Practice guideline

Detection of a persistent foramen ovale using echocardiography

Peter Wilmshurst

Abstract

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Right-to-left shunts can result in decompression illness in divers and lead to a number of other conditions. Transthoracic echocardiography with intravenous injection of bubble contrast, when performed according to a well-tested protocol by trained personnel, enables the safe, simple, rapid and inexpensive detection of right-to-left shunts, the assessment of the size of the shunts and the differentiation of atrial shunts from pulmonary shunts. This article summarises the author's views on the techniques available and his preferred protocol for transthoracic echocardiography.

Key words

Bubbles; decompression; patent foramen ovale; lung; right-to-left shunt; investigations

Introduction

Right-to-left shunting of blood from the venous to arterial circulations can be the result of complex cyanotic heart diseases (such as Tetralogy of Fallot), atrial shunts that rarely cause cyanosis (i.e., an atrial septal defect, ASD, or a persistent foramen ovale (PFO) also called patent foramen ovale) and pulmonary arteriovenous shunts, which only cause cyanosis when large. The type of shunt and its size are important. It is not unusual for small pulmonary shunts to be misdiagnosed as atrial shunts. Right-to-left shunts are associated with arterial hypoxaemia when very large; paradoxical thromboembolism and cryptogenic stroke; paradoxical gas embolism and decompression illness (DCI) (particularly neurological, cutaneous and cardio-respiratory manifestations), and migraine with aura.[1–5]

In divers, venous bubbles form during decompression from many dives. In the absence of a right-to-left shunt, venous bubbles return to the right side of the heart and pulmonary arteries. During passage of the bubbles through the alveolar capillaries, gas diffuses out of the bubble down the concentration gradient so that bubbles do not get to the arterial circulation unless it was a highly provocative dive that liberated so many bubbles that the pulmonary filter is overwhelmed. When there is a right-to-left shunt, venous bubbles can circumvent the pulmonary capillary filter to reach the systemic arterial circulation and be carried to the tissues. It is postulated that if the tissues are still supersaturated with dissolved nitrogen (or other inert gas), the embolic bubbles will be amplified as nitrogen diffuses out of the tissue down the concentration gradient and, depending on the tissue, the enlarging bubbles produce the local effects that cause some forms of DCI.

PFOs are numerically the most frequent cause of right-to-left shunts. The foramen ovale is an important part of the foetal circulation in which it has the function of diverting the oxygenated blood returning from the placenta via the ductus venosus and the right atrium across the atrial septum into the left atrium and hence mainly to the developing brain. Everybody has a foramen ovale at birth. It closes during childhood and adolescence in three quarters of the population. Observational data from a large series of post-mortem examinations reported that the foramen ovale persists into adulthood in approximately one quarter of the population with a median diameter of 5 mm.[6] In divers who have a shunt-related DCI the median PFO diameter is 10 mm, which equates to a defect area four times as large.[7] Compared with half the divers who have shunt-related decompression illness, only 1.3% of the general population have a PFO with a diameter of 10 mm or larger.[7]

Paradoxical thromboembolism is the usual cardiac indication to investigate a patient for the presence of a right-to-left shunt and in those patients the great majority of shunts detected are atrial (i.e., large PFO or ASD). Pulmonary shunts account for far less than 1% of episodes of paradoxical thromboemboli. As a result, some cardiologists lack experience of detecting pulmonary right-to-left shunts and may misdiagnose a pulmonary shunt on the rare occasion that one is present. Misdiagnosis exposes patients to unnecessary risk if procedures are performed to close non-existent PFOs. Some other shunt-related illnesses are more commonly associated with pulmonary shunts. In people with shunt-related DCI and migraine with aura, 5–10% of right-to-left shunts are pulmonary.[7,8] In these conditions, pulmonary shunts are often misdiagnosed as atrial.

Investigating right-to-left shunts – what technique is optimal?

An ideal test for a right-to-left shunt should have the following features:

- It should detect all clinically significant shunts.
- It should distinguish between different types of right-

Table 1
Comparison of the qualities of different ultrasonic techniques for detecting and assessing right-to-left shunts

	Transthoracic echocardiography	Transcranial Doppler	Transoesophageal echocardiography
Sedation usually used	No	No	Yes
Views of the atria	Yes	Never	Best
Ability to quantify shunt	Good	Best	Poor
Determination of shunt site	Best	Poor	Variable

to-left shunts.
- It should be safe, simple, easy, quick and inexpensive.

The presence of a right-to-left shunt is confirmed by detection of a marker in the systemic circulation that should not pass through the alveolar capillary filter. Three ultrasonic techniques are routinely used (Table 1) – transcranial Doppler, transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE), and all are coupled with intravenous injection of a contrast medium. The best contrast consists of large numbers of microbubbles of air. Some artificial colloidal contrast media will pass through the pulmonary capillaries and produce false positive tests.

The bubble contrast is produced by pushing approximately 8 ml of sterile saline, 1 ml of air and 1 ml of the patient's blood back and forth from one 10 ml luer-lock syringe connected via a three-way tap to another syringe, until no large bubbles remain visible. It is important to use some of the patient's blood, because it stabilises the microbubbles produced, so that one gets much better contrast filling the right heart.

The three ultrasonic techniques are operator-dependent and, therefore, individual investigators have their own preferences, but the best results are obtained by strict adherence to a tested protocol. My preference is TTE with injection of bubble contrast into a left antecubital vein, as described below.

It is commonly claimed that TOE is the gold standard test for detecting a PFO and that it detects all PFOs irrespective of their size. If this were true, it would be rare for a large PFO to be missed on TOE but found using a different technique. I have closed many large PFOs when cardiologists had reassured patients that they did not have a PFO because a TOE was negative and the patient had a further event, after which my TTE with bubble contrast showed a large atrial right-to-left shunt.[9] The reasons that TOE misses some large PFOs is that the sedation used and the presence of a large probe in the oesophagus prevent patients performing manoeuvres to accentuate right-to-left shunting, such as Valsalva manoeuvres and sniffing.

TTE protocol

TTE should be performed with imaging of the heart using the apical four-chamber view. That view minimises overlap of the right and left sides of the heart and hence avoids any contrast in the left heart being obscured by a higher density of bubble contrast in the right heart. One must inject a large amount of bubble contrast into an antecubital vein. Ideally one should use a left arm vein because that is better able to detect the rare instances when there is partial anomalous systemic venous drainage to the left atrium, such as via a left superior vena cava. Contrast should be injected with the arm elevated above the level of the heart to ensure rapid drainage to the right atrium. Injection of contrast into a vein in the back of the hand should be avoided because it does not make the blood in the right atrium adequately opaque. If there are no suitable antecubital veins, the contrast should be injected into a femoral vein. But if one can get the right atrial cavity totally opaque with injection into an antecubital vein as described, my experience is that femoral vein injection has no advantage for detection and is more uncomfortable for patients.

My current protocol is to give up to six injections of contrast. The first injection is with the patient at rest and breathing normally. If no significant shunt is demonstrated at rest, the next two injections are with release of a Valsalva manoeuvre. If they are also negative, I then give injections with the patient performing a short, sharp sniff when the right atrial cavity is totally opaque. The technique should be practiced because a deep sniff will cause the left lung to come between the imaging probe and the left heart, so that the heart will be obscured. It is important that contrast is seen adjacent to the atrial septum: false negative results can be obtained if blood containing no bubbles is streaming from the inferior vena cava to prevent the area adjacent to the interatrial septum being filled with contrast. A sniff will often rectify that.

With an atrial shunt, shunting occurs in 'boluses' of bubbles crossing the atrial septum when right atrial pressure and flow are greater than left atrial. Typically that occurs when a patient or subject breathes in, releases a Valsalva manoeuvre or sniffs. This results in a 'jerky' appearance of contrast in the left heart. Pulmonary shunting builds up beat by beat in a smoother manner and also declines more gradually. Contrary to common belief, the timing of shunting after contrast fills the right atrium is not an accurate way to determine whether shunting is atrial or pulmonary. When there is a large pulmonary shunt or cardiac output is high, shunting of contrast to the left heart via a pulmonary shunt can occur within two heartbeats and very occasionally one heartbeat after the right heart has filled with contrast. Conversely atrial

shunting may not occur for several heartbeats after the right heart is opaque until the patient takes a deep breath. When there is uncertainty whether there is a pulmonary shunt, a long imaging run should be recorded to see whether bubbles are still entering the left heart when the right heart contains fewer bubbles than the left heart. Obviously that appearance can never be the result of an atrial shunt.[10]

I find that only 1–2% of patients have image quality that is inadequate for shunt demonstration and in those cases other techniques must be used. The simplest of these is to use the stand-alone continuous wave Doppler probe on the echocardiogram machine to record over a carotid artery when bubble contrast is injected intravenously.[11] If a shunt is present, this produces displays rather like transcranial Doppler with bubble contrast. If bubble contrast is injected into a left antecubital vein, it is best to image the right carotid artery to reduce the chance of interference with the carotid images as a result of reflux of contrast from the subclavian vein into the internal jugular vein. Doing that test at the time of echocardiography means that the patient does not need to come back for another investigation on another occasion if the test is negative. If the test is positive, further tests will be required to distinguish an atrial shunt from a pulmonary shunt. One can also use TOE with bubble contrast, but a negative test does not exclude a PFO.[9] Other techniques are very rarely required to detect a right-to-left shunt.

I believe that the technique we use for detecting shunts is the most accurate for a number of reasons:

- In control populations, in which about one-quarter of individuals would be anticipated to have a PFO, and in most cases they would be expected to be small in size, we have consistently found that between 24 and 28% of individuals have right-to-left shunts consistent with a PFO, and the majority of the shunts are small.[4,12]
- In populations in which we would expect there to be a high prevalence of right-to-left atrial shunts, we find such high rates. For example, in individuals with cutaneous DCI we find that 75–80% of divers have a significant right-to-left shunt.[12] In the remaining divers who have no significant shunt, their dive profiles prior to their cutaneous DCI were much more provocative, in keeping with a mechanism different from paradoxical gas embolism.[12]
- We are frequently asked to investigate divers with a history consistent with shunt-related DCI, but in whom other cardiologists have found no shunt using TOE. In them, we consistently demonstrate the presence of an atrial shunt using our technique and confirm the presence of a large atrial shunt during transcatheter closure.[9]

In conclusion, I believe that transthoracic echocardiography with intravenous injection of bubble contrast, as described, is the method of choice for investigation of patients for possible right-to-left shunts.

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Peter Wilmshurst, Consultant Cardiologist, Royal Stoke University Hospital, Stoke-on-Trent, UK and UK Diving Medical Committee

Address for correspondence:
Dr Peter Wilmshurst
Royal Stoke University Hospital
Stoke-on-Trent, ST4 6QG, UK
E-mail: *<peter.wilmshurst@tiscali.co.uk>*