Percutaneous Closure of Patent Foramen Ovale in Patients With Paradoxical Embolism

To the Editor:

Windecker et al reported a series of 80 stroke patients with patent foramen ovale (PFO) treated by percutaneous closure1 and recommended a randomized trial. The accompanying editorial is less measured.2 Its author does not mention antplatelet treatment as a management option, despite acknowledging that PFO is “almost invariably benign.” He postulates that a randomized trial should compare anticoagulation and closure and that young patients with cryptogenic stroke and large PFO should currently be referred for closure if unsuitable for anticoagulant therapy.

The low recurrence rate in patients with cryptogenic stroke and PFO presents difficulties in trial design. A benign natural history means that large randomized trials will be required to demonstrate a significant benefit of interventional techniques. It also has implications for preliminary claims made on the basis of observational data. In the study by Windecker et al, annual risk of recurrence (using a combined end point of transient ischemic attack, cerebrovascular accident, and peripheral embolism) was 3.4%, the same as that reported in a medically treated cohort by a French multicenter group.3 In the French study, patients with PFO alone (n=69) remained event free; only patients with an associated atrial septal aneurysm (ASA) developed recurrence. Figures from the Lausanne Stroke Registry are similar.4 Both these series included patients treated with aspirin or warfarin, and neither found a significant difference between the 2 treatments.

The finding that persistent shunt is predictive of recurrence is important and warrants proper consideration of open surgery; reported rates of residual shunt after surgery are lower than those after percutaneous closure.5 No significant differences were found between patients who had only PFO and those with PFO and ASA in terms of recurrence, yet evidence from both case-control and follow-up studies indicates that both lesions in conjunction confer a particularly high risk. The numbers treated are too small to determine whether percutaneous closure of PFO is sufficient or whether additional correction of the ASA will improve prognosis.

Current recommendations for therapy vary considerably: a perfect backdrop for a randomized trial. This will be difficult to design and perform in the context of the observational data currently available. The considerations above dictate that antiplatelet therapy must be one of the strategies studied. Adaptive randomization techniques may enable both patients with small lesions and transient isolated symptoms and patients with larger lesions and recurrent stroke to be randomized to appropriate comparative therapies.

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Response

Overell et al suggest that the higher recurrence rate in patients with residual shunt in our study should give proper consideration for open surgery. The residual shunt rate in the study they quoted was 10% after surgical closure compared with 27% after percutaneous closure of patent foramen ovale (PFO).2 However, residual shunts were trivial in the majority of cases (16%, 1 to 5 bubbles crossing), leaving only 11% of patients with a significant leak (>5 bubbles crossing). What matters to patients are clinical end points as defined by procedural complications and recurrent thromboembolic events. The largest surgical PFO closure series (91 patients) from the Mayo Clinic2 reported an overall freedom from recurrence of 93% at 1 year and 83% at 4 years compared with 92% and 84%, respectively, in our study. Surgical PFO closure was associated with the typical complications of open heart surgery, including atrial fibrillation (12%), pericardial effusion requiring drainage (4%), reperfusion for bleeding (3%), and wound infection (1%), which amounted to a 21% morbidity rate.

Overell et al state that the number of patients with PFO and atrial septal aneurysm in our study (n=20) was too small to determine whether percutaneous PFO closure suffices. Although we acknowledge the low numbers treated in our study, the published data on surgical treatment of atrial septal aneurysm is similarly scarce, with only 17 patients treated in the Mayo Clinic series.3 The feasibility and efficacy of percutaneous treatment of atrial septal aneurysm with a right-to-left shunt is currently under investigation in a larger patient cohort.

We initiated an international, multicenter, randomized trial comparing the efficacy of medical treatment with percutaneous PFO closure in patients with Cryptogenic embolism (PC trial). Groups like that of Overell et al are invited to participate. Until results from this or similar trials are available, percutaneous and surgical PFO closure should be considered investigational and performed only in appropriately selected and fully informed patients.

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