Letter by Pirson et al Regarding Article, "Results From DEFUSE 3 Good Collaterals Are Associated With Reduced Ischemic Core Growth but Not Neurologic Outcome"

Letter to the Editor

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Letter by Pirson et al Regarding Article, "Results From DEFUSE 3 Good Collaterals Are Associated With Reduced Ischemic Core Growth but Not Neurologic Outcome"

To the Editor:

With great interest, we read the study by de Havenon et al[1] on the association of collaterals with ischemic core growth and neurological outcome in stroke patients with large vessel occlusion in the late time window (6–16 hours from last known well). In this study, the authors confirm the well-known association of collaterals with smaller infarct core volumes and reduced infarct core growth. However, the interaction between collaterals and treatment effect on functional outcome (modified Rankin Scale score, 0–2) could not be found.

In this study, the lack of interaction between collaterals and treatment effect on outcome is considered as an unexpected finding. In our opinion, this finding should be interpreted with caution for several reasons. First, the small and highly selected study population of patients with a very small ischemic core at baseline (median 9.8 [interquartile range, 1.7–23.4]) may have prevented a translation from infarct size to functional outcome, as would have been expected.[2] This highly selected study population is also reflected in a low percentage of absent (1.5%) and poor collaterals (25%), as mentioned by the authors. To fully investigate the association between collaterals and outcome, a cohort with a wider spread in collaterals is recommended.

Second, at baseline, the volume of the perfusion lesion in the group of poor collaterals was significantly larger than in the group of good collaterals. Larger perfusion deficit corresponds with more salvageable tissue and consequently higher expected clinical benefit. For this difference at baseline, no correction model was suggested by the authors.

Finally, collaterals were rated with the binary modified Tan scale. In a post hoc analysis of the MR CLEAN trial (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands),[3] using a 4-point collateral score based on the method of Tan, a shift in the distribution on modified Rankin Scale in favor of the intervention group across all collateral grades has been observed, with the exception of the patient group with absent collaterals. The association between collaterals and neurological outcome may have been diminished due to a dichotomized measure in the study of de Havenon et al,[1] especially when the relatively small sample size of this study is taken into consideration.

We agree with the authors that further study is needed to better understand the role of collaterals for anterior circulation large vessel occlusion stroke patients in the late therapeutic window, but we consider it of clinical importance to investigate the full spectrum of collaterals in the late time window (6–24 hours after last know well). By using a more pragmatic approach and broader inclusion criteria, patients with a much wider range of collaterals, and infarct core volumes, may be included in the MR CLEAN LATE trial (Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands for Late Arrivals).

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Disclosures

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References

1. de Havenon A, Mlynash M, Kim-Tenser MA, Lansberg MG, Leslie-Mazwi T, Christensen S, et al. Results from DEFUSE 3: good collaterals are associated with reduced ischemic core growth but not neurologic outcome. *Stroke*. 2019;50:632–638. doi: 10.1161/STROKEAHA.118.023407
2. Boers AMM, Jansen IGH, Beenen LFM, Devlin TG, San Roman L, Heo JH, et al. Association of follow-up infarct volume with functional outcome in acute ischemic stroke: a pooled analysis of seven randomized trials. *J Neurointerv Surg*. 2018;10:1137–1142. doi: 10.1136/neurintsurg-2017-013724
3. Berkhemer OA, Jansen IG, Beumer D, Fransen PS, van den Berg LA, Yoo AJ, et al; MR CLEAN Investigators. Collateral status on baseline computed tomographic angiography and intra-arterial treatment effect in patients with proximal anterior circulation stroke. *Stroke*. 2016;47:768–776. doi: 10.1161/STROKEAHA.115.011788

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