Letter by Zito et al Regarding Article, “Warfarin Versus Aspirin for Prevention of Cognitive Decline in Atrial Fibrillation: Randomized Controlled Trial (Birmingham Atrial Fibrillation Treatment of the Aged Study)”

To the Editor:

We read with great interest the article of Mavaddat et al reporting no differences between warfarin and aspirin on progressive cognitive decline as measured by the Mini-Mental State Examination (MMSE) in a large cohort of elderly people with atrial fibrillation.

Overall, the relationship between antithrombotic agents and cognitive function remains unclear with conflicting results in the literature, which may be the consequence of the lack of a thorough evaluation of geriatric domains shown to affect cognitive function over time. The latter is often neglected in vascular trials, possibly introducing significant bias in the analysis. Therefore, we feel that additional information is needed from the work of Mavaddat et al to fully appreciate the effects of anticoagulation or antiplatelets on cognitive function.

First, a baseline and follow-up comprehensive geriatric assessment of the study population is missing while decisive for the purposes of the study. The MMSE is not the ideal test to diagnose cognitive impairment and presents significant inter- and intrapatient variations because of several cofactors or comorbidities unrelated to cognition. Functional impairment (measured for instance by activities of daily living and instrumental activities of daily living) and cognitive reserve represent well-known independent risk factors of cognitive decline, and depression or other mood-affecting conditions can generate significant bias when administering the MMSE or any other neuropsychological test.

Finally, if a deterioration of ≤4 points in MMSE has to be expected for a 2-year time in about 59% of the population, the relative stability of the mean MMSE, largely unchanged from baseline, may point to selection bias. Because MMSE does not supply information about the cause of cognitive decline, some of the included patients could be affected by neurodegenerative disorders (ie, Alzheimer disease), and therefore significant changes in MMSE would be expected >33 months. Because the advent of new oral anticoagulants for stroke prevention in atrial fibrillation is expected to significantly improve cerebrovascular outcomes compared with warfarin, a thorough geriatric evaluation to appreciate the effects (if any) of anticoagulant treatment on cognition is essential before discarding any potential benefit. A better characterization of cognitive decline mechanisms (ie, vascular, neurodegenerative, or mixed) by neuroimaging of the brain could further unravel different effects on cognition by anticoagulants depending on background physiopathology.

Disclosures

None.

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