Frequency of Atrial Septal Aneurysms in Patients With Cerebral Ischemic Events

Yoram Agmon, MD; Bijoy K. Khandheria, MD; Irene Meissner, MD; Federico Gentile, MD; Jack P. Whisnant, MD; JoRean D. Sicks, MS; W. Michael O’Fallon, PhD; Jody L. Covalt, RN; David O. Wiebers, MD; James B. Seward, MD

Background—Atrial septal aneurysm (ASA) is a putative risk factor for cardioembolism. However, the frequency of ASA in the general population has not been adequately determined. Therefore, the frequency in patients with cerebral ischemic events, compared with the frequency in the general population, is poorly defined. We sought to determine the frequency of ASA in the general population and to compare the frequency of ASA in patients with cerebral ischemic events with the frequency in the general population.

Methods and Results—The frequency of ASA in the population was determined in 363 subjects, a sample of the participants in the Stroke Prevention: Assessment of Risk in a Community study (control subjects), and was compared with the frequency in 355 age- and sex-matched patients undergoing transesophageal echocardiography in search of a cardiac source of embolism after a focal cerebral ischemic event. The proportion with ASA was 7.9% in patients versus 2.2% in control subjects (P = 0.002; odds ratio of ASA, 3.65; 95% CI, 1.64 to 8.13, in patients versus control subjects). Patent foramen ovale (PFO) was detected with contrast injections in 56% of subjects with ASA. The presence of ASA predicted the presence of PFO (odds ratio of PFO, 4.57; 95% CI, 2.18 to 9.57, in subjects with versus those without ASA). In 86% of subjects with ASA and cerebral ischemia, transesophageal echocardiography did not detect an alternative source of cardioembolism other than an associated PFO.

Conclusions—The prevalence of ASA based on this population-based study is 2.2%. The frequency of ASA is relatively higher in patients evaluated with transesophageal echocardiography after a cerebral ischemic event. ASA is frequently associated with PFO, suggesting paradoxical embolism as a mechanism of cardioembolism. In patients with cerebral ischemia and ASA, ASA (with or without PFO) commonly is the only potential cardioembolic source detected with transesophageal echocardiography. (Circulation. 1999;99:1942-1944.)

Key Words: aneurysm • cerebral ischemia • echocardiography
Figure 1. Diagram of criteria for ASA. (1) Protrusion of interatrial septum, or part of it, ≥15 mm beyond plane of interatrial septum (a, ≥15 mm) or (2) phasic excursion of interatrial septum during cardiorespiratory cycle ≥15 mm in total amplitude (b, ≥15 mm) and diameter of base of aneurysmatic portion of interatrial septum measuring ≥15 mm (c, ≥15 mm). LA indicates left atrium; RA, right atrium.

Atrial Septal Aneurysm
ASA was defined according to criteria previously published by Hanley et al: (1) diameter of the base of the aneurysmatic portion of the IAS measuring ≥15 mm and either (2) protrusion of the IAS, or part of it, ≥15 mm beyond the plane of the IAS or (3) phasic excursion of the IAS during the cardiorespiratory cycle ≥15 mm in total amplitude (Figure 1).

Patent Foramen Ovale
A patent foramen ovale (PFO) was defined as a right-to-left interatrial shunt diagnosed by intravenous injections of agitated saline with the patient at rest and with provocative maneuvers (cough or release of Valsalva or both).

For the present study, all TEEs were reviewed systematically by an observer blinded to the initial diagnoses, with offline measurements of ASA dimensions. Any discrepancies between the initial and review diagnoses were settled by a third observer blinded to all previous diagnostic data.

Figure 2. Frequency of ASA in patients (solid bars) and control subjects (open bars) in 5 age subgroups. Total number of subjects in each age subgroup is given at bottom of figure.
Atrial Septal Aneurysm and Cerebral Ischemia

Additional Sources of Embolism in 28 Patients With Cerebral Ischemia and Atrial Septal Aneurysm

<table>
<thead>
<tr>
<th>Embolism Source</th>
<th>Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-cardiac thrombus</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Prosthetic valve†</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Aortic atherosclerosis‡</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Left ventricular dysfunction§</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

*More than 1 source of embolism was identified in some patients.
†Mitra1 mechanical prosthesis in 1 patient and aortic mechanical prosthesis in another.
‡Complex atherosclerosis (plaque thickness ≥5 mm and/or mobile plaque elements) in ascending aorta or aortic arch.
§Left ventricular systolic dysfunction (ejection fraction <40%).
| Atrial fibrillation during the TEE examination.

Frequency of ASA
The rate of ASA detection with echocardiography varies from 0.22% in consecutive transthoracic studies to significantly higher rates by TEE, the diagnostic technique of choice. The frequency of ASA is highly variable among TEE studies, reflecting differences in study populations as well as in ASA definition. Although any cutoff in ASA definition is arbitrary, the 15-mm cutoff adopted in the present study provides relatively high specificity for ASA diagnosis. According to this definition, the proportion of ASA in the general population is low (2.2%) and similar to a 1% proportion noted in a large autopsy series. This figure is lower than those of smaller population-based studies, which reported frequencies of 4.5% (no quantitative definition of ASA) and 13% (15-mm ASA definition).9

ASA and Cerebral Ischemia
A possible relationship between ASA and cerebral ischemia was suggested initially by retrospective observations of the high frequency of preceding cerebral ischemic events in patients with an echocardiographic diagnosis of ASA. This was confirmed subsequently in 2 multicenter studies. In addition, studies comparing the proportion of ASA in patients with cerebral ischemia with its proportion in those undergoing TEE for miscellaneous clinical indications have found a relatively high prevalence of ASA in association with cerebral ischemia. However, the control groups of such studies were highly prone to selection bias. Our study allowed an estimation of the relative frequency of ASA in patients with cerebral ischemia in comparison with a sample of the general population undergoing TEE.

Right-to-left shunting through a PFO (permitting paradoxical embolism), thrombus formation in the ASA, associated mitral valve prolapse, and supraventricular arrhythmias are the potential mechanisms of cardioembolism associated with ASA. Our data support only the first mechanism, although undiagnosed transient atrial arrhythmias as well as small or rapidly resolving thrombi in ASAs cannot be excluded.

Clinical Implications
Clinical follow-up data have suggested that ASA is associated with an increased risk of stroke recurrence. However, the optimal therapeutic regimen for secondary prevention and possibly primary prevention of stroke in subjects with ASA remains to be determined.

In summary, our study estimated the frequency of ASA in the general population, confirmed an association between ASA and cerebral ischemic events, and suggested that paradoxical embolism is a mechanism of cardioembolic stroke in patients with ASA.

Acknowledgment
This study was supported in part by a grant from the National Institute of Neurological Disorders and Stroke, National Institutes of Health (NS-06663).

References
Frequency of Atrial Septal Aneurysms in Patients With Cerebral Ischemic Events
Yoram Agmon, Bijoy K. Khandheria, Irene Meissner, Federico Gentile, Jack P. Whisnant, JoRean D. Sicks, W. Michael O'Fallon, Jody L. Covalt, David O. Wiebers and James B. Seward

Circulation. 1999;99:1942-1944
doi: 10.1161/01.CIR.99.15.1942
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/99/15/1942

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/