Check for updates

### **OPEN ACCESS**

EDITED AND REVIEWED BY Jean-Claude Baron, University of Cambridge, United Kingdom

\*CORRESPONDENCE Jenny P. Tsai ⊠ tsaij4@ccf.org

SPECIALTY SECTION This article was submitted to Stroke, a section of the journal Frontiers in Neurology

RECEIVED 02 January 2023 ACCEPTED 16 January 2023 PUBLISHED 06 February 2023

#### CITATION

Tsai JP, Schaafsma JD and Sarraj A (2023) Editorial: Management of acute stroke with large core. *Front. Neurol.* 14:1135886. doi: 10.3389/fneur.2023.1135886

#### COPYRIGHT

© 2023 Tsai, Schaafsma and Sarraj. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

# Editorial: Management of acute stroke with large core

## Jenny P. Tsai<sup>1\*</sup>, Joanna D. Schaafsma<sup>2</sup> and Amrou Sarraj<sup>3</sup>

<sup>1</sup>Cerebrovascular Center, Neurological Institute, Cleveland Clinic, Cleveland, OH, United States, <sup>2</sup>Division of Neurology, Department of Medicine, University of Toronto, Toronto, ON, Canada, <sup>3</sup>Programs of Neurology and Stroke, University Hospitals Cleveland Medical Center – Case Western Reserve University, Cleveland, OH, United States

#### KEYWORDS

stroke, thrombectomy, large ischemic core, cerebrovascular disease, neuroimaging

## Editorial on the Research Topic Management of acute stroke with large core

Owing to perceived poor outcomes and limited benefit from reperfusion therapies, acute stroke patients presenting with large infarct core on baseline imaging were consistently excluded from thrombolytic and endovascular therapy trials for the last two decades (1-10). Prioritizing finding an effective treatment for the majority of acute stroke patients has paved the way for the current standard-of-care, and improved survival and functional recovery for a vast number of individuals (11, 12). However, whether thrombolytic and endovascular therapies are safe and provide functional benefits in presence of large infarct cores is still unknown. As acute stroke research continues to expand the indication for both medical and endovascular therapies, management of acute stroke patients with large infarct core becomes the next frontier to explore (13–16).

Elucidating the best management of a recently established or evolving large infarct comes down to three key questions. First, what are the optimal imaging modalities and criteria to identify a "large core"? Second, are attempts at reducing the infarct core size *via* thrombolytic or endovascular reperfusion justified by their risk-benefit balance? And third, how can secondary injury and complications of acute large infarcts be minimized?

This review on the topic of acute strokes with large infarct core examines all three aspects. Koopman et al. present evidence that perfusion imaging is a reliable early biomarker to predict clinical outcome in this patient population. Yang et al. continue the discussion with evidence that patient age and perfusion profile may potentially define a ceiling to treatment benefits (17). To address this complexity of early outcome prediction, Chen et al. propose a model based on demographic and imaging biomarkers (18). As the discussion shifts to acute therapy, Hu et al. suggest a promising role for low-dose tirofiban (19). Meanwhile, Hassan et al. present data from the COMPLETE registry to reaffirm the importance of time in limiting infarct growth and improving clinical outcomes (20). DeHoff and Lau then round off our discussion with a review of medical management of cerebral edema resulting from large hemispheric infarcts (21).

The world of cerebrovascular medicine currently eagerly awaits the outcomes of randomized controlled trials on endovascular therapy for acute strokes with large infarct cores (22–24). While endovascular reperfusion may yet again promise the most effective treatment, the complexity of acute stroke patients presenting with large cores highlights the ongoing need for multi-faceted, collaborative research to optimize their outcomes. It is long overdue.

# Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

# **Conflict of interest**

AS reports grant support from Stryker Neurovascular for the SELECT2 clinical trial, is a member of the speaker bureau and advisory board for Stryker Neurovascular and has received consultant fees from AstraZeneca.

# References

1. Berkhemer OA, Fransen PSS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med.* (2015) 372:11–20. doi: 10.1056/nejmoa1411587

2. Campbell BCV, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med.* (2015) 372:1009–18. doi: 10.1056/nejmoa1414792

3. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med.* (2015) 372:1019–30. doi: 10.1056/nejmoa1414905

4. Saver JL, Goyal M, Bonafe A, Diener H-C, Levy EI, Pereira VM, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med.* (2015) 372:2285–95. doi: 10.1056/nejmoa1415061

5. Campbell BCV, Mitchell PJ, Churilov L, Yassi N, Kleinig TJ, Dowling RJ, et al. Tenecteplase versus alteplase before thrombectomy for ischemic stroke. *N Engl J Med.* (2018) 378:1573–82. doi: 10.1056/nejmoa1716405

6. 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.* (2017) 378:11–21. doi: 10.1056/nejmoa1706442

7. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med.* (2018) 378:708–18. doi: 10.1056/nejmoa1713973

8. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med.* (2015) 372:2296–306. doi: 10.1056/nejmoa1503780

9. Ma H, Campbell BCV, Parsons MW, Churilov L, Levi CR, Hsu C, et al. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. *N Engl J Med.* (2019) 380:1795–803. doi: 10.1056/nejmoa1813046

10. Group NI of ND, S rt-PSS. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med.* (1995) 333:1581–88. doi: 10.1056/nejm199512143332401

11. Goyal M, Menon BK, van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a metaanalysis of individual patient data from five randomised trials. *Lancet.* (2016) 387:1723– 31. doi: 10.1016/s0140-6736(16)00163-x

12. Albers GW, Lansberg MG, Brown S, Jadhav AP, Haussen DC, Martins SO, et al. Assessment of optimal patient selection for endovascular thrombectomy beyond 6 hours after symptom onset: a pooled analysis of the AURORA database. *JAMA Neurol.* (2021) 78:1064. doi: 10.1001/jamaneurol.2021.2319

13. Garcia-Esperon C, Bivard A, Johns H, Chen C, Churilov L, Lin L, et al. Association of endovascular thrombectomy with functional outcome in patients with acute stroke with a large ischemic core. *Neurology.* (2022) 99:e1345-e1355. doi: 10.1212/wnl.00000000201641

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

# Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

14. Moreu M, Pérez-García C, Rosati S, López-Frías A, Egido JA, Gómez-Escalonilla C, et al. Mechanical thrombectomy is cost-effective versus medical management alone around Europe in patients with low ASPECTS. *J Neurointerv Surg.* (2022) jnis-2022-019849. doi: 10.1136/jnis-2022-019849. [Epub ahead of print].

15. Sarraj A, Hassan AE, Savitz S, Sitton C, Grotta J, Chen P, et al. Outcomes of endovascular thrombectomy vs medical management alone in patients with large ischemic cores: a secondary analysis of the optimizing patient's selection for endovascular treatment in acute ischemic stroke (SELECT) study. *JAMA Neurol.* (2019) 76:1147. doi: 10.1001/jamaneurol.2019.2109

16. Tanaka K, Goyal M, Menon BK, Campbell BCV, Mitchell PJ, Jovin TG, et al. Significance of baseline ischemic core volume on stroke outcome after endovascular therapy in patients age  $\geq$ 75 years: a pooled analysis of individual patient data from 7 trials. *Stroke.* (2022) 53:3564–71. doi: 10.1161/strokeaha.122.039774

17. Yang H, Lin D, Lin X, Wu Y, Yi T, Chen W. Outcomes and CT perfusion thresholds of mechanical thrombectomy for patients with large ischemic core lesions. *Front Neurol.* (2022) 13:856403. doi: 10.3389/fneur.2022.856403

 Chen J, Li J, Xu Z, Zhang L, Qi S, Yang B, et al. Prediction model of early biomarkers of massive cerebral infarction caused by anterior circulation occlusion: establishment and evaluation. *Front Neurol.* (2022) 13:903730. doi: 10.3389/fneur.2022. 903730

19. Hu Y, Xiao Q, Shi Z, Hou Y, Chen Z, Cheng J, et al. Safety and efficacy of lowdose and long-course tirofiban in large hemispheric infarction. *Front Neurol.* (2022) 13:987859. doi: 10.3389/fneur.2022.987859

20. Hassan AE, Zaidat OO, Nanda A, Atchie B, Woodward K, Doerfler A, et al. Impact of interhospital transfer vs. direct admission on acute ischemic stroke patients: a subset analysis of the COMPLETE registry. *Front Neurol.* (2022) 13:896165. doi: 10.3389/fneur.2022.896165

21. DeHoff G, Lau W. Medical management of cerebral edema in large hemispheric infarcts. *Front Neurol.* (2022) 13:857640. doi: 10.3389/fneur.2022.857640

22. Sarraj A, Hassan AE, Abraham M, Ribo M, Blackburn S, Chen M, et al. A randomized controlled trial to optimize patient's selection for endovascular treatment in acute ischemic stroke (SELECT2): study protocol. *Int J Stroke.* (2021) 17:689–93. doi: 10.1177/174749302110 35032

23. Jabal MS, Ibrahim MK, Thurnham J, Kallmes KM, Kobeissi H, Ghozy S, et al. Common data elements analysis of mechanical thrombectomy clinical trials for acute ischemic stroke with large core infarct. *Clin Neuroradiol.* (2022) 1–11. doi: 10.1007/s00062-022-01239-x. [Epub ahead of print].

24. Yoshimura S, Sakai N, Yamagami H, Uchida K, Beppu M, Toyoda K, et al. Endovascular therapy for acute stroke with a large ischemic region. *N Engl J Med.* (2022) 386:1303–13. doi: 10.1056/nejmoa21 18191