

## Q: How often are atrial septal defects associated with thromboembolism? When should they be looked for?

Wael A. Jaber, MD

Department of Cardiology, Cleveland Clinic

Allan L. Klein, MD

Director, Cardiovascular Imaging Research, Professor of Medicine, Department of Cardiology, Cleveland Clinic

**A:** THE EXACT PREVALENCE of incompetent atrial septa (due to an atrial septal defect [ASD] or a patent foramen ovale [PFO]) and their causative relation to strokes are controversial. Diagnostic studies have shown, however, a greater likelihood of finding anomalies of the atrial septum among patients who had strokes than in control subjects, and larger defects in those who had suffered strokes.

In the absence of other causative conditions, an ASD or PFO may be presumed to be the underlying cause of cerebrovascular thromboembolism. The search for these defects will be more cost-effective in younger stroke patients who, unlike older patients, rarely have the cardiovascular conditions associated with advanced age that commonly cause strokes in the elderly.

### ■ DETECTING ATRIAL SEPTAL MALFORMATIONS

The atrial septum usually is evaluated with a combination of two-dimensional (2D) echocardiography, color flow Doppler, and contrast saline injection. A 2D echocardiogram will demonstrate a separation of the flap valve from the limbus of the fossa ovale. Color flow mapping will in some cases show left-to-right atrial flow.

Contrast saline injection increases the sensitivity of both transthoracic and transesophageal echocardiography in detecting interatrial shunting. In this procedure, agitated saline solution is injected into a peripheral

vein; the examination usually is considered positive if three or more microbubbles appear in the left atrium within three cardiac cycles after right atrial opacification.<sup>1</sup>

For the bubbles to pass from the right atrium to the left atrium, however, the pressure must be higher on the right than on the left—the opposite of the usual pressure gradient. Elevation of right atrial pressure can be physiologic (due to cough, the Valsalva maneuver, or increased intra-abdominal pressure) or pathologic (due to pulmonary hypertension, tricuspid regurgitation, or stenosis). During the procedure the patient is therefore asked to cough or perform the Valsalva maneuver.

### ■ INCIDENCE OF ATRIAL SEPTAL MALFORMATIONS

In 1984, Hagen et al<sup>2</sup> reported a 27% prevalence of atrial septal malformations in an autopsy study in 965 hearts believed to have been normal. The prevalence declined from 34% during the first 3 decades of life to 20% in the ninth and 10th decades.

The same year, Lynch et al<sup>3</sup> performed transthoracic echocardiography in 80 volunteers who had no symptoms and found an 18% prevalence of interatrial shunting.<sup>3</sup>

In 1988, Lechat et al<sup>4</sup> revisited this subject, performing contrast echocardiography in 100 patients with no history of stroke and in 60 patients with ischemic strokes. All patients in the study were 55 years or younger and had a normal cardiac evaluation. The prevalence of PFO was 10% in the control group and 40% in the stroke group ( $P < .001$ ).

Two reports in 1991 found transesophageal echocardiography to be superior to transthoracic echocardiography in identifying cardiac sources of emboli in patients with

Suspect an atrial septal defect if a young patient has a stroke



TABLE 1

### Prevalence of structural defects in stroke patients and control subjects on transesophageal echocardiography

	CONTROL SUBJECTS (N = 50)	STROKE PATIENTS (N = 100)	ODDS RATIO	PATIENTS WITH CRYPTOGENIC STROKE (N = 64)
Atrial septal aneurysm	4 (8%)	28 (28%)*	4.3	25 (39%)†
6–10 mm	3	8		7
11–15 mm	0	10		9
> 15 mm	1	10		9
Patent foramen ovale	9 (18%)	43 (43%)*	3.9	36 (56.3%)‡
Mitral valve prolapse	3 (6%)	8 (8%)		5 (7.8%)
Atrial septal aneurysm and patent foramen ovale	1 (2%)	22 (22%)	33.3	21 (32.8%)

\* $P < .005$  vs control subjects

† $P < .001$  vs control subjects

‡ $P < .0001$  vs control subjects

ADAPTED FROM CABANES L, MAS JL, COHEN A, ET AL. ATRIAL SEPTAL ANEURYSM AND PATENT FORAMEN OVALE AS RISK FACTORS FOR CRYPTOGENIC STROKE IN PATIENTS LESS THAN 55 YEARS OF AGE. A STUDY USING TRANSESOPHAGEAL ECHOCARDIOGRAPHY. STROKE 1993; 24:1865–1873.

transient ischemic attacks or strokes.<sup>5,6</sup> Transesophageal echocardiography had a diagnostic yield of 40%, compared with 19% for transthoracic echocardiography. The combined data from these two reports showed a 10% prevalence of PFO or ASD (13 of 129 patients). Moreover, transesophageal echocardiography identified other lesions that could act as cardiac sources of embolism (atrial septal aneurysms, left atrial and left atrial appendage thrombi, and spontaneous echo contrast).

#### ■ ASSOCIATION WITH STROKES

To determine the role of PFOs and ASDs as independent risk factors for strokes, Cabanes et al<sup>7</sup> performed transesophageal echocardiography in 100 consecutive patients with ischemic strokes and in a control group of 50 patients. PFOs were present in 43% of the stroke patients vs 18% of the control group ( $P < .05$ ) and 56.3% of patients with cryptogenic stroke ( $P < .0001$  vs controls). Larger atrial septal aneurysms were more prevalent in patients with stroke.

Furthermore, atrial septal aneurysms were found to have a synergistic effect. Only two patients (4%) in the control group had both a

PFO and an atrial septal aneurysm vs 22 (22%) of the patients in the stroke group and 21 (32.8%) in the group with cryptogenic stroke. The investigators concluded that there is a powerful association between ischemic strokes and the combination of PFO and atrial septal aneurysm (TABLE 1).

#### ■ WORKUP OF THE PATIENT WITH THROMBOEMBOLISM

The cardiac workup of patients with strokes should start with a complete transthoracic echocardiogram with contrast. If this does not reveal a cause of the stroke, a transesophageal echocardiogram should follow.

Most studies connecting atrial septal malformations with strokes were done in patients younger than 55 years. This population has the highest incidence of cryptogenic strokes, and in it echocardiographic investigation will produce a high yield. An older population (56 years or older), on the other hand, has a high prevalence of atherosclerosis of the large vessels (aorta, carotids), atrial fibrillation, valvular heart disease, or small artery disease. Pursuing other causes of strokes such as ASD and PFO in elderly patients might be less cost-effective.

Start the  
workup  
of stroke  
patients with  
a transthoracic  
echo

To incriminate an ASD or a PFO in the pathogenesis of cerebrovascular ischemic events, three criteria should be present<sup>8</sup>:

- Venous thrombus
- Venous-arterial defect (ASD or PFO)
- Systemic emboli without arterial causes (aortic atheroma, left atrial or ventricular thrombi, atrial fibrillation, or carotid disease).

## ■ MANAGEMENT

Once clinical investigation suggests an ASD or PFO as the cause of thromboemboli, available data suggest that management start with long-term antiplatelet therapy for patients at low risk or antiplatelet therapy combined with indefinite anticoagulation for those at higher risk. Patients who should not be taking anticoagulants or in whom anticoagulation is ineffective may be considered for surgical or percutaneous (catheter-based) closure of the defect.<sup>9</sup>

## ■ REFERENCES

1. De Castro S, Fiorelli M, Rasura M, et al. Morphological and functional characteristics of patent foramen ovale and their embolic implications. *Stroke* 2000; 31:2407–2413.
2. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc* 1984; 59:17–20.
3. Lynch JJ, Schuchard GH, Gross CM, Wann LS. Prevalence of right to left atrial shunting in a healthy population: Detection by Valsalva maneuver contrast echocardiography. *Am J Cardiol* 1984; 53:1478–1480.
4. Lechat P, Mas JL, Lascault G, et al. Prevalence of patent foramen ovale in patients with stroke. *N Engl J Med* 1988; 318:1148–1152.
5. Lee RJ, Bartzakis T, Yeoh TK, Grogin HR, Choi D, Schnittger I. Enhanced detection of intracardiac sources of cerebral emboli by transesophageal echocardiography. *Stroke* 1991; 22:734–739.
6. Pearson AC, Labovitz AJ, Tatineri S, Gomez CR. Superiority of transesophageal echocardiography in detecting cardiac sources of embolism in patients with cerebral ischemia of uncertain etiology. *J Am Coll Cardiol* 1991; 17:66–72.
7. Cabanes L, Mas JL, Cohen A, et al. Atrial septal aneurysm and patent foramen ovale as risk factors for cryptogenic stroke in patients less than 55 years of age. A study using transesophageal echocardiography. *Stroke* 1993; 24:1865–1873.
8. Meister SG, Grossman W, Dexter L, Dalen JE. Paradoxical embolism. Diagnosis during life. *Am J Med* 1972; 53:292–298.
9. Lock JE. Patent foramen ovale is indicted, but the case hasn't gone to trial. *Circulation* 2000; 101:838.

ADDRESS: Allan L. Klein, MD, Department of Cardiology, F15, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail [kleina@ccf.org](mailto:kleina@ccf.org).