Neurocrit Care (2020) 32:84–85
https://doi.org/10.1007/s12028-019-00841-1

NEUROCRITICAL CARE SOCIETY

INVITED EDITORIAL COMMENTARY

Predicting Malignant Cerebral Edema After Large Hemispheric Stroke

W. Taylor Kimberly*

Large hemispheric infarction (LHI) is an ischemic stroke of the middle cerebral artery (MCA) territory and leads to a disproportionate degree of disability and death [1, 2]. Poor functional outcome is further exacerbated when severe edema develops, which manifests as a decreased consciousness in association with displacement of midline structures of the brain [3]. This abrupt neurological decline, termed malignant cerebral edema (MCE) or malignant MCA infarction [4], occurs in the first 1–3 days after stroke onset [5]. There are limited treatment options for MCE, with surgical decompressive craniectomy (DC) offered to a subset of patients [6].

Despite several decades of research, the ability to predict which LHI patients will develop MCE remains imprecise. Several neuroimaging features can assist, including the presence of early computed tomography (CT) hypodensity involving more than half of the MCA territory [7], a lesion volume >82 cc on brain magnetic resonance imaging (MRI) in first 6 h [8], or a lesion volume >145 cc on MRI in first 14 h [9]. However, size alone is insufficient since some patients with LHI will not progress to MCE. Additional clinical characteristics that have been identified include headache and vomiting [7], a high National Institutes of Health stroke scale (NIHSS) [10], and decreasing level of consciousness [4, 11].

The rapid and accurate recognition of patients at risk for MCE is important for the initial triage of patients to stroke centers with neurocritical care units or other intensive monitoring capability. Predictive information not only prepares clinicians for potential impending deterioration, but can also guide discussions with patients and family members in clarifying the goals of care [12, 13]. Given the importance of accurately anticipating MCE, several groups have developed risk scores to predict edema [14–17].

Each of these scores, developed from cohorts at single centers, represents a trade-off between feasibility of the scoring criteria and the score's performance in discriminating MCE. For example, the diffusion-weighted imaging ASPECTS ≤ 3, anterior cerebral artery territory involvement, M1 susceptibility sign, and hyperglycemia score has a reported area under the receiver operating characteristic curve (AUC) of 0.88 but relies on brain MRI findings, which may not be generalizable to other institutions. In contrast, the thrombolysis risk Using mRS and NIHSS score is rapid, feasible, and generalizable, but has an AUC of 0.67 for predicting edema. From a practical perspective, if the goal is early triage and identification, then the time at which the score is assessed also becomes important.

In the current study by Cheng et al, the authors sought to validate and improve upon the performance of the enhanced detection of edema in malignant anterior circulation stroke (EDEMA) score in predicting MCE. The EDEMA score utilizes clinical and CT imaging features and may therefore represent a compromise between generalizability and discrimination. However, several points are worth noting. First, the original EDEMA score was designed to predict death with midline shift (MLS) >5 mm or DC. This endpoint is limited by the fact that MLS is used in both the scoring criteria and the outcome measure. Moreover, death is frequently confounded by withdrawal of care, which has both cultural and regional variation. Similarly, DC has recognized practice variation that potentially limits generalizability. This does not necessarily diminish the value of the EDEMA score *per*

*Correspondence: wtkimberly@mgh.harvard.edu
Massachusetts General Hospital, Lunder 644, 55 Fruit St, Boston, MA 02114, USA

This comment refers to the article available at https://doi.org/10.1007/s12028-019-00844-y.

Springer

se, but rather highlights the importance of the validation study now performed by Cheng et al.

Accordingly, the authors tested the EDEMA score and used MCE as the primary endpoint, followed by a secondary analysis using the original death or DC definition. The study was also conducted in a Chinese population, testing the performance of the EDEMA score in a group of patients with a different ethnic and cultural background.

What are the key take-aways? In both Western and Chinese populations, the EDEMA score performs moderately well in discriminating patients who develop MCE (AUC of 0.80). The addition of NIHSS, which is frequently incorporated into other stroke predictive scores, enhances prediction in the current study (AUC of 0.83). Whether this would also be the case in a similarly powered US-based study would require additional research. Taken together, the findings by Cheng et al. validate the original EDEMA score and identify the value of including the NIHSS.

However, it should be noted that even the revised EDEMA score had a sensitivity of 85% and a specificity of 62%. This emphasizes that there is room for further refinement prior to implementing in routine clinical practice. It is possible that additional neuroimaging characteristics [18] or plasma markers may be able to provide added information. Nevertheless, this study represents a useful advance in our understanding of cerebral edema after stroke and potentially informs the triage of these patients to stroke centers with neurocritical care expertise.

Source of Support
The author received funding from AHA 17CSA 33550004, NIH R01 NS099209-03, and NIH U01 NS113443-01.

Conflict of interest
The author received research grants from Biogen, and received consulting fees from Biogen.

Publisher's Note

Published online: 23 September 2019

References

1. Wijdicks EFM, Sheth KN, Carter BS, Greer DM, Kasner SE, Kimberly WT, et al. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014;45:1222–38.
2. Torbey MT, Bösel J, Rhoney DH, Rincon F, Staykov D, Amar AP, et al. Evidence-based guidelines for the management of large hemispheric infarction: a statement for health care professionals from the neurocritical care society and the german society for neuro-intensive care and emergency medicine. Neurocrit Care. 2015;22:146–64.
3. Huttner HB, Schwab S. Malignant middle cerebral artery infarction : clinical characteristics, treatment strategies, and future perspectives. Lancet Neurol Elsevier Ltd. 2009;8:949–58.
4. Hacke W, Schwab S, Horn M, Spranger M, De Georigia M, von Kummer R. "Malignant" middle cerebral artery territory infarction clinical course and prognostic signs. Arch Neurol. 1996:309–15.
5. Qureshi AI, Suarez JI, Yahia AM, Mohammad Y, Uzun G, Suri MFK, et al. Timing of neurologic deterioration in massive middle cerebral artery infarction: a multicenter review. Crit Care Med. 2003;31:272–7.
6. Vahedi K. Decompressive hemicraniectomy for malignant hemispheric infarction. Curr Treat Opt Neurol. 2009;11:113–9.
7. Krieger DW, Demchuk A, Kasner SE, Jauss M, Hantson L. Early clinical and radiological predictors of fatal brain swelling in ischemic stroke. Stroke. 1999;30:287–92.
8. Thomalla G, Hartmann F, Juettler E, Singer OC, Lehnhardt FG, Kohrmann M, et al. Prediction of malignant middle cerebral artery infarction by magnetic resonance imaging within 6 hours of symptom onset: a prospective multicenter observational study. Ann Neurol. 2010;68:435–45.
9. Oppenheim C, Samson Y, Manai R, Lalam T, Vandamme X, Crozier S, et al. Prediction of malignant middle cerebral artery infarction by diffusion-weighted imaging. Stroke. 2000;31:2175–81.
10. Kasner SE, Demchuk AM, Berrouschot J, Schmutzhard E, Harms L, Verro P, et al. Predictors of fatal brain edema in massive hemispheric ischemic stroke. Stroke. 2001/09/08. 2001;32:2117–23.
11. Cucchiara BL, Kasner SE, Wolk DA, Lyden PD, Knappertz VA, Ashwood T, et al. Early impairment in consciousness predicts mortality after hemispheric ischemic stroke. Crit Care Med. 2004;32:241–5.
12. Larach DR, Larach DB, Larach MG. A life worth living: seven years after craniectomy. Neurocrit Care. 2009;11:106–11.
13. Kelly AG, Robert GH. Health state preferences and decision-making after malignant middle cerebral artery infarctions. Neurology. 2010;75:682–7.
14. Asuzu D, Nyström K, Sreekrishnan A, Schindler J, Wira C, Greer D, et al. TURN score predicts 24-hour cerebral edema after IV thrombolysis. Neurocrit Care. 2016;24:381–8.
15. Shimoyama T, Kimura K, Uemura J, Yamashita S, Saji N, Shibazaki K, et al. The DASH score: a simple score to assess risk for development of malignant middle cerebral artery infarction. J Neurol Sci. 2014;338:102–6.
16. Ong CJ, Gluckstein J, Laurido-Soto O, Yan Y, Dhar R, Lee JM. Enhanced detection of edema in malignant anterior circulation stroke (EDEMA) score. Stroke. 2017;48:1969–72.
17. Jo KW, Bajgur SS, Kim H, Choi HA, Huh PW, Lee K. A simple prediction score system for malignant brain edema progression in large hemispheric infarction. PLoS ONE. 2017;12:e0171425.
18. Broocks G, Flottmann F, Scheibel A, Aigner A, Faizy TD, Hanning U, et al. Quantitative lesion water uptake in acute stroke computed tomography is a predictor of malignant infarction. Stroke. 2018;49:1906–12.