To the Editor:

Thaler and Wahl repeated characterize the CLOSURE I trial as having gone wrong. Such moralistic (mis)characterizations betray the prevalent bias toward devices in patients with cryptogenic stroke and a patent foramen ovale (PFO). Although disappointing to some, better to say CLOSURE I failed to prove that the StarFlex device was superior to medical therapy for stroke prevention, in this particular cryptogenic population with PFO. This result is neither wrong nor right.

Wrong patient–Contrary to clinical practice, CLOSURE I used an independently adjudicated and rigorous definition of transient ischemic attack (TIA). In clinical practice, failure to use a rigorous definition of TIA can lead to inappropriate device closure of a PFO for spells unrelated to ischemia or paradoxical embolism. If by wrong, Thaler and Wahl also meant patients were randomized who were more or less likely to have paradoxical embolism that is indeed possible, then the population could be optimized. It is another matter altogether to demonstrate that device is superior to medical therapy even in a population optimized for paradoxical embolism.

Wrong device–Devices indeed differ. For example, the Amplatzer device being used in RESPECT has recently been cited by the Food and Drug Administration for potentially fatal erosions, which may occur several years after implantation. Thaler and Wahl were misled by the reports of late erosion of an Amplatzer septal occluder device 6 years after placement. Late erosion of an Amplatzer septal occluder device 6 years after placement. J Thorac Cardiovasc Surg. 2012;142:221–222.

Wrong outcome assumptions–We agree stroke is the best endpoint. Possibly a stroke only event driven outcome will be more reliable cohort series. Furthermore, residual shunting did not seem to play a role in recurrent neurological events.

Wrong outcome assumptions–We agree stroke is the best end point. Possibly a stroke only event driven outcome will be more reliable and have sufficient power to be conclusive. We also agree that a longer follow-up or a larger sample size would be desirable (but possibly not feasible). However, in CLOSURE I, the stroke rates were identical at 2 years making it unclear how long patients would need to be followed to be confident there is no significant difference. Of note, a recent propensity observational study from Bern found no difference in stroke outcome at 9 years; the favorable outcome claimed for device was driven by (unspecified) TIA.

Despite disingenuous protests from some, many CLOSURE I patients possibly would have received off-label devices with no apparent benefit before this trial. CLOSURE I suggests that patient selection criteria for device closure must be restricted and more narrowly defined. Before CLOSURE I, we do not believe interventionalists were restricting device closure only to patients who met the humanitarian device exemption criteria, or who had magnetic resonance imaging demonstrated cortical infarction, or who first saw a board-certified neurologist. Would it be wrong to think reimbursement was a factor? Will Centers for Medicare & Medicaid Services require interventionalists to follow more restricted selection criteria if a device is approved? We hope the ongoing trials will build on the foundation laid by CLOSURE I and identify specific criteria for a subset of cryptogenic stroke patients who may benefit from device closure. Thaler and Wahl are right to say that no single trial provides all the answers (dangerous knowledge). But treating patients based on opinion or without considering all the evidence would be truly wrong.

Disclosures

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Letter by Furlan Regarding "Critique of Closure or Medical Therapy for Cryptogenic Stroke With Patent Foramen Ovale: The Hole Truth?"
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