JoS
JOURNAL OF STROKE

Journal of Stroke 2018;20(3):411-412
https://doi.org/10.5853/jos.2018.01186

Letter to the Editor

Manual Thrombus Density Measurement Depends on the Method of Thrombus Delineation

Liang Shu,[a,b] Johannes Meyne,[c] Olav Jansen,[a] Ulf Jensen-Kondering[a]

[a]Department of Radiology and Neuroradiology, University Hospital of Schleswig-Holstein, Kiel, Germany
[b]Shanghai Ninth People's Hospital, Shanghai, China
[c]Department of Neurology, University Hospital of Schleswig-Holstein, Kiel, Germany

Dear Sir:

We would like to comment on the review by Heo et al.[1] on computed tomography (CT) thrombus imaging in acute large intracranial vessel occlusion, with focus on manual thrombus delineation. As noted, better recanalization is achieved when hyperdense thrombi are subjected to intravenous thrombolysis or endovascular thrombectomy,[2-5] but this finding was inconsistent.[6-9]

To demonstrate the influence of manual thrombus delineation, we retrospectively assembled data from 20 patients with large intracranial vessel occlusion who underwent pretreatment, non-enhanced cranial CT (Brilliance 64, Philips, Amsterdam, the Netherlands; 120 kV, 320 mA, reconstructed slice thickness 2.5 mm). Regions of interest (ROIs) were placed by one reader using different methods (Fig. 1A). One (method 1)[4,6] or three (method 2)[2,9] circular ROIs were placed in the most hyperdense-appearing part of the occluded artery. Using method 3, the hyperdense artery was delineated with irregular ROIs for every CT slice,[3,5] yielding 124 ROIs. Hyperdensities with >100 Hounsfield units (HU) were considered calcifications and excluded. For methods 2 and 3, the mean density was calculated. Since interrater reliability was reportedly high,[10] 50 randomly selected ROIs were reanalyzed by a second, blinded reader. Mean density differences between the raters and the intraclass correlation coefficient (ICC) were calculated. Density

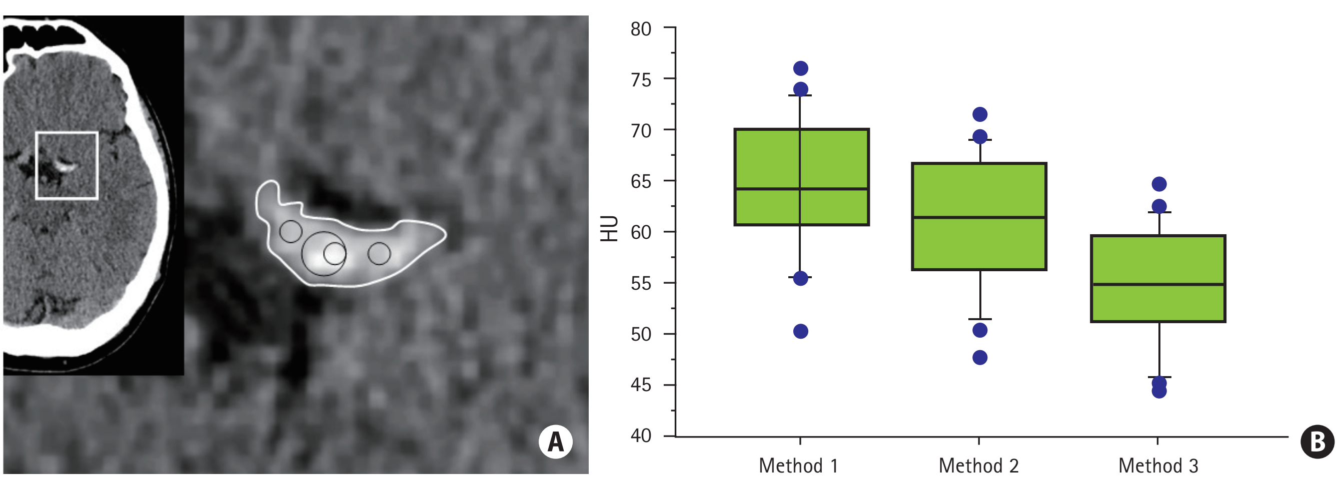

Figure 1. (A) Three methods of manual thrombus delineation. One (method 1, large circular region of interest [ROI]) or three (method 2, circular ROIs) were placed into the most hyperdense-appearing part of the vessel, or the whole hyperdense vessel was encompassed within an ROI on every slice on which the vessel was visualized (method 3, white outline). The mean density was determined (method 2 and 3). (B) Box and whisker plots of density values for the three methods. HU, Hounsfield unit.

values were subjected to the Kolmogorov-Smirnov test to verify normal distribution. One-way analysis of variance (ANOVA) was performed to detect between-group differences. The Tukey-Kramer *post hoc* test was applied to determine differences between groups, and $P<0.01$ was considered significant.

Density values were normally distributed ($P>0.999$). Differences between the two readers were small (2.8±1.2 HU) and ICC between raters was 0.93. Henceforth, only ROIs defined by the first observer were used for analysis. One-way ANOVA was significant ($P<0.0001$). The mean thrombus density was 65.04±6.59 (method 1), 60.92±6.65 (method 2), or 54.93±5.7 HU (method 3) (all $P<0.01$) (Fig. 1B). Mean differences in thrombus density were 5.98±2.34 (method 1 vs. 2), 4.12±2.48 (method 2 vs. 3), and 10.11±3.06 HU (method 1 vs. 3).

Thus, manual thrombus density measurements depend on the measurement method. Despite small sample size, measured densities were significantly different, with whole thrombus delineation yielding lowest density values. Further factors (slice thickness, treatment modality, heterogeneous thrombi, and beam hardening artefacts) must be considered. While automated algorithms[11] might be useful, we agree with Angermaier and Langner[7] that technical standards are needed for manual thrombus density measurements.

References

1. Heo JH, Kim K, Yoo J, Kim YD, Nam HS, Kim EY. Computed tomography-based thrombus imaging for the prediction of recanalization after reperfusion therapy in stroke. *J Stroke* 2017;19:40-49.
2. Froehler MT, Tateshima S, Duckwiler G, Jahan R, Gonzalez N, Vinuela F, et al. The hyperdense vessel sign on CT predicts successful recanalization with the Merci device in acute ischemic stroke. *J Neurointerv Surg* 2013;5:289-293.
3. Mokin M, Morr S, Natarajan SK, Lin N, Snyder KV, Hopkins LN, et al. Thrombus density predicts successful recanalization with Solitaire stent retriever thrombectomy in acute ischemic stroke. *J Neurointerv Surg* 2015;7:104-107.
4. Moftakhar P, English JD, Cooke DL, Kim WT, Stout C, Smith WS, et al. Density of thrombus on admission CT predicts revascularization efficacy in large vessel occlusion acute ischemic stroke. *Stroke* 2013;44:243-245.
5. Puig J, Pedraza S, Demchuk A, Daunis-I-Estadella J, Termes H, Blasco G, et al. Quantification of thrombus hounsfield units on noncontrast CT predicts stroke subtype and early recanalization after intravenous recombinant tissue plasminogen activator. *AJNR Am J Neuroradiol* 2012;33:90-96.
6. Yilmaz U, Roth C, Reith W, Papanagiotou P. Thrombus attenuation does not predict angiographic results of mechanical thrombectomy with stent retrievers. *AJNR Am J Neuroradiol* 2013;34:2184-2186.
7. Angermaier A, Langner S. Thrombus density measurement is promising but technical standards are needed. *J Neurointerv Surg* 2017;9(e1):e9-e10.
8. Topcuoglu MA, Arsava EM, Kursun O, Akpinar E, Erbil B. The utility of middle cerebral artery clot density and burden assessment by noncontrast computed tomography in acute ischemic stroke patients treated with thrombolysis. *J Stroke Cerebrovasc Dis* 2014;23:e85-e91.
9. Spiotta AM, Vargas J, Hawk H, Turner R, Chaudry MI, Battenhouse H, et al. Hounsfield unit value and clot length in the acutely occluded vessel and time required to achieve thrombectomy, complications and outcome. *J Neurointerv Surg* 2014;6:423-427.
10. Santos EM, Yoo AJ, Beenen LF, Berkhemer OA, den Blanken MD, Wismans C, et al. Observer variability of absolute and relative thrombus density measurements in patients with acute ischemic stroke. *Neuroradiology* 2016;58:133-139.
11. Santos EM, Niessen WJ, Yoo AJ, Berkhemer OA, Beenen LF, Majoie CB, et al. Automated entire thrombus density measurements for robust and comprehensive thrombus characterization in patients with acute ischemic stroke. *PLoS One* 2016;11:e0145641.

Correspondence: Ulf Jensen-Kondering
Department of Radiology and Neuroradiology, University Hospital of Schleswig-Holstein, Arnold-Heller-Str. 3, Haus 41, Kiel 24105, Germany
Tel: +49-431-500-16501
Fax: +49-431-500-16504
E-mail: Ulf.Jensen-Kondering@uksh.de

Received: April 24, 2018
Revised: May 24, 2018
Accepted: June 4, 2018

The authors have no financial conflicts of interest.