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Effect of Catheter-Based Patent Foramen Ovale Closure on the Occurrence of Arterial Bubbles in Scuba Divers

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Objectives This study sought to evaluate the effect of catheter-based patent foramen ovale (PFO) closure on the occurrence of arterial bubbles after simulated dives.

Background PFO is a risk factor of decompression sickness in divers due to paradoxical embolization of bubbles. To date, the effectiveness of catheter-based PFO closure in the reduction of arterial bubbles has not been demonstrated.

Methods A total of 47 divers (age 35.4 ± 8.6 years, 81% men) with a PFO (PFO group) or treated with a catheter-based PFO closure (closure group) were enrolled in this case-controlled observational trial. All divers were examined after a simulated dive in a hyperbaric chamber: 34 divers (19 in the PFO group, 15 in the closure group) performed a dive to 18 m for 80 min, and 13 divers (8 in the PFO group, 5 in the closure group) performed a dive to 50 m for 20 min. Within 60 min after surfacing, the presence of venous and arterial bubbles was assessed by transthoracic echocardiography and transcranial color-coded sonography, respectively.

Results After the 18-m dive, venous bubbles were detected in 74% of divers in the PFO group versus 80% in the closure group ($p = 1.0$), and arterial bubbles were detected in 32% versus 0%, respectively ($p = 0.02$). After the 50-m dive, venous bubbles were detected in 88% versus 100%, respectively ($p = 1.0$), and arterial bubbles were detected in 88% versus 0%, respectively ($p < 0.01$).

Conclusions No difference was observed in the occurrence of venous bubbles between the PFO and closure groups, but the catheter-based PFO closure led to complete elimination of arterial bubbles after simulated dives. (Nitrogen Bubble Detection After Simulated Dives in Divers With PFO and After PFO Closure; NCT01854281) (J Am Coll Cardiol Intv 2014;7:403–8) © 2014 by the American College of Cardiology Foundation

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Scuba (self-contained underwater breathing apparatus) diving is a popular sport that attracts millions of participants worldwide (1). The general risk of death or major injury during scuba diving is small (<0.001% per dive) (2). However, some risk associated with decompression sickness (DCS) still exists.

DCS is caused by nitrogen bubble formation in hypersaturated tissues during the diver's ascent (3). These bubbles either cause local tissue damage or embolize through venous blood (3). Small quantities of venous gas bubbles are believed to be common after most scuba diving (4,5).

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Although most divers remain asymptomatic, symptoms may occur with high bubble load (pulmonary gas embolism) or may be due to paradoxical embolism (arterialization of bubbles) in a diver with a transient right-to-left shunt. The connection between a patent foramen ovale (PFO) and DCS was first described in the 1980s (6,7). Since then, a high prevalence of PFO has been repeatedly reported in divers with the neurological or cutaneous form of DCS (8,9). Multiple brain lesions have also been suggested as possible chronic sequelae of repeated exposure to asymptomatic arterial embolisms (10). The high prevalence of PFO in the general population (11) raises concern among divers and involved medical professionals.

Abbreviations and Acronyms

DCS = decompression sickness

PFO = patent foramen ovale

TCCS = transcranial color-coded sonography

TTE = transthoracic echocardiography

It has been suggested that catheter-based PFO closure might prevent the arterialization of bubbles and reduce the risk of DCS (12–14). The effect of PFO closure to prevent paradoxical embolization of injected bubbles has previously been demonstrated (15). However, there are currently limited clinical data supporting the effectiveness of PFO closure in divers (12,13) and no data confirming its effect on post-dive reduction of arterial gas emboli. The aim of this study was to test the effect of catheter-based PFO closure on the occurrence of arterial bubbles after simulated dives.

Methods

Patients. A total of 183 consecutive divers were screened for PFO at our center. Transcranial color-coded sonography (TCCS) was used for screening, and the diagnosis of PFO was confirmed by transesophageal echocardiography. The right-to-left shunt was graded by means of TCCS according to the International Consensus Criteria (16): grade 1, 1 to 10 bubbles; grade 2, >10 bubbles but no curtain (uncountable number of bubbles); grade 3, curtain. Significant PFO (grade 3) was found in 47 divers. Twenty divers (age 38.8 ± 9.5 years, 80% men) with a history of unprovoked DCS underwent catheter-based PFO closure (closure group). The other 27 divers (age 33.0 ± 6.6 years, 81% men) were either asymptomatic or did not agree with PFO closure, or their PFO closure had not been performed prior to study onset (PFO group). A total of 136 divers (age 33.6 ± 8.3 years, 85% men) that did not have a grade 3 PFO were not included in the study. In this group, 118 tested negative for PFO, 13 had a grade 1 PFO, 5 had grade 2 PFO, mean body mass index was 25.9 ± 3.1 kg/m^2, mean number of logged dives was 225 ± 479, and mean number of logged decompression dives was 47 ± 136. A history of DCS was reported in 11 (8%) of the 136 divers.

Inclusion criteria for the closure group were as follows: age ≥19 years; a PFO that had been occluded by a catheter-based procedure; and a signed informed consent form. Inclusion criteria for the PFO group were: age ≥19 years; a previously diagnosed grade 3 PFO according to the International Consensus Criteria (16); and a signed informed consent form. Exclusion criteria for both groups were: another dive performed in the preceding 24 h and disagreement to being included in the study. The study was approved by the local ethics committee and all study subjects gave written informed consent to participate in the study.

Procedures. The PFO closure procedures were performed in a single center (with the exception of 2 divers) between February 1, 2006, and April 30, 2013. The Amplatzer septal occluder (AGA Medical Corporation, Golden Valley, Minnesota) was used in 5 (25%) divers. In the remaining 15 (75%) cases, the Occlutech Figulla PFO Occluder N (Occlutech GmbH, Jena, Germany) was used. The procedure was performed as previously described (17). In all divers, the indication for the procedure was a history of unprovoked DCS (i.e., without violation of decompression regimen) and the presence of a grade 3 PFO according to the International Consensus Criteria (16). There were no major complications, and bleeding at the puncture site with no need of intervention occurred in 1 (5%) patient.

Simulated dives. To test the effect of catheter-based PFO closure on the reduction of arterial bubbles, decompression dives according to the U.S. Navy Air Decompression Procedure 1996 (18) were used. This decompression procedure was previously reported to generate significant amounts of venous and arterial bubbles but no acute DCS symptoms (5,19). Two dive profiles were used. The divers chose 1 of the 2 simulated dives that best corresponded to their usual diving practice. Thirty-four divers performed a dive to 18 m with a bottom time of 80 min (dive A). The descent and ascent rate was equivalent to 9 m/min; the decompression stop was performed at 3 m for 7 min. Thirteen divers performed a dive to 50 m with a bottom time of 20 min (dive B). The descent and ascent rate was 9 m/min; decompression stops were performed at 6 m for 4 min and at 3 m for 15 min.

Bubble detection. Venous and arterial nitrogen bubbles were assessed within 60 min after surfacing (20). In both dives, the occurrence of venous and arterial bubbles and the incidence of symptoms were compared between the PFO and closure groups.

Venous bubbles were assessed by experienced echocardiographers (J.H. and J.J.) using transthoracic echocardiography (TTE). An ultrasound system, Philips HD-10, with a 2 to 3.7 MHz multifrequency probe (Philips, Amsterdam, the Netherlands) was used. Bubbles were visualized by pulse-wave Doppler in the right ventricular outflow tract from the parasternal short-axis view, and their detection was performed for 1 min. The test was considered positive if 1 or more bubbles were detected.

Arterial bubbles were detected by means of TCCS in the medial cerebral artery (21). An experienced neurologist (M.S.) who was blinded to whether the diver was in the closure or PFO group performed the examination. The same ultrasound equipment as for the echocardiographic examination was used. Bubbles were detected for 1 min during native breathing and subsequently 3× for 40 s after a Valsalva maneuver. The test was considered positive if 1 or more bubbles were detected.

The divers were observed and questioned for any DCS symptoms, with special attention to any neurological or cutaneous manifestations. If symptoms occurred, immediate treatment in a hyperbaric chamber was administered. Treatment Table 5 of the U.S. Navy Diving Manual Revision 6 (18) was used as the treatment protocol. The primary endpoint was the occurrence of arterial bubbles.

Definitions. Arterial bubbles were defined as high-intensity transient signals in the Doppler spectrum detected by TCCS in the medial cerebral artery (21). Venous bubbles were defined as high-intensity transient signals in the Doppler spectrum detected by TTE in the right ventricular outflow tract. Neurological symptoms of DCS were defined as headache, unusual fatigue, visual problems, limb weakness or paralysis, dizziness, and paresthesia reported by the patient ≤24 h after the simulated dive. A history of unprovoked DCS was defined as any DCS symptoms that originated ≤24 h after a dive performed within the limits of any commercially-available diving table or computer used by the diver.

Statistical analysis. Normally distributed data are presented as mean ± SD and non-normally distributed data as median (interquartile range). The distribution of data was evaluated by the Kolmogorov-Smirnov test. Fisher exact test and the Mann-Whitney *U* test were used when appropriate. A p value of ≤0.05 was considered to indicate a statistically significant difference.

Results

A total of 47 divers (age 35 ± 8.6 years, 81% men) were examined after a single air dive in a hyperbaric chamber.

Table 1. Baseline Characteristics of PFO and Closure Groups for Dive A

	PFO Group (n = 19)	Closure Group (n = 15)	p Value
Age, yrs	33.0 ± 7.6	40.6 ± 8.5	0.02
Male	80	79	1.00
BMI, kg/m^2	26.0 (22.2–29.7)	27.4 (24.7–30.9)	0.27
Logged dives	100 (39–150)	500 (100–1,880)	0.02
Logged decompression dives	2 (0–15)	150 (5–400)	0.01
DCS history	53	100	<0.01
Time between PFO closure and experimental dive, months	—	36 (17–81)	—

Values are mean ± SD, %, or median (interquartile range). — = data are not available.
BMI = body mass index; DCS = decompression sickness; PFO = patent foramen ovale.

TTE and TCCS were used to assess the occurrence of bubbles. In all divers, adequate visualization of the medial cerebral artery during the TCCS examination was possible. The occurrence of arterial and venous bubbles was compared between the PFO and closure groups separately for dives A and B. The baseline characteristics for dives A and B are shown in Tables 1 and 2, respectively.

Dive A. Dive A was a dive to 18 m for 80 min of bottom time. Thirty-four divers (19 in the PFO group [age 32 years, range 21 to 51; 74% men], 15 in the closure group [age 38 years, range 28 to 55; 80% men]) performed this dive. Venous bubbles were detected in 74% of divers in the PFO group versus 80% in the closure group (p = 1.0) (Fig. 1). Arterial bubbles were detected in 32% versus 0% of divers, respectively (p = 0.02) (Fig. 1). In 21% of divers with PFO and detected arterial gas bubbles, neurological symptoms of DCS were present (headache, unusual fatigue, transitory visual disturbances). No divers (0%) reported DCS symptoms in the closure group (p = 0.11).

Dive B. Dive B was a dive to 50 m for 20 min of bottom time. Thirteen divers (8 in the PFO group [age 31.5 years, range 26 to 40; 100% men], and 5 in the closure group [age 34 years, range 18 to 51; 80% men]) performed this dive.

Table 2. Baseline Characteristics of PFO and Closure Groups for Dive B

	PFO Group (n = 8)	Closure Group (n = 5)	p Value
Age, yrs	32.9 ± 4.8	33.4 ± 12.1	1.00
Male	100	80	0.38
BMI, kg/m^2	25.5 (23.6–26.9)	30.7 (23.0–32.6)	0.23
Logged dives	55 (17.5–185)	300 (35–2,310)	0.23
Logged decompression dives	0 (0–75)	100 (10–315)	0.13
DCS history	38	100	0.08
Time between PFO closure and experimental dive, months	—	31 (7–67)	—

Values are mean ± SD, %, or median (interquartile range). — = data are not available.
Abbreviations as in Table 1.

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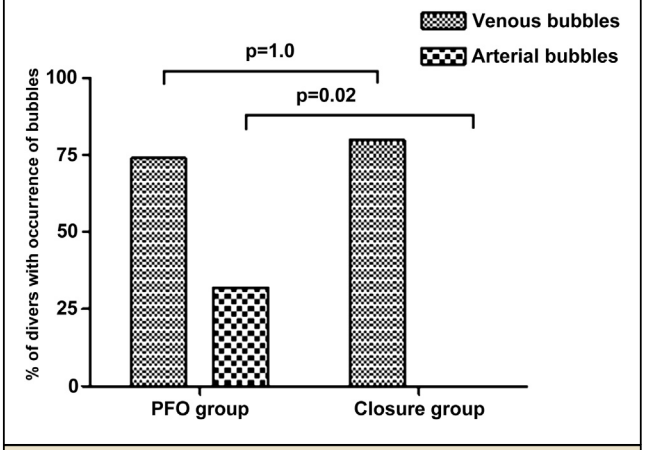

Figure 1. Occurrence of Bubbles After Dive A

The proportion of divers with the occurrence of venous and arterial bubbles after dive A in divers with patent foramen ovale (PFO group) and divers treated with a catheter-based patent foramen ovale closure (closure group). There was no difference in the occurrence of venous bubbles between the PFO and closure groups ($p = 1.0$), but no arterial bubbles were detected in the closure group ($p = 0.02$).

Venous bubbles were detected in 88% of divers in the PFO group versus 100% of divers in the closure group ($p = 1.0$) (Fig. 2). Arterial bubbles were detected in 88% versus 0% of divers, respectively ($p < 0.01$) (Fig. 2). In 25% of divers with PFO and detected arterial gas bubbles, mild neurological symptoms of DCS were present (headache, unusual fatigue, transitory visual disturbances, dizziness). No divers (0%) reported DCS symptoms in the closure group ($p = 0.49$).

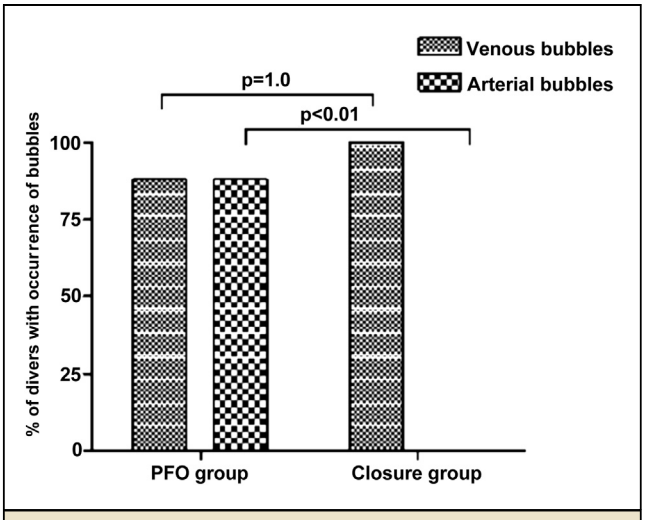

Figure 2. Occurrence of Bubbles After Dive B

The proportion of divers with the occurrence of venous and arterial bubbles after dive B in divers with patent foramen ovale (PFO group) and divers treated with a catheter-based patent foramen ovale closure (closure group). There was no difference in the occurrence of venous bubbles between the PFO and closure groups ($p = 1.0$), but no arterial bubbles were detected in the closure group ($p < 0.01$).

The typical appearance of post-dive venous bubbles in the right heart chambers and no arterial bubbles in the left heart chambers in a diver with a PFO closure device is shown in Figure 3.

Discussion

The present study is the first to our knowledge to demonstrate the effect of catheter-based PFO closure on the occurrence of arterial bubbles after simulated dives. In our study, no difference was found in the occurrence of venous bubbles between the PFO and closure groups. However, in the closure group, no arterial bubbles were detected. It is plausible, therefore, that the presence of a PFO plays a key role in paradoxical embolization of venous bubbles after scuba dives. Additionally, because PFO occlusion led to elimination of bubble occurrence in the medial cerebral artery, this closure strategy should have a role in the prevention of unprovoked DCS recurrence in divers.

Decompression sickness. DCS is caused by nitrogen bubble formation during the diver's ascent (3). The diver is exposed to an elevated pressure of nitrogen when breathing compressed air during the submersion (nitrogen can be exchanged for other inert gases such as helium or hydrogen in the breathing mixtures used by professional or technical divers). This excess nitrogen dissolves in all tissues at a rate dependent on their chemical composition and the density of capillaries (22). The total nitrogen load is determined by the depth profile (i.e., the partial pressure of nitrogen the diver is exposed to) and the duration of the dive (i.e., the duration of

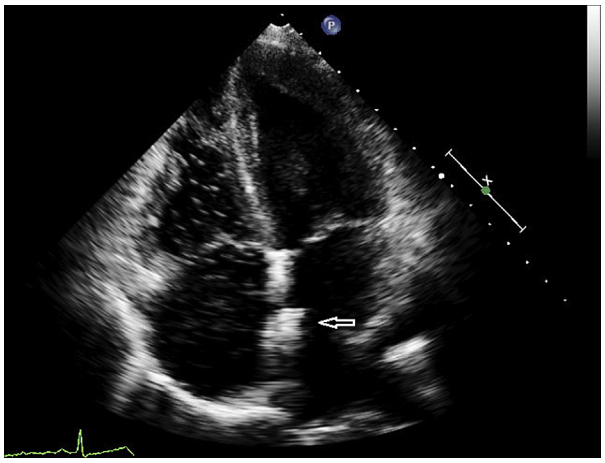

Figure 3. Post-Dive Venous Bubbles in a Diver After Foramen Ovale Closure

Transthoracic echocardiography (apical 4-chamber view) in a diver with a catheter-based patent foramen ovale (PFO) closure device after surfacing from a simulated dive. Venous bubbles are apparent in the right atrium and ventricle; no bubbles are visible in the left heart chambers. The PFO closure device is indicated by an **arrow**.

the exposure). During the ascent and hours after the dive, the excess gas is transported from the tissues back to the alveoli and exhaled. If the diver reaches the surface too early, the tissues get hypersaturated and intravascular and extravascular bubbles form and increase in size (3). To prevent DCS, divers perform the ascent according to decompression tables or a decompression algorithm implemented in a diving computer.

Small numbers of intravascular bubbles form in the capillaries and the venous blood even during a properly performed ascent (4). These bubbles are usually asymptomatic because most of the time, they are effectively filtered by the pulmonary circulation (3). If the bubble load is massive (in case of violation of the decompression regimen), the embolization manifests as a pulmonary DCS. In divers with PFO, a paradoxical embolization to the systemic circulation may occur and cause various, mostly neurological or cutaneous DCS symptoms even after a dive with an appropriate decompression regimen (unprovoked DCS) (3).

Paradoxical embolization results from increased right atrial pressure due to hemodynamic changes that occur in divers. After submersion, blood redistributes from the periphery to the thorax, which results in an increased right atrial pressure (23). Moreover, divers perform a Valsalva maneuver frequently during the dive (to equalize pressure in the middle ear), which further contributes to the increased right atrial pressure and leads to transient right-to-left shunting through the PFO.

PFO in divers. The connection between PFO and DCS was first described in the 1980s (6,7). Since then, a high prevalence of PFO has been repeatedly reported in divers with the neurological or cutaneous form of DCS (8,9). The possible chronic sequelae of repeated exposure to asymptomatic arterial embolisms have also been discussed. Knauth et al. (10) reported an association of PFO with multiple brain lesions in a follow-up study using magnetic resonance imaging. However, we have to bear in mind that these studies have several inherent limitations and are not generalizable.

PFO or other right-to-left cardiac shunt is present in about 27% of the normal population (11). However, the management of divers with PFO remains unresolved. Routine screening for PFO in divers is currently not recommended in most countries (24,25). Suggested recommendations for divers with diagnosed PFO and a history of DCS include the cessation of diving, a conservative approach to diving (26), and PFO closure.

It has been suggested by several investigators that a catheter-based PFO closure in divers might eliminate the arterialization of bubbles and prevent unprovoked DCS (12–14). No divers had arterial bubbles after PFO closure in this study; both the Amplatzer septal occluder and the Occlutech Figulla PFO Occluder N were highly effective. In the deeper dive, where the nitrogen load was greater, arterial gas bubbles were observed in all divers with a PFO and venous bubbles were detected. Moreover, 29% of these had cerebral DCS symptomatology. This is in agreement with the landmark case-controlled study by Germonpré et al. (27), who found high prevalence of high-grade PFO in divers suffering from unprovoked cerebral DCS. No divers in the closure group had DCS symptoms after either the 20-m or 50-m dive.

It has been suggested that the transpulmonary passage might also play an important role in the occurrence of post-dive arterial gas emboli. Ljubkovic et al. (28) observed arterial bubbles in 9 of 34 divers who tested negative for PFO and argued that transpulmonary arterialization would occur if a large amount of bubbles were produced and an individual exhibited a higher susceptibility for the transpulmonary passage. This was not observed in the closure group in our study, where no arterial emboli were detected, despite the fact that the occurrence of venous bubbles was not different from the PFO group. Also, clinical studies support the fact that PFO might be the major route of paradoxical embolization in divers. Torti et al. (8) reported that the odds of suffering a major DCS were 5× higher in divers with PFO and that the risk paralleled PFO size. Wilmhurst et al. (9) found that the incidence of PFO was 77% among 61 divers who had suffered the cutaneous form of DCS, compared with 28% in control subjects.

Study limitations. The absence of symptom-based clinical endpoints is the main limitation of this observational study. A randomized prospective follow-up trial would be necessary to assess the clinical efficacy of catheter-based PFO closure in divers. The primary endpoint was the occurrence of arterial bubbles, defined as 1 or more bubbles present. The binary grading of bubbles (none or any) might not have revealed a picture with enough differentiation. Another potential limitation is the experimental setting of the study. There is some evidence that wet dives generate more venous bubbles than dry dives do (29). In our study, only dive A was a dry dive, in dive B, the divers were submersed in a water reservoir inside the hyperbaric chamber using their usual scuba equipment.

Conclusions

We have demonstrated that in conditions of 2 simulated dives, catheter-based PFO closure was associated with the elimination of arterial bubbles. These results suggest that PFO occlusion might lead to a reduction of unprovoked DCS incidence in divers.

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Key Words: catheter-based closure ■ decompression sickness ■ paradoxical embolization ■ patent foramen ovale.