Prominence of the Eustachian valve in paradoxical embolism

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Aims

To investigate the relationship between Eustachian valve (EV) length and degree of atrial septal movement in patients with patent foramen ovale (PFO) and presumed paradoxical cerebral embolism. PFO is a well-established risk factor for cryptogenic stroke. However, due to the high prevalence of PFO, many of these are bystanders rather than true pathological entities. Other studies have sought to define which patients with PFO are particularly at risk of cryptogenic stroke by measuring various parameters of right atrial anatomy. We investigated the relationship between EV length and atrial septal movement.

Methods and results

Measurements of EV length and atrial septal movement were made prospectively from 72 consecutive patients referred to our centre for PFO closure following presumed cryptogenic stroke, by intracardiac phased array echocardiography. The most significant finding from this study was that patients with fewer than 10 mm atrial septal movement had significantly longer EVs than those in whom there was >10 mm septal movement (P = 0.003). The mean EV length with >10 mm septal movement is 6.35 mm, and 13.33 mm with fewer than 10 mm movement. The prevalence of septal movement beyond 10 mm was significantly less in our series than in previously published papers.

Conclusion

We propose that while a large degree of atrial septal movement significantly increases propensity to cerebral embolism in patients with PFO, its absence does not negate this risk. We have shown that long EV may function independently from atrial septal movement to potentiate paradoxical embolism.

Keywords

Patent foramen ovale • Paradoxical embolism • Atrial septal aneurysm • Eustachian valve

Introduction

Patent foramen ovale (PFO) is a recognized risk factor for cryptogenic stroke, although the absolute increase in risk is debated because PFO is common and some or many may be innocent bystanders in patients with cryptogenic stroke. The prevalence of PFO in the general population is ~25%, while that in patients with cryptogenic stroke is up to 50%.1,2

Recent research has focused on factors which, in addition to the presence of PFO, potentiate the risk of cryptogenic stroke. Such factors include PFO, size3 degree of spontaneous shunting,4–6 PFO tunnel length4 co-existent atrial septal aneurysm (ASA),4,6–9 and concurrent prominent Eustachian valve (EV).10,11

Data published by Alsheikh-Ali et al. emphasize the importance of recognizing these additional risk factors. Using mathematical modelling, they report that up to 33% of PFO is likely to be an incidental finding in patients with cryptogenic stroke. Interestingly, this figure decreases to 9% in the presence of a concurrent ASA.12

Indeed, there is much evidence to show that ASAs potentiate stroke risk in patients with PFOs, including a meta-analysis by Overell et al.7

In the foetus, the EV functions to direct the umbilical vein blood through the open foramen ovale. It would seem logical that the presence of a well-preserved EV in an adult with a PFO should place this individual at increased risk of paradoxical embolism. It has previously been suggested that a persistent EV may predispose to right-to-left shunting in patients with PFO and that by extension, this may increase risk of paradoxical embolism.10,11 However, there have been relatively few studies performed looking at stroke risk in this population and not all authors agree that
prominent EV predisposes to additional risk. Additionally, there have been few studies which have employed intracardiac echocardiography (ICE) to measure such variables as those mentioned above.

ICE is a widely used imaging modality for assessment of the interatrial septum, whose use is increasingly prevalent in occluder device placement in atrial septal defects and PFO. It is slowly replacing transoesophageal echocardiography (TOE) as the preferred imaging modality for these procedures. It is excellent for imaging the right atrium, including the insertion of the inferior vena cava (IVC) and EV (Figure 1). Manipulation of the ICE probe allows visualization of the interatrial septum from multiple planes allowing full delineation of the fossa ovalis, extent of any septal aneurysm and insertion point of the EV.

While the co-existence of ASA and PFO has been convincingly shown to correlate with increased stroke risk, the same cannot be said for a prominent EV and PFO. In a recent study by Rigatelli et al., the authors conclude that the presence of an EV should be considered an adjunctive risk factor for paradoxical embolism rather than a significant risk factor in its own right. Their study employed ICE to visualize the EV, although not phased array. TOE was used to assess movement of the interatrial septum.

We sought to investigate the relationship between EV prominence and ASA using phased array ICE, in a group of patients with cryptogenic stroke without evidence of an alternative aetiology, and a high probability of paradoxical embolism.

Method

We prospectively collected data from 72 consecutive patients referred to our centre for percutaneous PFO closure.

ICE was performed using an 10F 5–10 MHz linear phased array AcuNavTM catheter (Siemens Medical) via a 11F sheath in the right femoral vein. The interventional cardiologist performing the procedure recorded the length of the EV as well as the overall diameter of the right atrium. In addition, the degree of atrial septal movement beyond the septal plane was recorded from the imaging plane demonstrating the greatest movement between the left and right atria and graded from 1 to 4. Grades 1–4 corresponded to movement of 0–5, 6–10, 11–15, and 16 mm or more, respectively; a classification as previously employed by Cabanes et al.

Prominent EV is defined as being ≥1 mm thick and protruding for at least 10 mm within the right atrium from the border of the IVC. ASA is defined as excursion ≥10 mm of the atrial septum into the right or left atrium. Atrial septation was defined as the ratio of EV length to right atrial width.

Comparisons across groups was performed with ANOVA unpaired t-test and Fisher's Exact test (SPSS).

Results

There was no significant difference in age between the groups (P = 0.44). The mean age overall was 48.7 years (range 19–82 years). There were 36 men and 36 women, with no significant difference

<table>
<thead>
<tr>
<th>ASA group</th>
<th>n</th>
<th>M:F</th>
<th>Mean age (years) (SD)</th>
<th>Mean EV (SD)</th>
<th>Mean septation (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>16:18</td>
<td>45.6(14.1)</td>
<td>13.1(7.8)</td>
<td>0.43(0.29)</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>11:9</td>
<td>51.6(14.2)</td>
<td>13.5(9.1)</td>
<td>0.44(0.31)</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>5:6</td>
<td>44.9(12.8)</td>
<td>6.5(5.5)</td>
<td>0.20(0.17)</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>4:3</td>
<td>51.7(14.0)</td>
<td>6.1(11.1)</td>
<td>0.20(0.37)</td>
</tr>
</tbody>
</table>

ASA, atrial septal aneurysm; SD, standard deviation.
in proportion of either sex between groups. Table 1 describes the distribution of mean age, sex ratio, mean EV length and mean septation amount by ASA grade.

Of the 72 patients, 18 (25.0%) had ≥10 mm of septal movement and of these, 7 (9.7%) had a movement of >15 mm. Forty-six (63.9%) had an EV length of 10 mm or more.

The mean lengths of the EV for groups 1–4 were 13.15, 13.50, 6.55, and 6.14 mm, respectively. There was significant variation in EV length between the groups (P = 0.03). There was no significant difference in EV length between groups 1 and 2 or between 3 and 4. However, when groups 1 and 2 are combined and compared with groups 3 and 4 there is a significant difference in EV length (P = 0.003). There was also a significant difference between proportions of atrial septation (P = 0.003). There was no measurable EV in 13 of 72 (18%) patients, 7 in patients from groups 1 and 2, and 6 in patients from groups 3 and 4.

The proportion of EV 10 mm or more in length was 64% overall; 39% (7/18) in patients with ASA and 72% (39/54) in patients without; P = 0.022.

Inverse correlation between ASA and EV length is confirmed by linear regression (P = 0.01) as shown in Figure 2.

**Discussion**

ASA and persistent EV have previously been suggested to increase the risk of stroke in patients with PFO.6,8,10,11 Several studies have investigated right atrial anatomy in relation to PFO and presumed paradoxical embolism, but few have investigated the relationship between prominent EV and ASA. Fewer still have employed ICE.

A quarter of our patients had >10 mm of AS movement and just 9.7% had more than 15 mm of movement. Three-quarters of our patients do not qualify as having ASA, suggesting that some other predisposing factor is present. On the basis of the literature these could include a large degree of right-to-left shunting, large PFO size or perhaps long tunnel length. We propose that a significant predisposing factor in these patients is a prominent EV in conjunction with a PFO. We have clearly demonstrated that below 10 mm of septal excursion there is a higher incidence of a prominent EV, with an increase in mean length from 6.3 to 13.3 mm (P = 0.003). Seven of the 18 patients with ASA had a prominent EV (39%) while 39 of the 54 patients without ASA had prominent EV (72%); P = 0.022. Overall, the proportion of patients with prominent EV was 64%. Rigatelli et al.10 found a proportion of 73.4%. As with our study, these were patients who had suffered previous stroke or transient ischaemic attack, and who had been referred for PFO closure. Forty-six per cent of their patients also had ASA on TOE, a considerably higher proportion than in our study. This discrepancy may reflect the increased spatial resolution and anatomical accuracy of phased array ICE. It is not reported in
their publication whether there was any correlation between EV length and presence (or absence) of ASA.13

In contrast with our findings Homma et al. found that EV significantly correlated with the presence, not absence, of ASA.14 However, in their study it is unclear whether or not a large proportion of those with both prominent EV and ASA also had PFO. Sixty per cent of subjects with ASA in the Homma study also had prominent EV. However, this figure fell to 22% when a ‘large PFO’ was also present. Additionally, even in the absence of ASA there was still a co-incidence of 43% with prominent EV. Every patient in our series had PFO by definition since all measurements were made during the PFO closure procedure. Again, the difference between Homma’s data and our own may be partly explained by technical differences in equipment used. In addition there may be differences between the patient populations. Our study included patients who had experienced transient ischaemic attacks rather than stroke with lasting neurological deficit. Indeed, further research is merited in order to ascertain whether there is any correlation between phenotype and anatomical characteristics such as EV and ASA.

One potential explanation for our findings is that an aneurysmal atrial septum on its own leads to increased risk of right-to-left shunting, but when the atrial septum is not aneurysmal a prominent EV preferentially directs IVC blood flow to the atrial septum, hence also increasing the rate of paradoxical embolism.15,16 Another explanation is that potential ASA is masked in shunting, but when the atrial septum is not aneurysmal a prominent EV is probably independent, so both may be present in an individual, perhaps adding further to the risk of paradoxical embolism in this individual. Our data would suggest that in the absence of an ASA, the presence of a well-preserved EV may be an important alternative factor in placing the individual at risk of paradoxical embolism.

Absence of significant atrial septal movement on transthoracic or transoesophageal echocardiography should not falsely reassure the physician investigating cryptogenic stroke unless a prominent EV due to obstruction to septal movement although it is hard to imagine how the EV could significantly reduce the mobility of the AS. The presence of an ASA or EV is probably independent, so both may be present in an individual, perhaps adding further to the risk of paradoxical embolism in this individual. Our data would suggest that in the absence of an ASA, the presence of a well-preserved EV may be an important alternative factor in placing the individual at risk of paradoxical embolism.

In conclusion, we propose that a prominent EV is a risk factor for paradoxical embolism in patients with PFO but without ASA, and may account for a large proportion of otherwise ‘incidental’ PFOs in cryptogenic stroke where there is no ASA. This contrasts with the view of Rigatelli et al. who proposed that EV be considered an adjunctive risk factor. Further study is warranted to ascertain whether different anatomical variants correlate with defined phenotypic subgroups of stroke and TIA patients, including severity of disability and recurrence.

**Conflict of interest:** none declared.

**References**


