Neurocrit Care (2019) 31:451–452
https://doi.org/10.1007/s12028-019-00768-7

NEUROCRITICAL CARE SOCIETY

INVITED EDITORIAL COMMENTARY

CT Markers of Intracerebral Hemorrhage Expansion: Different Sides of the Same Coin?

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Hematoma expansion (HE) is common in the natural history of acute intracerebral hemorrhage (ICH), and its prevention appears as a valuable strategy to improve patients' outcome. Subjects at high risk of HE may be more likely to benefit from anti-expansion therapies, and therefore, accurate stratification of HE risk is a clinical research priority. The computed tomography angiography (CTA) spot sign is a robust and validated marker of HE, but CTA is not routinely performed in the workup of acute ICH [1]. Less than one in five patients underwent CTA in a large ICH randomized controlled trial [2]. Conversely, non-contrast CT (NCCT) is widely available and nearly all acute ICH cases are detected with this imaging technique. The first evidence of an association between NCCT features of ICH and hematoma growth came as early as 1994 [3]. Publications and research efforts on NCCT markers of HE have grown exponentially in the last 5 years.

In this regard, Dr. Chu and Colleagues reported a new NCCT marker of HE, namely minimal computed tomography attenuation value (MCTAV) [4]. This sign was described in a single center development cohort ($n = 148$) and validated in a multicenter population derived from three different institutions ($n = 311$). MCTAV detection requires manual drawing of a region of interest and CT attenuation measurement with an automated software. The presence of a MCTAV ≤ 31 Hounsfield Units was independently associated with HE and poor outcome after adjustment for potential confounders in multivariable logistic regression. MCTAV had excellent inter- and intra-rater reliability (Cohen's $k \geq 0.90$) and identified HE with 64% sensitivity and 92% specificity.

Although this study confirmed that NCCT features may be used to identify patients at high risk of HE and poor prognosis, some caveats should be kept in mind. It remains unclear whether this new marker provides additional yield in the stratification of HE risk. Good sensitivity and specificity for HE have been previously reported using markers that are easier to detect compared to MCTAV, requiring only a direct visual inspection of NCCT [5–7]. With the evidence available so far, a clear superiority of one NCCT sign over the others cannot be established. There is also significant overlap between different NCCT markers, with lack of consensus on the diagnostic criteria and optimal setting for detecting and reporting these signs.

From a clinical point of view, patients with NCCT markers do not derive clinical benefit from intensive blood pressure reduction [8]. The interaction between NCCT signs and clinical benefit from hemostatic treatments targeting HE remains unknown and deserves further investigations. Routine evaluation of NCCT markers in clinical practice may, however, identify subjects at high risk of neurological deterioration, requiring therefore a higher intensity of care and monitoring [9].

Several questions remain unanswered in the field of NCCT predictors of HE. First, a consensus on diagnostic criteria is needed. Second, future studies should investigate whether NCCT markers can improve the diagnostic performance of the currently available tools to predict HE [10]. Third, the relationship between NCCT features of ICH and the CTA spot sign remains unclear. Fourth, the pathophysiological mechanisms underlying NCCT signs are still unknown. Finally, several NCCT markers require prospective validation with assessment and comparison of their diagnostic accuracy and inter-rater reliability.

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This comment refers to the article available at https://doi.org/10.1007/s12028-019-00754-z.

In conclusion, several NCCT signs are associated with HE in patients with acute ICH, but a consensus on the standards for detecting and reporting these markers is needed. Given the wide availability of NCCT, stratification of HE risk with NCCT markers appears as a promising strategy to expand the pool of patients eligible for clinical trials and accelerate the discovery of acute treatments limiting active bleeding.

Source of support
None.

Conflict of interest
The author declare that he has no conflict of interest.

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Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Published online: 19 June 2019

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