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Exercise after SCUBA diving increases the incidence of arterial gas embolism

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Madden D, Lozo M, Dujic Z, Ljubkovic M. Exercise after SCUBA diving increases the incidence of arterial gas embolism. *J Appl Physiol* 115: 716–722, 2013. First published June 13, 2013; doi:10.1152/japplphysiol.00029.2013.—Arterialization of gas bubbles after decompression from scuba diving has traditionally been associated with pulmonary barotraumas or cardiac defects, such as the patent foramen ovale. Recent studies have demonstrated the right-to-left passage of bubbles through intrapulmonary arterial-venous anastamoses (IPAVA) that allow blood to bypass the pulmonary microcirculation. These passages open up during exercise, and the aim of this study is to see if exercise in a postdiving period increases the incidence of arterialization. After completing a dive to 18 m for 47 min, patent foramen ovale-negative subjects were monitored via transthoracic echocardiography, within 10 min after surfacing, for bubble score at rest. Subjects then completed an incremental cycle ergometry test to exhaustion under continuous transthoracic echocardiography observation. Exercise was suspended if arterialization was observed and resumed when the arterialization cleared. If arterialization was observed a second time, exercise was terminated, and oxygen was administered. Out of 23 subjects, 3 arterialized at rest, 12 arterialized with exercise, and 8 did not arterialize at all even during maximal exercise. The time for arterialization to clear with oxygen was significantly shorter than without. Exercise after diving increased the incidence of arterialization from 13% at rest to 52%. This study shows that individuals are capable of arterializing through IPAVA, and that the intensity at which these open varies by individual. Basic activities associated with SCUBA diving, such as surface swimming or walking with heavy equipment, may be enough to allow the passage of venous gas emboli through IPAVA.

SCUBA diving; exercise; VGE; arterialization; IPAVA

VENOUS GAS EMBOLI (VGE) ARE a common occurrence during decompression from SCUBA diving and are normally trapped and eliminated by the pulmonary microcirculation. Arterialization of these emboli is usually associated with septal wall defects in the heart, such as a patent foramen ovale (PFO) (26), that allow the emboli to cross over from the right to the left side of the circulation. Arterialization may also occur in individuals who do not possess PFO, when the quantity of VGE overwhelms the ability of the pulmonary circuit to trap and eliminate these bubbles (4). Investigations of arterialization at rest show incidents rates to range from 13 to 26% (11, 16, 18). Recent studies have used contrast bubbles to investigate intrapulmonary arterial-venous anastamoses (IPAVA) that allow blood to bypass the pulmonary microcirculation (24). These vascular pathways allow the passage of contrast bubbles from the venous to arterial circulation in laboratory conditions during exercise (9, 13), and we hypothesize that these vascular pathways provide the path for arterialization of VGE in divers in the field.

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Although the exact physiological role of IPAVA is not yet clear, recent studies have found that they open during physical activity and may serve to help regulate pulmonary arterial pressure (20, 24). The intensity of O_2 uptake ($\dot{V}O_2$) consumption at which this occurs is variable, ranging from rest to maximal effort, with few subjects not showing any evidence of opening at all (9). IPAVA are larger in diameter than the surrounding pulmonary microcirculation and may allow the easier passage of bubbles that would normally be trapped and eliminated. Stickland et al. (24) and Eldridge et al. (9) were the first to use injected contrast bubbles during exercise in PFO negative subjects to demonstrate this passage. Further studies have shown that the use of supplemental oxygen during exercise can prevent the opening of these shunts (21). Supplemental oxygen is currently a recommended first aid treatment for divers experiencing symptoms of decompression sickness (DCS) (19). Any additional information on the relationship between arterialization, IPAVA, and oxygen supplementation may provide guidelines and protocol for prophylactic use of oxygen in certain scenarios.

Multiple diving studies have produced the arterialization of emboli without any reported incidence of DCS or other related acute symptoms. However, PFO and arterializations still remain linked to neurological symptoms of DCS (10, 23, 27, 28) and chronic cerebral microvascular damage (15). These relationships warrant the continued investigation of the physiological conditions that lead to arterialization.

Therefore, the purpose of this study is to explore the impact of exercise in a postdive period on potential VGE arterialization. Furthermore, the effect of oxygen administration in the subject exhibiting the VGE passage to systemic circulation was also investigated.

METHODS

This study received approval from the University of Split Medical School Ethics Committee, and each subject gave written, informed consent before participation. All studies were performed in accordance with the Declaration of Helsinki.

Subjects. Twenty-three subjects (20 men and 3 women), age range of 23–65 yr, participated in the study. Diving experience of the subjects ranged from 2 to 41 yr (mean 19.25 ± 12.23 yr). Subjects selected have either been tested negative for PFO within the past 3 yr or were screened before participation in the study. PFO screening was conducted by an anesthesiologist using preestablished procedures (18). Twenty-five subjects volunteered for the study, 2 were excluded due to a positive PFO test, and 23 subjects completed the protocol. Pulmonary function, cycle ergometry, and anthropometric data are presented in Table 1. All subjects were apparently healthy and were cleared to dive at the time of the study, and there were no reports of illness during the duration of protocol.

Pulmonary function and maximum $\dot{V}O_2$ testing. Maximum $\dot{V}O_2$ ($\dot{V}O_{2max}$) and pulmonary function testing was performed by all divers at least 3 days before the diving experiment. Before testing, height, weight, and percent body fat for each subject were determined. Percent body fat was estimated by measurement of subcutaneous skin

Table 1. *Anthropometric data for male and female divers*

Parameter	Male (n = 20)	%Predicted	Female (n = 3)	%Predicted
Age, yr	40.7 ± 12.0		38.3 ± 5.0	
Height, cm	182.0 ± 6.0		168.0 ± 1.0	
Weight, kg	93.6 ± 10.0		58.0 ± 5.6	
FVC, liter	5.6 ± 0.8	110.5 ± 14.7	3.9 ± 0.3	110.6 ± 9.2
FEV_1, liter	4.3 ± 0.5	106.6 ± 13.6	3.3 ± 0.3	108.5 ± 12.4
FEV_1/FVC, %	78.7 ± 7.8	98.9 ± 9.6	84.8 ± 4.3	103.7 ± 6.2
MVV, l/min	172.5 ± 25.4	121.9 ± 25.4	126.4 ± 13.9	114.7 ± 15.9
$\dot{V}O_{2max}$, ml·kg^{-1}·min^{-1}	43.5 ± 7.3		47.0 ± 4.6	
$\dot{V}O_{2max}$ power, W	257.3 ± 37.1		175.0 ± 4.3	

Values are means ± SD; n, no. of subjects. FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; MVV, maximal voluntary ventilation; $\dot{V}O_{2max}$, maximum O_2 uptake, determined through graded maximal cycle ergometry test. Power (in Watts) is of last completed stage of cycle ergometer test.

fold thickness with a caliper (Harpenden skinfold caliper, Baty International, West Sussex, UK) at the three sites, as dictated by the Jackson Pollock equations for male and female subjects. Pulmonary function assessment included forced vital capacity and maximal voluntary ventilation tests. The $\dot{V}O_{2max}$ test was an incremental test conducted on a cycle ergometer (Marquette Hellige Medical Systems 900 ERG, Milwaukee, WI), beginning at 50 (for female subjects) or 80 W (male subjects) and increasing 15 W every minute until voluntary termination or until at least two of the three following requirements were met: *1*) a plateau of $\dot{V}O_2$ (<150 ml increase) with an increase in workload; *2*) respiratory exchange ratio > 1.1; and *3*) heart rate (HR) in excess of 90% of age predicted (220 − age) values. Once these criteria were met, the highest recorded $\dot{V}O_2$ was selected as the subject's maximal value. The ergometer has been modified to stabilize the torso to aid in transthoracic contrast echocardiography (TTE) imaging and was used in the field data collection portion of the study. Performing the test on this equipment allowed the subjects to familiarize themselves with equipment that would be used in the future. Briefly, the modifications consisted of a backboard fixed to the base of the ergometer that would provide a surface for the subjects to brace their back against in a 90° upright position. The bicycle's handlebars were lengthened to accommodate this new position and provide leverage for the cyclists to press their back into the board. This action, combined with straps, greatly reduced movement in the upper body during intense pedaling. Additionally, a support was made to hold the left arm in a 90° abducted and externally rotated position with a 90° bend at the elbow to open up the intercostal space for a better TTE window.

Diving protocol and location. This study was performed at a military installation of the Croatian Navy Force. The dive site was located in the vicinity of the base, within a short (~30 m) distance of the location where the experiments would take place. The site was chosen because of the minimal transit time between finishing the dive and beginning initial TTE analysis. All divers performed the dive at a depth of 18 m sea water (msw) with a 47-min bottom time. Decompression was performed at a rate of 9 msw/min, with direct ascent to the surface. Sea temperature at the bottom was ~16°C, and the outside temperature was ~26°C. Throughout the dive, divers performed swimming of moderate intensity.

Postdive exercise and echocardiography. Within 8–15 min after surfacing, the divers were placed in the supine position where an ultrasonic probe connected to a Vivid q echographic scanner (GE, Milwaukee, WI) was used to obtain a clear apical four-chamber view of the heart. This position was monitored continuously until 30 min postsurfacing, and initial bubble images were recorded and scored on a scale of 0 to 5, with 4 being subdivided into 4A, 4B, and 4C, according to the method described by Eftedal and Brubakk (8), and later modified by Ljubkovic et al. (16). Next the subject was moved to a seating position where a bubble score was obtained again after approximately 2–3 min to observe the effect of the posture change on the bubble score. The subject then continued on with one of two potential procedures based on the observation at rest in the supine position. If arterialization was observed in the supine position, defined by an agreement on two trained observers of the appearance of bubbles in the left heart, the subject completed the supine oxygen protocol (O_2) as described below. If the subjects displayed no arterialization, they advanced to the exercise protocol also described below.

O_2 protocol. In the supine position, the subject was continuously monitored in the apical four-chamber view via TTE by two experienced observers. O_2 (99.5%) was administered through a mouthpiece, while the subject wore nose clips. With a continuously running timer, the time was marked when there was no longer any observed arterialization, as defined by 20 consecutive cardiac cycles with no bubbles in the left heart. At this time, the subject was switched from O_2 to breathing room air. The next recorded time interval was when bubbles were again observed in the left heart, after being taken off of O_2. The final time interval was recorded when no more arterializations were observed.

Exercise protocol. After it was determined that a subject was not arterializing at rest, they were moved to an electronically braked cycle ergometer in an upright position. The torso was strapped into the support device as described above, and the left arm was moved into the abducted and externally rotated position. When a clear picture of the heart was obtained, the subject began the exercise procedure. The subjects completed a single incremental exercise test with a starting workload of 60 W and a 30-W increases every 2 min. After beginning exercise, on the first appearance of bubbles in the left heart (in divers in whom the arterialization was observed), the exercise was immediately suspended while TTE observation of the heart continued. The time was noted both when the bubbles first appeared in the left heart and when the left heart was clear of bubbles. The criterion for clearance of the bubbles was 20 consecutive cardiac cycles without appearance of bubbles in the left heart. This observation was used as an estimation of when, and at what workload, pulmonary shunting had occurred. Once the left heart was clear of bubbles, exercise was resumed at the same intensity from which it was suspended when the shunting occurred. The subjects continued with the protocol until bubbles were again observed in the left heart. At this second occurrence of arterialization, exercise was terminated, and oxygen at a concentration of 99.5% O_2 was immediately given. The time interval of the appearance and clearing of the bubbles was again recorded as before: the only difference was the use of O_2. For individuals who did not arterialize, the protocol was terminated when subjects could no longer maintain consistent power output. Expired gasses and HR were monitored and recorded during the initial $\dot{V}O_{2max}$ test and during the exercise protocols after diving via a portable metabolic system (Cosmed K4 B^2, Rome, Italy).

Oxygen subgroup. On a separate occasion, an additional subgroup of six divers, selected from the group of those who arterialized during exercise, completed a second dive. The goal of this dive was to see how, and on what schedule, VGE react to the

Table 2. *Subjects who arterialized at rest*

Subject No.	Age, yr	Sex	Initial Bubble Score Cardiac Chamber R	Initial Bubble Score Cardiac Chamber L	Upright Bubble Score Cardiac Chamber R	Upright Bubble Score Cardiac Chamber L	Time After Surfacing, min:s O_2 given	L chambers clear*	Arterialization resumes	L chambers clear
1	23	M	4B	2	3	0	25:52	26:55	29:51	51:41
2	23	M	4C	3	4C	3	10:47	11:58	12:26	46:35
3	44	M	4A	2	3	0	21:14	21:44	23:09	37:00

M, male; R, right cardiac chambers; L, left cardiac chambers. *No bubbles observed in L cardiac chambers.

administration of oxygen at rest after diving. After completing a dive of the same profile (18 msw, 47 min bottom time), divers preceded directly to the field laboratory for imaging. In the supine position, divers were given oxygen 30 min after surfacing, to match both the timing of the procedure, as well as peak bubble production, while under continuous TTE observation. Oxygen was given at 12 l/min for 20 min, and bubble score was recorded at 2-min intervals.

Statistical analysis. An independent samples *t*-test was used to compare the time of exercise after surfacing in the group that arterialized during exercise with the group that did not. A paired samples *t*-test was used to compare the time for arterialization to stop while breathing room air and while breathing oxygen in the exercise group. The supine and upright bubble score at rest of those two groups, as well as the oxygen subgroup was compared with a Mann-Whitney test.

RESULTS

Data obtained after the dive, exercise, and oxygen protocols are presented in Table 2. All subjects completed the dive as planned without showing any signs or symptoms of DCS or any other adverse effects. In *subjects 1–3*, we detected gas bubbles in both the right and left sides of the heart at rest. These divers then completed the oxygen protocol. *Subjects 4–23* displayed a range of emboli (bubble score 0-4B) in the right heart at rest, but without apparent arterialization, and advanced to the exercise protocol. *Subjects 4–15* displayed arterialization at some point during exercise to $\dot{V}O_{2max}$ (Table 3), while in *subjects 16–23* we did not observe arterialization at any point during the study (Table 4).

Oxygen protocol. Subjects who displayed arterialization at rest were given oxygen while under continuous observation via TTE in the supine position. The time between the first observation of arterialization and the application of O_2 ranged between 2 and 7 min. This includes the time to monitor the heart in the upright position, and the relatively wide range of time is the result of the extra time associated with obtaining a new cardiac window with the TTE probe, which varied in difficulty from subject to subject. When oxygen was applied, arterialization was no longer observed in any of the divers, with the mean time of 55 ± 22 s. After the left heart was clear of bubbles, and the subjects were switched back to room air, the arterialization resumed in all divers, within 96 ± 75 s. After arterialization was confirmed, the mean time for emboli in the left heart to clear, while breathing room air, was 1,397 ± 614 s.

Exercise protocol. The exercise intensity, as $\%\dot{V}O_{2max}$, at which arterialization was first observed in *subjects 4–23* is displayed in Fig. 1. Once arterialization was observed and exercise suspended, the mean time until the left heart was clear of emboli was 88 ± 41 s. Exercise was then resumed at the same intensity at which it was suspended. During the second round of exercise, supplemental O_2 (99.5%) was given once arterialization was observed and exercise was suspended. The $\%\dot{V}O_{2max}$ that elicited arterialization in the second round was variable within individuals. However, the workload in Watts at the time of the observed arterializations was equal in 9 of 10 subjects who arterialized in both rounds of exercise. The mean time until the left heart was clear of emboli was 46 ± 15 s. *Subjects 4* and *6* did not produce any observable emboli in the left heart during the second round of exercise.

Oxygen subgroup. Oxygen administration at rest reduced VGE over 20 min. Immediately after the application, there was

Table 3. *Conditions in which subjects arterialized during exercise*

Subject No.	Subject No. Prior Study	Age, yr	Sex	Initial BS† R	Initial BS† L	Upright BS R	Upright BS L	First Exercise Arterialization BS: Time of ex onset	Time of art	R	L	$\dot{V}O_{2max}$, %	Power, W	Time to clear‡	Time of ex resume	Second Exercise Arterialization BS: Time of 2nd art	R	L	$\dot{V}O_{2max}$, %	Power, W	Time to clear with O_2§
4	*30*	65	M	1	0	0	0	36:23	42:57	3	1	81	150	01:23	44:48	*	*	*	*	*	*
5	*6*	37	M	4A	0	3	0	37:46	40:32	3	1	25	60	00:58	41:57	46:00	3	1	22	60	01:09
6	*33*	52	M	4A	0	4A	0	38:38	42:34	4A	1	45	90	01:18	43:03	*	*	*	*	*	*
7	*1*	45	M	4B	0	3	0	38:32	41:45	4A	1	32	90	00:30	44:25	45:06	4A	1	46	90	00:29
8	*24*	43	M	3	0	3	0	37:49	44:52	4A	1	60	150	02:34	47:42	48:18	4A	1	56	150	00:34
9	*28*	39	M	4B	0	4B	0	37:18	45:15	4B	2	48	150	01:20	46:51	48:14	4B	1	56	150	01:02
10	*11*	39	M	3	0	3	0	30:00	30:47	4B	2	23	60	00:47	32:20	32:45	4B	2	38	60	00:40
11	*5*	33	F	4B	0	2	0	43:00	45:25	4B	2	55	135	02:45	48:30	51:00	4B	2	38	60	00:51
12	*32*	64	M	4A	0	3	0	34:10	40:52	4A	1	30	150	01:21	42:24	44:15	4A	1	79	150	01:00
13	*18*	44	M	3	0	2	0	39:24	50:40	3	1	92	210	01:40	54:10	54:58	3	1	94	210	00:33
14		45	M	4A	0	4A	0	36:25	40:41	4A	1	50	120	01:03	42:03	42:46	4A	1	41	120	00:30
15		39	F	3	0	3	0	32:58	33:40	4A	1	31	60	00:50	35:00	36:00	4A	1	28	60	00:49

Subject number from prior study, Ljubkovic et al. (18), is shown in Table 2, under same dive profile. Times are in min:s. BS, bubble score; F, female; art, arterialization; ex, exercise. *Subjects did not display arterialization during the second bout of exercise. †Initial BS is of subjects at rest during previous study (18). ‡Time to clear is time when arterialization of gas bubbles was no longer observed breathing room air. §Time to clear with O_2 is time when arterialization of gas bubbles was no longer observed breathing oxygen.

Table 4. *Subjects who did not arterialize during rest or exercise*

Subject No.	Subject No. Prior Study	Age, yr	Sex	Initial Bubble Score Cardiac Chamber R	Initial Bubble Score Cardiac Chamber L	Upright Bubble Score Cardiac Chamber R	Upright Bubble Score Cardiac Chamber L	Time of Ex Onset, min:s	Peak BS During Ex
16	*27*	41	M	2	0	1	0	38:50	1
17	*3*	46	M	3	0	2	0	32:55	3
18	*34*	30	M	1	0	0	0	36:06	1
19	*13*	30	M	0	0	0	0	34:00	1
20	*19*	24	M	0	0	0	0	42:53	0
21		50	M	1	0	0	0	37:41	0
22		29	M	1	0	0	0	33:20	0
23		43	F	0	0	0	0	32:10	0

Subject number from prior study, Ljubkovic et al. (18), is shown in Table 2.

no change in VGE (2 min $P = 0.634$, 6 min $P = 0.567$). The reduction was not significant until 16 min into the protocol ($P = 0.026$). Additional details are displayed in Table 5.

Determinants of arterialization. There was no difference in the time to starting exercise in the group that arterialized (*subjects 4–15*) and the group that did not (*subjects 16–23*) ($P = 0.58$). However, in subjects who arterialized with exercise, both the supine and upright resting bubble scores were significantly higher than in the subjects who did not exhibit exercise arterialization ($P = 0.001$ and 0.0009 for supine and upright position, respectively) There was a significant difference in the time for arterialization to stop after exercise when oxygen was used ($P = 0.035$).

DISCUSSION

The purpose of this study was to investigate the possibility that exercise may increase the incidence of arterial gas embolism after SCUBA diving, presumably via opening of IPAVA. Our results show that 12 subjects who were not arterializing at rest after SCUBA diving experienced arterialization during exercise on a cycle ergometer. Although the subjects were seated in an upright position during exercise, it is unlikely that the posture change alone was responsible for arterialization, since subjects were observed in both the seated and supine positions at rest. A recent study by Ljubkovic et al. (18) has detailed the conditions necessary to provoke arterialization of VGE after diving at rest. One of these conditions was a bubble score of at least 4B in the right heart. We have shown that, with postdive exercise, divers can arterialize with a bubble score as low as 3. For *subjects 16–23*, who we did not observe any arterialization, bubble score during exercise at $\dot{V}O_{2max}$ ranged from 0 to 3. It is possible that the IPAVA were open, providing a potential path to arterialization, yet there was a lack of adequate or even any observable VGE to pass through them. Of these eight subjects who did not arterialize, only one produced a bubble score of 3, while the rest produced peak scores of 0 or 1 throughout the duration of the study.

In subjects who were exposed to the exercise protocol, the timing of exercise after diving may impact arterialization, since divers typically reach peak bubble production 30–60 min after surfacing. It is thus possible that timing of exercise could be the difference between arterialization or not. However, in this study, there was no significant difference in the exercise start time between those who did and those who did not arterialize (*subjects 4–15* and *16–23*). Rather, there was a significant difference in the initial bubble score, both supine and seated, which may contribute to arterialization during exercise. It is possible that there is still a minimal bubble score required to arterialize, even if open IPAVA during exercise provide a pathway. For the subjects who arterialized at rest (*subjects 1–3*), two of them fit the requirements for arterialization at rest, as described before (18), while one was just below the threshold. It is possible that IPAVA could be the pathway if the activity between surfacing and arriving to the testing site was enough to open them, or it may be that the higher bubble score was enough on its own to overwhelm the pulmonary clearing capacity.

It has been proposed by Eldridge et al. (9) that exercise opens up normally closed arteriovenous intrapulmonary shunts

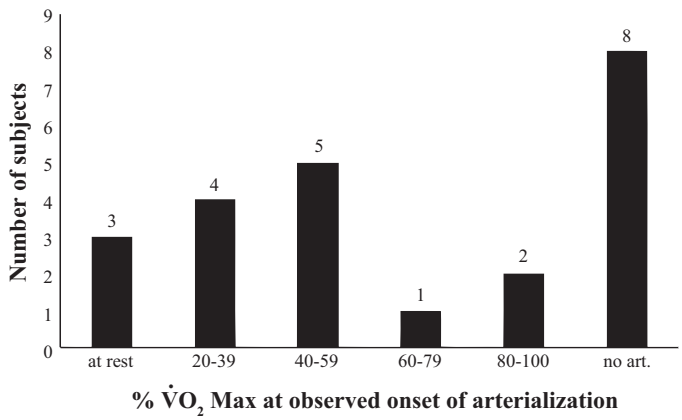

Fig. 1. Percentage of maximum O_2 uptake ($\dot{V}O_{2max}$) during observed arterializations. Histograms represent the distribution of intensity, as a percentage of $\dot{V}O_{2max}$ at which arterialization was observed during exercise. art., Arterialization.

Table 5. *Bubble score of all subjects during oxygen subgroup*

Subject No.	Bubble Score at Various Time Points, min 0	2	6	10	16	20
15	3	3	3	3	2	2
4	3	2	3	2	3	3
8	3	3	4	3	1	1
10	3	3	3	3	2	2
13	4	4	4	3	3	2
11	3	3	3	3	2	2
P value	n/a	0.634	0.567	0.248	0.026	0.009

in healthy humans. In their study, with incremental cycle ergometer exercise, 21 out of 23 PFO negative subjects demonstrated the passage of contrast bubbles from the right to left heart, as viewed in a four-chamber echocardiogram. This occurrence of shunting was again demonstrated by Lovering et al. (20, 21) and Stickland et al. (24) when eight of nine, seven of seven, and seven of eight subjects, respectively, shunted during exercise. Although Dujic et al. (7) reported previously that shunting did not occur with exercise after diving, in a case study presented by that same group in 2007 (22), in the current experimental setting, divers displayed a high level of VGE and shunting with exercise following a dive. There are at least four possible explanations for the discrepancies between our present findings and previous studies. *1*) We continuously monitored the subjects rather than only during select time points, so it is less likely that arterialization could have occurred during a period of time that we were not monitoring. *2*) This study has a higher number of subjects than previous studies with divers. *3*) As imaging technology improves, the investigators have decreased chances to miss the passage of emboli due to a lack of resolution. *4*) The subjects in this study exercised until voluntary termination rather than toward a predetermined HR or workload, so it is unlikely that those who did not arterialize failed to do so as a result of not exercising at a high enough intensity.

Asymptomatic venous bubbles are common after a dive and vary in size from 19 to 700 μm (12). The diameter of capillaries at the site of gas exchange ranges from 6 to 15 μm and does not allow easy passage of these bubbles from the venous to the arterial circulation. The trapped bubbles are commonly eliminated during gas exchange and ventilation. However, this system of clearing bubbles from the blood may be overwhelmed by a high bubble load in the circulation, greater than the pulmonary circuit is capable of clearing, allowing VGE to cross over to the arterial circulation, either through IPAVA, through distention of pulmonary capillaries, or through deformation of bubbles into cylindrical shapes (1). Under the theoretical, ideal conditions, larger bubbles may deform into a cylindrical shape to pass through smaller diameter vessels (3). Alternatively, as bubbles outpace the pulmonary circuit's ability to eliminate them through gas exchange, pulmonary arterial pressure may increase as a result of the stack of bubbles blocking local circulation (6, 17). This increase in pulmonary arterial pressure may then open the IPAVA and allow bubbles to pass, as previously suggested by Stickland et al. (24). In our laboratory's previous studies, it has been shown that a bubble score of 4B is likely a prerequisite for arterialization at rest (18). These studies excluded divers with PFO, so VGE may not cross over through defects in the septal wall. This may explain why during PFO testing, when large quantities of bubbles are injected in subjects who are found to be PFO negative, bubbles appear in the left heart in lower quantities after 10 or more cardiac cycles.

In this study, administration of oxygen upon detection of gas bubbles in the left heart, both resting and immediately after exercise, caused rapid cessation of arterialization in all tested individuals. Furthermore, the use of oxygen terminated arterialization quite rapidly compared with breathing room air. We hypothesize that this is related to the mechanism of closing IPAVA with the application of oxygen. One alternative to this proposal is that a decrease in arterialization is related to an increased rate of nitrogen elimination, seen as a reduction of bubble load in the right heart. Oxygen prebreathing is used in high-altitude flights and astronaut extravehicular activity to eliminate nitrogen from the blood via an increased concentration gradient, and this principle has also been applied to SCUBA diving (2). This denucleation protocol can last between 1 and 4 h for high-altitude excursions (30). Exercise can speed this process up by increasing cardiac output and blood flow though the pulmonary circuit, although even the shortened protocols studied last at least 15 min (29). Due to the rapid cessation of arterialization (46 s mean) and the relatively low duration of oxygen administration, the time frame matches up more closely with other exercise and IPAVA studies rather than nitrogen washout. Additionally, our subgroup of six divers breathing oxygen shows that, while oxygen did reduce VGE in divers at rest, this reduction was not significant until 16 min into the administration procedure. However, we cannot completely rule out the possibility that breathing 100% O_2, leading to an increased gradient for nitrogen elimination at the alveolocapillary membrane, may still reduce the amount of bubbles in the pulmonary microcirculation.

To our knowledge, this is the first study that demonstrates the use of supplemental O_2 can stop arterialization after SCUBA diving. The use of oxygen significantly decreased the time for arterialization to stop, compared with breathing room air, in exercise (*subjects 4–15*, $P = 0.035$). With only three subjects arterializing at rest, statistical conclusions are of little use; however, in this study, the difference in the time to stop arterializing with oxygen vs. room air is noticeable. In the case of both rest and exercise, once the subject was taken off the oxygen, arterialization resumed after a relatively short amount of time. Without the use of supplemental oxygen, the half-life of the bubble scores and arterialization at rest followed closely with previously observed results with similar dive profiles (25). The mean time for the reduction of the bubble score to zero in the left heart occurred at 45:05 min after surfacing, accompanied by a concurrent decrease in VGE in the right cardiac chambers. For the subjects who shunted with exercise, while oxygen did decrease the time to clear emboli from the left heart, for practical purposes, removing the exercise stimulus also stopped arterialization within a few minutes.

Study limitations. There are other possible explanations for VGE to appear in the left heart other than IPAVA. Bubbles will decrease in diameter as time passes and may become small enough to pass through the pulmonary microcirculation, although bubbles of this size would be much more difficult to visualize via TTE and less likely to survive until they reach the left side of the heart. Larger gas emboli may also deform into a cylindrical shape with a small enough diameters to pass through the pulmonary circulation to be visualized in the left heart. Regardless of these limitations, 65% of divers arterialized (exercise and rest) in the postdive period of our study. This proportion is much greater than is found in studies that examine these parameters for divers at rest, which range between 0 and 39% (16, 18). Another study by Gerriets et al. (11) observed arterialization in 7 of 13 dives where VGE were present; however, five of these incidences were associated with PFO. One of the primary drawbacks to using VGE resulting from decompression as a visualization agent is the relatively small load compared with a bolus injection. For optimal echo

imaging conditions, exercise was initiated 30–40 min after surfacing, so that observations would be made during the postdive time period in which divers tend to produce their peak bubble scores (5). It is possible that subjects could have arterialized with or without this exercise, even if they were not during the initial 30-min TTE evaluation. However, three subjects arterialized with a bubble score of 3, and six subjects with a score of 4A. These are lower scores than typical arterializations at rest.

Conclusions. The safety of exercise after diving has been debated for some time. We have shown that exercise may directly contribute to arterialization. It may be concluded that exercise directly increases vulnerability to arterialization of VGE after diving. In some individuals, specifically those who have a low workload threshold for opening of IPAVA, it is possible that even relatively mild physical exertion associated with surface swimming at the end of a dive, climbing onto a boat, or walking with heavy gear on would be enough to provoke arterialization. These could all be considered regular activities that occur within 0 to 90 min after surfacing. This study also demonstrates the possibility that divers without PFO under certain circumstances may arterialize much more than it was previously thought. Divers who shunt at rest or at very low levels of exercise may be at similar risk levels as those with PFO. Conservative diving has been shown to decrease the risk of DCS in divers with a PFO (14), a similar tactic may be useful for individuals with VGE at low exercise intensities. Although many studies have shown that divers can arterialize with no DCS symptoms, there still remains a correlation between neurological DCS and the presence of arterial bubbles. Finally, subclinical levels of damage related to microemboli in the brain should not be ignored, especially in career divers.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: D.M., M. Lozo, Z.D., and M. Ljubkovic conception and design of research; D.M. and M. Lozo performed experiments; D.M., M. Lozo, Z.D., and M. Ljubkovic analyzed data; D.M., M. Lozo, Z.D., and M. Ljubkovic interpreted results of experiments; D.M. prepared figures; D.M. drafted manuscript; D.M., M. Lozo, Z.D., and M. Ljubkovic edited and revised manuscript; Z.D. and M. Ljubkovic approved final version of manuscript.

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