Patent Foramen Ovale: A Review of Associated Conditions and the Impact of Physiological Size

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Patent foramen ovale (PFO) is implicated in platypnea-orthodeoxia, stroke and decompression sickness (DCS) in divers and astronauts. However, PFO size in relation to clinical illness is largely unknown since few studies evaluate PFO, either functionally or anatomically. The autopsy incidence of PFO is approximately 27% and 6% for a large defect (0.6 cm to 1.0 cm). A PFO is often associated with atrial septal aneurysm and Chiari network, although these anatomic variations are uncommon. Methodologies for diagnosis and anatomic and functional sizing of a PFO include transthoracic echocardiography (TTE), transesophageal echocardiography (TEE) and transcranial Doppler (TCD), with saline contrast. Saline injection via the right femoral vein appears to have a higher diagnostic yield for PFO than via the right antecubital vein. Saline contrast with TTE using native tissue harmonics or transmural pulsed wave Doppler have quantitated PFO functional size, while TEE is presently the reference standard. The platypnea-orthodeoxia syndrome is associated with a large resting PFO shunt. Transthoracic echocardiography, TEE and TCD have been used in an attempt to quantitate PFO in patients with cryptogenic stroke. The larger PFOs (approximately ≥4 mm size) or those with significant resting shunts appear to be clinically significant. Approximately two-thirds of divers with unexplained DCS have a PFO that may be responsible and may be related to PFO size. Limited data are available on the incidence of PFO in high altitude aviators with DCS, but there appears to be a relationship. A large decompression stress is associated with extra vehicular activity (EVA) from spacecraft. After four cases of serious DCS in EVA simulations, a resting PFO was detected by contrast TTE in three cases. Patent foramen ovales vary in both anatomical and functional size, and the clinical impact of a particular PFO in various situations (platypnea-orthodeoxia, thromboembolism, DCS in underwater divers, DCS in high-altitude aviators and astronauts) may be different. (J Am Coll Cardiol 2001;38:613–23) © 2001 by the American College of Cardiology

Patent foramen ovale (PFO) has been implicated in several pathologic processes, including paradoxical embolism in cryptogenic stroke (1–6) and venous-to-arterial gas embolism (AGE) in serious forms of decompression sickness (DCS) (an occupational hazard for underwater divers [7–9] and high altitude aviators and astronauts [10–13]). Enhanced right-to-left shunting of venous blood through a PFO in certain pathologic states (14–16), including the platypnea-orthodeoxia syndrome (17–24), may cause systemic hypoxemia. Only a few studies have attempted to quantitate the size of a PFO, either functionally or anatomically.

The availability of noninvasive techniques for assessment of PFO provides the opportunity for clinicians to diagnose pathologic states that were heretofore difficult to diagnose.

These techniques assess PFO risk based on anatomic and functional size.

EMBRYOLOGY

Patent foramen ovale is a remnant of the fetal circulation. Oxygenated placental blood enters the right atrium (RA) via the inferior vena cava (IVC) and crosses the valve of the foramen ovale to enter the systemic arterial system (25). The IVC flow preferentially flows toward the interatrial septum (IAS) and foramen ovale. The crista internerviens directs superior vena cava flow away from the IAS. Coronary sinus flow is also directed away from the IAS (26). At birth, pulmonary vascular resistance and right-sided cardiac pressures drop with a reversal of the RA-to-left atrium (LA) pressure gradient. The flap of the foramen ovale (septum primum) closes against the atrial septum (septum secundum), with fusion usually occurring within the first two years of life. Fusion is incomplete in about 25% of people, resulting in an oblique slit-like defect. Termed a PFO, it functions as a valve-like structure with the “door-jam” on the LA side of the atrial septum (25) (Fig. 1).
INCIDENCE

Two autopsy studies determined PFO incidence, with the first (n = 1,100) revealing a “probe” patent PFO (0.2 cm to 0.5 cm maximum dimension) in 29% and “pencil” patent PFO (0.6 cm to 1.0 cm) in 6% (27). The second study (n = 965) recorded a PFO incidence of 27.3%, with PFOs varying in size from 1 mm to 19 mm (mean 4.9 mm). The incidence of PFO declined with age, suggesting that anatomic closure may occur even in adulthood (28).

ASSOCIATED ANATOMICAL STRUCTURES

Attrial septal aneurysm (ASA) (29,30) (Fig. 2) and Chiari network (31) (Fig. 3) are associated with PFO. Atrial septal aneurysm incidence is 1% by an autopsy study (32) and 1.9% by transthoracic echocardiography (TTE) (10,803 subjects) (33), defining ASA as a septal excursion of $\geq 10$ mm, with a base diameter of $\geq 15$ mm. Another TTE study using an excursion of $\geq 15$ mm found an ASA incidence of 0.22% (34).

A monoplane transesophageal echocardiography (TEE) study (30) defined ASA excursion $\geq 11$ mm and base diameter of 15 mm to compare patients with embolic stroke (n = 133) with controls (n = 277). An ASA was present in 15% of the stroke group and 4% of controls. A PFO was diagnosed by saline contrast injection in 70% of stroke patients with an ASA and 75% of controls with an ASA. Of the 32 ASAs in this study, six had an associated Chiari network. Notably, TTE identified only 12/32 (37.5%) of the ASAs. A biplane TEE study (29) found an ASA in 28/355 (7.9%) of stroke patients and 8/363 (2.2%) of controls. A PFO was found by saline contrast in 56% of ASA patients. No other possible source of embolism was found in 24/28 (86%) of the stroke patients with an ASA. In another study, if a mobile IAS or fossa ovalis measured $\geq 14$ mm, there appeared to be an increased PFO incidence (35). These data indicate that an ASA occurs commonly in patients with unexplained stroke and is more frequently detected by TEE than by TTE.

The Chiari network is a remnant of the septum spurium and the right valve of the sinus venosus resulting from incomplete resorption of these structures (36). Lace-like remnants of the original septum may persist and be evident as coarse or fine fibers in the RA. These fibers originate from either the Eustachian or Thebesian valve and have attachments to the upper wall of the RA or IAS. The Eustachian valve may also be relatively mobile and fenestrated but does not attach to the upper wall of the right atrium or IAS and, therefore, should not be termed a “Chiari network.”

The autopsy incidence of the Chiari network has been reported as 2% to 3% (37). A TEE study found a Chiari network in 29/1,436 (2%), whereas TTE identified only 8. A TEE-determined PFO was found in 24/29 (83%) of these, with more “intense” right-to-left shunting noted. An ASA was found by TEE in 33/1,436 (2.3%), with 7/33 having a coexistent Chiari network (31).

DIAGNOSIS OF A PFO

Before the advent of echocardiography, diagnosis of a right-to-left shunt was problematic. A PFO without a significant resting right-to-left shunt is generally not associated with any abnormality of the patient history, physical

#### Abbreviations and Acronyms

- AGE = arterial gas embolism
- ASA = atrial septal aneurysm
- ASD = atrial septal defect
- DCS = decompression sickness
- EMU = extravehicular mobility unit
- EVA = extravehicular activity (spacewalk)
- IAS = interatrial septum
- ISS = International Space Station
- IVC = inferior vena cava
- LA = left atrium
- MRI = magnetic resonance imaging
- NTH = native tissue harmonics
- PAVS = pulmonary arteriovenous shunt
- PFO = patent foramen ovale
- PV = pulmonary vein
- RA = right atrium
- TCD = transcranial Doppler
- TEE = transesophageal echocardiography
- TMD = transmitral Doppler
- TTE = transthoracic echocardiography

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**Figure 1.** Longitudinal imaging transesophageal echocardiography in the midupper esophagus. A large patent foramen ovale (PFO) is evident. The arrow illustrates how to measure the PFO width. LA = left atrium; RA = right atrium.
examination, electrocardiogram or chest radiograph. Heart catheterization is generally inadequate for diagnosis of PFO, unless a right heart catheter crosses the IAS into the LA. On occasion, a transvenous pacemaker wire or pulmonary artery catheter may inadvertently cross into the LA via an atrial septal defect (ASD) or PFO. Dye dilution methods are cumbersome and invasive (38). A relatively noninvasive method using peripherally injected indocyanine with generation of a dye dilution curve from a dichromatic earpiece densitometer was reported in patients with cryptogenic stroke. A right-to-left shunt was detected in 24/59 (41%); however, it was not compared with any other diagnostic modality (39).

Echocardiographic techniques have emerged as the principle means for diagnosis and assessment of PFO (Table 1). In particular, TTE, TEE and transcranial Doppler (TCD) are commonly used. Peripherally injected agitated saline may be utilized with TTE to diagnose a right-to-left shunt, but the yield is rather low compared with TEE. Transcranial Doppler has been used for PFO diagnosis by detection of air microemboli in a middle cerebral artery after peripheral injection of agitated saline. With TTE, the Valsalva maneuver may enhance color Doppler or agitated saline contrast detection of a right-to-left shunt, but the acoustic window may be lost during the maneuver.

Transmitral Doppler (TMD) of mitral flow using peripheral injection of agitated saline was compared with TEE using both contrast and color Doppler for PFO detection (40). Transesophageal echocardiography detected PFO in 17/44 subjects (39%), with 16 detected by contrast and 1 only by color, the latter having a left-to-right shunt. Transthoracic echocardiography (TTE) was positive in only 12 of 17 positive TEE-detected PFOs, but all 16 contrast positive TEEs were positive by TMD. An additional positive TMD was not detected by TEE. A TMD “bubble score” and automated quantitative power score correlated with PFO size measured by TEE.

Transthoracic echocardiography, TTE with native tissue harmonics (NTH) and TEE were performed with saline contrast and the Valsalva maneuver in a consecutive group.

Figure 2. M-mode (left) and two-dimensional (right) transesophageal echocardiography longitudinal image in the midupper esophagus. The M-mode demonstrates marked interatrial septum (IAS) mobility, with an excursion >15 mm. By definition this is an atrial septum aneurysm. LA = left atrium; RA = right atrium; SVC = superior vena cava.

Figure 3. Transesophageal echocardiography in the midupper esophagus at 105°. The arrow points to the mobile Chiari network. IAS = interatrial septum; LA = left atrium; RA = right atrium; SVC = superior vena cava.
Table 1. Evaluation of Patients for Both Anatomical and Functional PFO Size

<table>
<thead>
<tr>
<th>TTE</th>
<th>Anatomy</th>
<th>Chiari network</th>
<th>Interatrial septum mobility/atrial septum aneurysm</th>
<th>Diameter of fossa ovalis</th>
<th>Evaluate IVC flow direction (Right-to-left shunt)</th>
<th>Measure slit between septum primum and septum secundum</th>
<th>Resting and Valsalva</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color Doppler</td>
<td>Evaluate IVC flow direction</td>
<td>Right-to-left shunt</td>
<td>Left-to-right shunt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline contrast</td>
<td>(Quantitate bubbles in left heart)</td>
<td>Resting injection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TEE</td>
<td>Anatomy</td>
<td>Chiari network</td>
<td>Interatrial septum mobility/atrial septum aneurysm</td>
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</tr>
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<td>Left-to-right shunt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saline contrast</td>
<td>(Timing of contrast arrival into LA)</td>
<td>(Quantitate bubbles in LA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCD</td>
<td>Performed in conjunction with TTE and TEE.</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

ASD = atrial septal defect; IVC = inferior vena cava; LA = left atrium; PFO = patent foramen ovale; TCD = transcranial Doppler; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

of patients referred to an echocardiography laboratory (n = 109) for TEE (41). Criteria for PFO detection included contrast found in the LA within three cardiac cycles after RA opacification, and “significant” shunts were categorized as >20 bubbles in the LA. Patent foramen ovale was identified by TTE in 9/109 subjects (8%), NTH in 31/109 subjects (29%) and TEE in 31/109 subjects (29%). A “significant” PFO shunt was found in 8 subjects (7%) by TTE, 17 (16%) by NTH and 12 (11%) by TEE. Two “significant” shunts detected by NTH were not detected by TEE. Native tissue harmonics failed to detect four nonsignificant PFOs that were detected by TEE. The advantage of NTH over TEE was explained by the difficulty patients had in performing the Valsalva maneuver due to the presence of an endoscope.

Transesophageal echocardiography is currently considered the reference standard for PFO diagnosis, allowing direct imaging of the IAS and saline contrast shunting through a PFO. If color flow Doppler or peripheral saline contrast injection detect right-to-left flow during normal respiration, this is termed a resting PFO. Enhanced right-to-left flow may be noted upon release of the Valsalva maneuver.

A methodologic study (n = 70) in patients with arterial embolism compared antecubital vein to femoral vein contrast injection (Table 2) (42). These data suggest that cough or the Valsalva maneuver increase the sensitivity of TEE PFO detection and that contrast injections via the femoral vein approach are superior to the antecubital route. A second study comparing the antecubital and femoral vein approach used TEE and TCD in young patients (n = 44) with unexplained neurologic events (Table 3) (43). Although the incidence of PFO by antecubital injection was much lower than that generally reported by other investigators, contrast injections via the femoral approach had a higher PFO detection rate.

A false-negative or false-positive TEE for PFO may occur. A false-negative TEE may result from inadequate visualization within the esophagus, elevated LA pressures preventing right-to-left passage of contrast (44,45), IVC-directed flow along the IAS preventing impingement of antecubital bubbles against the IAS (42) (Fig. 4) or an improperly performed Valsalva maneuver.

A TEE false-positive contrast study may occur with a true ASD (Fig. 5) or a pulmonary arteriovenous shunt (PAVS). Contrast that has a delayed appearance (>3 cardiac cycles) within the LA after opacification of the RA may result from a PAVS in which contrast may also be observed traversing one or more pulmonary veins (PVs). So-called “debris” entering the LA from PVs may result in a false-positive TEE (46). Thought to be related to transient PV stasis, especially during Valsalva maneuver release, flow was noted to enter the LA. This debris was usually noted with high gain settings.

**Table 2. TTE PFO Detection by Site of Injection (42)**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Spontaneous Respiration</th>
<th>Cough</th>
<th>Valsalva</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/70 (1%)</td>
<td>4/70 (6%)</td>
<td>9/70 (13%)</td>
<td>9/70 (13%)</td>
<td></td>
</tr>
<tr>
<td>Femoral</td>
<td>7/70 (10%)</td>
<td>14/70 (20%)</td>
<td>22/70 (31%)</td>
<td>22/70 (33%)</td>
</tr>
</tbody>
</table>

PFO = patent foramen ovale; TTE = transthoracic echocardiography.

**Table 3. TTE PFO Detection by Injection Site (43)**

<table>
<thead>
<tr>
<th>Femoral Vein</th>
<th>Spontaneous Respiration</th>
<th>Cough</th>
<th>Valsalva</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>14/70 (20%)</td>
<td>22/70 (31%)</td>
<td>22/70 (33%)</td>
<td></td>
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</tbody>
</table>

**PFO SIZE AND CLINICAL SIGNIFICANCE**

**Autopsy correlation.** Patients (n = 35) were examined for PFO with both TEE and at subsequent autopsy (47). Patent foramen ovale size was measured with TEE aided by color flow Doppler and by quantitating LA contrast using peripheral venous injections. Nine PFOs found at autopsy had all been correctly identified ante mortem by color Doppler TEE. Contrast TEE was negative in one subject described as having a long interatrial channel. Several patients with anatomically confirmed PFO had TEE detected left-to-right shunts. All had evidence of high LA pressures. Color flow Doppler slightly overestimated PFO size as determined by autopsy. Left atrium contrast was graded by the maximum number of microbubbles appearing in a single frame and subsequently compared with autopsy findings (Table 4).

**The platypnea-orthodeoxia syndrome.** The platypnea-orthodeoxia syndrome describes both dyspnea (platypnea) and arterial desaturation in the upright position with im-
The syndrome occurs with an intracardiac or intrapulmonary shunt and often with some form of lung disease. The post-pneumonectomy patient (usually the right lung [18,20]) may develop symptoms many months after the surgical procedure (17,18,50). A ventilation-perfusion lung scan, obtained for dyspnea and hypoxia, will reveal systemic uptake of isotope (21,22,50).

Diagnosis of a PFO with platypnea-orthodeoxia has been made with a tilt table and saline contrast TTE (17) and TEE (24). A typical patient history with a significant drop in oxygen saturation while in the upright position, along with a large PFO by TEE found as the only source of a shunt, has been considered diagnostic (22).

Cryptogenic stroke. Efforts to determine anatomical size and functional significance of a PFO have been expended most often in patients with embolic stroke (Fig. 6). Patients (n = 49) with stroke were evaluated by TTE, TEE and TCD (51). Transesophageal echocardiography diagnosed PFO in 19/49 subjects (39%). Transthoracic echocardiography was positive in 9/49 subjects (18%) and TCD in 13/49 subjects (27%). No PFOs were detected by TTE and TCD that were not detected by TEE. All six PFOs not diagnosed by TCD measured ≤2 mm by TEE, suggesting that TCD may only miss small defects.

Another study used TCD and monoplane TEE to compare 63 controls, 33 patients with stroke that was explained or “clarified” and 41 patients with cryptogenic stroke (52). Shunts were sized by quantitating the number of TCD detected spikes or TEE visualized microbubbles (Table 5). The TEE score distribution was relatively similar among the three groups. By TCD, however, the normal group had a minimal shunt score, and the cryptogenic group had the largest shunt score, suggesting that TCD may find predominately clinically significant shunts.

A TEE study with peripheral contrast injection (18 for source of embolism) detected 34 resting PFOs (53). These were divided into a small shunt subgroup (n = 18) with ≥3 and <20 LA microbubbles and a large shunt subgroup (n = 16) with 20. All patients were treated with aspirin or warfarin and were followed for 21 months. Of the large shunt subgroup (5/16), 31% had an ischemic event, whereas there were none in the small shunt subgroup.

Patients <60 years of age with unexplained neurologic
events were compared with normal controls by multiplane TEE (54) (Table 6). A PFO was diagnosed using peripheral contrast injection and by direct visualization of the IAS. Shunt size was measured during normal respiration and with the Valsalva. Patients with neurologic events had a significantly higher PFO incidence and size compared with controls. The large PFO size was found more commonly in the multiple cerebrovascular accident subgroup. An ASA was more common in the neurologic event group (12%) compared with controls (2%), and 19 of the 21 patients with an ASA had a large PFO (5 ± 2 mm). Peripheral saline contrast shunts were quantitated as minimal (few bubbles in LA), moderate (“cloud” in LA) or severe (intense opacification). Although contrast identified patients with PFO, there was no significant correlation between measured size and contrast shunt severity.

**Underwater diving and DCS.** Decompression sickness results from the formation of bubbles in body fluids as

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**Figure 5.** Longitudinal transesophageal echocardiography (TEE) imaging in the midupper esophagus. A 32-year-old male presented with an embolic stroke. He was found to have occult thrombi in both calf veins. Transthoracic echocardiography with peripheral saline contrast during normal respiration and Valsalva were negative for a right-to-left shunt. (A) TEE revealed a small restrictive secundum atrial septal defect (ASD) (arrow). Note how this appearance is different from that of a patent foramen ovale. (B) Color Doppler demonstrates a left-to-right shunt with a color mosaic pattern from the shunt in the right atrium (RA). The ASD was subsequently surgically repaired. LA = left atrium; SVC = superior vena cava.
ambient pressure is reduced. Arterial gas embolism is usually due to air emboli arising from pulmonary barotrauma or from bubbles in the systemic venous circulation entering the arterial system. An AGE through an ASD in a scuba diver was first reported in 1986 (55). Two TTE studies then demonstrated a relationship between PFO and otherwise unexplained DCS in divers (7,8). In the first study (n = 30), 11/30 subjects (37%) had a resting right-to-left shunt (8). Of the 30 divers, 18 had type II DCS (i.e., serious disease including neurologic or cardiopulmonary dysfunction as opposed to type I DCS in which only musculoskeletal pain is present), and all 11 divers with a resting shunt were in this group. None of the other 12 divers, who had type I DCS, had a shunt.

In the second study, antecubital injection was performed during normal respiration and “modified” Valsalva (7). The incidence of PFO was 23/53 (43%), but further quantification, by counting bubbles in the left ventricle, was not reproducible from one injection to the next.

A TTE, TEE and TCD study compared commercial divers (n = 26) with control subjects (n = 30) (9). Divers were categorized as “possible” DCS (transient nonspecific neurologic symptoms and a normal examination within 48 h of surfacing), “probable” (significant neurologic dysfunction but with a normal neurologic examination within 48 h) and “definite” (significant neurologic dysfunction and an abnormal neurologic examination). A TTE was considered positive if any bubble appeared in the left heart. By TEE, ≥3 bubbles in the LA were required for an examination to be classified as positive, and a study was considered “strongly positive” if ≥5 bubbles were seen in a single video frame. With normal respiration, no difference in PFO detection rate was noted. By Valsalva maneuver (Table 7), TCD had the best positive and negative predictive value for detection of PFO in divers with DCS and was felt to be better than TEE for delineation of a clinically significant shunt. In addition, all controls and divers with a strongly positive TEE had a positive TCD, and all with a positive TCD had a strongly positive TEE.

Asymptomatic sport divers (n = 87) were evaluated with bilateral TCD and a sonicated contrast medium injected into an antecubital vein (56). A shunt was considered to be of low relevance if <20 signals occurred after the Valsalva maneuver and high relevance if ≥20 signals were noted. Magnetic resonance imaging (MRI) brain scans were also performed (Table 8). All MRI lesions were 2 mm to 3 mm in size and located in the distribution of the anterior cerebral circulation. Of note, the three divers with many lesions had high relevance signals by TCD.

A multiplane TEE study with peripheral agitated contrast injection was performed in divers with DCS (n = 37) and control divers (n = 36) (57). Shunts were sized during Valsalva by quantitating microbubbles in the LA (Table 9). Of the 37 DCS divers, 20 had type II illness and, of these, 14/20 (70%) had a grade II PFO.

From these studies, it appears that a PFO is associated

<table>
<thead>
<tr>
<th>Grade (Number of LA Microbubbles)</th>
<th>Number of Patients</th>
<th>PFO Autopsy Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (1–5)</td>
<td>1</td>
<td>&gt;2 mm</td>
</tr>
<tr>
<td>II (6–25)</td>
<td>2</td>
<td>&gt;2 mm to &lt;10 mm</td>
</tr>
<tr>
<td>III (&gt;25)</td>
<td>3</td>
<td>≥10 mm</td>
</tr>
</tbody>
</table>

LA = left atrium; PFO = patent foramen ovale; TTE = transthoracic echocardiography.

Figure 6. Longitudinal transesophageal echocardiographic imaging in the midupper esophagus. Arrows point to a thrombus wedged through a patent foramen ovale and lodged in both the right atrium (RA) and left atrium (LA). SVC = superior vena cava.
with unexplained DCS. A resting PFO and one found by TCD seem to be associated. Recreational divers without a clinical history of DCS, but with \( \geq 20 \) signals detected by TCD on a single peripheral injection seemed to have a higher likelihood of lesions in the anterior cerebral artery territory, as detected by MRI brain scan.

**DCS in high altitude aviators and astronauts.** As the performance of aircraft has evolved over the course of the last century, both the achieved altitude and rate of climb have increased. Therefore, hypobaric DCS became a problem, particularly evidenced during high-altitude bomber flights in World War II. Several fatal cases occurred in which the pressure profile and postmortem findings were documented in some detail (58), with a PFO noted in 5/19 cases. However, no comment was made on the integrity of the IAS in the reports of several of the remaining autopsies. Nevertheless, it is clear that a PFO is not invariably present in all serious cases of altitude DCS.

Altitude exposures occur yearly in hypobaric chambers utilized by the armed forces of several nations to familiarize aircrew with the physiologic phenomena associated with hypoxia and rapid decompression. Altitude DCS is an uncommon but persistent problem in these exposures; an overall incidence of about 0.1% is experienced by the U.S. Armed Forces, with about 10% of these cases manifesting neurologic or other serious symptoms (59–61).

The contribution of a PFO to these cases of DCS is not clear, but the prevalence of PFO in U.S. Navy aviators with serious DCS is reported to be no different from case controls (10,62). However, these data may not be applicable to all types of hypobaric pressure profiles. Specifically, the pressure profile used in physiologic training exercises involves a short exposure (about 15 min) to a modest altitude (about 7,600 m) with subjects at rest. A long hypobaric exposure, during which heavy work is performed, may be distinct from these physiologic training profiles and may render a PFO more important. Presently, the relative risk for altitude DCS conferred by the presence of a PFO is not well characterized.

A large decompression stress is associated with extravehicular activity (EVA) from spacecraft. During the era of the International Space Station (ISS) construction and maintenance, two types of "space suits" were utilized, the Extravehicular Mobility Unit (EMU) developed by the U.S. and the Russian Orlan suit. To maximize space suit flexibility while maintaining an adequate alveolar oxygen partial pressure, the suits contain nearly pure oxygen at subatmospheric pressures. The absolute pressure within the EMU is 29.6 kPa, while in the Orlan suit it is 38.6 kPa. Under most conditions, the cabin atmosphere within all spacecraft utilized in this program (Space Shuttle, proposed "lifeboat" spacecraft, the Soyuz spacecraft and ISS itself) approximates sea-level conditions with a composition of 21% oxygen, balance nitrogen and trace gases, at an absolute pressure of 101 kPa. Consequently, when a crew member transitions from a spacecraft cabin into a space suit for EVA, there is a substantial decompression. If this decompression were performed without specific preparation, serious DCS would be virtually inevitable. To reduce risk of DCS during EVA,
during normal respiration and the Valsalva maneuver, with attention to proper timing during the Valsalva maneuver. It appears that femoral venous injection of contrast, as compared with antecubital injection, increases the incidence of right-to-left shunt detection, especially during TTE studies. During a TEE study, observation of agitated contrast adjacent to the RA-side of the IAS after antecubital contrast injection may be helpful in that the antecubital injection probably is accurate.

Individuals who have PFO can be subgrouped according to many PFO characteristics (large vs. small PFO, provoked vs. unprovoked trans-septal gas passage, associated anatomical structures). Which methodologic techniques for detection of those characteristics that are clinically important in assessing risk of embolic stroke, diver’s DCS and altitude DCS is not yet entirely clear. The size of PFO probably matters in determining risk, as does the ease with which trans-septal passage of emboli occurs in relation to intrathoracic pressure excursions. Patent foramen ovales are very common, and not all PFOs are the same. The challenge that remains is to determine which PFOs and clinical contexts confer an increased risk of significant disease.

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