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ORIGINAL ARTICLE

Patent Foramen Ovale Influences the Presentation of Decompression Illness in SCUBA Divers

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Background Few have examined the influence of patent foramen ovale (PFO) on the phenotype of decompression illness (DCI) in affected divers.

Methodology A retrospective review of our database was performed for 75 SCUBA divers over a 10-year period.

Results Overall 4,945 bubble studies were performed at our institution during the study period. Divers with DCI were more likely to have positive bubble studies than other indications ($p < 0.001$).
Major DCI was observed significantly more commonly in divers with PFO than those without (18/1,000 v. s. 3/1,000, $p = 0.02$). Divers affected by DCI were also more likely to require a longer course of hyperbaric oxygen therapy (HBOT) if PFO was present ($p = 0.038$). If the patient experienced one or more major DCI symptoms, the odds ratio of PFO being present on a transoesophageal echocardiogram was 3.2 ($p = 0.02$) compared to those who reported no major DCI symptoms.

Conclusion PFO is highly prevalent in selected SCUBA divers with DCI, and is associated with a more severe DCI phenotype and longer duration of HBOT. Patients with unexpected DCI with one or more major DCI symptoms should be offered PFO screening if they choose to continue diving, as it may have considerable prognostic and therapeutic implications.

Keywords Patent foramen ovale • Decompression illness • Hyperbaric oxygen therapy • Transoesphageal echocardiography • Bubble studies

Introduction

Patent foramen ovale (PFO) is present in approximately 27% of the adult population [1]. It is a vestige of the foetal circulation which persists beyond the early stages of life as a result of failed fusion between the septum primum and secundum. The one-way flap valve that forms over the fossa ovalis allows right-to-left shunting of blood flow when the right atrial pressure exceeds the left. Mechanistically, it has been implicated in various clinical syndromes including cryptogenic stroke [2–5], migraine [6,7], and neurological decompression illness (DCI) [8,9].

DCI occurs when there is a reduction in the ambient pressure surrounding the body, for example when a diver surfaces after a dive. It could either be caused by formation or expansion of existing inert gas bubbles (usually nitrogen) in the tissue causing local damage (decompression sickness, DCS), or intravascular gas bubbles passing into the arterial

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circulation with subsequent embolic complications (arterial gas embolism, AGE). The latter could either result from direct pulmonary barotrauma, or presence of a right to left shunt within the body such as a PFO.

Amongst all widely available diagnostic modalities, the trans-oesophageal echocardiogram (TOE) remains the investigation of choice for many institutions for the diagnosis and characterisation of PFO. PFO is detected via positive transeptal colour Doppler flow, transeptal flow of gas bubbles during bubble studies, or both, with or without the aid of Valsalva manoeuvres. In this report we reflect on our experience in 75 SCUBA divers referred for assessment following an episode of DCI treated at a major centre for Diving and Hyperbaric Medicine. Other studies to date have looked at divers as a whole and have not singled out divers affected by DCI as a group. It is our intention to characterise this specific subgroup in order to understand the relationship between DCI and PFO in these divers. To our knowledge this is the first time this specific group of patients has been studied in a moderate size cohort.

Methodology

This is a retrospective case series based on a review of our echocardiogram database and medical records between January 2004 and May 2013. All agitated saline bubble studies performed during the study period were identified. Clinical indications for the bubble studies were noted and divided into three groups: the ''source study'' group, where TOE was performed primarily to identify possible causes of cerebrovascular accident (CVA) and peripheral thromboembolic diseases, for divers with DCI, and for other miscellaneous indications. The latter group encompasses all other indications for TOEs including valve studies, TOE guided cardioversions, exclusion of endocarditis etc. For the purpose of this study these indications were grouped into one to distinguish them from studies aimed at identifying left-right shunts within the heart. All echocardiographic features were recorded.

The clinical notes of patients who underwent TOE following DCI were reviewed. Pertinent information including patients' demographics, co-morbidities, diving profiles, and details of decompression illness were recorded. Minor and major DCI are defined in Table 1. Divers with DCI were referred for TOE at the discretion of their diving physician; generally this was when the severity and/or symptoms of their DCI were incongruous with their dive profile and accumulated nitrogen load. Patients received treatment for their DCI prior to their TOE, so the need to treat and duration of treatment was determined without knowledge of their PFO status. TOE was performed in a single institution under sedation with midazolam and fentanyl, and following lignocaine anaesthetic spray to the oropharynx. The inter-atrial septum was interrogated with colour Doppler by sweeping the probe from the transverse to the longitudinal plane, looking for transeptal blood flow. Bubble studies were performed in the imaging plane where inter-atrial septum was most resolved, and by injection of 10 mL of contrast through an upper limb cannula. The echo-contrast medium consists of a mixture of saline, air and 1 mL of the patients' own blood taken from the intravenous cannula. When transeptal bubble flow was not immediately apparent, patients were asked to perform a Valsalva manoeuvre. A positive bubble study is defined as crossing of bubbles from right to the left atrium within four heartbeats.

Table 1 Definition of major and minor DCI.

Major DCI	Minor DCI
Cognitive Impairment	Dermatological manifestations
CNS dysfunction (cerebral cortex, cerebella, spinal cord)	Parasthaesia
Visual disturbances	Musculoskeletal Pain
Loss of consciousness	Abdominal discomfort
Amnesia to event	Constitutional symptoms (dyspnoea, headache, nausea, fatigue, unwell, light-headedness, and insomnia)
Inner ear disturbances	

Data collected was analysed using IBM SPSS Ver 20. Categorical data are expressed in absolute numbers and proportions, and statistical significance is tested with chi-square test. Continuous data are expressed as medians +/- inter-quartile ranges (IQR) if they are not normally distributed or mean+/- standard deviation (SD) if they are. Intergroup comparison of normally distributed data was tested with two-tailed student T test, while comparison of non-normally distributed data was performed through a two-tailed Mann-Whitney test. Statistical significance is defined as $p < 0.05$.

Results

Bubble Studies

Overall, 4,945 bubble studies were performed between January 2004 and May 2013 (Table 2). Seventy-five bubble studies (1.5%) were performed in patients with DCI, 1,385 (28%) in the ''source study'' group, and the remaining for other indications. Bubble studies were positive in 682 TOE (13.8%) overall. However, significantly more patients had positive bubble studies in the DCI group compared to the ''source study'' group and studies performed for other indications (52% v.s. 21% and 10% respectively, $p < 0.001$). When the bubble studies were positive, resting unprovoked transeptal flow of bubbles was more likely to be observed in patients with DCI, as compared with the ''source study'' group and studies performed for other indications ($p = 0.001$ and 0.03 respectively).

Table 2 Summary of Bubble Studies between January 2004 and May 2013.

	DCI	Source Study	Miscellaneous	Total
Indication for TOE	75/4,945 (1.5%)	1,385/4,945 (28%)	3,486/4,945 (70.5%)	4,945
Positive Bubble Studies	39/75 (52%)	291/1385 (21%)[a]	349/3,486 (10%)[a]	682/4945 (13.8%)
Positive *without* provocation	32/39 (82%)	176/291 (60%)[b]	239/349 (68%)[c]	479/682 (70%)

[a] $p < 0.001$ compared to DCI subgroup; [b] $p = 0.001$ compared to DCI subgroup; [c] $p = 0.03$ compared to DCI subgroup.

Divers with DCI

Of the 75 patients who underwent elective TOE following DCI, 46 were males (61%) and the mean age was 39 +/- 13. Thirty-nine patients (52%) had positive bubble studies, confirming the presence of a PFO in these patients. Those who had a positive bubble study tended to be older than those without (43+/-14 years v.s. 34+/-11, $p = 0.002$). Age however is not a predictor of DCI phenotype. There is also no significant difference in the divers' sex, incidence of migraine and regular medication use between the divers with or without a PFO (Table 3). For the majority of the 75 divers included in this review, the episode of DCI was their first event. However, 10 divers (19.9%) had experienced two or more episodes of DCI prior to this presentation. As such, the mean number of episodes of DCI experienced before these divers' TOE examination was 1.3. Overall, the median number of dives for our cohort was 93 (IQR: 181) prior to their first DCI, and 135 (IQR: 281) prior to their TOE. The mean depth and duration of dives preceding their present episode of DCI was 30.9 metres and 35.2 minutes respectively, although both varied significantly between individuals. The mean depth and duration of dives did not differ significantly between those with and without PFO (Table 3).

The mean rate of DCI in our cohort was 54 episodes per 1000 dives. There was no difference in the overall rate of DCI in patients with and without PFO (66 per 1,000 dives v.s. 43/1,000, $p = 0.23$). Thirty-two patients (43%) reported symptoms consistent with major DCI with a mean rate of 16 per 1,000 dives. Major DCI was observed significantly more commonly in divers with PFO than those without, with a rate of 18/1,000 and 13/1,000 respectively ($p = 0.02$). Divers without PFO who suffered DCI were more likely to have experienced a minor episode with a rate of 50/1,000 (v.s. 24/1,000, $p = 0.009$) (Tables 4 and 5). No single symptom was predictive of the presence of PFO in affected divers. However, if the patient experienced one or more major DCI symptoms, the odds ratio of PFO being present on TOE was 3.2 ($p = 0.02$) compared to those who reported no major DCI symptoms.

Overall, the symptoms of DCI lasted more than 24 hours in 73.3% of the divers irrespective of treatment status and the presence of PFO. While the duration of symptoms did not differ between divers with and without PFO (86% v.s. 69% with symptoms >24 hours respectively, $p = 0.12$), those who suffered a major episode of DCI were more likely to have symptoms that persisted beyond 24 hours irrespective of treatment status (91% v.s. 67%, $p = 0.02$).

Overall, 58 divers (77.3%) underwent recompression using a standard 2.8 ATA, 100% oxygen breathing treatment table (Royal Navy Table 62). Most also had a variable number of subsequent hyperbaric oxygen therapy sessions (HBOT) at 2.4 ATA breathing 100% oxygen for 90 minutes. The remaining patients who were not treated were those referred for elective assessment after symptom resolution. Overall, the mean number of hyperbaric sessions per treated diver was 3.1. Divers affected by DCI were more likely to require a longer course of HBOT if they had a PFO (3.6 ± 2.2 v.s. 2.6 ± 1.1 sessions, $p = 0.038$). Those who suffered from a major episode of DCI were also more likely to require longer course of therapy (3.8 ± 2.3 v.s. 2.6 ± 1.0 sessions, $p = 0.02$).

Table 3 Baseline Characteristics of Divers with DCI referred for TOE (n = 75).

	PFO (n = 39)	No PFO (n = 36)	p value
Age, mean (±SD)	43 (±14)	34 (±11)	0.002
Male	23 (64%)	23 (59%)	0.81
Migraine	6/39 (15.4%)	2/36 (5.6%)	0.27
Total Number of Dives Before First DCI Median (IQR)	100 (178)	65 (202)	0.57
Depth of Dive preceding DCI (m) Mean (SD)	29 (10)	32 (28)	0.25
Duration of dive preceding DCI (min) Mean (SD)	36 (15)	35 (23)	0.60
Medication use	9/39 (23%)	7/36 (19%)	0.78

Table 4 Clinical Features of Patients with Major DCI.

	PFO (N = 39)	No PFO (N = 36)	p values
Major DCI[a]	23 (60%)	9 (25%)	0.003
Rate of Major DCI (/1,000 dives); mean	18	13	0.02
Cognitive	6 (15%)	2 (6%)	0.27
Spinal	6 (15%)	1 (3%)	0.11
Cortical	5 (13%)	1 (3%)	0.20
Cerebellar	2 (5%)	2 (6%)	1
Visual	6 (15%)	3 (8%)	0.48
Consciousness	0 (0%)	1 (3%)	0.48
Amnesia	2 (5%)	0 (0%)	0.49
Inner Ear	8 (21%)	4 (11%)	0.35

[a]Clinical information missing in 1 patients.

Table 5 Clinical Features of Patients with Minor DCI.

	PFO (N = 39)	No PFO (N = 36)	p values
Minor DCI[a]	15 (40%)	27 (75%)	0.003
Rate of Minor DCI (/1,000 dives); mean	24	50	0.009
Dermatological	13 (33%)	9 (25%)	0.46
Peripheral nervous system	14 (36%)	17 (47%)	0.36
Arthralgia	1 (3%)	8 (22%)	0.01
MSK Pain	11 (28%)	14 (39%)	0.34
Abdominal Discomfort	2 (5%)	0 (0%)	0.49
Dyspnoea	1 (3%)	1 (3%)	1
Constitutional	20 (51%)	24 (67%)	0.24

[a]Clinical information missing in 1 patients.

Table 6 TOE characteristics in patient with DCI and PFO.

	Major DCI	Minor DCI	p value
Need for provocation	5 (22%)	2 (13%)	0.68
Presence of transeptal colour flow	15 (65%)	7 (47%)	0.32
Atrial Septal Aneurysm (Septal excursion $\geq$ 10mm)	16 (70%)	12 (80%)	0.71

Finally, no specific echocardiographic features of PFO were found to predict the severity of DCI (Table 6).

Discussion

PFO has long been established as a risk factor for the development of serious neurological DCI, as it permits arterialisation of venous gas bubbles as a diver ascends [10,11]. Our study confirmed the trend by demonstrating a higher prevalence of PFO in referred divers with DCI when compared to historical normal control. Our series also confirms the association between the presence of PFO and severity of DCI in affected divers, as well as the number of HBOT sessions required.

Transoesophageal echocardiogram remains the gold standard for diagnosing inter-atrial shunts. A positive diagnosis is achieved through demonstration of colour Doppler flow across the inter-atrial septum, and/or by visualisation of transeptal bubble flow on agitated saline bubble study. In an adequately performed study, the specificity of a positive bubble study for the presence of inter-atrial shunt is 100%, while the sensitivity approaches 93% [12]. The latter however, is heavily operator dependent, and may be affected by the site and number of contrast injections, as well as the type and adequacy of provocation manoeuvres attempted [13].

In our cohort of patients undergoing TOE for purposes other than to exclude left-right shunt, the sensitivity of TOE in identifying a PFO is markedly reduced when compared against its expected prevalence in the community. TOE performed in these settings were often targeted, and therefore the number of contrast injections during the bubble studies may be limited, while provocation manoeuvres may not have been adequate. For studies performed for our divers however, effort was made to ensure adequate interrogation of the inter-atrial septum by observing bowing of the inter-atrial septum to the left upon release from various Valsalva manoeuvres and that bubble studies were repeated to confirm the absence of inter-atrial shunt. Even then the true prevalence of PFO in this population may still be underestimated.

Within this limitation, the prevalence of PFO in our selected cohort of divers was significantly higher than the historical normal control. Indeed, previous series have reported a prevalence as high as 62% in patients with major DCI [14], which correlates closely with our observation. Further, the presence of PFO is closely linked to increased severity and increased number of HBOT sessions, with our results showing a significant increase in the risk of suffering a major DCI in divers with PFO than those without. This has both health and economic implications, with divers with PFO often needing an extra HBOT session before achieving symptomatic resolution. A previous study has demonstrated the importance of PFO size as an independent predictor of DCI [8], utilising a grading system where the quantity of bubbles observed across the inter-atrial septum was used as a surrogate measure. We further observed that *spontaneous* transeptal bubble flow occurred more often in divers with DCI than other patient groups. We postulate that this may be an additional feature of use in stratifying risk of embolisation in divers with PFO as well as in other patient groups. Indeed, a similar observation was made by De Castro et al in their study characterising the relationship between the presence of PFO and thromboembolic complications in stroke patients [15].

While it is generally accepted that screening for intracardiac shunt is not indicated in prospective professional or recreational divers, guidelines are less clear on the selection criteria for divers who present after an episode of DCI. In our institution, TOE is currently offered to divers who have experienced an episode of DCI out of proportion to their compressed air exposure and who wish to continue diving for either recreational or occupational reasons. Focus is placed in particular on patients who reported recurrent symptoms on minor exposures, or symptoms associated with DCI either in the neurological system including the CNS, spine and inner ear, or the skin. This is in alignment with published recommendations from other nations [16]. The high prevalence of PFO in our cohort is a testament to the value of careful patient selection, as TOE in this setting can be extremely high yielding and instructive clinically. Indeed, patients who describe one or more symptoms consistent with major DCI should be considered for PFO screening, as the chance of finding a PFO is more than three times that of a patient who had no major DCI symptoms in a carefully selected sample of divers.

In divers who are diagnosed with a PFO in the context of DCI, it is our practice to initially counsel them against further diving activities. While modification of diving practice including reduction in nitrogen loading [17] and depth of dive [18] may reduce DCI recurrence, the protection is not absolute and the risk of recurrent DCI does not return to baseline level. In a previously published report [19] and our own series [20], there were no reported recurrences of major DCI in divers who continue to dive after percutaneous PFO closure. For divers who are unable to change their diving practice for occupational reasons, or in whom DCI occurs despite modification of standard diving tables, PFO closure appears to be the only viable protective strategy against future DCI. Screening for the presence and characterisation of PFO in divers affected by ''undeserved'' DCI not only provide important diagnostic and prognostic information, but also have considerable therapeutic implications and facilitate discussion regarding possible short and long term management strategies with these individuals.

Limitations

As DCI is ultimately a clinical diagnosis based on historical features, the accuracy of patients' accounts of the events may significantly influence the true incidence of major and minor DCI in our study. This is pertinent as our cohort was heterogeneous in their diving experience, and study has shown that experience does influence the incidence and severity of self-reported symptoms of DCI [21]. However, as the final diagnosis was adjudicated by experienced hyperbaric physicians, the validity of the information gathered should be acceptable. This potential recall bias may also be somewhat ameliorated by the fact that patients were not aware of their PFO status at the time of review, and therefore its effect should be balanced across the board and its influence on our final analysis should be minimised.

Being an observational study, this report is also likely to be affected by confounders that were not or cannot be accounted for during analyses. This includes differences in individuals' diving habit such as the rate of ascent, pre-dive fatigue or dehydration, alcohol consumption, and environmental factors such as the water temperature. Furthermore, our cohort is relatively small, and as such the results from this study should be interpreted with caution and viewed only as hypothesis generating.

It has been suggested that transthoracic echocardiogram (TTE) and TOE play complimentary roles in the diagnosis of PFO, as false negatives may occur secondary to poor acoustic window and inadequate Valsalva manoeuvres, respectively [22]. A combined approach may therefore improve the diagnostic accuracy of contrast echocardiography. TTE were routinely performed for all our patients prior to their TOE, although only few had transthoracic bubble studies. It is possible that the true incidence of PFO was underestimated

in our cohort of patients due to inadequate provocation with Valsalva manoeuvres as a result of sedation. TOE however remains the gold standard for visualising the interatrial septum and characterising the PFO, especially when percutaneous closure is contemplated.

Conclusions

PFO is more prevalent in divers who suffered DCI compared to patients referred for TOE for other indications, and is associated with a more severe DCI phenotype and longer duration of hyperbaric therapy. The presence of baseline unprovoked right to left shunt is more common in patients with DCI when compared to other patient groups, and may be an additional risk factor for thromboembolic complications associated with PFO. Finally, patients with unexpected DCI with one or more major DCI symptoms should be offered PFO screening if they choose to continue diving, as the incidence of PFO is significantly increased in this group.

Conflict of interest

The authors have no conflict of interest to declare.

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