Disputes & Debates: Editors' Choice

Steven Galetta, MD, FAAN, Section Editor

Editors' note: Early hemodynamic predictors of good outcome and reperfusion injury after endovascular treatment

To better characterize (1) the success of endovascular recanalization and (2) the functional outcomes observed following thrombectomy for acute large vessel occlusion (LVO), Dr. Baracchini and colleagues prospectively followed 185 patients with acute anterior circulation LVO using serial transcranial color-coded ultrasonography postoperatively. All patients were treated within 6 hours of the time they were last known well, had moderate-to-severe deficits (NIHSS >6), and had favorable baseline CT findings (ASPECTS 6–10). After excluding patients who died within 1 week of treatment (8%), the investigators found that successful recanalization (TICI 2b or 3) was associated with a higher probability of normal peak systolic velocities on transcranial ultrasound than partial recanalization (TICI 2a), 96% vs 32%. However, early normalization of the blood flow velocity—irrespective of post-thrombectomy recanalization success—was strongly linked to better long-term outcomes using the modified Rankin Scale. Among those with normal blood flow velocities by 48 hours, 66% of patients with TICI 2b/3 recanalization and 57% of patients with TICI 2a recanalization achieved functional independence by 90 days. Higher velocities also correlated with an increased risk of intracranial hemorrhage, as suggested in previous literature. In response, Drs. Gattringer et al. found the elevated post-thrombectomy peak systolic velocity of the previously occluded artery alarming (279 cm/s in patients with TICI 2b/3). They also commented that other serologic and neuroimaging biomarkers of hyperperfusion injury might prove useful for prognostication after thrombectomy. Dr. Baracchini and colleagues recognize that their observed peak systolic velocities exceed what had been previously published, but they acknowledge that previous studies documented velocities 72 hours after thrombectomy as opposed to immediately following the procedure, as in this investigation.

James E. Siegler III, MD, and Steven Galetta, MD
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Reader response: Early hemodynamic predictors of good outcome and reperfusion injury after endovascular treatment

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We read with interest the study by Baracchini et al.[1] reporting dynamic blood flow velocity (BFV) changes on transcranial Doppler (TCD) after recanalization by mechanical thrombectomy (MT). In line with our work,[2,3] they found abnormal postinterventional BFV to be associated with poor outcome and, specifically, increased BFV indicating subsequent intracerebral bleeding. The main strengths of their study are the availability of (1) neurosonography follow-up, demonstrating increased BFV is mostly a temporary condition with normalization within the first days after MT, and (2) control angiography 24 hours post-thrombectomy. Although these findings point toward hyperperfusion as the most likely pathophysiologic mechanism behind elevated BFV after MT, we are surprised by the mean peak systolic velocity of ~280 cm/sec

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immediately post-thrombectomy. Such impressive elevations have not been observed in previous TCD studies a few hours post-recanalization.[2–4] Hence, what was the exact time point of the first TCD and was the increased BFV observed in the whole artery segment or rather locally? Further serial TCD studies in combination with postinterventional neuroimaging, including perfusion scans[5] and (blood) biomarkers for endothelial/blood-brain-barrier dysfunction, are warranted to better understand the pathophysiology of such findings. This could help individualizing blood pressure management post-thrombectomy, using an easy repeatable bedside tool (i.e., more strict control in hyperperfusion to avoid bleeding vs permissive hypertension in case of dampened BFV to augment collateral perfusion).

1. Baracchini C, Farina F, Palmieri A, et al. Early hemodynamic predictors of good outcome and reperfusion injury after endovascular treatment. Neurology 2019;92:e2774–e2783.
2. Kneihsl M, Niederkorn K, Deutschmann H, et al. Abnormal blood flow on transcranial duplex sonography predicts poor outcome after stroke thrombectomy. Stroke 2018;49:2780–2782.
3. Kneihsl M, Niederkorn K, Deutschmann H, et al. Increased middle cerebral artery mean blood flow velocity index after stroke thrombectomy indicates increased risk for intracranial hemorrhage. J Neurointerv Surg 2018;10:882–887.
4. Ikenberg B, Scharsich B, Mönch S, et al. Neurosonography after mechanical thrombectomy for acute stroke treatment. J Neuroimaging 2019;29:364–370.
5. Yu S, Liebeskind DS, Dua S, et al. Postischemic hyperperfusion on arterial spin labeled perfusion MRI is linked to hemorrhagic transformation in stroke. J Cereb Blood Flow Metab 2015;35:630–637.

Author response: Early hemodynamic predictors of good outcome and reperfusion injury after endovascular treatment

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We apologize for a late response to Gattringer et al.'s comment to our study.[1] First, the velocity measurements on the recanalized vessel were performed along the entire segment, thus avoiding misinterpretation with residual stenosis. Second, high-velocity values were also encountered in patients with TICI-3 (complete recanalization) and in recanalized M2 occlusions, pointing toward hyperperfusion. Two technicalities might have also influenced our mean peak systolic findings: angle correction and ultrasound contrast agent. Another point should be mentioned: our first postprocedural ultrasonographic examination was performed immediately after mechanical thrombectomy, in contrast to previous studies that report the baseline examination within 72 hours.[2–4] Yet, a common message is conveyed by these studies: independently from absolute velocity values, the velocity ratio between the recanalized vs contralateral arterial segment proved to be a strong and early predictor of clinical outcome in patients with stroke undergoing mechanical thrombectomy. We do hope that a more extensive application of noninvasive dynamic studies will improve the management of these patients.

1. Baracchini C, Farina F, Palmieri A, et al. Early hemodynamic predictors of good outcome and reperfusion injury after endovascular treatment. Neurology 2019;92:e2774–e2783.
2. Kneihsl M, Niederkorn K, Deutschmann H, et al. Abnormal blood flow on transcranial duplex sonography predicts poor outcome after stroke thrombectomy. Stroke 2018;49:2780–2782.
3. Kneihsl M, Niederkorn K, Deutschmann H, et al. Increased middle cerebral artery mean blood flow velocity index after stroke thrombectomy indicates increased risk for intracranial hemorrhage. J Neurointerv Surg 2018;10:882–887.
4. Ikenberg B, Scharsich B, Mönch S, et al. Neurosonography after mechanical thrombectomy for acute stroke treatment. J Neuroimaging 2019;29:364–370.

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Editors' note: MRI predicts intracranial hemorrhage in patients who receive long-term oral anticoagulation

For the HERO investigators, Drs. Martí-Fàbregas et al. report their results from the prospective, multicenter observational cohort that sought to estimate the long-term risk of intracranial hemorrhage (ICH) among patients aged >65 years with cardioembolic stroke and treated with an oral anticoagulant. Nearly 1,000 patients were followed over mean of 2 years. Ninety percent of patients had atrial fibrillation as the primary indication for anticoagulation, and two-thirds of patients were treated using warfarin. The annualized rate of ICH was 1%/yr—as has been previously reported—with a higher rate among patients with cerebral microhemorrhages (2.5%/yr with >1 microhemorrhage), with moderate/severe microvascular changes on MRI (2%/yr), and with both of these findings (3.8%/yr). Dr. Vilanilam and colleagues highlight a study limitation that included patients were not evaluated using identical MRI magnet strength (16% underwent 3T MRI) or MRI sequences (49% underwent SWI; 91% underwent GRE with or without SWI). The authors acknowledge that this could have affected their findings and stressed the uniformity of MRI magnet strength and consistency of sequences for future studies.

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Reader response: MRI predicts intracranial hemorrhage in patients who receive long-term oral anticoagulation

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We read, with interest, the impressive study by Martí-Fàbregas et al.[1] As discussed, the HERO study and the CROMIS-2 study together have elaborated on the safety of oral anticoagulation (OA) in patients with cerebral microbleeds (CMBs).[1,2]

The nonuniformity of brain MRI protocols was discussed as a limitation in this study.[1] This is of importance, as CMBs are radiologic constructs and pathologically represent perivascular hemorrhages.[3] It is also well known that a higher magnetic strength and susceptibility-weighted imaging (SWI) sequence are associated with a higher burden of CMBs.[4] Where unification of imaging protocols is impossible due to the retrospective nature of studies or due to technical constraints in prospective studies, a statistical correction for MRI field strength and specific blood-sensitive sequences will add novelty and increase confidence in the results. In this study,[1] there were about 150 (16%) patients who underwent MRI with a 3T scanner and about 450 patients with an SWI sequence. It is unclear whether statistical adjustment for MRI field strength or blood-sensitive sequence was performed. To our knowledge, only 1 study to date has performed this correction for technical confounders.[5]

1. Martí-Fàbregas J, Medrano-Martorell S, Merino E, et al. MRI predicts intracranial hemorrhage in patients who receive long-term oral anticoagulation. Neurology 2019;92:e2432–e2443.
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Author response: MRI predicts intracranial hemorrhage in patients who receive long-term oral anticoagulation

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We thank Vilanilam et al. for their interest in our study. As reflected in our study,[1] the heterogeneity of the images obtained, both in relation to the MRI field strength and in the MRI sequences used, is an important limitation of our study. We are therefore in complete agreement on the need for future studies to consider the technical characteristics of obtaining and evaluating images. However, our study reflects the reality of care—at least in Spain—where each institution updates its MRI devices and uses the sequences used for each clinical reality according to local protocols.

1. Martí-Fàbregas J, Medrano-Martorell S, Merino E, et al. MRI predicts intracranial hemorrhage in patients who receive long-term oral anticoagulation. Neurology 2019;92:e2432–e2443.

RETRACTIONS

Retraction: High prevalence of vitamin D deficiency and reduced bone mass in Parkinson's disease

Neurology® 2020;94:804. doi:10.1212/WNL.0000000000009358

The editors of *Neurology* retract the article "High prevalence of vitamin D deficiency and reduced bone mass in Parkinson's disease" by Sato et al.[1]

An expression of concern was published on September 6, 2017,[2] to alert readers to possible unreliability because of known issues leading to several retractions of papers by Y. Sato et al. Further statistical analyses by our editors found implausible reporting of the same measurements on key endpoints in different control groups in different manuscripts. In addition, although the paper stated that the Human Investigation Committee of the Futase Social Insurance Hospital approved the study, the hospital did not have an ethics committee at that time.

References

1. Sato Y, Kikuyama M, Oizumi K. High prevalence of vitamin D deficiency and reduced bone mass in Parkinson's disease. Neurology 1997;49:1273–1278.
2. Does compensatory hyperparathyroidism predispose to ischemic stroke? Decreased bone mass and increased bone turnover with valproate therapy in adults with epilepsy; An alternative to vitamin D supplementation to prevent fractures in patients with MS; High prevalence of vitamin D deficiency and reduced bone mass in Parkinson's disease [Expression of Concern]. Neurology 2017;89:1312.

Retraction: Decreased bone mass and increased bone turnover with valproate therapy in adults with epilepsy

Neurology® 2020;94:804–805. doi:10.1212/WNL.0000000000009359

The editors of *Neurology* retract the article "Decreased bone mass and increased bone turnover with valproate therapy in adults with epilepsy" by Sato et al.[1]

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An expression of concern was published on September 6, 2017[2] to alert readers to possible unreliability because of known issues leading to several retractions of papers by Y. Sato et al. We have since been notified that the president of Kurume University, where the research for this article was done, established a formal investigative committee that investigated papers written during Dr. Sato's tenure at Kurume University. The committee concluded the article was falsified and recommended retraction.

References

1. Sato Y, Kondo I, Ishida S, et al. Decreased bone mass and increased bone turnover with valproate therapy in adults with epilepsy. Neurology 2001;57:445–449.
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Retraction: Does compensatory hyperparathyroidism predispose to ischemic stroke?

Neurology® 2020;94:805. doi:10.1212/WNL.0000000000009357

The editors of *Neurology* retract the article "Does compensatory hyperparathyroidism predispose to ischemic stroke?" by Sato et al.[1]

An expression of concern was published on September 6, 2017,[2] to alert readers to possible unreliability because of known issues leading to several retractions of papers by Y. Sato et al. We have since been notified that the president of Kurume University, where the research for this article was done, established a formal investigative committee that investigated papers written during Dr. Sato's tenure at Kurume University. The committee concluded the article was classified as malpractice due to inappropriate authorship and recommended retraction. In addition, the work was conducted without ethics approval, as Kurume University did not have an ethics committee at the time. The committee found that none of the co-authors of Dr. Sato were involved in research misconduct.

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1. Sato Y, Kaji M, Metoki N, Satoh K, Iwamoto J. Does compensatory hyperparathyroidism predispose to ischemic stroke? Neurology 2003;60:626–629.
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Retraction: Does compensatory hyperparathyroidism predispose to ischemic stroke?

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