To Close or Not to Close: PFO’s and CVA Prevention
Allison Wolfe, MD

Story from the Front Lines:

A 65 year old man with a history of COPD, hyperlipidemia, and hypertension was scheduled for a hospital follow-up to ensure he was still doing well and recovering from a recent hospital admission. He was admitted to an outside facility one week prior to our visit. He presented at that facility with slurred speech and aphasia and was diagnosed with a left MCA ischemic infarct. TPA was administered with a positive outcome: he spent one week in the hospital and made a remarkable recovery. The only residual defect was numbness in three digits in his right hand impacting his dexterity, but improving with therapy. There was no immediately obvious cause for his stroke: no deep venous thrombosis was seen on ultrasound, carotid ultrasound showed normal arteries, he did not have a thrombus in his left atrium, and a hypercoagulable work-up was pending. However, he was found to have a patent foramen ovale (PFO) on trans-esophageal echocardiography (TEE). He reported that the cardiologists at the OSH wanted to close this PFO to prevent further strokes and was under the impression that by closing his PFO any future clots would be shunted to his lungs. He seemed to be enthusiastic about this course of treatment and unaware of the data surrounding the efficacy of this as well as the risks inherent in the procedure itself.

Teachable Moment:

Cerebral vascular accidents (CVA) cause more than 130,000 deaths per year and is the fourth leading cause of death in the United States.\(^1\) In 33% of strokes, a cause is never found, leaving these patients and their physicians with the unsatisfactory diagnosis of cryptogenic stroke.\(^2\) Unfortunately, physicians and patients alike may find this diagnosis frustrating. In these patients further work-up with a TEE may be performed to exclude a high-risk cardiac cause (e.g. left atrial thrombus, aortic thrombi, or PFO).\(^3\) Some have proposed that a proportion of cryptogenic strokes may actually be caused by a venous embolism passing through a PFO becoming an arterial embolus.\(^4\) Despite the mechanical plausibility of this theory, the role of PFO in CVA remains unclear and less than 10% of people with a PFO were found to have a DVT.\(^5\) The ambiguity of the role of PFO in CVA has led to a wide range of therapies from surgical intervention to anticoagulation to no treatment at all.

In CLOSURE 1, the first multicenter, randomized controlled trial addressing this issue, researchers tried to determine what kind of therapy should be pursued in patients with cryptogenic stroke or transient ischemic attack (TIA) and a PFO: medical therapy or PFO closure using the STARFlex Septal Closure System. They found no significant difference in the primary end point: a composite of stroke or transient ischemic attack during 2 years of follow-up, death from any cause during the first 30 days, or death from neurologic causes between 31 days and 2 years (5.5 versus 6.8 percent, hazard ratio [HR] 0.78, 95% CI 0.45-1.35).\(^4\) Two other randomized trials, RESPECT and PC, also failed to show a reduction in recurrent stroke with PFO closure using the Amplatzer PFO occluder device.\(^6,7\)

In the CLOSURE 1 trial, risks for PFO closure compared to medical therapy alone included atrial fibrillation (5.7% vs 0.7%) and major vascular complications (3.2% vs 0%).\(^4\) Though rates of atrial fibrillation were lower in the RESPECT and PC trials, concerns
remain given the vascular complications reported in CLOSURE 1 and a trend toward a higher rate of right atrial thrombus and pulmonary embolism with PFO closure in RESPECT.

The role of PFO in the etiology of cryptogenic stroke remains unclear. The existing evidence does not show a clear benefit in recurrent stroke prevention with PFO closure compared to medical therapy alone. Furthermore, the possibility of net harm has not been excluded given the low event rate in randomized trials designed to address this question. The perils associated with PFO closure, while uncommon, can be serious and may well outweigh the benefit of closure in many patients.

References: