New Insights in Neuroprotective Acute Stroke Treatment

In this issue, Amaro et al. [1] from Spain presented an outstanding randomized clinical trial on 411 alteplase-treated patients, part of them ($n = 211$) also received 1,000 mg uric acid or placebo ($n = 200$) before the end of the alteplase treatment. In this study, a smaller group of patients (40 placebo and 44 uric acid) were followed according to the results of a pretreatment CT-angiography showing a proximal carotid occlusion. Excellent collaterals were defined as 100% collateral supply on pretreatment CT-angiography. Regression models assessed the interaction between therapy (uric acid/placebo) and collaterals on the main outcome (ordinal-modified Rankin Scale shift at 90 days). Overall, excellent collaterals were associated with improved outcome. There was a significant interaction between therapy and pretreatment collaterals (p interaction = 0.02) for the prediction of improved modified Rankin Scale shift. The largest treatment contrast in favor of uric acid was found in patients with excellent collaterals (adjusted OR 9.2; 95% CI 1.23–68.6; $p = 0.03$). The authors suggest that collaterals were associated with the neuroprotective effect of uric acid therapy, highlighting the importance of assessing the collateral status in neuroprotection trials. Given the negative results of many studies in recent decades, designed to evaluate the effect of early neuroprotective drugs for the benefit of stroke outcome, the authors need to be applauded for their new and careful study design. Hopefully other similar sophisticatedly prepared investigations will follow and confirm recent investigators' hope to use neuroprotective agents for the benefit of stroke patients.

Among the other studies, we recommend 2 particularly interesting contributions: Tashiro et al. [2] from Japan, who studied adult moyamoya disease patients with superficial temporal artery-middle cerebral artery anastomosis. They observed a complex and unique pathophysiological condition, the so-called “watershed shift (WS) phenomenon,” which is defined as a paradoxical decrease in the cerebral blood flow at the adjacent cortex near the site of local cerebral hyperperfusion. The incidence of the WS phenomenon was as high as 10.9% after STA-MCA anastomosis for adult moyamoya disease. The clinical outcome of the WS phenomenon is generally favorable, but there is a potential risk for perioperative cerebral infarction. Thus, routine cerebral blood flow measurement in the acute stage after revascularization surgery is recommended to avoid surgical complications.

Another study was presented by Renard et al. [3] from France. Stimulated by recent observations of finger-like projections and subarachnoid hemorrhage extension of lobar intracerebral hemorrhage on acute CT together with ApoE4 genotype in a prediction model for histopathologically proven cerebral amyloid angiopathy, they re-studied MRI scans from 46 patients with similar findings. In acute lobar intracerebral hemorrhage patients, finger-like projection and subarachnoid hemorrhage extension on acute/early subacute phase MRI are associated with probable cerebral amyloid angiopathy diagnosis.

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References

- 1 Amaro S, Renú A, Laredo C, Castellanos M, Arenillas JF, Llull L, et al.; on behalf of the URICO-ICTUS investigators. Relevance of collaterals for the success of neuroprotective therapies in acute ischemic stroke: insights from the randomized URICO-ICTUS trial. *Cerebrovasc Dis*. 2019;47:171–7.
- 2 Tashiro R, Fujimura M, Kameyama M, Mugikura S, Endo H, Takeuchi Y, et al. Incidence and risk factors of the watershed shift phenomenon after superficial temporal artery-middle cerebral artery anastomosis for adult moyamoya disease. *Cerebrovasc Dis*. 2019;47:178–87.
- 3 Renard D, Parvu T, Thouvenot E. Finger-like projections in lobar haemorrhage on early magnetic resonance imaging is associated with probable cerebral amyloid angiopathy. *Cerebrovasc Dis*. 2019;47:121–6.