Exercise-induced intrapulmonary shunting of venous gas emboli does not occur after open-sea diving

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Dujić, Željko, Ivan Palada, Ante Obad, Darko Duplančić, Alf O. Brubakk, and Zoran Valic. Exercise-induced intrapulmonary shunting of venous gas emboli does not occur after open-sea diving. J Appl Physiol 99: 944–949, 2005. First published April 21, 2005; doi:10.1152/japplphysiol.01431.2004.—Paradoxical arterializations of venous gas emboli can lead to neurological damage after diving with compressed air. Recently, significant exercise-induced intrapulmonary anatomical shunts have been reported in healthy humans that result in widening of alveolar-to-arterial oxygen gradient. The aim of this study was to examine whether intrapulmonary shunts can be found following strenuous exercise after diving and, if so, whether exercise should be avoided during that period. Eleven healthy, military male divers performed an open-sea dive to 30 m breathing air, remaining at pressure for 30 min. During the bottom phase of the dive, subjects performed mild exercise at ~30% of their maximal oxygen uptake. The ascent rate was 9 m/min. Each diver performed graded upright cycle ergometry up to 80% of the maximal oxygen uptake 40 min after the dive. Monitoring of venous gas emboli was performed in both the right and left heart with an ultrasonic scanner every 20 min for 60 min after reaching the surface pressure during supine rest and following two coughs. The diving profile used in this study produced significant amounts of venous bubbles. No evidence of intrapulmonary shunting was found in any subject during either supine resting posture or any exercise grade. Also, short strenuous exercise after the dive did not result in delayed-onset decompression sickness in any subject, but studies with a greater number of participants are needed to confirm whether divers should be allowed to exercise after diving. No evidence of intrapulmonary shunting found. Decompression sickness; echocardiography; maximal oxygen consumption; human

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avoid exercise immediately after diving, especially due to the relatively low intensity of exercise at which shunts become functional.

Exercise after diving, as well as shortly before or after decompression to altitude, can promote bubble formation (9, 20). Webb et al. (40) recently failed to show that moderate dynamic exercise after altitude exposure resulted in either delayed onset of DCI or recurring DCI. This finding has to be confirmed in diving.

Accordingly, the primary hypothesis of the present study was to confirm that exercise-induced I-P shunts after diving could cause paradoxical arterialization of the venous gas bubbles. A secondary hypothesis was to investigate whether short, strenuous exercise after diving induces delayed-onset DCS.

METHODS

Study population. The study was carried out on 12 Croatian Navy divers aged 29–41 yr. Their anthropometrical parameters are presented in Table 1. The subjects were all experienced divers with considerable diving experience (both air and oxygen diving). Only one of them experienced DCS in the past during high-altitude diving on the lake. Three of the divers were smokers (5–40 cigarettes/day). At the time of the study, all had a valid medical certificate for diving and were clear of all symptoms of acute illness. All experimental procedures were conducted in accordance with the Declaration of Helsinki and were approved by Ethics Committee of the University of Split School of Medicine. Each method and potential risks were explained to the participants in detail, and subjects gave written, informed consent before the experiment.

V\(\text{O}_2\) max. V\(\text{O}_2\) max and maximum heart rate (HR) were determined in all divers 1 wk before the experiments using incremental protocol on the cyclic ergometer (Marquette Hellige Medical Systems 900 ERG). Height and weight of subjects were determined on arrival at the laboratory. Percent body fat of each participant was estimated by triple measurement of subcutaneous fat tissue thickness with a caliper (Harpenden skinfold caliper, BodyTrends, Carpinteria) at chest, abdomen, and thigh regions. Subjects were exposed to an initial work rate of 50 W at the pace of 60 cycles/min. They were told to maintain the constant frequency, and the work rate was increased each following minute by 25 W up to exhaustion. This occurred within 9–13 min in all subjects. During the entire test, V\(\text{O}_2\) and pulmonary ventilation were measured with a cardiopulmonary exercise testing unit (Quark b\(^2\), Cosmed, Rome, Italy), and HR was registered continuously with Polar S810i HR monitor (Polar Vantage). Criteria for assessment of V\(\text{O}_2\) max included (1) HR in excess of 90% of age-predicted maximum (220 – age), (2) respiratory exchange ratio of \(\geq 1.1\), and (3) plateau (\(\leq 150\)-ml increase) in V\(\text{O}_2\) with an increase in workload. If at least two of the three criteria were met, the highest V\(\text{O}_2\) measured was chosen as the subject’s V\(\text{O}_2\) max. Mean V\(\text{O}_2\) max was 41.2 ± 6.3 ml·kg\(^{-1}\)·min\(^{-1}\) (mean ± SD), and the maximum HR at V\(\text{O}_2\) max was 177 ± 8 beats/min (mean ± SD).

Location and duration of the study. The study was performed at the military base of the Croatian Navy Forces over a 2-wk period. The diving site was located in the vicinity of the base, where the divers were transported by powerboat during a 10-min ride. The site was chosen because it allowed us to perform dives of the suitable depth and duration. Sea temperature at bottom and at the decompression stop was 15°C for all dives, and outside temperature varied between 8 and 16°C.

Diving protocol. All dives were performed by divers equipped with wet suits in accordance with the Croatian Navy and US Navy diving manual (34). Depth of the dive was set to 30 m with a 30-min bottom time. Decompression was performed at a rate of 9 m/min with a 3-min stop at 3 m. Each pair of divers was supplied with a diving computer (Mosquito, Suunto, Finland) interfaced with a personal computer for later verification of the diving profile. The divers were told to swim on the bottom to the distance of 500 m, which was controlled by the personnel on the powerboat and mimicked 30% of their V\(\text{O}_2\) max. During the decompression period, divers were told not to perform any exercise. This protocol was chosen because, from our experience, it is reliable to produce a significant amount of venous bubbles even if proper decompression procedures were followed. HR was continuously monitored in all divers during diving with a Polar S810i HR monitor.

After-dive monitoring and bubble analysis. After the completion of diving protocol, divers were transported to the facility where they took a brief shower before further monitoring. After the shower, subjects were placed in the supine position, and an echocardiographic investigation with a phase-array probe (1.5–3.3 MHz) using a Vivid 3 Expert ultrasonic scanner (GE, Milwaukee, WI) was conducted. All echocardiographic investigations were performed by the same experienced cardiologist. High-quality images were obtained in all subjects and stored on S-VHS tape for later evaluation and analysis. Monitoring was performed in the resting supine position and after the two cough procedures (32) at 20, 40, and 60 min after reaching surface pressure. Additionally, after the measurements at 40 min after reaching surface pressure, subjects were transferred to cycle ergometer to test the possibility of transfer of the bubbles through pulmonary shunts. This time was selected because we have previously shown (11) that bubble formation is the greatest at this time point after the dive. Each diver started cycling at 50 W for a duration of 1 min. Intensity of the exercise was increased by 50 W each minute until they reached 250 W (this represented ~ 85% of their V\(\text{O}_2\) max, as previously determined). During cycling, high-quality images of the left atrium and ventricle were obtained in all subjects for determination of the possible transfer of the venous bubbles through pulmonary circulation. Images were graded on a scale from 0 to 5, according to a previously reported method (12). This grading system has been used extensively in several animal species as well as in humans. It has also been demonstrated that the grading system for Doppler (30) coincides with that used for images (3).

Statistical analysis. Data are presented as means ± SD and as median and range for bubble grade. Nonparametric Wilcoxon matched-pairs test was used to examine increases in venous bubble grade in response to two cough procedures due to small sample size (\(n = 11\)). Level of statistical significance was set at \(P < 0.05\).

Table 1. Anthropometric characteristics of divers and venous gas bubble grades during the observational period in supine rest position and after 2-cough procedure

<table>
<thead>
<tr>
<th>Diver No.</th>
<th>Age, yr</th>
<th>Weight, kg</th>
<th>Height, m</th>
<th>Body Fat, %</th>
<th>20 min Positive</th>
<th>40 min Positive</th>
<th>60 min Positive</th>
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<tr>
<td>1</td>
<td>41</td>
<td>83</td>
<td>1.81</td>
<td>9.82</td>
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<td>2</td>
<td>1</td>
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<tr>
<td>2</td>
<td>39</td>
<td>90</td>
<td>1.80</td>
<td>20.91</td>
<td>4</td>
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<td>1.83</td>
<td>20.88</td>
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Note that diver 7 did not show any bubbles during the observation period, so he was excluded from ergocyclic procedure and further analysis.
RESULTS

All 12 divers successfully completed the designed protocol, and none developed any signs of DCI. Their mean weight and height were 85.8 ± 10.4 kg and 1.82 ± 0.05 m. On average, they had 16.7 ± 4.4% body fat. Their mean forced vital capacity was 115.9 ± 8.7%, and mean forced expired volume in first second was 109.6 ± 7.7% of the predicted normal values. One participant showed no bubbles during the first 40 min of rest supine observation, and he was excluded from cyclic ergometer procedure and further analysis.

Figure 1 represents a characteristic echocardiographic presentation of venous gas bubbles within the right chambers of the heart after the described diving protocol. The heart of the diver was recorded with apical four-chamber view during supine resting (Fig. 1A) and immediately on completion of two forced coughs (Fig. 1B). It is clearly visible that, in the same subject, performance of the coughing procedure considerably increases the number of venous gas bubbles recorded in the routing through the right chambers of the heart.

Summary data on bubble grades at 20, 40, and 60 min of echocardiographic observation, for both supine rest and forced coughing, are presented in Table 1. During the resting phase, bubble grades reached maximal occurrence during 20 and 40 min after the dive (median grades 1 and 2, respectively) and slowly started to decay by 60 min of observation. Executing two forced coughs produced statistically significant (P < 0.05) increase in recorded venous gas bubble grades at 20, 40, and 60 min postdive (median grades 2, 3, and 3, respectively).

Figure 2 shows a representative echocardiographic image of the heart for the period of performing graded exercise in one typical diver. The figure clearly reveals the presence of a significant number of venous gas bubbles within the right chambers of the heart. During the 5 min of exercise, not a single transfer of the venous gas bubbles could be detected to the left chambers of the heart. Interestingly, we noticed that number of venous gas bubbles arriving to right side of the heart decreased during cycle ergometry compared with supine rest and forced coughing. Unfortunately, due to our concentration on the left side of the heart and technical difficulties (moving of the subjects, forced breathing), we were unable to precisely quantify this observation.

DISCUSSION

This study demonstrates that, in 0 of 11 divers who performed open-sea air dives, there were any postdive indications of right-to-left shunting of the VGE during supine rest or upright incremental exercise. This was the case despite rather high bubble grades observed up to 60 min after the dives and a level of exercise similar to that used in recent reports of exercise-induced I-P shunts by Eldridge et al. (13) and Stickland et al. (31). The results suggest that anatomical I-P shunts...
were not recruited in our subjects. Additionally, short, strenuous exercise after diving did not result in delayed-onset DCS in any subject. These results must be treated with caution but may indicate that divers need not refrain from exercising immediately after diving due to lack of anatomical I-P shunt recruitment during exercise. Further studies are required to evaluate the effect of exercise characteristics (type, timing, duration, and intensity).

**Venous gas bubbles and opening of I-P shunts.** Venous bubbles have been detected frequently during asymptomatic dives. They range in size from 19 to 700 μm (19), and they become lodged in the pulmonary vessels. The effect of VGE on the cardiopulmonary system shows variations depending on the animal model that has been employed, as well as the method used to produce gas bubbles (5). Generally, gas injected as a bolus will be eliminated in a rather short time compared with continuous infusion of gas. After decompression, bubbles are continuously released to the pulmonary vascular bed, with initial abrupt increase in the number of bubbles (peak 20–40 min), followed by slow decline up to 120 min postdive.

A lower VGE load, in experimental animals, will lead to an initial increase in PAP, followed by a decrease in arterial oxygen tension (37, 39). If the rate of production of the VGE is matched to the organism’s capability to effectively resolute gas bubbles, elevation of PAP will reach a plateau (39). The transpulmonary passage of emboli may be quite different from that of the solid particles. Gas bubbles are easily deformable and, by changing shape, may move in the smaller vessels and can coalesce into columns of gas by addition of the incoming gas bubbles (38). These emboli are continually absorbed either in the tissue or alveoli by diffusion process. The filtering capacity of the pulmonary microcirculation may be overwhelmed by excessive venous bubbling (6). The transpulmonary passage of gas emboli occurs after reaching a threshold dose, and above this a dose dependency exists (38). The spillover of gas does occur also in humans, as was demonstrated after excursions during deep saturation dives (4). In that study, arterial bubbles were reported in 10 of 12 excursions from 300 to 250 m of sea water, and although the incidence of PFO was not determined, this passage has to be related via a transpulmonary route since the prevalence of PFO is much lower than the observed passage of the bubbles.

At present, we cannot explain why our divers did not shunt VGE either during supine rest or during incremental exercise, whereas this was the case in almost all healthy subjects in two recent reports (13, 31). The onset of I-P shunting developed at submaximal exercise levels (13–84% \( V_{O_2\text{max}} \)) (13), and in two of the subjects shunting occurred during supine rest (31). This was explained by higher PAP in the supine posture and better perfusion of the lung apices. The anatomical shunt vessels in humans can have a diameter larger than 500 μm, and they seem to be located in the lung apices (33). The supernumerary arteries (29) have a muscle baffle valve that might open with increased pressure and flow, as occurs during exercise (13). However, this is still controversial since others have argued whether these shunts/channels exist in normal lungs (7, 18).

Agitated saline contrast echocardiography is a standard technique for detecting righ-to-left shunts (41), although not usually used during exercise. The contrast is administered as a bolus in a rather short time (several seconds). The bubble grade observed in our study was rather high (e.g., in 7 of 12 divers, the grade was 3–5 on the scale, where 5 is maximal), although much lower than the bubble grade in two reports with contrast (grade 5) (13, 29).

Other possible explanations for the observed differences between the present study and two current reports (13, 31) include differences in the bubble density and the size distribution of injected contrast and endogenous bubbles. Because an ultrasonographic image only visualizes a fraction of the bubbles transiting the heart, it is possible that “endogenous contrast” is an inherently less sensitive technique than agitated saline contrast echocardiography and fails to detect shunts that may be present. The source of ultrasound contrast injected peripherally is related to microbubbles present in the injectant (22). The contrast bubble diameter in vivo is not known precisely. However, it has been estimated that the size distribution of peripherally injected contrast bubbles entering the pulmonary circulation is in the range of 60–90 μm (28).

Decompression bubbles are even less defined than injected bubbles, both for their size and for the time course of arrival at the lungs (2). Hills and Butler (19) have attempted to measure the size of decompression bubbles in the inferior vena cava of dogs and found it to vary with time. The size of bubbles ranged from 24 to 30 μm 5 min after decompression, increasing up to 50–160 μm between 25 and 35 min. If the bubbles are broken in greater number of smaller bubbles while flowing through the right heart, the diameter of most bubbles entering the pulmonary artery are well below 100 μm (2). Therefore, the size distribution of endogenous bubbles is likely to be very similar with contrast bubbles. The density of both types of bubbles is also essentially the same since air (~79% nitrogen) is used in ultrasound contrast, whereas nitrogen is the main gas filling decompression bubbles. Therefore, we believe that factors other than the density or the size distribution of bubbles are accountable for the observed discrepancy in results.

Bolus application of agitated contrast may acutely overwhelm the filtering capacity of pulmonary microcirculation and open the I-P shunts. Thus we suggest that the results observed in this study are related to a lower, acute bubble load compared with the two other reports. In future studies, contrast echocardiography should be repeated with lower bubble load to investigate whether shunts open in that situation. Our findings are supported by the fact that the incidence of DCS was only 2% in 3,500 dives in which VGEs were detected in 56% cases (25).

**Exercise and DCS.** Exercise is intrinsic activity during military and commercial diving and has been considered an additional risk factor for DCI (8). Cavitations in supersaturated fluids produces gas nuclei, and it is generally accepted that gas bubbles grow from preexisting nuclei (44). Vigorous exercise immediately before diving may produce microscopic muscular injuries, which could promote bubble formation (36). We have shown that a single bout of exercise 24 h before dive significantly reduces the number of bubbles in the right heart of divers (11), and the results are in accordance with previous studies in rats (43). The uptake and elimination of inert gas is dependent on blood flow. Exercise during the bottom phase of a dive will increase the amount of gas taken up (14), whereas mild exercise during decompression increases gas elimination (14) and reduces the number of venous bubbles detected after diving (20, 21). Webb et al. (40) recently showed that moderate dynamic exercise (3 times, 15-min dual-cycle ergometry) after altitude exposure does not result in either delayed onset of DCI...
or recurring DCI. This is the first study in divers to support these findings. Our subjects exercised (at ~85% \( \dot{V}_{O_2 \text{max}} \)) 40 min after dive because our laboratory has previously shown highest bubble grade at that time (11). Future studies should investigate the effect of postive exercise characteristics such as timing, duration, intensity, and type on DCI incidence.  

**Study limitations.** This study was performed on a limited number of subjects; therefore, results have to be viewed with caution before recommendation is given to divers to exercise freely immediately after a dive. We have investigated military divers without previous DCI incidents, except for one diver (mild DCS type I). Pilmanis et al. (26) reported that five of six subjects with altitude-induced AGE had a high incidence of DCS and VGM during previous research chamber flights. Five of six subjects became symptomatic (joint pain and skin mottling) soon after AGE onset. However, altitude data have to be viewed with caution since altitude DCS involves decompression from the saturation condition, whereas subsaturation decompressions are associated with diving. Thus it is thought that more VGMs occur at altitude exposure and that cerebral symptoms are more frequent in altitude DCS than in diving (15). Further study is necessary to evaluate the present findings in divers with a history of DCS.  

Transthoracic echocardiography was used in the present study as method of detection of the crossover of VGM. Pilmanis et al. (26) have used transthoracic echocardiography, but also transthephageal echocardiography, as a more reliable method for detection of small atrial septal defects and PFOs. We feel that transthoracic echocardiography is an adequate technique for the current aim of this study if performed always by the same experienced cardiologist.

The duration of the postive exercise was short (5 min), but rather strenuous, ending at 250 W, which is ~85% \( \dot{V}_{O_2 \text{max}} \). Anecdotial reports, heard from this group of divers, indicated that some have previously performed 10- to 15-km races freely immediately after a dive. We have investigated military divers without previous DCI incidents, except for one diver (mild DCS type I). Pilmanis et al. (26) reported that five of six subjects with altitude-induced AGE had a high incidence of DCS and VGM during previous research chamber flights. Five of six subjects became symptomatic (joint pain and skin mottling) soon after AGE onset. However, altitude data have to be viewed with caution since altitude DCS involves decompression from the saturation condition, whereas subsaturation decompressions are associated with diving. Thus it is thought that more VGMs occur at altitude exposure and that cerebral symptoms are more frequent in altitude DCS than in diving (15). Further study is necessary to evaluate the present findings in divers with a history of DCS.

In conclusion, this study has demonstrated that I-P shunting is not evident during exercise after diving in man. No signs of DCI were observed, suggesting that exercise after a dive may not be associated with an increased risk for DCI.

**GRANTS**

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