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Reply: Transcatheter aortic valve implantation and covert brain injury: does silence equal reassurance?

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We sincerely thank Dr Pyrpyris and colleagues for their thoughtful comments[1] regarding our recent publication, the AUREA trial[2].

We fully agree with their perspective on the complex and multifactorial nature of cerebral microembolism during transcatheter aortic valve implantation (TAVI) procedures. Despite significant procedural advances, the cerebral impact of microembolic events, often silent, remains a major concern, particularly in elderly patients already at risk of cognitive impairment.

In line with the authors' comments, we emphasise the critical need to identify novel and reliable biomarkers of cerebral microembolism after TAVI. Current approaches to detect brain injury, including magnetic resonance imaging (MRI), though highly sensitive, are not always practical in daily clinical settings due to availability, cost, and patient frailty. Developing blood biomarkers such as glial fibrillary acidic protein, neurofilament light chain, tau and its peptides, and β-synuclein[3] that are not only sensitive and specific but also easy to use and interpret could greatly enhance early detection, monitoring, and risk stratification of patients undergoing TAVI, as well as prediction of complications and clinical outcomes at follow-up.

In addition, artificial intelligence-enhanced imaging enables accurate quantification of vascular and valvular calcium burden[4]. Beyond improving procedural planning, it may allow identification of patients at highest embolic risk and support tailored neuroprotective strategies.

Equally important is the implementation of standardised neurocognitive assessments before and after the procedure. Cognitive outcomes after TAVI are variable and may depend on multiple factors, including baseline status, cerebral perfusion changes, embolic burden, and systemic inflammation. Objective neurological testing, both clinical and through validated cognitive questionnaires, should be routinely incorporated in TAVI trials and, when feasible, in clinical practice[5]. This would allow more accurate characterisation of cognitive trajectories and identification of patients at risk of deterioration or, conversely, those likely to experience neurocognitive improvement.

We also fully agree on the potential role of cerebral embolic protection devices (CEPDs). Although current evidence on clinical outcomes remains mixed, these devices consistently demonstrate their potential to reduce cerebral lesion volume and embolic burden[6]. The integration of CEPDs in TAVI, especially in selected high-risk patients or as part of comparative strategy trials (ClinicalTrials.gov: NCT05873816, NCT03130491), may prove beneficial in minimising microembolisation and its consequences[7]. Furthermore, combining CEPDs with refined antithrombotic approaches could offer synergistic protection and deserves exploration.

Finally, as the authors mention, the identification of pharmacological strategies targeting both thrombotic and inflammatory pathways post-TAVI is a promising avenue. The interplay between prosthetic material, residual native leaflets, and flow dynamics can trigger proinflammatory and prothrombotic cascades, potentially leading to leaflet thrombosis and cerebral embolisation. Recent results with colchicine are promising, although they should be interpreted with caution given the reported increased risk of stroke in treated patients[8]. Further studies evaluating

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combinations of antiplatelet agents (ClinicalTrials.gov: NCT05283356), anticoagulants, and anti-inflammatory therapies (NCT06076824) are warranted to define optimal post-TAVI regimens that balance ischaemic, embolic, bleeding, and cognitive risks.

In conclusion, the prevention and understanding of covert brain injury in the TAVI population must become a multidimensional effort: identifying feasible biomarkers, integrating neurocognitive assessment, evaluating device-based protection, and refining pharmacological strategies.

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Conflict of interest statement

The authors have no conflicts of interest to declare regarding this manuscript.

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