Title
Patent foramen ovale: What cardiologists and neurologists need to know

Journal
Catheterization and Cardiovascular Interventions, 93(6)

ISSN
1522-1946

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Publication Date
2019-05-01

DOI
10.1002/ccd.28293

Peer reviewed

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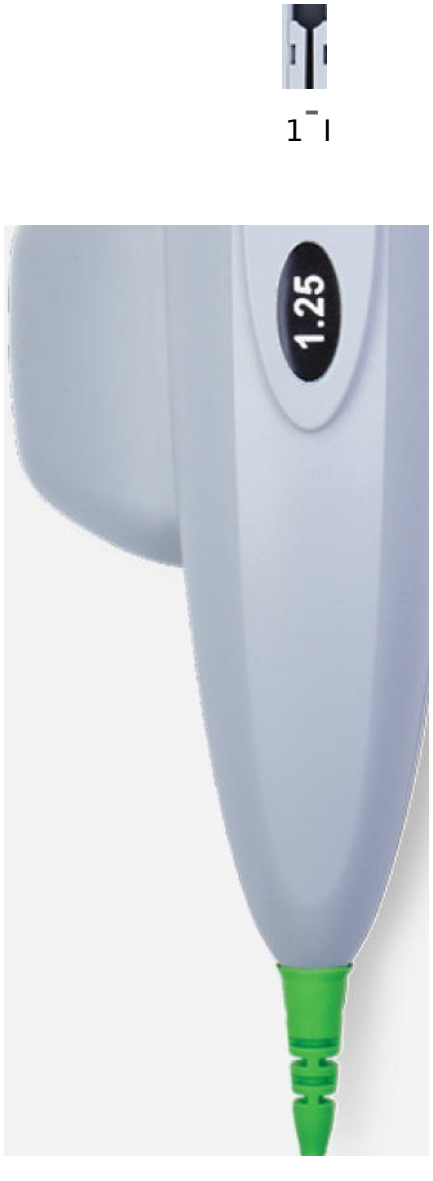

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Received: 1 April 2019Accepted: 4 April 2019

DOI: 10.1002/ccd.28293

EDITORIALCOMMENT

WILEY

Patent foramen ovale: What cardiologists and neurologists need to know

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a tran- sient ischemic attack is indistinguishable from a complex migraine. Both have transient neurologic deficits with a normal MRI.
n for closure. A stroke or peripheral embolus associated with a PFO is the indication for closure.
he warning that about 1 in 500 cases require device removal through open-heart surgery.

Percutaneous patent foramen ovale (PFO) closure is a simple and safe outpatient procedure that replaces the need for open-heart surgery. There are now four randomized clinical trials (RCTs), which show that device closure is preferable to standard-of-care medical therapy to prevent recurrent stroke in patients with stroke of unclear etiology associated with a PFO. In addition to stroke, several other conditions are associated with a PFO; the most common are migraine with aura and transient neurologic deficits without cephalgia, such as visual migraine, recurrent paresthesia, or aphasia. The jury is still out whether PFO should be closed to prevent migraine, but a new trial is scheduled to start this year that will address this issue and clarify the target patient population. PFO can also cause profound hypoxemia, which is a form of congenital right-to-left shunt and should not require a RCT to prove that closure is the appropriate method of treatment.

There are several interesting facts about PFO that may be useful for doctors to discuss with their patients. Since 20% of all individuals have a PFO, it is by far the most common congenital heart defect. In comparison, a bicuspid aortic valve occurs in 1–2% of the general population. Because a PFO does not create a murmur, most people go through life without knowing that they have one. However, 50% of people who have migraine with aura have a PFO, so you can use this clinical association to consider the diagnosis. The estimated occurrence of stroke per year is about 1 in 1000 people with a PFO, so longitudinal studies of populations are unlikely to identify an increased incidence. Once someone has had a stroke, the risk of recurrent stroke is 1% per year, and this appears to be continuous; that is, the risk is 10% at 10 years and presumably the risk continues at this rate. For a young person with a life expectancy of 50 more years, extrapo- lating from the RCTs suggests that there will be a 50% risk of stroke recurrence in that person's lifetime. The frequency of PFO in people who present with cryptogenic stroke is 60%, and if they have migraine with frequent aura, this increases to 93%.[1]

The PFO itself does not cause a stroke but rather serves as the pathway for a right-to-left shunt. If a venous clot is present secondary to conditions such as deep vein thrombosis, varicose veins, or prolonged immobility from a plane or car trip, then the thrombus is able to enter the arterial circulation through the interatrial shunt. This may explain why migraineurs have a higher risk of stroke. Migraine with aura is an indication that a PFO pathway may be present, and the presence of risk factors for thrombus formation, such as exogenous estrogen use (birth control or hormone replacement therapy), smoking, or varicose veins (any woman who had a child), provides the ammunition to enter the pathway and produces an embolic stroke, renal infarction, or peripheral embolus.

Although 20% of people in general have a PFO, the defect is genetically distributed, and 60% of first-degree relatives of a proband with a PFO-associated condition will have a PFO. Daughters of a PFO-

associatedstrokepatientshouldbetestedforthepresenceofaPFO,
andifoneispresent,Iadvisethemtoavoidusingexogenousestrogen (birthcontrolpillsorcervicalrings).

Transesophagealechocardiography(TEE) underestimates PFO sizecomparedwith a sizing balloon, so that theanatomicalsize by ultra-soundshouldnotbeacriteriaforclosure.Alargestrokecanoccureven witha"small"PFO.Thesizeofthethrombusisagreaterdeterminant of strokemagnitudethanPFOsize.[2] ThepresenceofaPFO-associatedstrokeis enough to justify closure. It is inconsistent with the data to statethatthePFOissmallbyTEEandthereforecouldnotbeculpable.

TheriskofaPFOclosureprocedureshouldbeminimal(<1%).Themajor concern is a 5% risk of new-onset atrial fibrillation 2–6weekspost-procedure due to irritation from the device. A second concern is that 1 in 500 patients develop excessive scar tissue with chestpain,or more rarely, atrial perforation with tamponade, which requires surgical removal of the PFO closure device. Perhaps, a 0.2% risk of open-heart surgery is not terrible as, without these devices,allpatients would have undergone surgery or remained at elevatedrisk

for recurrent stroke. However, 0.2% is not a negligible risk, and all patients should be warned of this during the informed consent process. The development of new devices without these drawbacks provides an opportunity for innovative thinkers.

With these observations as background, let us interprettheaccompanying article by Snidjer et al (Percutaneous patent foramen ovale closure using the Occlutech Figulla device: More than1,300patient-years of follow up). This group from the Netherlandspro-vides an observational study of 250 people who had the Occlutech Figulla device placed to close a PFO. The primary reason (89%) for PFO closure was transient ischemic attack (TIA) or stroke. With a mean follow-up of 5.9 years, the risk of recurrent stroke was 3% (8/250). The authors arrived at this value by combining TIA patients and stroke patients but it should have been calculated using only the stroke patients. For example, if they only had 150 patientswithMRI-documented stroke, then the risk of stroke recurrence is5%(8/150). In the stroke RCTs, the recurrence rate for medicaltreat-ment was 1% per year, so the Occlutech device does not impress one as being superior to medicaltherapy. Of course, themajorweakness of this study is that it is not a RCT, so we do not know how this device compares with medical therapy or other devices. Speaking of other devices, those of us in the United States will never see this device because it was ruled to infringe ontheAmplatzer PFO Occluder (Abbott, Chicago, IL) patent, to whichtheOcclutech product is sinisterly similar. But even using thec u r r e n t study data, the results are not impressive because the residualshunt rate was fairly high at 6%, and that was derived using transthoracic echocardiogram, an imaging modality less sensitive thanotherultrasoundtechniques,suchastranscranialDoppler.Forco mparison, the Gore Cardioform Septal Occluder (W.L. Gore and Associates, Flagstaff, AZ) provides effective closure in 99% ofcases.

Lastly, it is clinically impossible to distinguish between aTIA,whichisthoughttobeembolic,andacomplexmigraine,whichis pre- sumed to be triggered by a chemical (serotonin or low-oxygenated venous blood) that bypasses the lungs through the interatrial shunt. Both entities produce a transient neurological deficit with noabnor-mality on brain magnetic resonance imaging. Authors of outcome studies that count TIA prevention as due to the PFO closure maybefooling themselves in that they are actually inhibiting migraines,andthe“recurrentstrokerate”wouldnaturallybelow.O fcourse,botharegoodresults,buttherisksoftheprocedurehaveto bejustifiedbythe clinical syndrome that is purported to havebenefitted.

REFERENCES

1. West BH, Noureddin N, Mamzhi Y, et al. Frequency of patentforamen ovale and migraine in patients with cryptogenic stroke. Stroke.2018;49(5):1123-1128.https://doi.org/10.1161/STROKEAHA.117.020160.
2. Akhondi A, Gevorgyan R, Tseng C-H, et al. The association of patent foramenovalemorphologyandstrokesizeinpatientswithparadoxical embolism. Circ Cardiovasc Interv.2010;3:506-510.