PFO AND DECOMPRESSION ILLNESS: AN UPDATE

Richard Moon and Joseph Kisslo

Key Words

Bubbles, cardiovascular, decompression illness, medical conditions and problems.

Introduction

It has been known for many years that blood clots originating in the leg veins can pass from the right to the left sides of the heart via a patent foramen ovale (PFO), resulting in paradoxical thromboembolism. When it occurs it usually manifests as stroke. A clot passing through a PFO is a rare event, and it has traditionally been made at post mortem examination. However, the availability of techniques to detect PFO in live people, in recent years there has been a considerable amount on interest in the role PFO might play in otherwise inexplicable diseases. In 1988 Lechat reported a group of young individuals who had what appeared to be embolic stroke with no other risk factors and found that 40% of these individuals had a PFO demonstrable using bubble contrast echocardiography. The usual prevalence of PFO in the normal population is around 20%, suggesting that embolism through the PFO was the explanation.[1]

The left atrial pressure is higher than the right and the design of the inter atrial septum is a flap valve mechanism. Even with a patent foramen ovale, the doorway, the flap valve should be closed by the normal inter-atrial pressure gradient. How, then, could a PFO result in shunting from the right side to the left? When the left atrial and the right atrial waveforms are examined in detail, there is a small portion of the cardiac cycle in which right atrial pressure actually exceeds the left, during which blood and other materials such as clots could be shunted from the right to the left side of the heart.

Why does this have any importance for divers? After a dive one can demonstrate in some divers, by Doppler techniques, intravascular bubbles on the right side of the heart (venous gas embolism, VGE).[2] Dick Dunford of the Virginia Mason Institute in Seattle has demonstrated that during a week of diving, VGE may exist at some time in virtually every individual studied.[3]

That being the case, if someone does have an inter-atrial communication, the normal filtering ability of the lung may be bypassed, which would allow bubbles to travel from the right atrium into the left, and may then cause arterial occlusion in the central nervous system, or localised activation of a mediator, such as complement. A case report suggested that right-to-left shunting of bubbles through an atrial septal defect (ASD) might precipitate DCI.[4]

After deciding to investigate PFO as a possible risk factor for decompression illness (DCI), our first case was a man who had been diving off the North Carolina coast with his girl friend. After a dive the two of them were driving back to their hotel when he suddenly realised that he did not know the way. A couple of minutes later, as related by the girl friend, he looked quizzically at her and stated that he did not recognise her. Feeling rather disconcerted by this she took him to the hospital. After evacuation and evaluation at Duke Hospital it was evident that he was profoundly abnormal neurologically. He was confused, and had a rash, which he said had occurred after a dive several weeks before, at which time he had also been confused. His MRI showed numerous white spots in the sub cortex and he also had a PFO.

Examination for a patent foramen ovale is quite straightforward. The easiest method is to use transthoracic echocardiography (TTE) and inject a suspension of microbubbles. To make the suspension one can put a three way stopcock into an intravenous line, attach two syringes with a small quantity of air and 5 ml of saline in each and then rapidly flush the solution back and forth between syringes until it goes milky. The bubble suspension is then rapidly injected into a peripheral vein via an indwelling catheter. A few drops of the subject's blood will stabilise the bubbles and permit a better study. A few seconds after injection a cloud of bubbles will be observed traversing the right side of the heart. In the presence of a PFO bubbles will be observed also in the left heart (see Fig. 1). Alternatively, one can use commercially available, stabilised bubbles. The routine is to try it once while the individual is resting comfortably, and if there is no demonstrable shunt, then have the patient perform a Valsalva manoeuvre, injecting the contrast during the release phase. This can demonstrate a shunt which is not visible during normal resting breathing.

There are other ways of doing it, such as using transcranial doppler rather than 2-D echocardiography to detect the bubbles. With this technique, by applying a probe to the head in the appropriate orientation, one can examine the intracranial arteries and observe a pulsatile flow wave, usually in the middle cerebral artery. If one then injects bubbles as described bubbles traversing a PFO can be observed as aberrant spikes in the ultrasound waveform. Others have used transoesophageal echo (TEE), which provides clearer images than transthoracic imaging, and a few additional instances of PFO can be detected using this technique. However, as will be demonstrated below, the minimal right-to-left flow through a PFO which can be demonstrated exclusively with TEE is probably of minor consequence with regard to DCI risk.

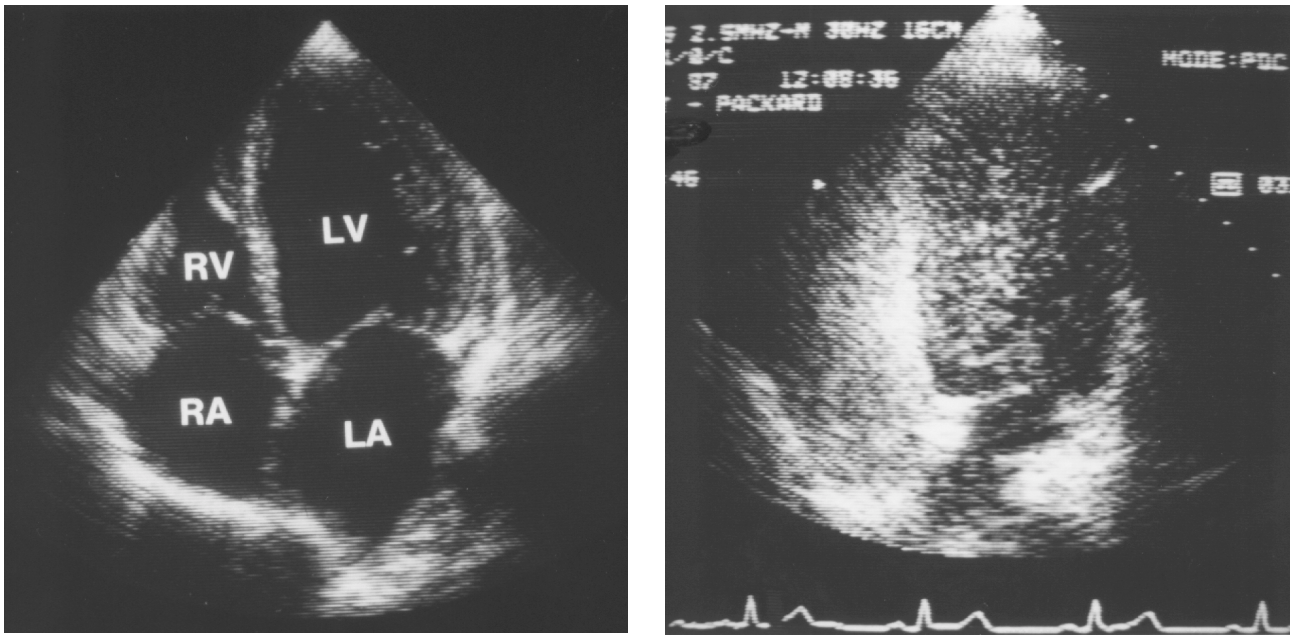

Figure 1. Transthoracic bubble contrast echocardiograph images. On the left, pre-injection, with cardiac chambers labelled. On the right after intravenous injection of bubble suspension in a 48 year old male diver who, a few minutes after a 30 metre 17 minute dive, developed back and epigastric pain, dyspnoea, leg weakness and numbness. He had paraparesis, urinary retention and a T12 sensory level. Bubbles can easily be observed in the left atrium and ventricle.

Findings in divers

In order to examine this problem systematically we identified a group of divers who had varying degrees of predominantly neurological bends. We arbitrarily defined these as serious (cerebral, vestibular or motor weakness), or mild, which included pain, with or without paraesthesia or hypaesthesia. This was simply an operational definition, and was not intended to imply that the latter category is less important than the former.

A total of 91 divers who had had decompression illness and 100 volunteers were studied.[5] Eleven percent of the volunteers had right-to-left shunt during spontaneous breathing and an additional 9% shunted after Valsalva, for a total of 20%. Of the divers with decompression illness, 32% shunted at rest and a total of 43.2% (including those who shunted during resting breathing) shunted after Valsalva manoeuvre. Of the 57 serious cases, as defined above 39% shunted during resting breathing and a total of 47% shunted after Valsalva manoeuvre. There were 31 non-serious cases of which six (19.4%) shunted during spontaneous breathing and a total of 11 (35.5%) shunted after Valsalva.

All subjects underwent colour flow doppler evaluation prior to bubble contrast injection, and few inter-atrial shunts were detectable, confirming the lack of sensitivity of this technique for the detection of PFO.

We studied onset latency and found that the odds ratio was statistically different from 1 in those bends with onset less than 10 minutes and 10-60 minutes after surfacing, but not for those with longer latency onset. I am uncertain as to the significance of this because there is a strong relationship between the severity of DCI and its onset time: serious cases tend to have a shorter time between surfacing and the onset of symptoms. The statistical significance of latency could be because of this correlation.

A similar relationship has been found by Peter Wilmshurst of the UK.[6] He found that 24% of normal divers had right-to-left shunt through a PFO, compared with 65% of those with early onset neurological bends. The prevalence of PFO in divers with late onset bends was not different from control values.

Patent foramen ovale therefore appears to be associated with serious neurological bends (Duke study) and early onset neurological bends (Wilmshurst study) and, at least in our study, there was a relationship between the degree of shunt (resting vs. Valsalva-induced shunt). The reason for this relationship remains an open question. I believe the most tenable hypothesis is that VGE, which would otherwise be filtered by the pulmonary capillaries, may become arterialised in the presence of a PFO. However, there are other hypotheses. It is conceivable that the presence of a PFO is linked genetically to an unrelated factor which predisposes to DCI. In other words the presence of a PFO may be merely a marker for the "real" predisposition, in the same way that xanthomata are not the cause of coronary artery disease, but external markers for the underlying predisposing condition,

hypercholesterolaemia. Another possibility is that DCI induces PFO, or enlarges it. A possible mechanism for this might be right atrial hypertension. However, the only form of DCI in which this is likely to occur is massive venous gas embolism causing pulmonary hypertension and secondary right heart failure, an extremely rare but easily recognisable event. There were no such cases in our series of DCI in which PFO was examined. Therefore I believe that is unlikely.

While surgical correction of a PFO in order to correct one's risk of DCI would be considered too radical by most diving consultants, recent development of techniques to correct cardiac septal defects may have changed the picture. Some years ago, one of our commercial divers with a PFO underwent placement of one the first transvenous occlusion devices. After ascertaining that his neurological exam was normal, and, using bubble contrast echocardiography, that there was no residual right-to-left shunt, we cleared him to return to diving. This technique has been published by Peter Wilmshurst recently in the British Medical Journal.[6]

As a follow-up study we were interested in what would happen to right-to-left shunts when immersed. Divers, particularly professional divers, may spend significant periods of time decompressing in the water. We wanted to know what happened if they were experiencing VGE while they decompressed. We hypothesised that, because of translocation of 500-800 ml of blood from the legs into the thorax (causing an increase in cardiac volume),[8,9] immersion would increase right-to-left shunt through a PFO.

We studied 11 individuals, all of who had a PFO demonstrated by bubble contrast echocardiography, under rest and exercise conditions in the dry and immersed to the neck in water. We measured at end-diastolic and end-systolic left ventricular diameter under resting and increasing exercise conditions and in the supine position. Exercise studies were performed in the dry or immersed to the neck in thermoneutral (35°C) water. Upon immersion there was a significant increase in left ventricular end-diastolic and end-systolic volumes, exactly as one would expect. We used a semi-quantitative measure of the degree of shunt after bubble contrast injection, as follows: "0" represented no right-to-left shunt, "1" represented partial opacification of the left side of the heart and "2" represented total opacification. During a separate sitting we performed the same manoeuvres after placing arterial and pulmonary artery catheters in the same volunteers, and used using the technique of multiple inert gas elimination[10,11] to assess right-to-left shunt (which in this case would include both intracardiac and intrapulmonary shunt). Using either technique, there was no effect of immersion upon the degree of shunt.[12,13] Within the limits of this relatively small study, it appears that neither immersion in water nor supine position increases right-to-left shunt through a PFO.

A recent study

A recent article from the British Medical Journal has created a stir within the recreational diving community in the United States.[14] These investigators examined 87 dive club volunteers, each of whom had made more than 160 recreational scuba dives. Using a 1.5 Tesla scanner each volunteer underwent MRI of the brain, and scans were examined for the presence of subcortical areas of high T2 intensity. In order to detect right-to-left shunt through a PFO, transcranial Doppler, after intravenous injection of bubble contrast, either with or without a Valsalva manoeuvre was used. They diagnosed a right-to-left shunt (RLS) when there were more than 5 bubbles in either middle cerebral artery. Table 1 shows the patient group. Twenty-five individuals (28.7%) had a right-to-left shunt, 62 (71.3%) did not have a shunt, approximately the proportions that one might expect in the normal population. Heights, weights, ages and diving exposures were similar. Cigarette smoking was a little heavier in the group without shunt, while the self-reported amount of alcohol consumed was the same in each group.

TABLE 1

PATIENT DEMOGRAPHICS (Knauth[14]**)**

	RLS*	**No RLS**
Number	25	62
Weight (kg)	69.9	80.0
Height (cm)	174	177
Age (years)	35.4	35.9
Total dives	574	562
Decompression stop dives	89	100
Cigarette smoking (pack-years)	1.8	5.2
Alcohol intake (g/day)	30.9	33.1

* RLS = Left to right shunt

They further classified these shunts as either low or high haemodynamic significance based upon an arbitrary score of either less than 20 bubbles or more than 20 bubbles (Table 2).

TABLE 2

HIGH (HHS) AND LOW (LHS) HAEMODYNAMIC SIGNIFICANCE RIGHT TO LEFT SHUNTS
(From Knauth[14])

Lesions	**HHS**	**LHS**	**No RLS**	**Total**
0	10	11	55	76
1	0	1	7	8
5	1	0	0	1
12	1	0	0	1
16	1	0	0	1
Total	13	12	62	87

When one examines the "0" or "1" lesion group, there is actually no relationship between the existence of a lesion and right-to-left shunt. However, there were three individuals, with 5, 12 and 16 brain lesions, respectively, each of whom had a right-to-left shunt of high haemodynamic significance. The original data can be summarised in Table 3.

TABLE 3

SUMMARY OF RESULTS (Knauth[14]**)**

Lesions	HHS	LHS	No RLS	Total
0	10	11	55	66
1	0	1	7	8
> 4	3	0	0	3
Total13	12	62	87	

HHS High haemodynamic significance RLS
LHS Low haemodynamic significance RLS
RLS Right to left shunt

The authors concluded that right-to-left shunt through a PFO in divers is a risk factor for the development of brain lesions visible on MRI.

There are several reasons why this study cannot be accepted at face value. First, although all of these individuals were divers, they had no non-diving control group, so there was actually no evidence that even if there is a relationship between PFO and brain lesions, it has anything to do with diving. An alternative hypothesis to explain the data is that the lung may be important in breaking down metabolic compounds that may produce MRI lesions. The lesions could also have been due to subclinical thromboembolism. PFO has already been demonstrated to be a risk factor for stroke, presumably by allowing small venous clots to traverse the inter-atrial septum.[15,16] Second, the described relationship depended in this study only on three individuals suggesting an apparent relationship where there may not be one. Finally, the clinical significance of these brain lesions is speculative, and the authors presented no functional data (e.g. psychometric testing) with which to demonstrate clinical relevance. Therefore, although further studies may be warranted, to conclude that PFO is a risk factor for subliminal brain damage in divers is unwarranted.

Conclusions

To summarise, the evidence suggests that the risk of serious neurological DCI or early onset DCI is increased in divers with a resting right-to-left shunt through a PFO. There is, at present, no evidence that PFO is related to mild or late onset bends. This issue raises several questions:

Should all recreational divers be screened for PFO?

No. Even with a PFO the probability of DCI is low, especially those types of DCI that are associated with PFO. A case could be made that screening is appropriate for divers whose work experience is likely to subject them to VGE for prolonged periods (e.g. saturation divers).

If a diver experiences bends frequently and appears to be predisposed to DCI should a bubble echo study be done?

No. If a diver has an intrinsic susceptibility to bends, identification of just one of many possible risk factors (most of which are probably as yet undiscovered) is not useful unless surgical correction is contemplated (e.g. of an ASD).

Should a person with a known intracardiac shunt ever dive?

Because of the extremely high probability of cerebral gas embolism, a person with any significant right-to-left shunt (e.g. Tetralogy of Fallot) should never scuba dive. Because of the small pressure difference between the right and left atria, and the potential for reversal of the usual left-to-right shunt, people with atrial septal defects should also not dive.[4]

In the presence of a PFO, the advice I usually give depends upon the degree to which the individual is risk averse. The most conservative advice is not to dive. The liberal approach states that even if the probability of experiencing serious neurological bends is five fold higher than a person without a PFO and five times a small risk is still small. A middle philosophy is to minimise the probability of VGE, for example by using bottom times that are at most one half of the USN air diving no-stop times.[2]

For individuals with ventricular septal defects (VSD), provided the shunt is unidirectional, left-to-right and not haemodynamically significant, small changes in intracardiac pressures induced by respiratory manoeuvres will not significantly affect the large pressure gradient between the ventricles. Therefore it is extremely unlikely that VGE could enter the left side of the heart via a VSD, and such a condition should not preclude diving.

Questions

Unidentified speaker

In 1991 there was a study from Norway on 120 professional divers who had been examined with MRI, demonstrating that there were not any more bright spots in the MRI scans of professional divers than in a control group.[17]

Secondly in the professional divers the number of bright spots seemed to decrease as the diving career increased. This may of course be the healthy diver effect, that most injured divers leave their job, but it did not look like that because the same divers were used for examination of neurological symptoms and a number of

them had neurological symptoms. Anyway, there was no clear relationship between diving and neurological symptoms from diving and the bright spots.

Reply

That is exactly right. In fact, in that study, the number of white spots was less in the divers than it was in the controls, who were policemen.

Unidentified speaker

Should all prospective divers have a thorough cardiac examination, and have the physician listen carefully for murmurs?

Richard Moon

I believe the answer to your question depends upon the type of diving. For recreational divers I believe that there is no need for a screening examination to look for patent foramen ovale. The only relationship that we have found between PFO and DCI is for serious neurological bends, a rare disorder, and largely attributable to risk factors which are associated with the dive itself, such as depth, bottom time and rate of ascent. On the other hand, for a person who plans to perform dives that have a high risk of venous gas embolism for long periods of time, for example saturation diving, then I would recommend a PFO study.

The method of looking for a PFO must be a bubble contrast echo. Colour flow doppler is insufficiently sensitive. It is impossible to detect inter-atrial shunts on physical examination unless there is a frank atrial septal defect, which produces a fixed split of the second heart sound, or a pulmonic valve systolic flow murmur. These physical signs therefore cannot be used as a method of screening for PFO. However, if there are physical signs of an ASD, the diver needs to be examined more thoroughly using echocardiography.

Unidentified speaker

Two comments. I would like to emphasise that in the Norwegian study, it is my understanding that those controls as you mentioned were policemen and given the combative nature of that work, that may not have been a wise control group to use, as far as head injuries are concerned. But the second thing is I have been desperately seeking some reassurance that the test is not worse than the disease, particularly after hearing Des' work and being familiar with Brian Hills' work. Do we have any assurance that putting these saline bubbles thorough the brain and elsewhere does no harm?

Richard Moon

It appears that in the absence of a pre-existing inert gas load, the transient gas embolism of the degree which is engendered by this test is fairly harmless. In our series of about 170 people on whom we did this test, two experienced transient paraesthesias, but neither had a right-to-left shunt. The general opinion among cardiologists is that it is a safe procedure that does not result in any serious morbidity.

Ian Millar

Any comments on the comparability or preference for testing techniques, given that there were two clearly techniques, one looking at the heart specifically, one sampling the end target organ, and yours using agitated saline, versus recent studies which as I understand it used a contrast medium which has contrast microbubbles in it, which would be significantly smaller than the saline bubbles.

Richard Moon

The sensitivity of the two techniques in detecting PFO in normal subjects appears to be similar. Transoesophageal echo (TEE) has clearer images than transthoracic echo, but it is a little less popular with divers because swallowing the probe is extremely uncomfortable. It has a higher sensitivity,[18,19] presumably because of the increased clarity of the images. There are, at present, no data showing that PFOs seen with TEE that cannot be detected using TTE represent a risk factor for DCI. I feel that such PFOs are probably small and of minimal significance in the pathophysiology of decompression illness.

Paul Langton

Most of the studies that have looked in the neurological series where they have had lots of cases and compared transthoracic and transoesophageal, certainly do find a higher detection rate of PFO from transoesophageal, but at complete loss of specificity. They are detecting lots of small lesions that they can detect in control subjects as well, so the specificity goes out the window with the alleged improved sensitivity.

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A CASE OF RECURRENT DECOMPRESSION ILLNESS

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Key Words

Case report, decompression illness, sequelae, treatment.

General practitioners see their patients repeatedly. This puts them in an excellent position for follow up studies on divers who have suffered decompression illness (DCI) to discover what the usual clinical progress is likely to be. Very little has been published about the long term follow up of divers. Case 1 is from my records. Follow up of divers suffering decompression illness treated with recompression is often revealing.

Case 1

A 50 year old mechanic has been diagnosed as DCI on 4 separate occasions. His only other disability has been symptoms of carpal tunnel syndrome. He was treated at the Royal New Zealand Navy (RNZN) Hospital on 3 occasions between 1988 and 1996. He has suffered from a series of subtle but significant disabilities for years.

December 1988

After an evening of moderate to heavy alcohol consumption he did a single dive to 21 m (70 ft) for 60 mins. He ran out of air and made a rapid ascent. 24 hours later he consulted me complaining of skin itch, pain in his hands and feeling very tired and light headed. He had pain at the base of his spine and in the buttocks.

Physical examination was neurologically normal, except for a sharpened Romberg Test (SRT) of 25 seconds. He was slow counting down from 100 by sevens. The audiogram showed a mild high frequency loss R>L.

He was transferred to the RNZN recompression chamber (RCC) at the Naval Hospital in Auckland, about 150 km, where he needed three treatments before his