Editorial

Transcatheter occlusion of patent foramen ovale: A prevention for decompression illness?

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In 1986 Wilmshurst and colleagues observed neurological decompression sickness in a recreational scuba diver after a 15 minute dive to 38 m, and attributed its cause to venous gas embolism (VGE) passing through a previously undocumented atrial septal defect (1). Embolization of thrombus through a patent foramen ovale has been described for over 50 years (2), and the concept of venous to arterial embolization led to the notion that venous gas bubbles, common after recreational dives but usually silent due to filtration by the pulmonary vasculature, could traverse an intracardiac shunt and cause infarcts in susceptible target organs such as the brain and spinal cord. While large atrial septal defects such as the one demonstrated in Wilmshurst's case are rare, small defects (patent foramen ovale, PFO) are present in up to 30% of the population (3), and could provide a similar route for bubbles to enter the arterial blood. Indeed, several investigators have demonstrated an association between PFO and certain types of decompression illness, predominantly cerebral, spinal cord and, possibly, inner ear (4-10). PFO has also been associated with skin bends (11). In these studies right-to-left shunt has been demonstrated in as many as 89% of symptomatic divers (inner ear DCS), but more typically 60% (cerebral or spinal cord bends), compared with 20-30% of control subjects.

The general diving public has enthusiastically latched onto this concept. During fitness to dive evaluations, questions about PFO are always near the top of divers' lists; the Divers Alert Network is bombarded with PFO queries. This interest has gained momentum with the development of transvenous occluder devices, which can be used to close PFOs in an outpatient procedure in as little as 30 minutes. In Europe these devices are commercially available and approved for closure of hemodynamically significant ASD or recurrent presumed paradoxical thromboembolism. In the US, transvenous occluders are available only under the humanitarian device exemption for the closure of a PFO in patients with recurrent cryptogenic stroke due to presumed paradoxical embolism and who have failed conventional drug therapy.

This concept has been extended to diving. Wilmshurst and colleagues first reported the use of a transcatheter occlusion device in an attempt to reduce the risk of DCI in a professional diver (12). Walsh and colleagues reported the use of transcatheter occlusion to treat PFO in 7 divers with neurological DCI (13). The authors noted that after occlusion there were no further

neurological decompression episodes in any of the patients over a 3–12 month follow up period. However, without knowing more about their diving patterns before and after the procedure it is difficult to be sure that this represents a true reduction in risk.

Those who undertake or sign up for such a procedure should be aware of several issues. First, while there is an association between PFO and severe neurological bends, causation is unproven. Indeed there is a disconnection between the purported mechanism and many observations. In recreational divers venous bubbles are almost ubiquitous. In multi-day, repetitive, multi-level exposures venous bubbles were observed by Doppler in 61 of 67 recreational divers (91%) (14). While 20-30% of divers might be expected to have a PFO, the incidence of DCI among recreational divers using standard decompression procedures is only 1/20,000 to 1/1,200 dives (15-18). The estimated probability of a DCI incident with characteristics of those correlated with PFO is between 1/60,000-1/3,600 dives. It can be concluded that in order for DCI to occur there must be other factors, such as bubble load or a tissue factor.

It is also conceivable that a PFO represents a marker for susceptibility but is not involved directly in the pathophysiology (19). After all, no one has yet correlated the presence of left atrial bubbles after a dive with the type of decompression illness that is commonly correlated with PFO. While Pilmanis and colleagues reported left ventricular bubbles in 6 instances of simulated altitude exposure, only 5 experienced symptoms, and not of the type related to PFO (4 pain, one skin mottling; no cerebral symptoms). Moreover, of the 5 subjects who were tested, a PFO was present in only two (20). In the attempt to find the 'smoking gun', as yet investigators have observed only the smoke.

Second, studies to date have focused on the correlation of PFO with neurological injuries, particularly serious ones, but these represent only a small proportion of DCI incidents (around one third). The majority of DCI cases in both recreational and commercial diving consist of pain or sensory abnormalities (16,17), and no one has yet shown that PFO is related to most of these cases. The exception is skin bends, but this is uncommon. Only around one third of cases of DCI in recreational divers are considered severe (16,17). If 60% of these have a PFO, and 25% of the remainder have one, then it can be estimated that the majority of cases of cases of bends must occur in divers *without* a PFO.

The error of associating a common finding with an uncommon disease is well known, and has been discussed in the context of mitral valve prolapse (21). This error is referred to as "referral bias", and is likely to be involved in the data regarding DCI and PFO.

Finally, placement of a transvenous occluder is not without risk. According to data submitted to the US Food and Drug Administration by the manufacturer of the AMPLATZER PFO Occluder™, in 442 insertions there were 7 major adverse events, including cardiac arrhythmia requiring major treatment, device embolization requiring either percutaneous or surgical removal and failure of the delivery system (http://www.fda.gov). More recent publications have continued to report device malposition, device embolization, arrhythmias, pericardial effusion, iliac vein dissection, hemorrhage, sizing balloon rupture and both right and left atrial thrombus (22-25). Late complications have included peripheral embolization and sudden death (22).

Even for recurrent thromboembolism, the effectiveness of transcatheter devices has not been demonstrated, and no benefit-risk ratio for transcatheter closure has been established (26). For PFO and DCI, one can conclude, even less so. A thoughtful debate about PFO closure in

cryptogenic stroke (27,28) points out the need for prospective randomized trials to find the true answer.

We do not exclude the possibility that closure of a PFO might reduce the probability of some types of DCI, but, the evidence indicates, only a minority. It must be understood that: 1) there are uncertainties in the PFO hypothesis; 2) there are probably more powerful (as yet undiscovered) predictors of DCI; and 3) the transcatheter procedure has hazards. If it is true that the presence of a PFO in a diver with VGE predisposes to DCI by providing a route through which bubbles can pass into the arterial circulation, then the safest strategy might be to focus on reducing the venous bubble load for susceptible divers, by developing different decompression procedures, limiting bottom time or by the appropriate use of oxygen.

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