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Author(s): George Harston

Iris Grunwald

Alastair Buchan

Letter by Harston et al. Regarding Article, "Alberta Stroke Program Early CT Score Versus Computed Tomographic Perfusion to Predict Functional Outcome After Successful Reperfusion in Acute Ischemic Stroke"

George WJ Harston DPhil[1,2]; Iris Grunwald PhD[3]; Alastair M Buchan FMedSci[4]

1. Acute Stroke Service, Oxford University Hospitals NHS Foundation Trust; John Radcliffe Hospital; Oxford, OX3 9DU, UK; George.harston@rdm.ox.ac.uk
2. Brainomix Limited, Oxford, UK
3. Anglia Ruskin University, Cambridge, UK
4. Radcliffe Department of Medicine, University of Oxford, UK

Demeestere et al.[1] investigated the ability of Computed Tomography Perfusion (CTP)-defined ischemic core, conventional ASPECTS, and e-ASPECTS to predict a variety of dichotomized outcomes in a subgroup of patients in the CRISP (Computed Tomographic Perfusion to Predict Response to Recanalization in Ischemic Stroke Project) Study. The relationship of baseline imaging with outcome is important if imaging is to be used to make treatment decisions in patients with acute stroke, and head-to-head comparisons are necessary to advance the field. However, it is not clear that the conclusions in this paper reflect the results of the analysis, and several key limitations have not been discussed.

The results show that both e-ASPECTS and CTP ischemic core statistically associate with good outcome when multivariate regression analysis is used, appropriately correcting for other variables. Despite this, the conclusions state that CTP alone predicts outcome, which does not reflect the results presented. Furthermore predictive ability is better quantified using Receiver Operator Characteristic (ROC) curve analysis rather than odds ratios or p-values, which should not be used for head-to-head comparisons.[2] Could the authors please explain why ROC curve analysis was only shown for CTP data?

There are also significant limitations to the study which are not mentioned in the manuscript, and which make drawing any firm conclusions challenging. Importantly, the core imaging laboratory removed artifacts from CTP imaging *post hoc*, whereas no such corrections were made for e-ASPECTS software. This has the potential to have introduced significant bias. Despite this, it was demonstrated that e-ASPECTS outperformed conventional ASPECTS without any corrections, but the retrospective consensus scores tended to identify more ischemia than the automated score, inconsistent with previous work.[3-5] This discrepancy may be due to non-blinding raters to other imaging modalities such as CTP when defining ASPECTS, although this is unclear from the manuscript. Raters tend to overestimate ischemic injury in this setting.

Finally, the results presented differ from independent work using less selective inclusion criteria and with larger infarct cores, which showed e-ASPECTS correlated more strongly with good outcome than CTP.[5] In this CRISP substudy, not only was analysis restricted to those who went on to have successful recanalization, but investigators used the CT and CTP data before making decisions to treat. This may explain the small number of patients with a low e-APSECTS score or large core on CTP. It is likely that these few patients were selected for intervention despite adverse imaging profiles and because of other confounding factors, necessitating caution when comparing to those with favourable imaging profiles. The limited number of patients with less favorable imaging profiles may also explain the modest ability of CTP to predict outcome in this cohort. The stated aim of identifying patients likely to benefit from mechanical thrombectomy is limited using these data.

In summary, while head-to-head comparisons of imaging biomarkers are necessary in patients with large vessel occlusion stroke, this study has significant limitations restricting the scope of the inferences that can be drawn, and the results presented do not support the stated conclusions.

Disclosures

GH is employed part-time by Brainomix. IG and AMB have equity interest in and are consultants for Brainomix.

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