Review articles

The role of persistent foramen ovale and other shunts in decompression illness

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Abstract

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A persistent foramen ovale (PFO) and other types of right-to-left shunts are associated with neurological, cutaneous and cardiovascular decompression illness (DCI). A right-to-left shunt is particularly likely to be implicated in causation when these types of DCI occur after dives that are not provocative. It is believed that venous nitrogen bubbles that form after decompression pass through the shunt to circumvent the lung filter and invade systemic tissues supersaturated with nitrogen (or other inert gas) and as a result there is peripheral amplification of bubble emboli in those tissues. Approximately a quarter of the population have a PFO, but only a small proportion of the population with the largest right-to-left shunts are at high risk of shunt-mediated DCI. The increased risk of DCI in people with migraine with aura is because migraine with aura is also associated with right-to-left shunts and this increased risk of DCI appears to be confined to those with a large PFO or other large shunt. Various ultrasound techniques can be used to detect and assess the size of right-to-left shunts by imaging the appearance of bubble contrast in the systemic circulation after intravenous injection. In divers with a history of shunt-mediated DCI, methods to reduce the risk of recurrence include cessation of diving, modification of future dives to prevent venous bubble liberation and transcatheter closure of a PFO.

Key words

Right-to-left shunt; persistent foramen ovale (PFO); arterial gas embolism; decompression illness; bubbles; percutaneous closure; review article

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Introduction

Paradoxical thromboembolism across a persistent foramen ovale (PFO) as a cause of stroke was first postulated in 1877,[1] but it was believed to be a rare event until 1988 when two case control studies showed that this mechanism may be numerically important, particularly in young stroke patients.[2,3] It was around that time that the role of paradoxical gas (nitrogen) embolism as a cause of decompression illness (DCI) in divers was first proposed.[4]

Until then, the prevailing hypothesis was that what we now call decompression illness in divers had two distinct mechanisms. One mechanism is arterial gas embolism (AGE), which is caused by pulmonary barotrauma on ascent, so that alveolar gas invades the pulmonary veins and is carried to the systemic circulation. The onset of symptoms should be during or immediately after ascent and should affect tissues with the greatest blood flow, particularly the brain. The second mechanism is decompression sickness (DCS) resulting from excessive amounts of bubble liberation from solution in solid tissues and venous blood.

Some venous bubbles are liberated after many dives that are not provocative, but as the bubbles pass through alveolar capillaries, the gas diffuses out of the bubbles into the alveoli down the concentration gradient. Therefore, venous bubbles liberated after dives generally should not reach the systemic circulation, unless massive amounts of bubbles are liberated and overwhelm the alveolar filter. In theory, there should be a delay in liberation of bubbles and hence of onset of DCS after surfacing unless the dive profile is extremely provocative, when there can be a very rapid onset, similar to that in AGE secondary to pulmonary barotrauma. According to this hypothesis cutaneous manifestations and joint pain could not be the result of gas embolism.

A difficulty with this hypothesis was that many divers who have had DCS with some latency in onset of symptoms and, therefore, not the result of pulmonary barotrauma of ascent, are certain that their dive profiles were conservative. The later advent of decompression computers confirmed that the majority of episodes of DCS follow a dive with a profile generally considered to be conservative.

The possibility that DCS in divers might result from paradoxical gas embolism was proposed in 1986: A diver who had cerebral and spinal DCS after an air dive with a profile that had a risk of causing venous gas nucleation but was of a low risk of causing DCS was discovered to have an atrial septal defect (ASD).[4] It was proposed that even when there is relatively little venous bubble formation during decompression, a right-to-left shunt may allow paradoxical gas embolism. In that way the venous bubbles evade the pulmonary filter and pass into the systemic circulation where bubble emboli invade critical tissues and cause DCI.[4] This

mechanism requires that the gas emboli pass into tissues that are supersaturated with nitrogen, so that the embolic bubbles are amplified as nitrogen passes out of the supersaturated tissue into the bubble.[5] This amplification of embolic bubbles is critical to the postulated pathophysiological mechanism of manifestations of DCI.

Echocardiography with bubble contrast is a common procedure in hospitals when testing for a right-to-left shunt, but patients do not suffer symptoms and signs of DCS, even when large numbers of bubbles cross the communication. That is because, in that situation, their tissues are not supersaturated with inert gas. During contrast echocardiography, the injected air bubble emboli have a higher partial pressure of nitrogen than the tissues they invade, so the nitrogen rapidly diffuses out of the bubble down the concentration gradient.[5]

If a diver with a large right-to-left shunt performs a dive such that many bubbles are liberated and, as a result, many small bubbles cross the communication, the bubbles will be distributed widely according to tissue blood flow. In that situation, the manifestations of DCI will be determined largely by whether the tissues invaded by bubble emboli are still supersaturated and hence able to amplify embolic bubbles. This may explain the fact that shunt-mediated DCI can manifest both in tissues with high blood flow and hence high emboli load, such as the brain, but also in tissues with low blood flow, such as skin and subcutaneous tissues.

Neurological decompression illness

In 1989, Moon and colleagues reported that 11 of 18 patients with a history of serious neurological DCS had a right-to-left shunt consistent with the presence of a PFO on transthoracic contrast echocardiography (TTE) compared with a shunt in only nine of 176 (5%) historic controls (reported by different investigators using a different technique) ($P = 0.0001$).[6] No shunt was detected in 12 divers with mild DCS, defined as joint pain or sensory symptoms only.

The same year, a blind case controlled study compared the findings on contrast echocardiography in 61 divers with DCS divided into pre-defined sub-groups with 63 control divers.[7] Shunts were detected in 15 of 63 controls compared with 19 of 29 divers with neurological symptoms of DCI with onset within 30 minutes of surfacing ($P < 0.01$). Of the remaining 10 divers in this sub-group, four had lung disease. When latency of neurological symptoms exceeded 30 minutes, four of 24 had a shunt. Shunts were present in one of six with joint pain but in three of five with cutaneous DCS (three of those with skin bends also had neurological symptoms). Shunts were present in significantly more divers (16 out of 25) who had DCS after dives that were not provocative than in divers who had symptoms after provocative dives (nine of 36). Provocative dive profiles were significantly more often associated with late onset neurological DCS (22 of 26, $P < 0.001$) and joint DCS (seven of eight, $P < 0.01$) than with neurological DCS with latency less than 30 minutes (nine of 31). Spinal manifestations appeared to be related to having a shunt.

The findings in the study were extended by increasing the number of affected divers to 97 and control divers to 109.[8] Shunts were present in 26 of 109 (24%) of controls, but in significantly more divers with neurological DCS with latency within 30 minutes (33 of 50), cutaneous DCS (12 of 14) and cardiorespiratory DCS (seven of 12). The prevalence of shunts in divers with neurological DCS with latency greater than 30 minutes (nine of 35) and joint pain (three of 20) did not differ significantly from the control group.

Risk factors for DCS were present in 29 of 38 dives (not divers) preceding neurological DCS with latency more than 30 minutes and 20 of 23 of dives followed by musculoskeletal DCS. The proportions of provocative dives preceding neurological manifestations with onset within 30 minutes (21 of 58), cutaneous rashes (seven of 29) and cardiovascular manifestations (four of 12) were significantly fewer.

At the time, these findings were controversial. So a replication study was performed under the supervision of the Medical Research Council and the MRC Decompression Sickness Panel, which supported the reported findings.[9] Since then, many studies in divers with DCI have provided more information about the types of DCI associated with shunts and the type and size of shunts responsible.

A blind case control study to determine the relationship between different manifestations of neurological DCI and its causes in 100 consecutive divers with 115 episodes of neurological DCI and 123 historical control divers found that the size of right-to-left shunts was critical to the development of DCI.[10] A large shunt was seen after a single injection of bubble contrast at rest in 41 of 100 (41%) cases compared with six of 123 (4.9%) controls ($P < 0.001$). A Valsalva manoeuvre increased the rates of large shunts detected to 51% of cases and 7.3% of controls ($P < 0.001$). Shunts graded large or medium in size were present in 52% of affected divers and 12.2% of controls ($P < 0.001$). Spinal decompression illness occurred in 26 of 52 affected divers with large or medium size shunts and in 12 of 48 without a significant shunt ($P < 0.02$). Five of the 52 large or medium shunts were pulmonary, not intracardiac shunts and three of these five divers had spinal DCI.

The distribution of latencies of DCI symptoms and signs differed markedly between the 52 divers with a large or medium shunt (63 episodes with median latency 20 minutes, of which 10 episodes had a latency of five minutes or less), and the 30 divers who had either lung disease (on chest X-ray and/or pulmonary flow-volume loops) or had performed a provocative dive (31 episodes, of which 20 had a latency

of 5 minutes or less). In the 18 divers who had 21 episodes of neurological DCI after non-provocative dives but had no significant shunt or lung disease on the tests performed, a short latency was associated with a significantly higher prevalence of smoking than in other groups of divers.

Since then, other studies have consistently confirmed that a right-to-left shunt and, in particular, a large shunt is strongly associated with cerebral and cochleovestibular DCI.[11,12] A transcranial Doppler study comparing 101 divers with DCI and 101 controls found that "*major shunts*" were present in 11.9% of controls, but in significantly more divers with cochleovestibular (24 of 34), cerebral (13 of 21) and spinal bends (10 of 31). Only two of 15 with joint pains had major shunts.[12]

Thromboembolic events frequently affect the brain and rarely affect the spinal cord. This predilection for affecting the brain is attributed to the considerably greater blood flow to the brain compared with the spinal cord. But the frequencies with which neurological DCI affects the spinal cord and brain are much more comparable. So, the possibility that spinal DCI might result from an embolic process was controversial. However, a number studies have found a significant relationship between spinal DCI and large right-to-left shunts.[7,10,12–14] In a study of 49 divers with spinal DCS (17 cervical and 32 thoraco-lumbar) and 49 controls, the prevalence of right-to left shunts was reported to be significantly greater in divers with spinal DCS than controls, and particularly so for thoraco-lumbar spinal DCS.[14]

However a study using transoesophageal echocardiography (TOE) with bubble contrast reported that the prevalence of PFO in divers with neurological DCS (22 of 37) did not differ from in control divers (13 of 36).[11] In a sub-group analysis, 20 divers with a history of "*cerebral DCS (cerebral, cerebellar, high-spinal, vestibular or cochlear symptoms)*" were compared to 20 controls and 17 divers with "*spinal DCS*" were compared to 16 controls. The level that differentiated spinal DCS from high spinal and the number of high spinal cases that were in the "*cerebral DCS*" group are not stated. One quarter of the controls for the cerebral DCS group but half of the controls for the spinal DCS group had a PFO. The authors stated that "*in the sub-group of divers with cerebral DCS, the prevalence of PFO (16 of 20) was significantly higher than in control divers (five of 20). In contrast, for the subgroup of divers with spinal DCS, PFO prevalence (six of 17) was comparable to the prevalence in their control group (eight of 16)".*[11]

At first sight it may seem surprising that spinal injury is a common manifestation of DCI that appears to be the result of paradoxical gas embolism across a right-to-left shunt. An explanation is provided by experiments performed on pigs which were compressed to 507 kPa for 30 minutes breathing air and then rapidly decompressed.[15] Immediately after decompression, there were few bubbles detected in venous blood, but the numbers increased and peaked between 5 and 30 minutes after decompression. Arterial bubbles were detected in all six pigs that were found to have a PFO but only two of eight pigs without a PFO. In both groups the peak arterial bubble count was detected between 15 and 30 minutes after surfacing, and only one pig had arterial bubbles detected less than seven minutes after surfacing. These data in pigs may explain the observation in divers that the incidence of spinal DCI is frequent and also that the median latency of onset of cerebral DCI is 3 minutes compared with median latency of 10 minutes for spinal DCI.[16]

Most bubbles crossing a shunt into the systemic circulation will pass to the tissues with the greatest blood flow, such as the brain, but because of the brain's rapid nitrogen elimination half-life, there are few bubbles present in venous blood and even fewer in arterial blood during the brief period after a dive when the brain is supersaturated with dissolved nitrogen and thus able to amplify embolic bubbles. Any bubbles that do enter the brain at that early stage will be amplified because the brain is supersaturated and cause cerebral DCI. Later, larger numbers of venous bubbles are liberated and larger numbers can cross a PFO or other shunt. At that time, large numbers of bubbles invade the brain, but it is no longer supersaturated, so the gas passes out of the bubble down the concentration gradient and dissolves. Far fewer bubble emboli enter the spinal cord, but those that do invade the spinal cord arrive at a time when, because of its slower nitrogen elimination half-life, it is still supersaturated and able to amplify bubble emboli. Dive profiles that result in even later peaks in venous bubble liberation and hence later paradoxical embolism in divers with a right-to-left shunt are likely to account for non-neurological shunt-mediated DCI.

Cutaneous decompression illness

The unexpected observation in a small number of early reports,[7,8] that cutaneous decompression illness occurred in individuals with a right-to-left shunt has been confirmed in a larger study.[17] This case control study compared the prevalence and sizes of right-to-left shunts determined by contrast echocardiography performed blind to history in 61 divers (including one caisson worker), who had a history of cutaneous DCI and 123 historical control divers. Twenty-nine divers had had a single skin bend, and 32 had had multiple episodes. It was found that 47 of the 61 cases had a shunt compared with 34 of 123 (27.6%) control divers ($P < 0.001$).[17] The size of the shunts in those with cutaneous lesions was significantly larger than in the controls. Of 61 cases with cutaneous DCI, 30 had a large shunt at rest compared with six of 123 (4.9%) of the controls ($P < 0.001$). Five of the 47 shunts in those with cutaneous DCI were pulmonary. During transcatheter closure procedures, 17 of these divers had a significant inter-atrial shunt; the mean diameter of the PFO being 10.9 mm. Cutaneous DCI occurred after dives that were provocative in those without shunts and after shallower dives that were not provocative

in those with shunts. These findings strongly support the hypothesis that cutaneous DCI is usually due to paradoxical gas embolism with peripheral amplification of bubble emboli in skin and subcutaneous fat that is supersaturated with nitrogen. When cutaneous decompression illness occurs in divers who do not have a shunt it nearly always occurs after deep and provocative dives. It is possible that in those cases the mechanisms include the lung filter being overwhelmed by massive amounts of venous bubbles or of autochthonous bubble formation (i.e., bubble nucleation in the skin rather than bubble embolism).[15,17]

In this study some divers with significant right-to-left shunts had pain in a shoulder associated with an overlying rash.[17] We have observed this in a number of other cases since then. This appears to be the exception to the rule that joint DCI is not associated with a shunt.

Sub-atmospheric decompression illness

Decompression illness can also occur during sub-atmospheric decompression in high altitude aviators and in astronauts on space walks. Human terrestrial hypobaric chamber experiments indicate that gas nucleation occurs in body tissues with all decompression protocols studied.[18] Monitoring the pulmonary artery with Doppler ultrasound reveals that heavy burdens of circulating gaseous emboli are present in between 6% and 39% of those subjected to subatmospheric decompression.[18] In these hypobaric chamber studies serious DCI has been encountered, including massive cutaneous 'marbling' (characteristic of cutaneous DCI), severe cerebral dysfunction and circulatory shock.[19] The National Aeronautics and Space Administration tested four individuals who had serious DCI resulting from space-walk simulations, in three of whom contrast TTE detected a PFO at rest.[18]

The link between decompression illness and migraine

It has been recognised for 70 years that individuals who have migraine with aura have an increased risk of neurological DCI and often experience migraine symptoms, particularly migraine visual aura, during sub-atmospheric decompression.[20] The relationship between shunts and migraine with aura were reported more recently.[21,22] Divers who have migraine with aura (typically visual aura but sometimes with hemiplegia, hemisensory abnormalities, dysphasia or cognitive features) also often experience an identical migraine aura with or without headache following dives.[23] This nearly always occurs in divers who have a clinically significant right-to-left shunt (usually a large PFO but sometimes a pulmonary shunt) and in them it occurs after dives with profiles that are expected to liberate venous bubbles.[23] In some cases a similar migraine aura is experienced after right-to-left shunting of bubbles during contrast echocardiography.[23] Therefore, it appears that the association between a history of migraine with aura and the increased risk of DCI is because migraine with aura is an indicator of an increased prevalence of large right-to-left shunts.

In a study of 400 divers who had contrast echocardiography following DCI, there was a relationship between the size of right-to-left shunts and prevalence of migraine with aura.[24] A large shunt at rest was present in 170 (42.5%). A further 33 (8.25%) had a large shunt with a Valsalva manoeuvre. Twelve (3%) had a medium shunt, 24 (6%) had a small shunt and 161 (40.25%) had no shunt. Small shunts are not considered to have clinical significance and, in those divers as well as in those with no shunt, DCI was thought usually to be the result of a provocative dive profile or pulmonary barotrauma as a result of lung disease. In those with no shunt or only a small shunt, the lifetime prevalence of migraine with aura was similar to that in the general population (11%). Ninety of the 170 (53%) with large shunts at rest had migraine with aura. In those with large shunts with a Valsalva manoeuvre or a medium shunt, the lifetime prevalence of migraine with aura was intermediate at 21% and 25% respectively.

Detection and estimation of the size of a shunt

The amount of shunting across a PFO is dynamic; it varies from beat to beat of the heart and with respiration. The factors affecting shunting include the dimensions of the PFO, the size of the flap covering the left atrial side of the PFO, the mobility and compliance of the flap, the pressure gradient between the atria and the atrial flow characteristics. The last two are variable.

The main reason for testing a diver to determine whether they have a PFO or other right-to-left shunt is to advise about the risks of future diving. If a shunt is present, the diver should be counselled on the options.[25] These are to stop diving; to modify diving to reduce the chances of venous bubbles forming and to reduce tissue nitrogen loading after dives; or to have transcatheter closure of their PFO. It has been estimated that the presence of a PFO possibly increases the risk of DCI in a diver by 2.5 times, namely to approximately 5/10,000.[26] However, it is clear that risk is related to the size of the shunt rather than the presence or absence of a PFO.[10,17,27]

There are three ultrasound techniques used commonly for detecting a PFO – transcranial Doppler, transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE). Each technique requires confirmation of a right-to-left shunt by detecting contrast in the arterial circulation following intravenous injection. There are proponents of each technique, and this is probably because the techniques are operator dependent. Therefore, operators favour the technique that they judge gives them the best results. One thing is certain, one must use bubble contrast because other types of intravenous contrast give false positive results. In addition, if one wishes to determine

whether venous nitrogen bubbles pass through a shunt into the arterial circulation, it is logical to test that using intravenous bubbles of air, which is predominantly nitrogen.

Transcranial Doppler with bubble contrast is quick, simple and is probably the most sensitive technique for detecting a right-to-left shunt but, because it does not image the heart, it does not differentiate inter-atrial from pulmonary shunts.

Cardiologists often consider TOE to be the 'gold standard' for detecting a PFO but that view is based on poor evidence. About one-quarter of the general population have a PFO and in high-risk groups, such as patients with stroke, the proportion of patients with a PFO should be greater. Yet some studies using TOE have reported prevalence rates of PFO as low as 3.2% in groups who might be expected to have prevalence rates of around 25% or greater.[28] This low prevalence came from a group that reported that TOE with contrast and colour-flow mapping were the "*methods of choice for the detection of atrial level shunts*".[29] One presumes some PFOs must have been missed by their technique. My colleagues and I have closed a large number of sizable PFOs after other cardiologists had reported that their TOE assessment had excluded the presence of a PFO (unpublished obseervations). Clearly TOE often fails to detect a large PFO in some patients and part of the reason may be that performance of Valsalva manoeuvres and sniffing to promote right-to-left shunting are difficult to perform during transoesophageal echocardiography.

In a study describing repeat TOE assessments for PFO in 40 divers with the second assessment six to eight years after the first, shunt size was graded as 0 (none), 1 (less than 20 bubbles in the left heart) or 2 (more than 20 bubbles in the left heart).[30] Twenty divers had no shunt on the first assessment, but on the second assessment three of the 20 had a grade-1 shunt and one had a grade-2 shunt. Of nine that had a grade-1 shunt at the first assessment, three had no shunt and five had a grade-2 shunt at the second assessment. The 11 grade-2 shunts at the first assessment remained grade-2 at the second assessment. The authors reported that during seven years "*significant increases in prevalence and size of PFO were found*" which they attributed to "*de novo opening or increasing permeability of PFOs*". A more plausible explanation is probably that TOE with contrast assessment for the presence and size of a PFO is not reproducible from one test to another. My own unpublished experience using TTE with contrast is that PFO size does not change significantly over 20 years of follow up.

One reason why TOE may miss a large PFO is that performance of a Valsalva manoeuvre and other manoeuvres designed to promote shunting are difficult for patients who are sedated and have a probe in their oesophagus. The use of sedation and passage of the probe also involve risk to the patient and increase the time taken for the procedure and the recovery of the patient.

My preference is for TTE with bubble contrast.[10] It can be performed quickly, without sedation and allows visualisation of the heart including the inter-atrial septum. Also, one can see whether provocative manoeuvres are being performed correctly. In addition, one can also distinguish between atrial and pulmonary shunts.[31] We consistently find that about one-quarter of normal controls have a shunt, but most of their shunts are small.[7,10,24] We consistently find higher rates of shunts and larger-sized shunts in high risk groups, such as divers with DCI and patients with paradoxical thromboembolism and migraine with aura.[7,10,17,24,32] We also detect very high rates of pulmonary shunts in patients with hereditary haemorrhagic telangiectasia, in whom there is a very high prevalence of large pulmonary arteriovenous malformations.[31] Our clinical assessments are consistently confirmed at closure procedures.

As stated, divers with the largest shunts have the greatest risk of DCI, as a result of paradoxical gas embolism, but other critical factors, including a dive profile that results in venous bubble formation and that loads critical tissues with inert gas (nitrogen) at the time of paradoxical embolism, are important.

Transcatheter closure of atrial shunts to prevent recurrence of DCI in divers was first reported in 1996.[33] Initially the procedure was restricted to commercial divers, for whom inability to return to unrestricted diving had serious financial consequences. Increasingly amateur divers who have had shunt-mediated DCI request PFO closure to permit unrestricted diving.[34–36] My colleagues and I have closed atrial shunts in about 300 divers with a history of shunt-mediated DCI. At the time of PFO closure in 200 of these, the median diameter of defects was 10 mm as reported in another paper in this issue.[35] A post-mortem study of 965 individuals showed that although 27.3% of the populations have a PFO, only 1.3% have a PFO that is 10 mm diameter or greater.[37] Extrapolating from this it seems that the 1 to 2% of divers with the largest right-to-left shunts experience half of the episodes of shunt-mediated DCI, which accounts for the majority of episodes of neurological and cutaneous DCI. Therefore, the available evidence suggests that the risk of a diver having shunt-mediated DCI is related to the size of their shunt, which in the case of shunting across a PFO, is largely determined by the diameter of their PFO.

However, it is also clear that shunting across a PFO is increased by some manoeuvres, such as release of a Valsalva manoeuvre. The amount of shunting across a significant PFO varies during the respiratory cycle, being maximal during inspiration. One typically sees a bolus of bubbles crossing to the left atrium during inspiration, with lesser amounts and sometimes no shunting during other phases of respiration.

The appearance with a pulmonary shunt is different, with the amount of shunting affected little at different phases of the respiratory cycle.[31] As a result, a more significant

pulmonary shunt may appear visually less impressive than a smaller atrial shunt, because a moderate degree of pulmonary shunting on every heart beat may result in more bubbles shunting to the arterial circulation than a larger number of bubbles shunting across a PFO on, say, every fourth heart beat that corresponds with peak inspiration or even less frequently if shunting only occurs when the diver releases a strain or Valsalva manoeuvre.

We also need to realise that our assessments are usually performed at rest. Shunting can be affected by the activities of an individual at the time of appearance of bubbles in the right heart. Shunting across a PFO may be increased in some individuals by exertion.[38] Pulmonary shunting is much more likely to increase with exertion.[39,40] As a result, some authorities recommend that the counselling of divers with DCI and their assessment for a shunt should be performed by a combination of a cardiologist and a doctor with knowledge of diving medicine.[41]

Before referring a diver for transcatheter closure of a PFO, I recommend that all five of the following criteria below should be satisfied:

- There is no other potential cause for DCI; therefore, a provocative dive profile and lung disease that could cause gas trapping should be excluded.
- The dive profile was likely to have liberated some venous bubbles.
- The symptoms and latency of symptom onset are consistent with shunt-mediated DCI.
- Investigations demonstrate a significant right-to-left shunt with features consistent with an atrial shunt.
- The patient understands the risks of the procedure including the possibility that transcatheter closure of a PFO is not always successful.

We anticipate successful complete closure of a PFO in more than 90% of cases, but it must be realised that there are considerable differences in the successful rate of PFO closure with different devices.[42] Therefore, the device used should be one with the best record of successful closure when the patient's anatomy is taken into consideration. It is essential that, before return to diving after PFO closure, contrast echocardiography should confirm that there is no significant residual shunt.[25]

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