



LETTER TO THE EDITOR

Ischemic stroke and homocysteine: To test or not to test?



AVC isquémico e homocisteinemia: testar ou não estar?

Ischemic stroke is the second leading cause of death in patients under 65 years old and contributes significantly to loss of quality of life, since most stroke survivors live with disabilities.¹

Studies have shown that homocysteine levels are elevated in young patients with stroke and that high homocysteinemia is a cardiovascular risk factor independent of other risk factors such as diabetes, smoking, or hypertension. Also, patients with high homocysteine levels are more likely to have a vascular event before the age of 30.²

It has also been shown that some vitamin B deficiencies are associated with increased homocysteine levels, since these vitamins are a cofactor of homocysteine metabolism.³

Randomized clinical trials have set out to understand the benefit of lowering homocysteine using vitamin B supplements. One such trial, VITATOPS,⁴ concluded that the impact of lowering homocysteine in preventing cardiovascular events was very low and that treatment with vitamin B supplements was of dubious benefit in preventing major vascular events among patients with a history of recent stroke or transient ischemic attack.

Hence, measuring homocysteine levels is not consensual in young patients admitted with a diagnosis of ischemic stroke.

To address this issue, we conducted an exploratory observational retrospective study, including all patients aged under 65 years admitted to a tertiary hospital due to stroke. Using data from electronic records, we aimed to determine the frequency of requests for homocysteine levels, and how many showed high homocysteine levels ($>12.0 \mu\text{mol/l}$).

Over a period of one year, 850 patients were admitted with ischemic stroke. Of those, 147 (17%) were aged under 65 years and were analyzed. The majority (71%) were male, 42 (28%) were female, and mean age was 52.8 ± 10.0 years.

Homocysteine levels were determined in 72 patients (48.97%). The median level was $12.9 \pm 10.91 \mu\text{mol/l}$. Using

a cut-off of $12.0 \mu\text{mol/l}$, 40 (55.56%) of these patients had high levels. However, only four (8%) patients with high homocysteinemia had no other risk factors for ischemic stroke, such as hypertension, diabetes, smoking, or dyslipidemia. The majority of patients with high homocysteine levels were aged between 30 and 39 and between 60 and 65 years.

Even when considering the 15 (out of 46) stroke patients under 50 years old with hyperhomocysteinemia, only three (20%) had no other risk factor.

In our center, homocysteine is included in the protocol of 'Stroke in young patients'. This might overestimate the frequency of requesting this analysis, which could be lower in other hospitals. We consider homocysteinemia should only be requested in young patients with ischemic stroke if no other risk factor is present and/or for research purposes. Besides, since there is no direct treatment for hyperhomocysteinemia, the cost-effectiveness of such testing in clinical practice is questionable..

Conflicts of interest

Mariana Alves has received support for attending meetings and/or travel from Boehringer-Ingelheim, Bristol-Myers-Squibb, Merck Sharp & Dohme, AstraZeneca, Tecnimede and Bayer. Sofia Julião has received support for attending meetings and/or travel from Bayer and Sanofi.

References

1. Niazi F, Aslam A, Khattak S, et al. Frequency of homocysteinemia in young ischemic stroke patients and its relationship with the early outcome of a stroke. *Cureus*. 2019;11:1–10.
2. Ganguly P, Alam SF. Role of homocysteine in the development of cardiovascular disease. *Nutr J*. 2015;14:1–10.
3. Palma Reis R. Homocysteinemia and vascular disease: where we stand in 2022. *Rev Port Cardiol*. 2022;41:821–2.
4. VITATOPS Trial Study Group. VITATOPS, the VITamins TO Prevent Stroke Trial: rationale and design of a randomised trial of B-vitamin therapy in patients with recent transient ischaemic attack or stroke (NCT00097669) (ISRCTN74743444). *Int J Stroke*. 2007;2:144–50.

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