EDITORIAL COMMENT

The PFO Gets Blamed Again...Perhaps This Time it Is Real*

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Patent foramen ovale (PFO) closure is the thing to do these days in the interventional laboratory. Closures are done for strokes, migraine headaches, and postural cyanosis, and for divers who are at risk for decompression sickness. Atrial septal defect closures are also done in the interventional laboratory, but these are known to reduce the significant left-to-right intracardiac shunt that eventually, when large enough, results in pulmonary hypertension, an Eisenmenger syndrome, and permanent lung injury. We have seen the image of a thrombus partially protruding through the PFO, threatening a major stroke (1), and seen the retrospective data indicating that there is a higher incidence of PFOs in patients with cryptogenic strokes, and in some forms of decompression sickness (2). But, the Reverend Bayes continually reminds us that an increased incidence of PFO in a stroke population is not the same as an increased incidence of stroke in a PFO population, particularly with the high incidence of PFO in the general population (3) or, in Bayesian terms, the high prior probability of PFO presence. Prospective randomized clinical trials of PFO closure for cryptogenic stroke have to date been disappointing in that they have not demonstrated a reduced stroke rate after closure (4,5), and the value of PFO closure for relieving migraine headaches has also been inconclusive (6). Similar concerns regarding the role of a PFO in decompression sickness have been a topic of discussion in altitude (7), space (8), and undersea exposures (9,10). All of these environments commonly produce venous gas emboli (VGE) from supersaturated nitrogen dissolved in blood and tissues that converts to a free-gas phase during exposure to lowered ambient pressure (11,12). Astronauts in space suits, aviators flying at high altitude, and divers returning from underwater exposures all experience this risk, and under circumstances of high degrees of supersaturation, will demonstrate VGE and, eventually, clinical evidence of decompression sickness (DCS) (13,14). The syndrome of DCS has been described for over 100 years (11,12), and the circumstances that result in DCS are well understood. Protocols for minimizing risk and prevention are well accepted; indeed, most sport divers now carry decompression computers on their wrist while diving to aid in safe decompression (15). Yet, there remains some unpredictability in DCS, and the question of whether a PFO contributes to DCS has been debated. Studies so far have been inconclusive, but as in stroke and migraine, a higher than expected incidence of PFO has been noted in divers with unexplained DCS (2), and a Bayesian meta-analysis suggests that a PFO does increase risk for DCS (16). Torti et al. (17) observed an increased incidence of DCS in divers with large PFOs compared with those with small or no shunt. Germonpré et al. (18) found an increased incidence of large PFOs in divers with evidence of diving-related cerebral injury compared with symptom-free divers with similar exposures, and the work of Billinger et al. (19) showed magnetic resonance imaging bright objects in divers with a PFO.

In this issue of JACC: Cardiovascular Interventions, Honék et al. (20) report an important study that helps elucidate the relationship between PFO and DCS. They exposed a group of sport divers to 2 acceptable (though risky) depth-time exposures and found a very high occurrence of VGE in the divers. These exposures are not recommended for sport diving by most diving organizations around the world, but are commonly followed by commercial divers, and recently by extension of sport diving to “technical diving,” where exposures to deeper depths, special gas mixtures, and need for staged decompression procedures all increase risk for DCS. Honék et al. (20) focused their study on divers found to have a large PFO who had previously experienced DCS symptoms when diving. A comparator group of divers without a PFO or with a small PFO was found to have a low incidence of DCS. As expected, the VGE were found to arterialize in the presence of a large PFO. Their detection method (transcranial Doppler) detected arterial bubbles signals in 32% of 18-m divers without closure and 0% of divers with closure of the PFO, and in 88% of the 50-m divers without closure and 0% of such divers with PFO closure. These exposures actually caused clinical evidence of neurological DCS in 20% to 25% of divers with an unclosed PFO and 0% of divers who had their PFO closed. Although the frequency of arterial gas emboli (AGE) was significantly reduced (p = 0.02) with PFO closure, the reduction of DCS incidence did not reach statistical significance (p = 0.11 for the 18-m dive and p = 0.49 for the 50-m

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dive). Yet, these data are compelling. Experienced dive supervisors have known for many years that a 50-m dive for 20 min using compressed air as the breathing gas results in an increased incidence of DCS even when the proper decompression schedules are observed, and as a result, often extend the decompression time to lower the DCS incidence (personal observation). One could speculate that a 10% to 15% incidence of DCS following this exposure occurred in the 10% to 15% of divers who had a large PFO. Similarly, the 18-m exposure for 80 min requires staged decompression (21,22) and increases the risk for DCS.

The study by Honék et al. (20) provides several important observations. They demonstrated that diving exposures requiring staged decompression are likely to produce a high incidence of VGE that will become AGE in the presence of a large PFO. This finding supports the recommendations for sport diving that depth should not exceed 130 feet (40 m), and exposure time should be limited to avoid staged decompression (no-decompression diving). They also demonstrate that closing the PFO eliminates the arterialization of VGE. However, their data do not confirm that closure will reduce the incidence of DCS. We know that AGE from pulmonary barotrauma (23) or iatrogenic AGE (24) can result in profound neurological injury, and logic would lead to the conclusion that AGE resulting from a large venous bubble load in the presence of a large PFO would result in neurological symptoms of DCS.

Their study would have benefitted from a similar exposure of divers with a small or no PFO for a true control group. However, a large, prospective, randomized clinical trial is unlikely to be supported to obtain a definitive answer regarding DCS and PFO closure. Importantly, one should not conclude that commercial and technical divers who are exposed to risky dive profiles be screened for a PFO or have a PFO closed prophylactically, but commercial divers who have multiple recurrences of unexplained DCS should be screened for a PFO, and if found, a decision to close the shunt should be made by the diver and physician together, depending on career goals, work requirements, and risk of complications of the closure procedure. Sport and technical divers who have experienced a DCS event with or without a PFO should be advised to reduce risk by limiting depth and time to safe exposures.

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