Transcatheter Closure of Patent Foramen Ovale

Therapeutic Overkill or Elegant Management for Selected Patients at Risk?

Werner G. Daniel, MD

Patent foramen ovale (PFO), the most common postnatal residue of the fetal circulation, has for many years been considered to have almost no clinical relevance. In an autopsy study from the Mayo Clinic, PFO was found in 27% of 965 normal human hearts, with an incidence declining with increasing age (34% in the first three decades and 20% in the ninth and 10th decades).1 PFO size ranged between 1 and 19 mm (mean, 4.9 mm) and showed a tendency for larger-sized communications that present in older age groups. There were no significant differences in incidence or size between males and females. Similar findings had been reported earlier by Thompson and Evans,2 who observed a “pencil patent” PFO in 6% and a “probe patent” PFO in 29% of 1,100 consecutive necropsies. A PFO is not associated with typical findings detectable by physical examination or basic laboratory tests. It can be diagnosed by cardiac catheterization or by detection of right-to-left echocardiographic contrast passage using transcranial Doppler ultrasound.3 Currently, however, the methods of choice for PFO diagnosis combine two-dimensional contrast4-5 or color Doppler6 echocardiography, with the transesophageal approach being more accurate than the transthoracic technique.7-9 Transesophageal echocardiography has an acceptably low risk for performance even in elderly or neurologically impaired patients,10 and the biplane mode in particular provides superb images of the atrial septum in virtually all patients. Consequently, PFO can be detected during life in a percentage of patients approaching that at autopsy.

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As PFO is detected more often, our knowledge about its potential clinical significance has increased considerably. In 1988, two independent case–control studies reported an unusually high incidence of PFO (54% and 50%) in young stroke patients.11,12 Our own investigations confirm these data.9 Therefore, a series of studies analyzing the value of transesophageal echocardiography for detecting cardiac sources of embolism has included PFO as one of the potential sources.13-15

Assuming that PFO may be responsible for more arterial embolic events than previously realized, what treatment would be appropriate for PFO patients with stroke or peripheral arterial embolism who have no other detectable sources? In this issue of Circulation, Bridges et al16 present data from a multicenter study that offers a fascinating solution: transcatheter closure of a PFO. Thirty-five patients with a PFO (and one patient with a small atrial septal defect) documented by transesophageal and/or transthoracic echocardiography were included. Three patients had associated atrial septal aneurysms, and 22 (61%) patients were <45 years old. All patients had suffered one or more cerebral events (33 patients), peripheral arterial embolic episodes (three patients), or brain abscess (two patients) considered most likely the result of paradoxical embolism. After thrombotic material in the femoral veins had been ruled out to avoid embolization induced by catheter manipulations, a Clamshell umbrella device was implanted successfully in all 36 patients, without major procedural complications. Follow-up of 1–24 months (mean, 8.4 months) revealed complete PFO closure in 28 (82%) of 34 patients restudied by echocardiography. Five patients showed small (<1 mm) leaks, and one patient showed a somewhat larger (2–3 mm) communication. During follow-up, one patient continued to suffer from episodes of focal paresthesia and weakness identical to those observed before PFO closure. In this patient, the diagnosis of presumed embolic events was revised, and symptoms were finally considered to be the result of cerebral vasculitis. A second patient experienced a vague episode of transient bilateral leg and arm weakness, and two other patients had experienced a transient focal deficit during follow-up. In three of these four cases, echocardiography had shown complete closure of the atrial defect. Major late complications such as stroke, systemic arterial embolism, embolization of the closure device, or endocarditis have not been observed.

In considering the pros and cons of transcatheter closure of a PFO, three questions must be asked. Is PFO really an important (and previously underestimated) cause of paradoxical embolism? What diagnostic procedures should be performed to identify PFO patients at increased risk for paradoxical arterial embolic events? What is effective and prudent treatment of those patients with increased risk at the present time?

The first question concerning the clinical relevance of PFO cannot be answered satisfactorily. However, there is definite proof that PFO allows right-to-left atrial shunting under normal hemodynamic conditions,4,5 and particularly in patients with increased right heart pres-
sure. Even high left-to-right atrial pressure gradients, which sometimes are observed in patients with an iatrogenic Lutembacher syndrome after incomplete percutaneous Lutembacher valveoplasty, may become reversed by a Valsalva maneuver or coughing, thereby allowing right-to-left shunting. The shunt via a PFO not only may result in impaired oxygenation in some patients but also may allow passage of thrombotic material from the venous bed into the arterial circulation. This has been documented by both autopsy and echocardiographic studies showing a thrombus lodged in a PFO and also has been suggested by a number of clinical investigations documenting a high prevalence of PFO in young patients with otherwise unexplained cerebral or peripheral arterial embolic episodes. In addition, air embolism during neurosurgical procedures and decompression sickness in divers may be explained by the presence of a PFO.

Which patients with a PFO are at increased risk for paradoxical embolism, how can they be identified reliably, and what is the recurrence rate of paradoxical embolism? Paradoxical embolism implies a source of embolism in the right atrium or venous circulation. Consequently, all patients with suspected paradoxical embolism should be screened carefully by angiography or ultrasound for the presence of deep venous thrombosis. Unfortunately, deep venous thrombosis often is clinically silent, and venous angiography is not infrequently negative, even in patients with proven pulmonary embolism. Thrombi as small as 1 or 2 mm (and frankly undetectable by any imaging technique) may be sufficient to cause stroke, and the average size of a PFO easily allows their passage into the arterial circulation. Thus, failure to document venous thrombi does not actually exclude paradoxical embolism in a PFO patient. On the other hand, deep venous thrombosis in a hemiplegic stroke patient may be the consequence of immobilization rather than the cause of stroke.

There is an increasing need for systematic studies of deep venous thrombosis in PFO patients as early as possible after an otherwise unexplained cerebral or peripheral arterial embolic event. There are also other indirect factors increasing the likelihood of paradoxical embolism, such as preceding episodes of pulmonary embolism or patients’ activities immediately before the arterial embolic event (e.g., Valsalva maneuver, coughing, defecation, or any other maneuver that raises right atrial pressure). However, unless we actually detect the thrombus lodged in a PFO and straddling the atrial septum, we must acknowledge that the diagnosis of paradoxical embolism involves different degrees of likelihood rather than definite proof. Furthermore, there are as yet no definite studies documenting the recurrence rate of paradoxical embolism.

The dilemma of a presumed but not proved diagnosis certainly does not facilitate the proper management of patients with a PFO and suspected paradoxical embolism. Accordingly, these patients have been treated empirically with anticoagulants or antiplatelet drugs, thrombolytics, implantation of a caval filter or interruption of the inferior vena cava, temporary PFO closure using catheter balloon systems, or permanent PFO closure by surgery. All of these options have some risks. The report by Bridges et al. of successful closure of a Clamshell umbrella device introduces an intriguing new option that may have merit compared with the other treatments available; it is permanent (as opposed to drugs) yet less invasive than surgery, and it should be effective also for intracardiac clots (which inferior vena cava procedures do not treat). Transcatheter closure of atrial septal defects and other congenital or acquired shunt lesions (including PFO closure in selected patients) has been performed successfully in clinical series during the past few years, and Bridges and coworkers certainly have been pioneers in this exciting method of treatment. However, there are a number of unanswered concerns about the implantation of these devices. First, the procedure itself, which requires a high level of training, is not without risk and may lead to bleeding complications, dislodgement of venous thrombi, and even embolism of the entire device. Second, long-term studies will be necessary to clarify the risk of late infective and thromboembolic complications and to define the incidence and clinical implications of arrhythmias, fracture of device arms, and other potential modes of device failure.

Bridges and coworkers have proposed a promising and elegant way to treat patients with PFO at risk of paradoxical embolism. At present, the key issue is proper patient selection, and in this context, there are more good questions than answers. A single unexplained transient neurological event without detectable peripheral venous thrombosis and without history of pulmonary embolism, as in some patients in the series by Bridges et al., may not be sufficient to justify transcatheter implantation of a PFO closure device. Perhaps some day, transesophageal echocardiography will provide anatomic clues to those PFOs that are more likely and those that are less likely to allow paradoxical embolism. Unless we can define strict indications for PFO closure, we risk ending up with therapeutic overkill, exposing some patients to unnecessary risks and perhaps unforeseen complications of treatment. For the present, Bridges and coworkers deserve praise for having described a new way of managing patients with PFO at high risk for recurrent paradoxical embolism.

References
5. Strunk BL, Cheitlin MD, Stulbarg MS, Schiller NB: Right-to-left interatrial shunting through a patent foramen ovale despite normal intracardiac pressures. Am J Cardiol 1987;60:413-415
9. Hausmann D, Mügge A, Becht I, Daniel WG: Diagnosis of patent foramen ovale by transesophageal echocardiography and association with cerebral and peripheral embolic events. Am J Cardiol 1992; 70:668–672

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W G Daniel

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