Clinical Medicine 26 (2026) 100600

Contents lists available at ScienceDirect

Clinical Medicine

journal homepage: www.sciencedirect.com/journal/clinical-medicine

CME: Cardiology

Persistent (patent) foramen ovale assessment and closure for the general physician

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ARTICLE INFO

Keywords:
Arterial hypoxaemia
Decompression sickness
Echocardiography
Migraine with aura
Paradoxical embolism
Persistent (patent) foramen ovale
Stroke
Transcatheter occlusion
Transcranial Doppler

ABSTRACT

One-quarter of adults have a persistent (patent) foramen ovale (PFO). Right-to-left shunting through a PFO can facilitate paradoxical thromboembolism, cryptogenic stroke, paradoxical gas embolism, decompression sickness, arterial hypoxaemia and migraine with aura. Atrial septal defects and pulmonary shunts are also associated with these diseases, and investigation must differentiate them from a PFO. The detection and assessment of PFOs and other right-to-left shunts uses ultrasound techniques augmented with intravenous injection of bubble contrast. When diseases are attributed to a PFO, the PFO is usually large, typically about 10 mm diameter and associated with a large right-to-left shunt. Transcatheter closure of a PFO is relatively simple, but it is not always effective. Therefore, patients require careful pre-procedure counselling about risks, benefits, success rates and alternative treatments.

Introduction

One-quarter of adults have a persistent or patent foramen ovale (PFO).[1] The presence of a PFO is associated with a several diseases, including paradoxical thromboembolism, ischaemic stroke, certain types of decompression sickness (resulting from venous bubbles liberated during decompression bypassing the lung filter), migraine with aura and arterial hypoxaemia.[2–5]

PFO closure will only prevent these diseases if the association is causal, if patient selection is appropriate and if the procedure adequately occludes the PFO. Evidence of causal associations is that other right-to-left shunts produce the same diseases, and the probabilities of having the diseases are related to shunt size.

The most frequent reason for investigating a patient for the presence of a PFO is to prevent recurrence of cryptogenic stroke, ie when investigations detected no other reason for the first stroke.[6] In some patient groups, particularly young patients, PFO closure is followed by less frequent stroke recurrence than medical treatments.[6]

There are a number of difficulties.

Paradoxical thromboembolism is a much less frequent cause of stroke than other reasons, such as atrial fibrillation, left heart disease or carotid disease, whereas one-quarter of patients with a stroke for other reasons have a PFO. Therefore, far more stroke patients have a coincidental PFO than have a PFO that facilitated their stroke by permitting paradoxical thromboembolism.

Exclusion of other risk factors for stroke as the first step in selection of patients for the presence of a clinically relevant PFO has flaws. All investigations can produce false negative results, and a true positive finding of a risk factor does not mean that particular risk factor caused the stroke.

Therefore, in most cases, we cannot be sure that a stroke was caused by paradoxical thromboembolism, and we base clinical decisions on probability from adding up points for risk factors. A rare exception is when stroke and pulmonary embolism occur at the same time, so we are sure that thrombus passed through the right atrium when the patient had a stroke, making paradoxical embolism highly likely.

In contrast, that degree of certainty is the norm when there is shunt-mediated decompression sickness. Paradoxical embolism of gas liberated because of reduction of ambient pressure is the major cause of decompression sickness. Paradoxical gas embolism was the cause of 370 (58%) of 636 consecutive cases of illness resulting from decompression.[7] The remaining 42% had other identified causes such as missed decompression stops, rapid ascents and lung disease. There are also differences in onset time after a dive and clinical manifestations of decompression sickness in those who had paradoxical gas embolism when compared with those who had different mechanisms.[3] In some cases, the clinical manifestations are pathognomonic of shunt-mediated decompression sickness. Crucially, when decompression sickness results

This article has an accompanying continuing medical education (CME) activity. Completion of this CME activity enables RCP members to earn two external CPD credits. The CME questions are available at: https://cme.rcp.ac.uk/.

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https://doi.org/10.1016/j.clinme.2026.100600
Received 24 March 2026; Received in revised form 11 May 2026; Accepted 15 May 2026

Table 1
Prevalence of right-to-left shunts detected by transthoracic echocardiography with bubble contrast in divers with neurological and cutaneous decompression sickness and unaffected control divers.[3,4]

	Right-to-left shunts of any size detected	Large shunts seen with single injection without provocative manoeuvres	Large shunt seen with multiple injections and provocative manoeuvres
Divers with no history of decompression sickness	28%	5%	7%
Neurological decompression sickness	57%	41%	51%
Cutaneous decompression sickness	77%	49%	67%

from paradoxical gas embolism, comparison of the dive profiles with published data shows high likelihood of venous gas nucleation post-dive.

Therefore, divers with shunt-mediated decompression sickness are comparable to the few people who have simultaneous stroke and pulmonary embolism, and from them, the characteristics of PFOs (anatomical diameter and shunt size on bubble echocardiography) that permit paradoxical gas embolism can be determined. It is reasonable to assume that PFOs that facilitate paradoxical thromboembolism are as large, because thrombi are larger than post-dive venous bubbles.

Characteristics of culprit PFOs

The percentage of divers with neurological and cutaneous decompression sickness who have a right-to-left shunt is two to three times the percentage of control divers who have shunts, but the percentage of large shunts during normal respiration in divers with neurological and cutaneous decompression sickness is eight to ten times that in controls (Table 1 and Fig. 1).[3,4]

In patients with severe migraine with aura, the prevalence of right-to-left shunts was 60% (approximately double that in the general population) but the prevalence of large shunts was 43% (about six times that in the general population).[5]

In 200 divers who had transcatheter closure of atrial shunts after shunt-mediated decompression sickness, the median defect diameter was 10 mm, whereas an autopsy study of 965 normal hearts showed that only 1.3% of the population have a PFO of 10 mm diameter or greater[7] (Fig. 2).

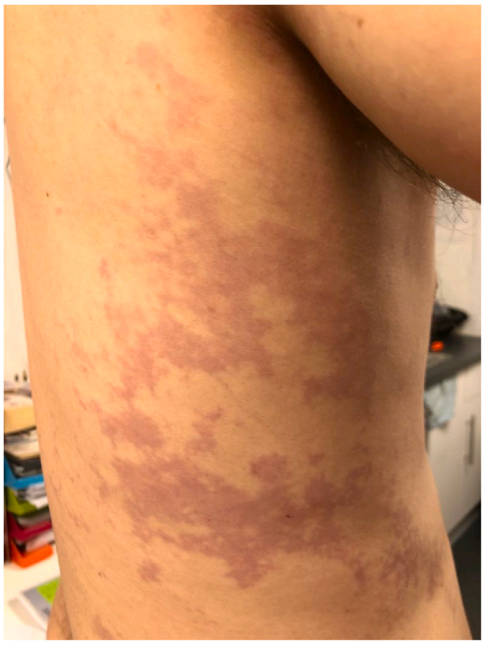

Fig. 1. Cutaneous decompression sickness is a mottled or marbled pink, red and/or purple rash which can be pruritic or slightly tender and situated on parts of the body where there is significant subcutaneous fat. Divers with cutaneous decompression sickness after one dive are at high risk of neurological decompression sickness after other dives.

In a study using similar assessment methods, patients who had PFO closure following stroke attributed to paradoxical embolism had a similar mean PFO diameter, ie 9.8 ± 4.1 mm.[8]

Therefore, the cross-sectional area of a PFO is an important determinant for paradoxical embolism in preference to emboli passing through the tricuspid valve, which has a cross-sectional area of about 8 cm^2. A PFO orifice that is circular and 10 mm in diameter has a cross-sectional area of 0.8 cm^2, whereas a PFO of 5 mm diameter has an area of only 0.2 cm^2. The pressure gradient across the atrial septum, septal mobility and atrial flow characteristics, which are affected by congenital remnants of the Eustachian valve or Chiari network, contribute to shunting.

Reasons for testing for a PFO

The most frequent reason for investigating whether a patient has a PFO is cryptogenic stroke.[6]

People at risk of shunt-mediated decompression sickness include divers, hyperbaric tunnel workers and healthcare staff working inside hyperbaric chambers. In divers, testing for a PFO is recommended if there is a history of decompression sickness, stroke or migraine with aura, or a family history of PFOs or atrial septal defects.[9,10]

Venous air embolism occurs in 25–75% of patients during posterior fossa neurosurgery in the sitting position.[11] Some authorities advocate pre-operative assessment of patients having such surgery and use of an alternative position for those who have PFO to reduce the occurrence of paradoxical air embolism.[12]

PFOs are rare causes of arterial hypoxaemia. When the right atrial pressure is increased either chronically (eg by lung diseases) or acutely (eg by pulmonary embolism), right-to-left shunting across a PFO can exacerbate arterial hypoxaemia from the primary disease,[13] but in this situation, PFO closure needs careful haemodynamic assessment. Measurement of changes in arterial saturation and haemodynamic parameters during temporary occlusion of the PFO with a balloon catheter may be helpful.

Detection and assessment of a PFO

The ideal test for detecting a PFO and quantifying its size should be safe, accurate, quick and inexpensive. Three ultrasound techniques augmented with intravenous injection of bubble contrast are commonly used. The amount of air injected is small, and the risk from paradoxical embolism of the air is extremely low, because the gas in the bubbles dissolves in the tissues they invade.

Transcranial Doppler of flow in a cerebral artery (usually middle cerebral artery) allows detection of bubbles after intravenous injection of bubble contrast if a right-to-left shunt is present. Shunt size is graded according to the maximum number of bubbles detected and whether the shunt is present when the subject is breathing normally or only when a Valsalva manoeuvre is released. The test requires an intravenous cannula for injection of bubble contrast, but is otherwise non-invasive. Performance is quick. It does not differentiate atrial from pulmonary shunts. Therefore, if a shunt is detected, another test is required to determine the location. Transcranial images cannot be obtained in a small number of patients.

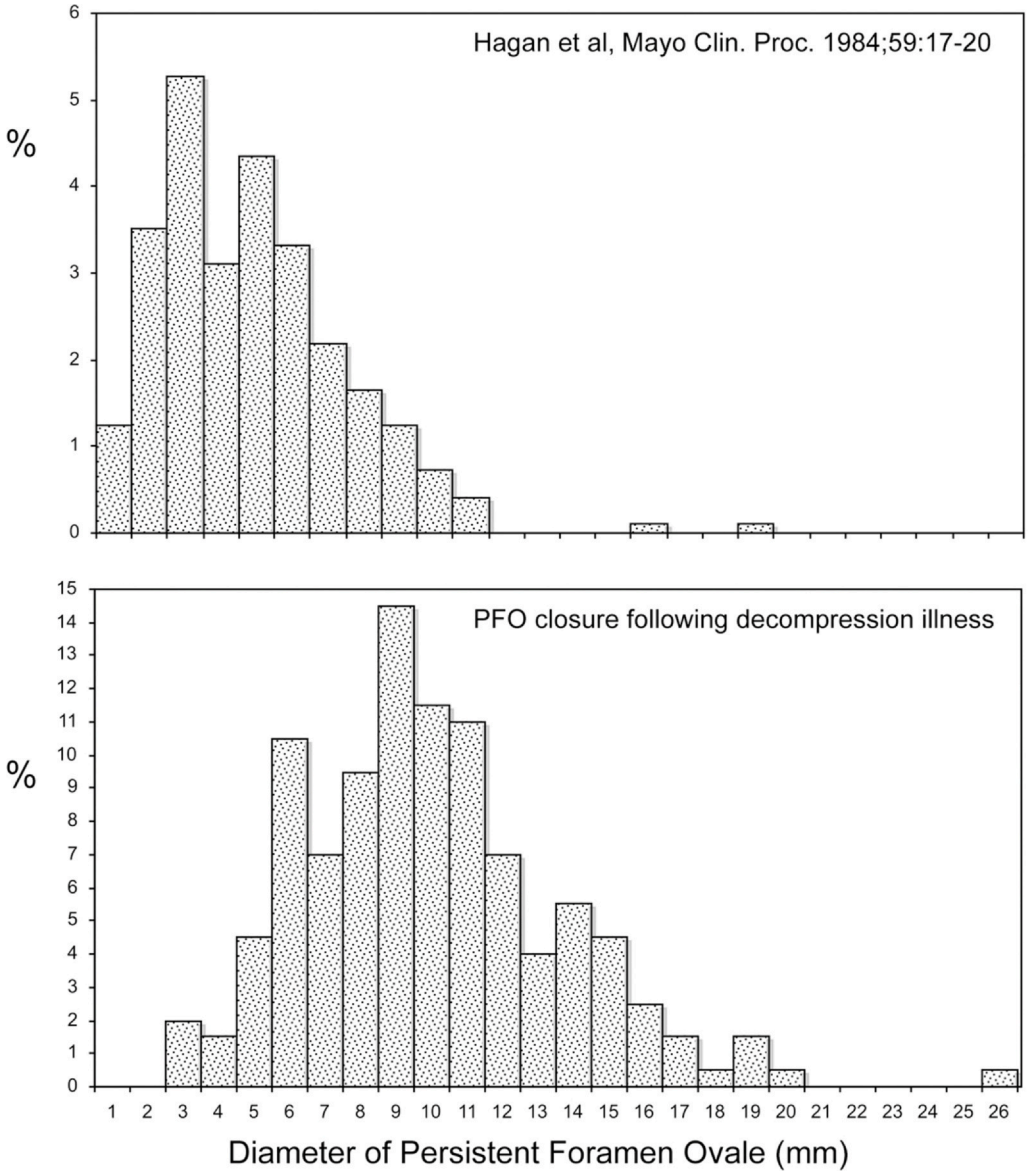

Fig. 2. Histograms showing the distribution of diameters of persistent foramen ovale (PFO) in the general population (upper panel) and the distribution of the diameters of PFO (n = 189) and atrial septal defect (n = 11) in divers with shunt-mediated decompression sickness (lower panel).

Transoesophageal echocardiography provides the best images of the atrial septum. Therefore many cardiologists presume that it is the investigation of choice for diagnosis of a PFO despite lack of proof.[6] Few studies compared the findings of a PFO using transoesophageal echocardiography with an objective standard, i.e., autopsy or cardiac catheterisation.[14,15] In those studies, most patients had pathology that would likely increase right-to-left shunting, and very few were investigated because of suspected paradoxical embolism.[14,15] A recent report of real-world experience found that transoesophageal echocardiography had a sensitivity of 32% for detection of PFOs that caused paradoxical embolism, were detected by transthoracic echocardiography with bubble contrast and were confirmed during transcatheter closure. The median diameter of the PFOs that transoesophageal echocardiography failed to detect was 10 mm.[16]

Failure of a transoesophageal echocardiogram with bubble contrast to detect a PFO may be because of difficulty performing a Valsalva manoeuvre with a probe in the oesophagus. In addition, transoesophageal echocardiography is the most invasive of the techniques, with a small risk of serious complications, and some patients cannot tolerate it without general anaesthesia.

The joint position statement on atrial shunts and diving of the South Pacific Underwater Medicine Society and the UK Diving Medical Committee recommends use of transthoracic echocardiography with bubble contrast for detecting a PFO in divers.[9] The test is quick. It requires several intravenous injections of bubble contrast during normal respiration and with provocative manoeuvres (sniff and release of a Valsalva manoeuvre) to promote right-to-left shunting.[10] The size of the shunt is graded according to the maximum number of bubbles seen in the left heart.[10] When performed with attention to details, it is very accurate for detection of clinically significant atrial shunts and differentiating atrial from pulmonary shunts. An online appendix provides detailed instructions for optimal performance of the test.[10]

Should a large PFO be closed?

Counselling patients requires discussion of the indications and risk of the closure procedure, the probability of the procedure being effective and the risk and efficacy of alternative treatments.

The most frequent reason for transcatheter closure of a PFO is to prevent recurrence of stroke after an earlier cerebral ischaemic event.[6]

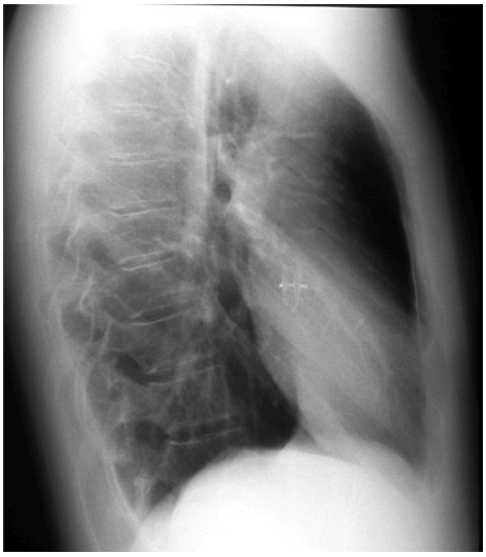

Fig. 3. Lateral chest X-ray showing an Amplatzer PFO device in position. The smaller disc is in the left atrium, and the larger disc is in the right atrium.

Many guidelines have been produced for when patients have cryptogenic stroke.[6,17,18] Some rely on the ROPE (Risk of Paradoxical Embolism) score and the PASCAL (PFO-Associated Stroke Causal Likelihood) classification in order to guide management. The ROPE score is based on whether risk factors for stroke are present (such as hypertension, diabetes, smoking and age).[6] The PASCAL classification is based on the appearance of the PFO on transoesophageal echocardiography, which is unhelpful when a different test is used. These scores do not take into account the probability that venous thrombosis was present.

In general, when there is cryptogenic stroke and a large PFO, PFO closure followed by antiplatelet therapy is preferred to either anticoagulation alone or antiplatelet therapy alone.[6,17,18] If a stroke was associated with proven venous thrombosis and there is continuing risk of venous thrombosis, PFO closure and anticoagulation to prevent pulmonary embolism may be appropriate.[6]

In divers with a large PFO, the options are to stop diving, modify dive profiles so that venous bubbles are not liberated, or PFO closure.[9]

PFO closure is indicated in platypnoea–orthodeoxia syndrome, but pulmonary arteriovenous malformations commonly cause this condition and must be excluded.

PFO closure is not currently indicated for migraine with aura except as part of a clinical trial.

Closing a PFO

Closure of a PFO is performed using a transcatheter technique with general anaesthesia or sedation. It takes less than 1 hour.

A number of types and sizes of transcatheter occlusion device are available. Most consist of two discs connected by a narrow waist. They incorporate nitinol wire – a metal alloy that has a memory, which allows the devices to have a low profile during insertion and to expand to the required shape when deployed.

The collapsed device is passed to the heart through a cardiac catheter inserted into a femoral vein. The device is deployed with the waist sitting across the PFO so that one disc sits in each atrium. The discs sandwich the interatrial septum to clamp the PFO closed (Fig. 3). Selection of type and size of the occlusion device is based on size and morphology of the PFO. The device is positioned using fluoroscopy and either transoesophageal or intracardiac echocardiography.

Antiplatelet drugs are usually prescribed long term after device implantation when PFO closure was for stroke, but for up to 6 months when the procedure was to prevent decompression sickness.[6,9]

There is considerable variation in the success of different devices in occluding a PFO.[19] One study of three devices showed final residual shunt rates of 11% with Amplatzer, 18% with Premere and 33% with Helex.[19]

Because there can be significant residual shunts after PFO closure, it is essential that patients have repeat transthoracic echocardiography with bubble contrast, particularly if patients plan to return to diving.[9] In some cases, insertion of an additional occlusion device may be required to produce a satisfactory result.

CRediT authorship contribution statement

Peter Wilmshurst: Conceptualization, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Consent for publication

Written consent was obtained from the patient for the use of Figure 1.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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