Atrial Septal Aneurysm and Stroke: A Transesophageal Echocardiographic Study

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The prevalence and morphologic characteristics of atrial septal aneurysms identified by transesophageal echocardiography in 410 consecutive patients are described. Two groups of patients were compared: Group I consisted of 133 patients referred for evaluation of the potential source of an embolus and Group II consisted of 277 patients referred for other reasons.

An atrial septal aneurysm was diagnosed by transesophageal echocardiography in 32 (8%) of the 410 patients. Surface echocardiography identified only 12 of these aneurysms. Atrial septal aneurysm was significantly more common in patients with stroke (20 [15%] of 133 vs. 12 [4%] of 277) (p < 0.05); right to left shunting at the atrial level was demonstrated in 70% of patients in Group I and 57% of patients in Group II by saline contrast echocardiography. Four patients in Group I had an atrial septal defect with additional left to right flow. There was no difference between the two groups in aneurysm base width, total excision or left atrial or right atrial excision. However, Group I patients had a thinner atrial septal aneurysm than did Group II patients.

It is concluded that an atrial septal aneurysm occurs commonly in patients with unexplained stroke, is more frequently detected by transesophageal echocardiography than by surface echocardiography and is usually associated with right to left atrial shunting. Treatment (anticoagulant therapy vs. surgery) of atrial septal aneurysm identified in stroke patients can be determined only by long-term follow-up studies.

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Atrial septal aneurysm is a localized outpouching of the fossa ovalis region of the atrial septum that has been identified in 1% of autopsies (1). Initially identified by angiographic techniques (2,3), with the advent of two-dimensional echocardiography it has been more widely recognized in patients before death (4,5). It has also been associated with a systolic click (6), atrial septal defect (4-8), atioventricular valve prolapse or obstruction (9-11) and pulmonary venous obstruction (12), but it has also been identified in asymptomatic subjects with a totally normal heart (13). A major association between atrial septal aneurysm and peripheral arterial embolism was first identified by Gallet et al. (14) in 1985. This association was further strengthened by Belkin et al. (15), who noted that 10 of 36 consecutively identified cases of atrial septal defect were found in patients with unexplained stroke.

Although up to 20% of strokes are believed to be cardioembolic in origin, the cardiac source frequently remains unidentified by surface echocardiography (16). We have recently reported (17) on the improved diagnostic yield of transesophageal echocardiography in unexplained stroke. Specifically, transesophageal echocardiography identified more patients with stroke who had left atrial spontaneous contrast or thrombus, patent foramen ovale and atrial septal aneurysm than did surface echocardiography. In this report the characteristics of atrial septal aneurysm found by transesophageal echocardiography are described and its relation to stroke is further detailed.

Methods

Study group. The study group consisted of 410 consecutive patients referred for transesophageal echocardiography between October 1988 and February 1990. The study was performed prospectively as part of a prospective study of patients presenting with unexplained stroke. Adequate transesophageal echocardiographic studies were obtained in all patients.

Two groups of patients were compared: Group I patients were referred for evaluation of a potential cardiac source of embolus (n = 133) and Group II patients were referred for other reasons (n = 277). The indications for transesophageal echocardiography in Group II patients were as follows: native valvular disease, 21%; prosthetic valve, 14%; suspected endocarditis, 7%; congenital disease, 7%; intraoperative, 14%; trauma, 8%; suspected aortic dissection, 6%; left ventricular function, 7%; technically difficult surface study, 5%; miscellaneous, 4%. There were no differences between

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groups in gender distribution (Group I was 50% male and Group II was 53% male) or mean age (the mean age was 53 years in Group I and 62 years in Group II). Spontaneous atrial contrast was noted significantly more often in Group I patients (12% vs. 5%, p < 0.05).

All Group I patients, as part of the prospective study, underwent a complete history and physical examination; a complete neurologic evaluation was performed by an attending neurologist. These patients had a documented cerebrovascular accident with a residual neurologic deficit or a confirmed transient ischemic attack or residual ischemic neurologic deficit documented by the neurologist. In addition, one patient with documented systemic embolism was included in this group. All Group I patients underwent transesophageal echocardiography after giving informed written consent, and complete studies were obtained with particular attention to identification of a cardiac source of embolism.

In our laboratory (17), a complete transesophageal echocardiographic study for cardiac source of embolism consists of exclusion of 1) left atrial and left atrial appendage thrombus or tumor, 2) left ventricular thrombus, 3) atrial septal aneurysm, 4) patent foramen ovale (by contrast administration) or atrial septal defect, 5) vegetations, and 6) mitral valve prolapse. Intravenous contrast injections were performed in all patients to evaluate right to left shunting with use of 10 ml agitated saline solution during normal respiration, cough and Valsalva maneuver. The entire study group of 410 patients was evaluated for an atrial septal aneurysm.

Study protocol. Transesophageal echocardiography was performed after administration of pharyngeal anesthesia with either 14% benzocaine or 10% lidocaine spray. The majority of patients were given intravenous sedation with diazepam, midazolam or Demerol (meperidine) either alone or in combination to achieve adequate sedation. Studies were performed with one of two ultrasound systems: a Hewlett-Packard 77020 with a 5 MHz single-plane transesophageal echocardiographic probe or an Interspec Vingmed CFM 700 with a 5 to 7.5 MHz transesophageal echocardiographic probe. The latter was used primarily at 5 MHz for imaging. Both systems were capable of both Doppler color flow and spectral Doppler interrogation. The probe was advanced to a depth of 25 to 30 cm and then manipulated to optimize imaging of the atrial septum. Standard transesophageal views were obtained with particular attention to the atrial septum.

All patients in Group I were evaluated for right to left atrial shunting across the interatrial septum with intravenous injection of agitated saline solution to provide contrast. Ten milliliters of saline solution was agitated by passing it between two syringes by means of a three-way stopcock and injections were performed at an antecubital vein site whenever possible. All such injections resulted in excellent right atrial opacification. A patent foramen ovale was diagnosed if microbubbles were visualized in the left atrium immediately after appearance in the right atrium and no atrial septal defect was identified. Contrast injections were performed during cough and Valsalva maneuver to elicit right to left shunting in patients that did not have obvious shunting during normal respiration.

The videotapes of all patients in both groups thought to have an abnormally redundant and mobile atrial septum were digitized with use of a commercially available computer system and custom-made software. With this system, measurements of excursion of the atrial septum into the left and right atria were performed, along with measurements of base width, thickness and duration and timing of the excursion of the atrial septum (Fig. 1). Surface echocardiography was also performed to evaluate the interatrial septum.

Surface echocardiograms were read by an experienced echocardiographer unaware of the results of the transesophageal echocardiogram. Associated cardiac abnormalities, including mitral valve prolapse, congenital heart disease, valvular disease, spontaneous contrast and wall motion abnormalities, were evaluated.

Criteria for diagnosis of atrial septal aneurysm were 1) base width ≥ 1.5 cm with 2) ≥ 1.1 cm excursion into either the left or the right atrium or a sum of the total excursion into the left or right atrium ≥ 1.1 cm. Forty-three patients were identified as having an atrial septum that appeared abnormally redundant or mobile. Atrial septal aneurysms were classified according to their movement by the schema of Hanley et al. (8) as type IA, continual protrusion into the right atrium (Fig. 2): type IB, predominant protrusion into the right atrium with passive left atrial excursion; and type II, persistent protrusion into the left atrium. For patients with a type IB aneurysm exhibiting left atrial excursion with every
cardiac cycle (Fig. 3), a new classification, type IC, was developed.

Statistics. All results are expressed as mean values ± SD. An unpaired t test was used to compare continuous variables between the two groups. Chi-square analysis was used to compare proportions between the two groups. A p value < 0.05 was considered significant.

Clinical characteristics of patients with atrial septal aneurysm (Tables 1 and 2). Atrial septal aneurysm was diagnosed by transesophageal echocardiography in 32 (8%) of the 410 patients. Of these 32, 18 were male and 14 female, with a mean age of 57 years (range 20 to 80). Associated two-dimensional echocardiographic abnormalities included Chian’s network in five patients, mitral valve prolapse in five, mitral valve replacement in one, tricuspid valve endocarditis in two and mitral regurgitation in one. Only 12 (37.5%) of the 32 atrial septal aneurysms were detected by surface echocardiography.

Atrial septal aneurysm was significantly more common in patients with stroke than in patients without stroke (20 [15%] of 133 vs. 12 [4%] of 277) (p < 0.05). The characteristics of patients with atrial septal aneurysm in both groups along with quantitative characteristics of the atrial septal aneurysms are presented in Table 2.

Classification of atrial septal aneurysm. The size, excursion and timing of excursion of the aneurysms varied considerably (Fig. 2). Two patients had marked excursion exclusively into the right atrium (type IA). Both of these

Results

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patients were in the stroke group, were young and did not demonstrate shunting. Three patients had excursion exclusively into the left atrium (type II). One of these three was in the stroke group; of the three, two had shunting and one of the two was in the stroke group.

Twenty-seven patients had atrial septal aneurysm classified as type IB. Four of the 27 patients demonstrated phasic excursion of the aneurysm during every cardiac cycle with predominant right atrial excursion and left atrial movement during early systole intensified by inspiration or Valsalva maneuver (type IC). Two of the four patients with a type IC atrial septal aneurysm were in the stroke group, two were not. Of these four, three underwent contrast imaging and all three demonstrated heavy shunting with normal respiration. The two patients in the stroke group also had an atrial septal defect. The remaining 23 patients had exclusive right atrial protrusion throughout the cardiac cycle with intermittent phasic excursion into the left atrium during inspiration. Fifteen of these 23 were in the stroke group and 20 (83%) demonstrated shunting.

**Morphologic characteristics.** There was no difference between the two groups in aneurysm base width and total, left atrial or right atrial excursion. Group I patients had a thinner aneurysm than did Group II patients (1.6 vs. 2.2 mm, p < 0.05). Thrombus was identified in one Group I patient on the right atrial side of the aneurysm. Five patients had an

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*Contrast injection not performed. ASA = atrial septal aneurysm; ASD = atrial septal defect; Chari = Chari's network; end = endocarditis; Exc = excursion; LA = left atrium; MV = mitral valve; MVP = mitral valve prolapse; MVR = mitral valve replacement; RA = right atrium; RV = right ventricle.
### Table 2. Characteristics and Classification of 32 Patients With Atrial Septal Aneurysm

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Aneurysm measurements (mm) (mean ± SD):

- Base width: 20 ± 4, 19 ± 5, 23 ± 7
- Total excursion: 18 ± 4, 17 ± 4, 19 ± 4
- Left atrial excision: 12 ± 4, 11 ± 5, 12 ± 5
- Right atrial excision: 6 ± 4, 6 ± 4, 6 ± 4
- Thickness: 1.8 ± 0.6, 1.6 ± 0.6, 2.2 ± 0.4

Unless otherwise indicated, data represent number of patients. *p < 0.01* vs. Group II. F = female; M = male.

Aneurysm with a roughened or irregular appearance. Roughened appearance was not more prevalent in the stroke group.

**Shunting.** Right to left shunting consistent with patent foramen ovale was identified in 14 (70%) of the 20 Group I patients with an atrial septal aneurysm, compared with 6 (75%) of the 8 Group II patients who underwent contrast echocardiography. Four patients in Group I had a defect of the atrial septum with left to right flow, demonstrated by Doppler color flow mapping consistent with atrial septal defect (Fig. 4).

**Figure 4.** Atrial septal aneurysm with associated atrial septal defect. AO = aorta; other abbreviations as in Figure 1.

**Discussion**

Silver and Dorsey (1) in 1978 provided the best pathologic description of atrial septal aneurysm: "the septum is severely redundant and it bulges far into the right or left atrial cavity." They also described tiny tags of fibrin or thrombus material similar to Lamb’s excrecescences that roughened the convex surface and thrombus in the circumferential pit at the base of the aneurysm. They found this anomaly in 1% of necropsies of adults performed over a 4-year period. These investigators (1) believed that the aneurysm could cause a heart murmur, obstruction of either the tricuspid or the mitral valve, pulmonary or systemic embolism and transient ischemic attack, or it could be associated with an atrial septal defect. Results of 8 of the 16 necropsies showed a probe-patient foramen ovale. The cause of the aneurysm was thought to be bulging of the septum primum through the fossa ovalis.

**Atrial septal aneurysm and surface echocardiography.** With the development of two-dimensional echocardiography, atrial septal aneurysm has been readily identified in patients before death. The largest series of echocardiographically detected atrial septal aneurysm was reported by the Mayo Clinic (8), which described 80 aneurysms studied over a 6-year period from 36,200 surface echocardiograms. The prevalence of atrial septal aneurysm increased from 0.09% in the first 3 years to 0.29% in the last year of the study (8).

Several conditions have been associated with atrial septal aneurysm, including atrial septal defect, atrial arrhythmias, mid-systolic click and cerebral ischemic events. Belkin et al. (13) described 30 consecutively identified patients with atrial septal aneurysm. Ten of these had a cerebrovascular event: five had a completed stroke of definite embolic origin on the basis of clinical, angiographic and computed tomographic findings; two had a transient ischemic attack of probable embolic origin and one had a peripheral embolus. Of the patients in that series (15), 90% demonstrated interatrial shunting by contrast echocardiography, including four with an atrial septal defect demonstrated angiographically. Three of the four had multiple fenestrations in the aneurysm at surgery. Gallet et al. (14) described 10 patients with atrial septal aneurysm identified over 3 years by echocardiography. Three patients had an atrial septal defect, two had a stroke and three had mitral valve prolapse.

**Atrial septal aneurysm and transesophageal echocardiography.** Transesophageal echocardiography is ideal for assessment of the atrial septum owing to the proximity of the esophagus to this structure, and the availability of nonparallel interrogation and higher frequency probes in comparison with surface echocardiography. Previous reports have emphasized the superiority of transesophageal echocardiography in detecting atrial and atrial septal abnormalities, including atrial septal defect (18-20) and left atrial thrombus (21). Our study indicates its clear superiority in identifying an aneurysm of the atrial septum. Only one-third of the aneurysms were detected by surface echocardiography.
This study also strengthens the previously noted association between atrial septal aneurysm and cerebrovascular accident: 15% of patients who had had a stroke had an atrial septal aneurysm detected by transesophageal echocardiography compared with only 4% of patients who had not had a stroke. There are two possible mechanisms for cardioembolic stroke. First, the high prevalence of right to left atrial shunting (75%) indicates the possibility of paradoxical embolism. Second, the aneurysm itself may be thrombogenic. As reported by Silver and Dorsey (1), thrombus has been observed within the circumferential pit of the atrial septal aneurysm as well as in the fibrin or thrombus tags on the convex surface. Although preliminary reports have described a high frequency of thrombus-like echoes in atrial septal aneurysm, we identified thrombus in only one patient.

Morphologic aspects of atrial septal aneurysm. The criteria for atrial septal aneurysm proposed by the Mayo Clinic (8) include a base width of 1.5 cm and an excursion ≥1.5 cm beyond the plane of the atrial septum or phasic excursion during the cardiorespiratory cycle >1.5 cm. Calle et al. (14) used localized bulging of the interatrial septum >6 mm. For our study we selected a base width ≥1.5 cm in combination with a total excursion ≥1.1 cm for two reasons. 1) Those measurements correspond more closely to the range described for aneurysms by the largest and most authoritative pathologic study, that of Silver and Dorsey (1); the smallest aneurysm in their series bulged 1.1 cm. 2) Five atrial seps that appeared clearly aneurysmal measured from 1.1 to 1.5 cm in total excursion; Figure 3 is an example of a clearly aneurysmal atrial septum with total excursion of 1.1 cm. All five of these atrial seps were associated with intratrial shunting by contrast echocardiography.

The appearance of atrial septal aneurysm could be classified into three different types as categorized by Hanley et al. (1b). Two patients (6%) had a type IA aneurysm that bulged continually into the right atrium and demonstrated little or no motion during the cardiorespiratory cycle. Both of these patients had had a stroke but no shunting. In the Mayo Clinic series a much higher percent of atrial septal aneurysms were classified as type IA (32 [40%] of 80). As in the current study, results of contrast echocardiography were normal in the four patients in the Mayo Clinic series with type IA atrial aneurysm. Thus, type IA aneurysms, although associated with stroke, are not associated with shunting.

Twenty-seven patients (84% of the patients with an atrial septal aneurysm) demonstrated predominant right atrial excursion with phasic oscillation during the cardiorespiratory cycle into the left atrium and would be classified as Mayo Clinic type IB. Only 13 (16%) of the 80 patients in the Mayo Clinic series were so classified. Of those 13, 8 were examined for atrial septal defect and 6 were thought to have an atrial septal defect (3 by surgical confirmation, 3 by Doppler study). This type of aneurysm had a higher prevalence of shunting in the current series (23 [88%] of 26 patients) and all four atrial septal defects were identified in this group.

A subset of the type IB aneurysm was identified in which phasic oscillation into the left atrium occurred during every cardiac cycle, not just with inspiration. We have termed these type IC aneurysms, and all such aneurysms examined were associated with shunting. Significantly, the two type IC aneurysms in patients with stroke were associated with a secundum type atrial septal defect. The differences in the relative prevalence of type IA versus type IB and the recognition of type IC aneurysms between the previous surface echocardiographic study (8) and the current study probably reflect the added sensitivity of transesophageal echocardiography in recording the movements of these aneurysms.

Type II atrial septal aneurysm, which demonstrates protrusion exclusively into the left atrium, was identified in only three patients: one with stroke and two with shunting. In contrast, 22 of the 80 patients in the Mayo Clinic series (8) had a type II aneurysm and 4 of 11 examined (2 with confirmation by catheterization) were thought to have an atrial septal defect. As Hanley et al. (8) have hypothesized, the direction of protrusion of the atrial septal aneurysm and its motion during the cardiac cycle are undoubtedly a reflection of the pressure gradient from the left to the right atrium. In support of this hypothesis is the easily observed ability to cause left atrial bulging of even a type IA aneurysm during the release phase of the Valsalva maneuver. This bulging can be detected only by transesophageal echocardiography because images are distorted by respiratory movement during surface imaging.

Comparison with previous transesophageal echocardiographic studies. Schneider et al. (22) and Zabalgoitia-Reyes et al. (23) recently published their experience with transesophageal echocardiographic imaging of atrial septal aneurysm. The results are consistent with the current study, with 85% (15 of 18) in the study of Schneider et al. (22) and 85% (11 of 20) in that of Zabalgoitia-Reyes (23) demonstrating contrast shunting compared with 72% in the current study. Schneider et al. (22) detected atrial septal aneurysm in 3% of studies performed for nonembolic indications and in 11% of studies performed for embolic indications, compared with 4% and 15%, respectively, in the current investigation.

Schneider et al. (22) found >5 mm thickening of the aneurysmal membrane in 9 of 12 patients with stroke and consider this a risk factor for thrombotic events. However, in the current study, patients with stroke did not demonstrate atrial septal aneurysm with such thickening. Part of this discrepancy may be explained by the ease with which a tangential cut across an atrial septal aneurysm membrane leading to a sparsely thickened appearance can be obtained by single-plane transesophageal echocardiography.

Limitations. Several limitations to this study need to be noted. First, not all patients in Group II underwent contrast imaging. However, the prevalence of a shunt was similar in both Group I and Group II patients with atrial septal aneurysm. Even if all patients in Group II had a shunt present, there would not have been a statistically significant difference in the prevalence between the two groups. Sec-
ond, selection bias may have been introduced into the study by the need for referral for transesophageal echocardiography. However, the ages of patients in Groups I and II were not significantly different and the male to female distribution also did not differ between these two groups. Finally, there was no independent reference standard for comparison. Currently the noninvasive standard for diagnosis of atrial septal aneurysm is surface echocardiography. However, transesophageal echocardiography is clearly superior to surface echocardiography in this evaluation of the atrial septum. Because most patients in this relatively low risk group did not undergo surgery or die, comparison with an independent standard was impossible.

Clinical implications. The cause of stroke remains unexplained in up to 20% of patients despite exhaustive clinical testing for coagulation abnormalities, cerebrovascular disease and cardiac sources of embolism. The strong association between atrial septal aneurysm and stroke in patients in this study and in previous studies implies a possible etiologic role. Two mechanisms have been hypothesized: paradoxic embolism across a patent foramen ovale or atrial septal defect, and thrombus within the atrial septal aneurysm. For either of these mechanisms there are three clinical options: anticoagulant therapy, antiplatelet therapy or surgery. The results of the present study do not allow recommendations for treatment. Only long-term follow-up of these patients will allow determination of which therapeutic option is best.

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References