European Journal of Applied Physiology
https://doi.org/10.1007/s00421-018-3854-7

ORIGINAL ARTICLE

Variability in circulating gas emboli after a same scuba diving exposure

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Received: 16 June 2017 / Accepted: 22 March 2018

Abstract

Purpose A reduction in ambient pressure or decompression from scuba diving can result in ultrasound-detectable venous gas emboli (VGE). These environmental exposures carry a risk of decompression sickness (DCS) which is mitigated by adherence to decompression schedules; however, bubbles are routinely observed for dives well within these limits and significant inter-personal variability in DCS risk exists. Here, we assess the variability and evolution of VGE for 2 h post-dive using echocardiography, following a standardized pool dive in calm warm conditions.

Methods 14 divers performed either one or two (with a 24 h interval) standardized scuba dives to 33 mfw (400 kPa) for 20 min of immersion time at NEMO 33 in Brussels, Belgium. Measurements were performed at 21, 56, 91 and 126 min post-dive: bubbles were counted for all 68 echocardiography recordings and the average over ten consecutive cardiac cycles taken as the bubble score.

Results Significant inter-personal variability was demonstrated despite all divers following the same protocol in controlled pool conditions: in the detection or not of VGE, in the peak VGE score, as well as time to VGE peak. In addition, intra-personal differences in 2/3 of the consecutive day dives were seen (lower VGE counts or faster clearance).

Conclusions Since VGE evolution post-dive varies between people, more work is clearly needed to isolate contributing factors. In this respect, going toward a more continuous evaluation, or developing new means to detect decompression stress markers, may offer the ability to better assess dynamic correlations to other physiological parameters.

Keywords Echocardiography · Venous gas emboli · Ultrasound · Decompression sickness · Microbubble

Abbreviations

DCS Decompression sickness
VGE Venous gas emboli

Introduction

Decompression sickness (DCS) is a pathophysiology which can result from inert gas bubbles during or after scuba diving, with symptoms of varying severity ranging from skin itching to death. DCS risk is well managed by adhering to decompression algorithms dictating slow ascent and time at certain depths before surfacing to allow sufficient time for efficient degassing. Nevertheless, especially in the

Communicated by Susan Hopkins.

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Published online: 03 April 2018

recreational diving setting including multi-level, repetitive, multi-day exposures by a physiologically diverse population, there is increasing evidence of significant intra-personal and even inter-personal differences in DCS risk. These differences are currently unaccounted for by decompression models which use probabilistic models for estimating the risk of a particular exposure based on big databases. Furthermore, these databases are based on square dive profiles performed by physically fit, young, male divers often in a military research context and are not necessarily representative of the recreational diver populations or exposures.

During the ascent portion of a scuba dive, inert gas (nitrogen and/or helium) supersaturation often results in gas emboli formation and circulation in the bloodstream. The exact formation mechanism and formation site of these bubbles in vivo are not elucidated, but it is generally accepted that gas nuclei pre-dive are triggered to growth during decompression forming expanding gas bubbles in preferential sites with lower nucleation/growth thresholds due to morphological or surface chemistry characteristics (Papadopoulou et al. 2013a). The gas emboli formed in this way are termed "venous gas emboli" or VGE in scuba decompression research; please note however that VGE are sometimes observed in the arterial circulation as well, as explained hereafter.

Although any diving exposure can result in DCS, the execution of dive profiles believed to create a high DCS risk for recreational diving research purposes is not approved by many academic institutions. It is well established that even shallow recreational dives that are well within current decompression guidelines can sometimes result in some degree of detectable gas emboli. Although there does not exist an exact threshold for VGE resulting in DCS, and in fact some divers with significant VGE do not get DCS, whereas conversely others with no observed VGE develop DCS, a higher VGE score has been shown to correlate to higher probability of DCS (Eftedal et al. 2007; Sawatzky 1991; Nishi et al. 2003). There is also new evidence for long-term cognitive effects of scuba diving even for recreational divers with no history of DCS (Balestra et al. 2004; Hemelryck et al. 2014; Balestra and Germonpré 2016). As such, and in keeping with the aim of personalizing exposure guidelines for diverse recreational populations and diving purposes, we hypothesize that a decompression stress exposure index could be developed to minimize physiological stress even below the DCS threshold. One component of this decompression stress index has to incorporate limiting VGE post-dive, since these correlate to higher likelihood of DCS. Diving is also associated with reactive oxidative species that may contribute to vascular endothelial impairment (Brubakk et al. 2005; Lambrechts et al. 2013, 2017; Wang et al. 2015), so another feature of this index could be related to the oxidative stress associated with the exposure. Importantly, such an index could eventually be used as an alternative decompression algorithm validation endpoint, redefining the aim of scuba decompression modeling to limit the decompression stress of the exposure instead of solely avoiding DCS.

VGE are detectable using ultrasound, either as signals on Doppler audio recordings or as circulating bright spot on 2D B-mode imaging (usually echocardiography). VGE are normally visible in the venous circulation, but not in the arterial circulation as they are filtered by the lungs which act like a microbubble filter that traps and dissolves them (Papadopoulou et al. 2014). As such, ultrasound imaging of the heart or echocardiography offers a unique site of evaluation, with the right heart chambers offering a view of venous blood and the left heart chambers being filled with arterial blood after lung filtering. Indeed, recreational scuba dives often result in VGE, visible in half the heart chambers for this reason. Echocardiography is also particularly well suited to evaluate potential paradoxical entry points of VGE into the arterial circulation, from either overly aggressive decompression (too many or too large emboli overpowering the pulmonary filter), or physiological arterio-venous shunting (patent foramen ovale—PFO—in the heart or intrapulmonary arteriovenous anastomoses—IPAVA—in the lungs) (Germonpré et al. 1998; Madden et al. 2013).

There are data showing inter-subject variability recordings after open sea dives using Doppler assessment (Carturan et al. 2002; Gennser et al. 2012), but very few studies looking at bubble evolution post-dive with B-mode echocardiography. Of these, Ljubkovic et al. investigated the grade of bubbles on B-mode echocardiography from multiple dive profiles, taking measurements every 20 min for 2 h post-dive, and subdivided grade 4 to A, B and C subsets to better describe inter-personal variability (Ljubkovic et al. 2012). We have recently shown that a counting-based method allows for better inter- and intra-rater consistency in assessing VGE post-dive on 2D echocardiograms than current grading methods with minimal training (Germonpré et al. 2014). This assessment could be automated via computer analysis to save experimenter time, as it is currently time consuming, and initial evaluation on the same dataset is promising (Papadopoulou et al. 2013c). Due to the discontinuous nature of bubble grades, it may be that some differences observed between individual divers could be over- or underestimated by grading and thus better captured on a continuous scale, with the ability to automate this assessment an exciting prospect. Thus, assessing VGE inter-subject variability with this counting method is of interest here. In addition, real exposure diving in open sea conditions is extremely difficult to control due to its very nature, with water temperatures, rough sea conditions, thermal protection differences, exercise during preparation to enter the water and then post water-exit, etc, possibly contributing to the differences in bubbles observed between divers. For this reason, recordings in controlled pool conditions with the new counting method have been previously carried out by our group, but only with two time points of measurement post-dive. Two recent reviews on ultrasound assessment post-dive reinforced the need for more regular recordings (Blogg and Gennser 2011; Mollerlokken et al. 2016). Finally, discussion to date with respect to regular time points has primarily concentrated on the need to capture the peak of VGE, and little consideration has been given to their post-dive *evolution* (time course).

For these reasons, in this study, we investigate the variability in VGE counting detection post-dive on B-mode echocardiograms for subjects undergoing a standardized dive profile in a pool with controlled temperature and ideally calm conditions, measured regularly until just over 2 h post-dive. Variability is assessed looking at the following metrics, both between subjects and for the same subjects diving on consecutive days: (1) VGE vs no VGE, (2) differences in peak VGE measured, (3) differences in time to peak.

Materials and methods

Experiments were conducted in accordance with the Declaration of Helsinki (World Medical Association 2013) after approval by the Academic Ethical Committee of Brussels, as well as informed consent from each volunteer.

Study population

Male healthy scuba diver volunteers, non-smokers with no history of DCS and not on any cardioactive medication, were recruited from a larger sports diver population. Divers needed to be certified to at least "autonomous diver" level (EN 14153-2 or ISO 24801-2), have a minimum of 50 logged dives to participate in the study and be cleared 'fit to dive' by a medical doctor. All volunteers were informed of the study protocol and consented to participate, understanding they were free to withdraw at any time.

Diving protocol

Due to pool availability constraints, the experiments were planned over two consecutive evenings so that a maximum of ten single dives by ten divers diving in pairs could be performed each day. Each diver pair started its dive 7 min after the previous pair, so that staggered measurements post-dive could be performed in a way that guaranteed that each pair was monitored at the same time relative to their own dive. Each volunteer could only dive a maximum of once per day and was free to choose whether to dive on day 1, day 2 or on both day 1 and day 2 (24 h surface interval). The volunteers were asked to not dive during the 7 days preceding their first dive for the study, as well as to refrain from vigorous exercise 24 h prior to both their dives and avoid caffeinated beverages for 3 h pre- and post-dive.

A support crew for diving safety was also present, with three divers in the water at set depths at all times during the diving portion of the experiment, two other divers outside the water monitoring volunteers and schedules, and a hyperbaric qualified medical doctor present each day with open communication line to the hyperbaric chamber.

The diving profile was chosen as the same standardized Nemo 33 m for 20 min pool dive as other studies by our group (Balestra et al. 2016; Germonpré and Balestra 2017). Each diver pair descended to a depth of 33 m freshwater (mfw) (400 kPa) at a rate of 20 m/min and ascended at 10 m/min after 20 min without decompression stops, since this profile falls within no-decompression limits (NAVSEA 2016). The depth chosen (33 mfw) corresponded to the deepest and narrowest bottom section of the pool (shaped in the form of a well) and divers were asked to hover calmly on the bottom for the duration of the dive, swimming in a relaxed and slow pace around the bottom of the well. The water temperature in the pool was kept at 33 °C, so the divers dived wearing their swimming suits without additional thermal protection. The ambient air temperature around the pool where all pre-dive and post-dive measurements were taken was kept at 29 °C.

Echocardiography recordings and bubble counting

Table 1 shows the measurement time points used for assessment. The experimental schedule and timings were constrained by having the diver pairs rotate every 7 min through a total of four experimental stations (concurrent international collaboration measurements), of which the second included the echocardiography data presented here. A minimum interval between subsequent echocardiography time points of 4×7 min = 28 min was therefore inherent to this study design. To allow for up to ten divers per day, we chose to increase this to 5×7 min, resulting in 35 min between measurements. Finally, the first time point post-dive was at 21 min due to allowing 14 (a multiple of 7) min for the divers to exit the water, remove their gear and dry themselves, as well as rotate through the previous measurement station before echocardiography.

Table 1 Time points of echocardiography measurement

Pre-dive	Pre-dive
Postdive1	Post-dive, 21 min post water-exit
Postdive2	35 min after Postdive1, 56 min post water-exit
Postdive3	70 min after Postdive1, 91 min post water-exit
Postdive4	105 min after Postdive1, 126 min post water-exit

A Mindray M9 portable ultrasound machine (Mindray Bio-Medical Electronics Co, Shenzhen, China) was used for all recordings, with a sectorial cardiac probe (SP5-1S). A modified four-chamber view B-mode echocardiography recording (Mindray standard adult cardiac mode, frequency 3.4 MHz, 30 frames per second (fps), mechanical index MI = 1.2) was acquired for each time point to evaluate circulating gas bubbles post-dive using a validated methodology for assessing the VGE load corresponding to each dive (Germonpré et al. 2014). Briefly, B-mode echocardiography videos, comprising at least ten cardiac cycles, were saved for post-processing. The number of bubbles is counted on ten consecutive heart cycles, on a frame with the tricuspid valves open, and the average taken as the 'bubble score' for the video.

Data analysis and statistical methods

For each time point, the VGE load assessed as per the Germonpré et al. (2014) counting methodology was recorded. Statistics were performed on GraphPad Prism version 5.01 (GraphPad Software, San Diego, California, USA). Statistical significance levels were set at $p < 0.05$ (*), $p < 0.01$ (**) and $p < 0.001$ (***). Inter-subject variability was assessed by the median and spread of the data at each time point. Variability between time points was assesses using the Friedman test for paired subject-wise VGE evolution after negative normality test (assessed using Kolmogorov–Smirnov test), with Dunn's multiple comparison post-test.

Results

A total of 17 dives were performed over the 2 days of the study, by 14 divers (3 of the divers who dived on day 1 also dived on day 2), with no DCS occurrences. The mean and standard deviations of the divers' demographics were respectively: age 42 ± 7 years, BMI = 25.2 ± 1.9 kg m^{-2}. Ten dives were performed on day 1 (five pairs) and seven dives on day 2 (four pairs, with one of the divers volunteering to act as a safety support buddy only), of which three dives were performed by volunteers having dived on day 1 also.

The number of bubbles counted for each dive was shown to vary significantly between the four time points measured post-dive ($p < 0.0001$) over the 2 h post-dive monitoring period, as well as between volunteers (Figs. 1, 3). Figure 1 displays the number of bubbles counted for each dive. The maximum number of bubbles counted for this same exposure varied from over 30 to 0 between subjects and did not show any trend with increasing age or BMI of the divers. 14/17 dives resulted in visible VGE post-dive (defined as a bubble count average over ten cycles > 0 for at least one of the time points measured). For 12/14 dives, the peak number of bubbles counted appeared either for Postdive1 (7/12) or Postdive2 (5/12) time points, with the remaining 2/14 peaking at Postdive3, and Postdive4 consistently being the minimum bubbles counted. It should be noted that both dives for which the peak score appeared at Postdive3 had a low bubble count throughout the post-dive monitoring, each peaking with an average count over the ten cardiac cycles of only 1.3 at Postdive3. Bubbles were still present at Postdive4 for 9/17 dives, although for eight out of these nine divers with visible bubbles, the average count over the ten cardiac cycles was below 1 (the other was 9.9).

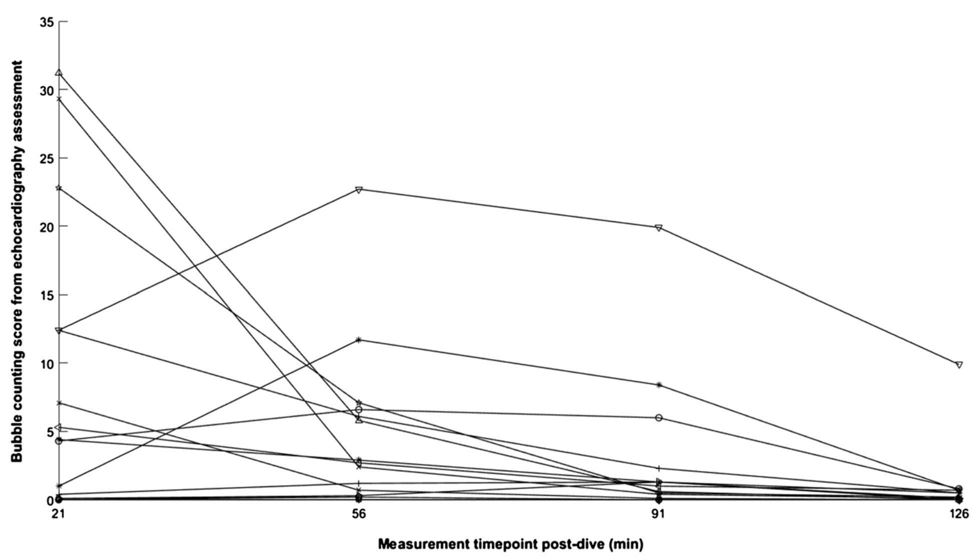

Fig. 1 Evolution of bubble counting score post-dive (17 dives)

Figure 2 shows the differences in bubbles counted between the 2 days of consecutive diving for the three volunteers that dived on both days. No VGE were detected on either dive for one of these divers. Fewer VGE were observed on the second dive for another subject, and more for the other but the time decay post-dive was faster.

Figure 3 displays the data as box plots showing the number of bubbles counted at each post-dive measurement time point for all dives after excluding the second day dives of the three subjects that dived on both days ($n = 14$), showing that VGE counts decrease with time (there were significant decreases in VGE counts for later, compared to earlier, measurement time points). It is also clear that the data are not normally distributed, as it follows a longer tail in higher VGE counts. It should be noted also that grouping the data in this manner masks individual trends for VGE evolution post-dive, as the differences in peak VGE with respect to measurement time point (Fig. 1) are no longer visible.

Discussion

VGE evolution for the NEMO profile

It is known that dive exposure (depth and time, as well as conditions) will affect VGE presence probability, as well as how long these are detected for post-dive. Since the NEMO profile has been extensively used in previous literature, it is important to document VGE evolution for it. This profile can then be compared with any similar depth–time profiles from the literature, so these are included below.

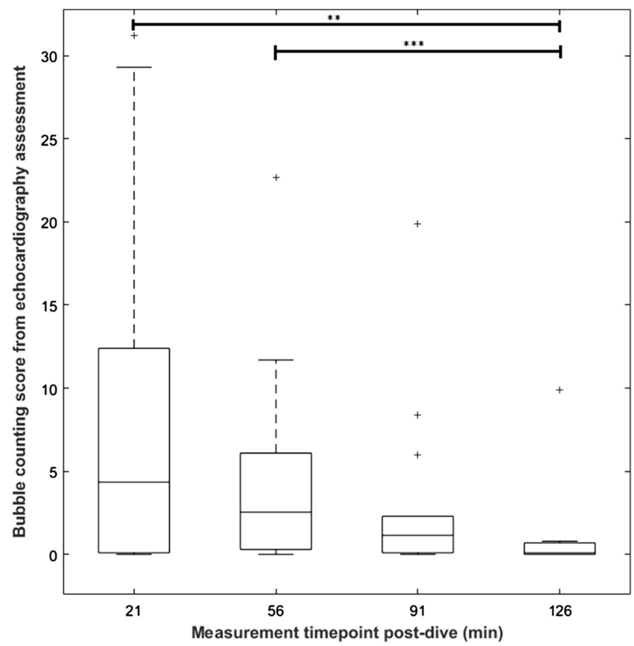

Fig. 3 Box plot representation of counted bubble score per measurement time point for all first dives (14 dives by 14 divers, excluding the repeated dives for the three divers that also dived the subsequent day)

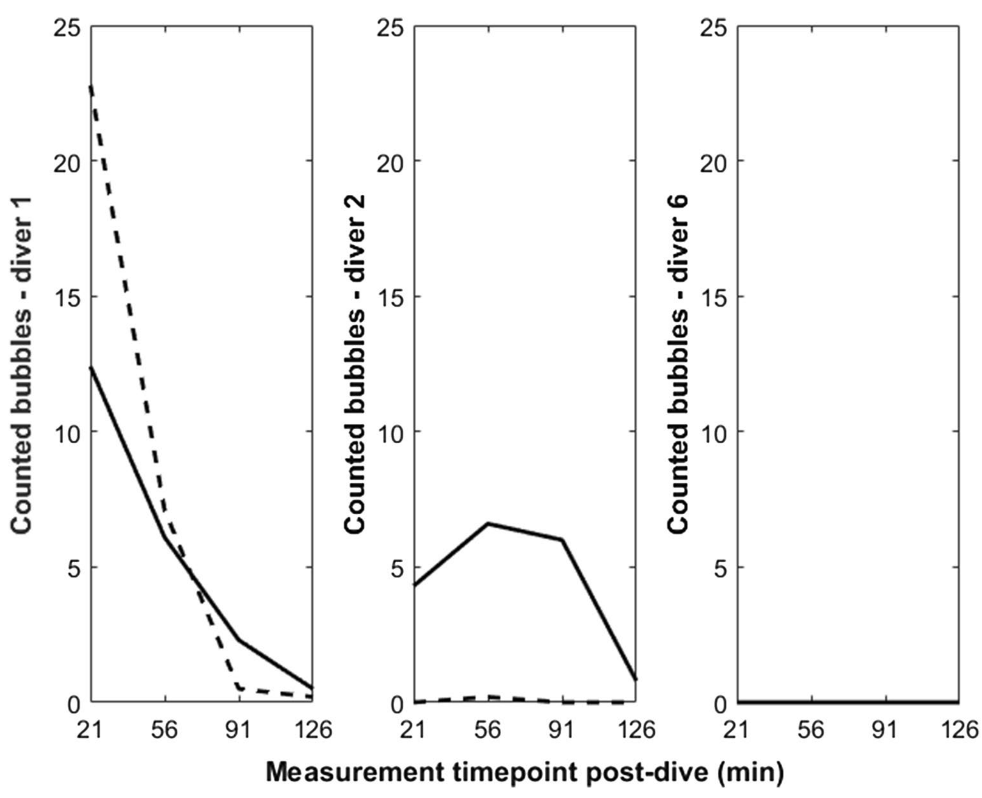

Fig. 2 Comparison of bubble dynamics post-dive for the three divers that dived on both days illustrating intra-personal variability in peak bubbles and time evolution; solid line—VGE count on day 1, and dashed line—VGE count on day 2 (note that for diver six both counts are superimposed, as there were no visible VGE on either day)

In a 2002 study, 50 divers dived to 35 m for 25 min with decompression stops, twice (different ascent rates) with a 24-h interval in open sea. A total of 28 divers were monitored every 10 min for 60 min, and 22 divers only at 60 min post-dive, all with Doppler recordings assessed using the Spencer scale (Carturan et al. 2002). The pressure excursion used here is slightly more aggressive (450 kPa) and two decompression stops were used, but significant bubbling that remains relatively high for most subjects until 60 min post-dive was found. A more recent study included one profile to 33 msw for 20 min in open sea and detected VGE with B-mode echocardiography assessed using a modified Eftedal and Brubakk grading system (Ljubkovic et al. 2011); however, only the median of the max VGE grade for the population was reported without details on time course or inter-subject variability. The median bubble grade observed 40 min post-surfacing was four (out of a maximum of five) and 10/12 of the divers tested did exhibit a grade 4 for this profile, with one subject arterializing also. Only one subject in our study showed arterial bubbles (known PFO). In our counting method for VGE assessment, any count > 1 corresponds by definition to at least a grade 3 on this scale (3—at least one bubble per four cardiac cycles for more than one set of four cycles) and most of our subjects would fall into grade 4 (continuous bubbling). In this respect, our results are therefore consistent with those of Ljubkovic et al. for the same profile in cold water conditions (16-C–18-C, with thermal protection) (Ljubkovic et al. 2011).

Inter- and intra-subject variability

In the current study, inter-subject variability in echocardiography VGE assessment appears in the presence of detectable VGE and peak VGE variability, but also importantly in the time to peak and rise/decay rate. The *evolution* of VGE post-dive clearly differs between individuals even when they have undergone the same dive profile in controlled conditions. In particular, in divers for whom circulating bubbles are visible, the peak score varies and is observed at earlier or later time post-dive (Fig. 4). For better illustration, Fig. 4 presents a frame of the videos analysed for two different subjects, showing how subject (a) peaks around Postdive2, whereas subject (b) peaks around Postdive1.

A limitation of the study design includes the gender restriction of the subjects, as only male participants were recruited. Volunteer and pool availability, as well as funding restrictions limited the possible sample size of our experiments to a single sex study. In this regard, however, it is worth noting that few studies have investigated differences in DCS risk or VGE between female and male divers and there is some evidence that the female hormonal cycle could influence risk (Boussuges et al. 2009). Further studies are needed since there is a large population of female divers. Similarly, since the amount of both older and younger recreational scuba divers is increasing, as is that of divers with pre-existing medical conditions (and/or taking medications), these are also inter-personal factors that should be further examined. With regard to the diving protocol, great care was taken to standardize the dive conditions and dive profile through the use of a pool, as well as controlled descent, ascent and swimming conditions during bottom

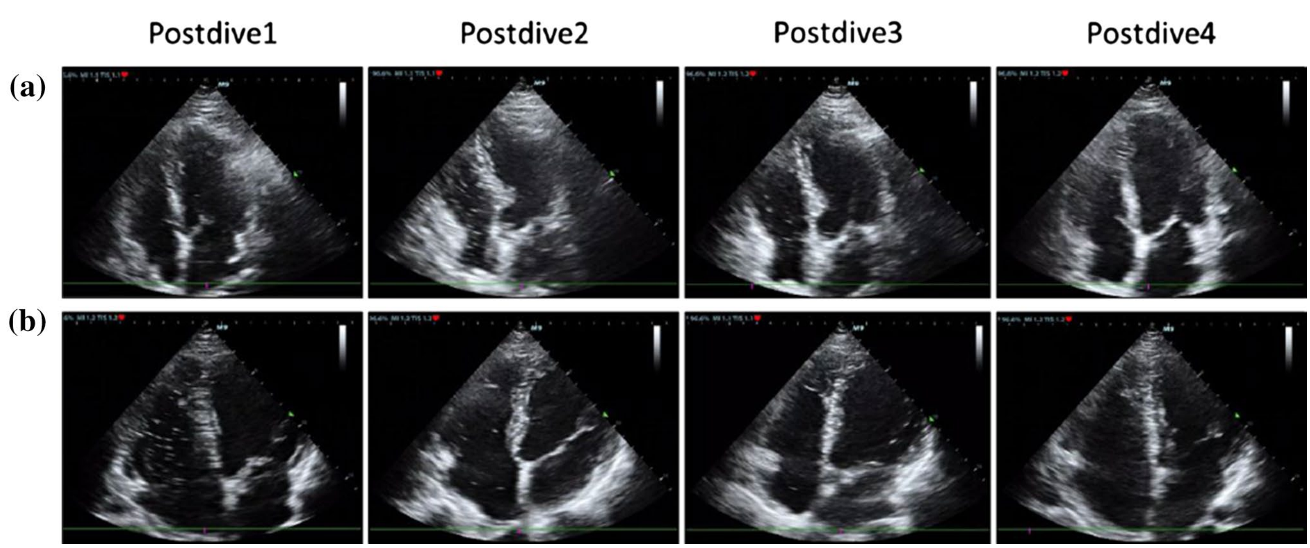

Fig. 4 Example of echocardiography frames for two subjects, (**a, b**), at all four post-dive measurement time points, illustrating the difference in VGE time to peak; VGE are seen as bright spots in the venous chambers of the heart [right heart of the subject, on the left of the images (inversed)]. Subject **a** shows maximum VGE at Postdive2, whereas subject **b** VGE peak appears at Postdive1

time. Nevertheless, minor variations in execution cannot be excluded since activity was not recorded underwater and this could have contributed to the variability observed. For this reason, having means to measure the activity level underwater precisely would be greatly advantageous in future experiments.

For the three subjects who dived on the second day also (intra-subject variability), from the literature it could be expected that fewer VGE would be present due to acclimatization thought to result from micronuclei population depletion (Montcalm-Smith et al. 2010; Zanchi et al. 2014), thus resulting in fewer VGE post-dive as fewer bubble precursors are excited to growth during ascent from a same depth–time profile. It should be noted that the limited number of second day dives in this study ($n = 3$ repeated dives after 24 h) does not allow to draw conclusions and is thus mostly illustrative. No VGE were present in either dive for one subject and some VGE were counted in the other two. For one of those, the second dive did indeed yield fewer VGE overall, but for the other more VGE were counted, albeit with a faster decay post-dive between measurement time points. The rate of VGE decay post-dive has not been extensively studied with respect to repetitive diving or other preconditioning interventions, focusing instead mainly on reporting the subjects' median bubbles with only the "peak" bubbles of each subject considered, and disregarding dynamic analysis post-dive.

On monitoring intervals

It is clear from this experiment that the VGE evolution pattern post-dive varies, even for the same exposure in a controlled pool environment. Previous studies relying on grading from Doppler recordings confirm these findings. Looking at unrestricted recreational dives (so different depth–time profiles performed) monitored only once 20–40 min post-dive between 1989 and 1991 (Dunford et al. 2002) showed that the likelihood of finding a high bubble grade (HBG) decreased by a factor of 0.78 for each 10 min delay in recording compared to their planned timeline of recording (20–40 min post-dive). The authors concluded that delaying monitoring by 25–30 min could underestimate the VGE peak by 20%. They also found a positive correlation between the likelihood of HBG with exposure severity, repetitive diving and male and/or older divers, but a lower incidence of HBG over the course of the days from multi-day diving trips pointing to possible adaptation.

One limitation of the current study relates to the choice of the monitoring interval (here 35 min). This was chosen as a compromise between the operational and availability constraints around the experiment and the aim to capture multiple time points post-dive at precisely set intervals for each dive pair to assess VGE presence and evolution. A recent review paper on this subject looked at Doppler and B-mode VGE monitoring protocols and concluded that the current protocols, most often monitoring twice post-dive around the 30 and 90 min points, are not frequent enough (Blogg and Gennser 2011). In a study with frequent post-dive measurements every 15 and 30 min using Doppler KM grading (Gennser et al. 2012), the authors found different results from other studies regarding the influence of pre-dive exercise, which may be linked to their more frequent measurement protocol. The current study follows the original recommendation for bounce diving (Nishi et al. 2003; Eatock and Nishi 1986) of starting measurement within 20 min of surfacing (almost, we started at 21 min to be precise) and measuring every 30–40 min for at least up to 2 h (we did every 35 min, in part due to operational constraints of pool availability).

The importance of short measurement intervals was further emphasized in the 2016 workshop on ultrasound monitoring for diving research (Mollerlokken et al. 2016), which proposed a new maximum of 20 min interval between recordings. Interestingly, very few studies measure multiple time points post-dive when using echocardiography to assess VGE (Mollerlokken et al. 2016). As pointed out by Blogg and Gennser, earlier Doppler studies relied on much more frequent measurements post-dive and this has been overlooked with the switch to more recent B-mode echocardiography assessment (Blogg and Gennser 2011). This could result in missing the peak of the diver's population median to a dive profile (Blogg and Gennser 2011). In contrast to the Doppler studies also, even when authors have measured at relatively regular time points post-dive, only the peak VGE grade is reported, with no information on the time to peak. For those few studies using B-mode echocardiography that report the median grade per measurement time point post-dive, only the median for all divers is usually given. As such, and as illustrated by the difference between Figs. 1 and 3, the inter-subject variability for time-to-peak information is lost. Despite all divers having followed the same dive profile in pool, temperature-controlled conditions, the rate of bubble production and clearance shows differences that remain unexplained. The likely peak VGE score has been shown to depend on the time–depth profile of the diving exposure, but for a fixed profile, the variability in degassing dynamics remains unexplained. This is an area that has received little attention to date, possibly due to the use of grading assessment that is coarser.

Optimizing the assessment?

Since the evolution of post-dive off-gassing dynamics follows different trends for different people, it may be advantageous to have a scoring system that allows for more "continuous" evaluation post-dive. Having a dynamic standardized measurement endpoint for testing the effect of physiological interventions, such as antioxidant supplementation or exercise/oxygen preconditioning (Balestra et al. 2016; Lambrechts et al. 2017), could shed light onto the underlying mechanisms. Instead of correlating the overall peak VGE to some intervention, dynamic evolution of different physiological parameters post-dive could be investigated in future studies.

In this regard, taking multiple echocardiograms is advantageous; however, manual VGE counting is very time consuming, so semi-automatizing this for experimenter ease and speed is needed. Once all frames from each video were extracted to a folder to allow scrolling between them, it took on average 8.1 ± 3.8 min to implement the scoring. As expected videos with no or extremely few visible VGE were faster to score (less than 4 min) and the videos with the most bubbles took the longest (above 12 min). Taking into account all the process from frame extraction to the final score obtained per video, the time is therefore about 10 min for a human rater manually counting (and often more for very high bubble scores). Toward this direction, having the capability to record echocardiograms at multiple time points post-dive, in conjunction with other physiological parameters, presents advantages, as it allows for the dynamics of degassing post-dive to be investigated. Nevertheless, since each echocardiogram takes around 10 min to analyze manually, it is clearly important to go toward automation of the counting methodology for maximum use and benefit of this new assessment technique. Indeed, efforts in that direction are underway (Parlak et al. 2011; Papadopoulou et al. 2013b).

In addition, the assessment itself may be further optimized to allow for smaller gas emboli detection in tissues with dual-frequency (Swan et al. 2011) or multi-pulse linear signal cancellation techniques (Papadopoulou et al. 2017; Hensel et al. 2018). Finally, the effect of ultrasound on VGE should also be considered, in the context of bioeffects in supersaturated tissues. In particular, ultrasound may transiently deplete VGE (with possible associated bioeffects) or facilitate cavitation, which needs to be further studied.

Toward a decompression stress exposure index

Going beyond simply VGE appearance post-dive as assessed in this study, there are many physiological changes associated with scuba diving which do not necessarily result in DCS. Measurements post-dive compared to pre-dive show that diving is often associated with VGE (as assessed by ultrasound) and oxidative stress (flow-mediated dilation, FMD, impairment measured at the brachial artery). In addition, cognitive performance metrics can assess narcosis to some extent, with marked decrease in speed of reaction time and critical flicker fusion frequency (CFFF) at depth that can extend to post-dive periods (Balestra et al. 2012).

Bubbles, oxidative stress and cognitive impairment are short-term markers of scuba diving stress and return to baseline after normal diving after some time (few hours to few days, depending on the exposure severity and marker considered). As such, beyond the binary pathophysiological threshold of DCS, these short-term normal responses to stress can be assessed in asymptomatic diving with healthy subject volunteers under different conditions and for different populations. In that context, the overall goal of decompression physiology research can be to limit the amount and duration of bubbles, oxidative stress and cognitive impairment. This amounts to safer diving since significant increases in bubbles are correlated to higher DCS risk, but also to faster physiological recovery and better performance underwater which becomes paramount when the diving purpose is task-oriented. Additionally, this would likely positively affect any long-term exposure effects as stressors are minimized or physiological responses to them are mitigated. Eventually, the goal of decompression algorithms could shift from DCS prevention to encompass enhanced human performance by personalizing recommendations or pre-dive interventions (preconditioning).

As a future research direction, the ability to assess all of these markers continuously before, during and after the dive would allow for time series analysis, with the ability to correlate these markers to anthropomorphic measurements and assess complex interactions between them. It is known for instance that bubbles can account for some vascular oxidative stress, although hyperoxia seems to be an independent contributing pathway. In this context, experimental research dives in controlled conditions with non-invasive and minimally disruptive sensors (that have been shown as safe to use for continuous monitoring pre-, during and post-dive) would be ideal.

Conclusions

Evaluating decompression gas emboli on echocardiograms distinguishes both the venous and arterial circulations, thus offering the ability to assess paradoxical arterio-venous shunting to some degree. Inter- and intra-personal differences in VGE post-dive were demonstrated despite all divers following the same diving protocol in controlled pool conditions. The detection or not of VGE, peak VGE and time-to-peak were shown to differ. In this respect, more work is clearly needed to isolate contributing factors and going toward a more continuous evaluation post-dive, or developing new means to detect decompression stress markers, may offer the ability to better assess dynamic correlations to other physiological parameters. Capturing VGE dynamics post-dive could inform underlying physiological mechanics by allowing time series analysis of the data. This could shed light on some of the inconsistencies found in the literature with respect to specific pre-conditioning effects on VGE for instance, as well as provide valuable information for decompression stress modeling to better account for physiological variability down the line.

Acknowledgements The authors wish to thank the NEMO33 pool for kindly hosting us after hours, all the volunteers who so generously donated their time, as well as Mindray for technical support. This work was supported in part by the PHYPODE project, funded by the European Union under a Marie Curie Initial Training Network (FP7-PEOPLE-2010-ITN program, Grant Agreement No. 264816), as well as the Divers Alert Network/R.W. (Bill) Hamilton Memorial Dive Medicine Research Grant (VP award 2017) administered by the Women Divers Hall of Fame.

Author contributions VP, PG, DC, MXT and CB substantially contributed to conception and design of the study. VP, GO and AB acquired all the data. ST supervised and coordinated all diving and measurement schedule adherence. VP, PG, DC, RJE, PAD, GO, AB, MXT, ST and CB substantially contributed to data analysis and interpretation. VP drafted the article. PG, DC, RJE, PAD, GO, AB, MXT, ST and CB revised the article critically for important intellectual content. Additional information: sadly, coauthor David Cosgrove (DC) passed away. All other authors read and approved the final version of the manuscript.

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