with aphasia, along with excellent parallel form reliability. The rigorous development of the LASTen justifies the fully funded multisite validation that we are now commencing in consecutive acute stroke patients. We will finally establish the diagnostic accuracy of the LASTen, permitting dissemination and implementation worldwide, to enable precocious identification of aphasia and sustained care for stroke survivors.

Corresponding author

Heather L. Flowers, PhD, 451 Smyth Road (RGN 3071), Ottawa, ON, K1H8M5, Canada. E-mail address: heather.flowers@uottawa.ca.

References

1. Flowers H, Skoretz SA, Silver F, et al. Poststroke aphasia frequency, recovery, & outcomes: a systematic review and meta-analysis. J Phys Med Rehabil 2016;97:2188-201.
2. Ellis C, Simpson AN, Bonilha L, Mauldin PD, Simpson KN. The one-year attributable cost of poststroke aphasia. Stroke 2012; 43:1429-31.
3. Flowers HL, Silver FL, Fang J, Rochon E, Martino R. The incidence, co-occurrence, and predictors of dysphagia, dysarthria, and aphasia after first-ever acute ischemic stroke. J Commun Disord 2013;46:238-48.
4. Boulanger JM, Lindsay MP, Gubitz G, et al. Canadian stroke best practice recommendations for acute stroke management: prehospital, emergency department, and acute inpatient stroke care, 6th edition, update 2018. Int J Stroke 2015;10:949-84.
5. Girma N, Darling S, Pother L, Flowers HL. Developing a tracking protocol for the management of communication impairments after acute stroke: a quality improvement initiative. Int J Stroke 2015;10:82.
6. Flamand-Roze C, Falissard B, Roze E, et al. Validation of a new language screening tool for patients with acute stroke: the language screening test. Stroke 2011;42:1224-9.
7. El Hachioui H, Visch-Brink EG, de Lau LM, et al. Screening tests for aphasia in patients with stroke: a systematic review. J Neurol 2017;264:211-20.
8. Eusebi P. Diagnostic accuracy measures. Cerebrovasc Dis 2013; 36:267-72.
9. Ivanova MV, Hallowell B. A tutorial on aphasia test development in any language: key substantive and psychometric considerations. Aphasiology 2013;27:891-920.
10. Flowers HL, Flamand-Roze C, Denier C, et al. English adaptation, international harmonisation, and normative validation of the Language Screening Test (LAST). Aphasiology 2015;29:214-36.
11. Kertesz A. Western Aphasia Battery. New York (NY): Grune and Stratton; 1982.
12. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Ger Soc 2005;53:695-9.
13. Bernhardt J, Hayward KS, Kwakkel G, et al. Agreed definitions and a shared vision for new standards in stroke recovery research: the Stroke Recovery and Rehabilitation Roundtable taskforce. Int J Stroke 2017;12:444-50.
14. Salter K, Jutai J, Foley N, Hellings C, Teasell R. Identification of aphasia post stroke: a review of screening assessment tools. Brain Inj 2006;20:559-68.
15. Snyder D, Body R, Parker M, Boddy M. Sheffield Screening Test for Acquired Language Disorders. Windsor: NFER-NELSON; 1993.
16. Enderby PM, Crow E. Frenchay aphasia screening test: validity and comparability. Disabil Rehabil 1996;18:238-40.
17. Enderby PM, Wood V, Wade D, Langton Hewer R. The Frenchay aphasia screening test: a short simple test appropriate for nonspecialists. Int Rehabil Med 1987;8:166-70.
18. Nakase-Thompson R, Manning E, Sherer M, Yablon SA, Gontkovsky SL, Vickery C. Brief assessment of severe language impairments: initial validation of the Mississippi aphasia screening test. Brain Inj 2005;19:685-91.
19. Cray MA, Haak NJ, Malinsky AE. Preliminary psychometric evaluation of an acute aphasia screening protocol. Aphasiology 1989;3:611-8.
20. Reitan RM. Aphasia Screening Test. 2nd ed. Tuscon, AZ: Reitan Neuropsychology Laboratory; 1985.
21. Doesborgh SJC, van de Sandt-Keonderman WME, Dippel DWJ, van Harskamp F, Koudstaal PJ, Visch-Brink EG. Linguistic deficits in the acute phase of stroke. J Neurol 2003;250:977-82.
22. Thommessen B, Thoresen GE, Bautz-Holter E, Laake K. Screening by nurses for aphasia in stroke – The Ullevall Aphasia Screening (UAS) test. Disabil Rehabil 1999;21:110-5.
23. Choi YH, Park HK, Ahn KH, Son YJ, Paik NJ. A telescreening tool to detect aphasia in patients with stroke. Telemed J E Health 2015;21:729-34.
24. Kim H, Kim J, Kim DY, Heo J. Differentiating between aphasic and nonaphasic stroke patients using semantic verbal fluency measures with administration time of 30 seconds. Eur Neurol 2011;65:113-7.
25. Azuar C, Leger A, Arbizu C, Henry-Amar F, Chomel-Guillaume S, Samson Y. The aphasia rapid test: an NIHSS-like aphasia test. J Neurol 2013;260:2110-7.
26. Keong-Bruhin M, Vanbellingen T, Schumacher R, et al. Screening for language disorders in stroke: German validation of the language screening test. Cerebrovasc Dis Extra 2016;6:27-31.
27. Yang H, Tian S, Flamand-Roze C, et al. A Chinese version of the language screening test (CLAST) for early-stage stroke patients. PLoS One 2018;13:e019664.