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Patent Foramen Ovale Closure and Decompression Sickness Among Divers

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ABSTRACT

Background: Decompression sickness is a diving-related disease that results in various clinical manifestations, ranging from joint pain to severe pulmonary and CNS affection. Complications of this disease may sometimes persist even after treatment with hyperbaric oxygen therapy. In addition, it may hamper the quality of life by forcing divers to restrict their recreational practice. The presence of a patent foramen ovale (PFO) increases the risk of decompression sickness by facilitating air embolization. Therefore, PFO closure may play a role in reducing such complications. However, PFO closure remains associated with its own set of risks and complications. We sought to assess the benefit and harm of PFO closure for the prevention of decompression sickness in divers.
Methods: We conducted a comprehensive search of MEDLINE, Embase, CENTRAL, and Web of Science. Two-armed studies comparing the incidence of decompression sickness with or without PFO closure were included. We used a random-effects model to compute risk ratios comparing groups undergoing PFO closure to those not undergoing PFO closure.
Results: Four observational studies with a total of 309 divers (PFO closure: 141 and no closure: 168) met inclusion criteria. PFO closure was associated with a significantly lower incidence of decompression sickness (PFO-closure: 2.84%; no closure: 11.3%; RR: 0.29; 95% CI: 0.10 to 0.89; NNTB = 11), with low heterogeneity ($I^2 = 0\%$). The mean follow-up was 6.12 years (Standard deviation 0.70). Adverse events occurred in 7.63% of PFO closures, including tachyarrhythmias and bleeding.
Conclusion: PFO closure may potentially reduce the risk of decompression sickness among divers; however, it is not free of potential downsides, with nearly one in thirteen patients in our analysis experiencing an adverse event.

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Patent foramen ovale (PFO) is an intra-atrial shunt that fails to close following birth. PFO is associated with decompression sickness (DCS) through arterial nitrogenous gas embolization [1]. The presence of a PFO increases the risk of venous bubble formation and subsequent DCS by facilitating systemic air embolization. DCS results in various clinical manifestations, ranging from joint pain to severe pulmonary and nervous system affection. PFO closure has shown to be effective and safe for secondary prevention of PFO-related stroke [2]. Therefore, PFO closure may play a role in reducing DCS-associated complications. Our study aimed to assess the procedural safety and effectiveness of catheter-based PFO closure in the prevention of DCS in divers.

MEDLINE/PubMed, Embase/OVID, CENTRAL, and Web of Science databases were searched from inception to August 2021. This PROSPERO-registered (CRD42021238147) systematic review included all two-armed studies comparing catheter-based PFO closure with conservative management among divers. All records were screened against the inclusion criteria by two independent authors (M.M. and A.S.).

The primary endpoint was long-term prevention of DCS at the longest follow-up available across all studies. Risk ratios (RRs) with 95%

Abbreviations: PFO, patent foramen ovale; DCS, decompression sickness; CI, confidence interval; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis.

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Table 1
Baseline characteristics and follow-up duration of included studies.

Study	Divers (N)		Age (years)		Gender (females %)		Total number of dives at baseline (N)		Professional divers (N)		History of decompression sickness (DCS) at baseline		Follow-up duration (years)	
	PFO closure	No PFO closure	PFO closure	No PFO closure	PFO closure	No PFO closure	PFO closure	No PFO closure	PFO closure	No PFO closure	PFO closure	No PFO closure	PFO closure	No PFO closure
Billinger et al. [4]	26	98	41	38	12	18	1208	689	6[a]		Major DCS: 7.3/10^4 dives	Major DCS: 4.8/10^4 dives	5.3	5.2
Koopsen et al. [5]	18	23	44.7	38.8	42.9	57.1	N/A	N/A	N/A	N/A	100% had a history of decompression sickness		6.8[a]	
Anderson et al. [3]	42	8	45.5	52	47.6	47.8	231	213	17	8	Confirmed DCS: 13.1/10^4 dives	Confirmed DCS: 12.8/10^4 dives	6	5
Honek et al. [1]	55	39	40.3	35.2	22	15	32,897	108,158	N/A	N/A	Unprovoked DCS: 4.13/10^3 dives	Unprovoked DCS: 0.11/10^3 dives	7.1	6.5

N/A: information not available.
[a] Information only available for the entire cohort rather than on a per-group basis.

confidence intervals (CIs) were estimated using the random-effects model. Study variability was estimated using the DerSimonian-Laird method and estimates were pooled using Mantel-Haenszel method. Additional fixed-effect analysis was performed to ensure the robustness of our results. Heterogeneity was quantified via the I^2 measure. Number needed to treat for an additional beneficial outcome (NNTB) was calculated based on the mean baseline risk of the control group. Analyses were conducted using R, version 4.1.0., 2021.

From a total of 202 records, 4 studies [3 prospective [1,3,4] and 1 retrospective [5]] were included in our meta-analysis. 309 divers were included (PFO closure: 141 and no closure: 168), of whom 223 (72.2%) were men. The weighted mean age across included studies was 40.8 years (standard deviation [SD] 3.76). PFO closure was performed electively in all divers. Baseline characteristics of all included studies are summarized in (Table 1). At a weighted mean follow-up of 6.12 years (SD 0.70), PFO closure was associated with a significant reduction in the risk of DCS (PFO-closure: 2.84%; no closure: 11.3%; RR: 0.29; 95% CI: 0.10 to 0.89; NNTB = 11), with no evidence of statistical heterogeneity (I^2 = 0%) (Fig. 1). Results using the fixed-effect model were similar (RR: 0.23; 95% CI: 0.08 to 0.70; NNTB = 10). Three studies [1,3,5] reported adverse events in sufficient depth. A total of nine adverse events occurring following 118 PFO closures (7.63%) (2 cases of minor bleeding, 4 atrial arrhythmias, 1 case with palpitations/syncope, 1 case of migraine with auras, and 1 allergic reaction during anesthesia).

To our knowledge, this is the first meta-analysis to assess the effectiveness of catheter-based PFO closure for preventing the clinical manifestations of DCS among divers. Our analysis suggests that divers with PFO may benefit from undergoing PFO closure. Nevertheless, selection bias might exist given the observational nature of the included studies. Moreover, the decision to perform PFO closure should take place in the context of a risk-benefit discussion with the patient. Such interventions may enable life-long protection from PFO-related stroke in higher-risk divers' cohort, and may provide assurance to practice diving at the desired diving depth.

Previous data showed that large PFOs likely contribute to DCS; however, identifying high risk divers is challenging. Moreover, offering an invasive procedure to otherwise healthy divers might be a challenge given the absence of RCTs in this population. Accordingly, routine screening is not currently recommended in healthy individuals. In certain high-risk cases, such as those with previous neurological DCS or a family history of PFO, screening may be considered, although this is not based on RCT-derived evidence [6]. Therefore, further feasibility RCTs are needed to further elucidate the benefit of PFO closure among divers. This meta-analysis is limited by the inherent limitations of the included studies, including self-reporting of endpoints, observational rather than randomized-nature, and loss to follow-up. Given the observational nature of the included studies, several potential confounders to DCS apart from preexisting PFO might alter outcomes, such as diving depth, duration, temperature, post-diving air travel, and physical fitness. Therefore, future RCTs are of paramount importance to help balance these factors between the intervention and control groups to accurately elucidate the impact of PFO closure. Further, as our analysis was solely based on raw events, we could not adjust for baseline differences or different follow-up durations. Moreover, the variable incidence of adverse events post-PFO closure across included studies (3.6–14.2%) [1,3,5] suggests that procedural skill may significantly alter the benefit-risk discussion. In conclusion, the present meta-analysis suggests that PFO closure might be associated with a lower risk of DCS among divers, but benefits must be weighed against the risk of adverse events. Although difficult to undertake, a future RCT evaluating the feasibility and effectiveness of PFO closure among high-risk divers is encouraged.

CRediT authorship contribution statement

Omar M. Abdelfattah: Conceptualization, Methodology, draft writing **Ahmed Sayed:** Data curation, Data Collection, data analysis. Writing- Original draft preparation. **Islam Elgendy:** manuscript

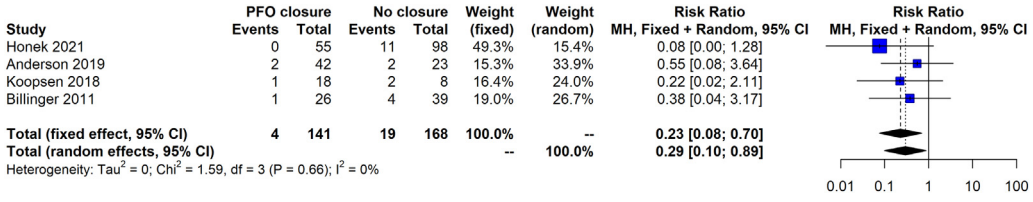

Fig. 1. Forest plot comparing patent foramen ovale closure to conservative management in divers.

drafting, critical revision, Writing- Reviewing and Editing. **Makak Munir:** Data curation, Data Collection. **Yehia Saleh:** Supervision, editing original draft**. Samir Kapadia:** Writing- Reviewing and Editing, Conceptualization. **George S. Abela:** revision of original draft, supervision, Validation. **Hani Jneid:** Writing- Reviewing and Editing, Conceptualization.

Declaration of competing interest

Dr. Elgendy has disclosures unrelated to this manuscript content including receiving research grants from Caladrius Biosciences, Inc. The other authors have nothing to disclose.

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None.

Ethical approval

This study was exempted from the institutional review board's approval because it used anonymized and de-identified data in a publicly available database.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2021.11.017.

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