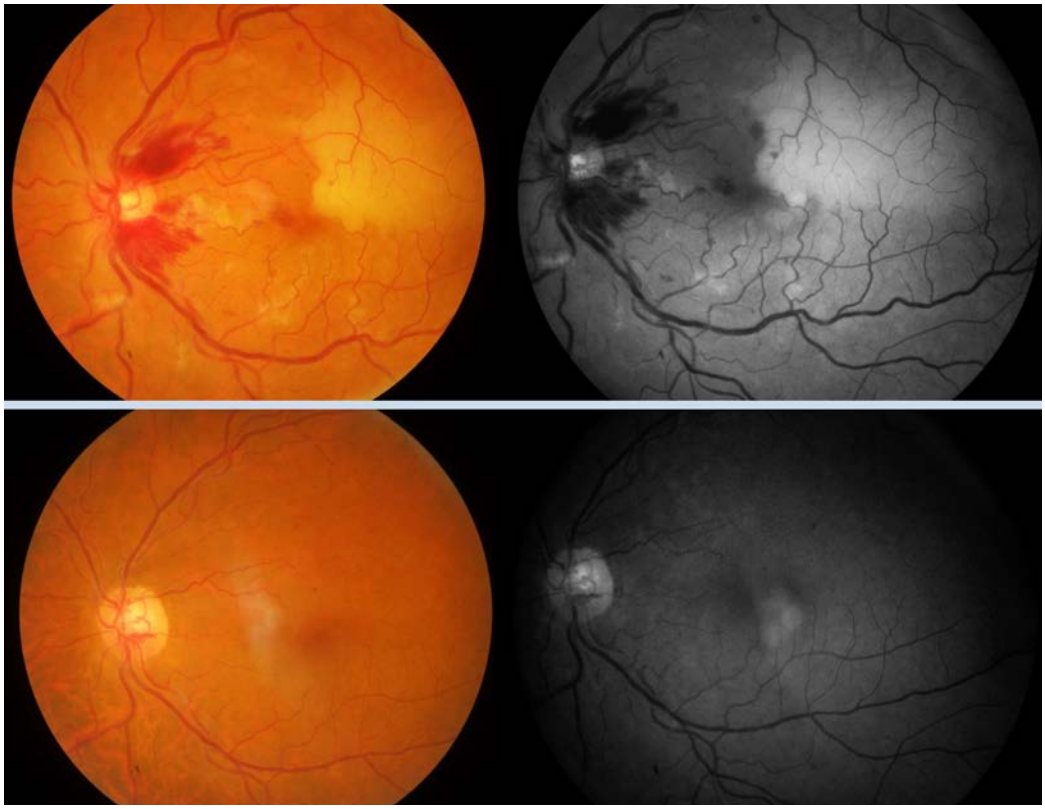
Diving and Hyperbaric Medicine

The Journal of the South Pacific Underwater Medicine Society and the European Underwater and Baromedical Society©

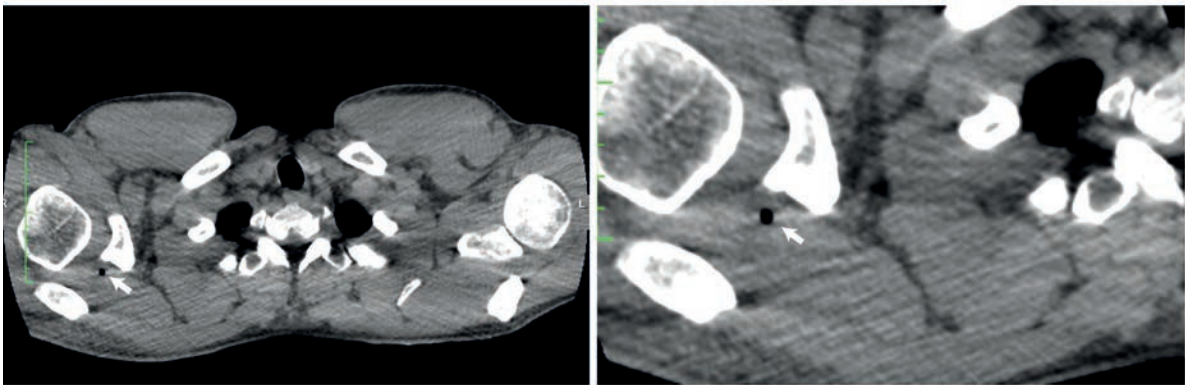
SPUMS

Volume 50 No. 4 December 2020

EUBS



HBOT for central retinal vein and cilioretinal artery occlusion



Residual tissue bubbles after recompression

E-ISSN 2209-1491

ABN 29 299 823 713

CONTENTS

Diving and Hyperbaric Medicine Volume 50 No.4 December 2020

Diving and Hyperbaric Medicine is indexed on MEDLINE, Web of Science® and Embase/Scopus
Articles from 2017 are deposited in PubMed Central®

PURPOSES OF THE SOCIETIES

To promote and facilitate the study of all aspects of underwater and hyperbaric medicine
To provide information on underwater and hyperbaric medicine
To publish a journal and to convene members of each Society annually at a scientific conference

---

DIVING AND HYPERBARIC MEDICINE

www.dhmjournal.com

Editor
Simon Mitchell editor@dhmjournal.com

European (Deputy) Editor
Lesley Blogg euroeditor@dhmjournal.com

Editorial Assistant
Nicky Telles editorialassist@dhmjournal.com

Submissions: https://www.manuscriptmanager.net/dhm

Subscriptions and print copies of back issues to 2017
Steve Goble admin@spums.org.au

***Diving and Hyperbaric Medicine* is published online jointly by the South Pacific Underwater Medicine Society and the European Underwater and Baromedical Society**
E-ISSN 2209-1491; ABN 29 299 823 713

The Editor's offering

Welcome to the final issue of *Diving and Hyperbaric Medicine* for 2020, our 50th publication volume. To say that 2020 has been a strange year would be a gross understatement, and I wish to acknowledge once again the difficult work and stress that many of our colleagues will have experienced. Many clinicians with an interest in diving and hyperbaric medicine are also front line in other disciplines, and will have been thrust to the forefront of caring for patients with Covid-19 in jurisdictions where outbreaks have been severe. This is particularly true of our European and American colleagues. Australia, New Zealand and several Asian nations have been largely spared this experience through combinations of bold leadership decisions, and aggressive testing, contact tracing and isolation programs. For this we are very grateful.

The world of medical publishing has been significantly affected by the pandemic. There has been a predictable explosion of Covid-19-related studies submitted to medical journals, and in the appropriate pursuit of rapid information sharing, never before has there been such a concerted effort to publish quickly and freely through combinations of pre-review publication, expedited review, and on-line publishing.

Interestingly, there are anecdotal reports that journal submissions on non-Covid-19 subjects have also increased substantially during the pandemic. One obvious explanation for this is that some authors have had more time to write up data during lock-downs and reductions in non-Covid-19 clinical activity. We have seen evidence of this at DHM. With a month to go at the time of writing, we have had approximately 50% more submissions in 2020 than we had for the entire year in 2019. Although a good 'problem' to have, this unanticipated and substantial increase has placed stress on the editorial capacity of our small but high-quality niche-field societal journal. There are no economies of scale with manuscripts; each adding linearly to the workload. This has resulted in longer delays to publication of some accepted papers than we would like, despite compiling record size issues in both final quarters of 2020. We try to ensure that an accepted manuscript never misses more than one issue after acceptance, and have failed in that regard with only two manuscripts in 2020. To those authors we apologise, and we will ensure that there is no disadvantage in relation to release of the published papers on PubMed Central.

Not surprisingly, Covid-19 related manuscripts have also appeared in our field, though to this point no randomised trials or even substantive cohort studies have been published exploring the proposal that hyperbaric oxygen may be a useful adjunctive treatment in Covid-19. It is known that several such studies are underway,[1] and we will await these with interest. The impact of Covid-19 on fitness for diving has attracted attention, and will continue to do so after the pandemic has subsided. A protocol for selection of appropriate investigations for candidates (or returning divers) wishing to dive after Covid-19 infection was published in the last issue of the journal,[2] and this issue contains another excellent summary of relevant considerations.[3]

This issue contains a record 12 original articles along with a guideline on the perennially controversial topic of children in diving, a technical report, three short communications and two case reports. Topics covered by the original articles include: training strategies for improving recovery after breath-hold dives; hyperbaric oxygen in spinal cord infarction; disinfection of hyperbaric chambers; a composite Chinese herbal preparation as a potential adjunctive therapy in decompression sickness; antiplatelet or anticoagulant drug effects on the risk of otic barotrauma during hyperbaric oxygen treatment; effects of free diving on the middle ear; oxygen store depletion during breath-hold diving; the effect of closing a persistent (patent) foramen ovale on decompression sickness risk; decompression sickness cases treated in Switzerland; the utility of critical flicker fusion frequency for measuring nitrogen narcosis; insulin sensitivity during hyperbaric oxygen exposure; and dysbaric osteonecrosis in diving fishermen.

In closing the DHM year, I must thank all our reviewers and the Editorial Board who provide such an important service to the field in ensuring that we are a credible evidence-based speciality. As previously, we will publish a list of our reviewers for 2020 in the March 2021 issue of the journal. Thanks also to the society presidents Dr Neil Banham and Dr Ole Hyldegaard for their unwavering support, and the Journal Governance Committee and SPUMS Treasurer Dr Soon Teo for their invaluable administrative work. The previous editor, Associate Professor Mike Davis has remained on the Editorial Board and has put his deep corporate knowledge of the journal to work in a special project to establish compliance with registration requirements with the Committee on Publication Ethics. This is deeply appreciated. Finally, I must thank our editorial assistant Nicky Telles for stepping up to the substantial workload challenge that 2020 has brought, and for her tireless accurate work. Here's hoping that 2021 will see the world start trending back toward normality.

References

1 Mitchell SJ. Diving and hyperbaric medicine in the SARS-CoV-2 pandemic. Diving Hyperb Med. 2020;50(2):90–1. doi: 10.28920/dhm50.2.90-91. PMID: 32557408.

2 Sadler C, Alvarez Villela M, Van Hoesen K, Grover I, Lang M, Neuman T, Lindholm P. Diving after SARS-CoV-2 (COVID-19) infection: Fitness to dive assessment and medical guidance. Diving Hyperb Med. 2020;50(3):278–87. doi: 10.28920/dhm50.3.278-287. PMID: 32957131.

3 Elia A, Gennser M. Considerations for scuba and breath-hold divers during the COVID-19 pandemic: A call for awareness. Diving Hyperb Med. 2020;50(4):408–11. PMID: 33325024.

Professor Simon Mitchell
Editor, Diving and Hyperbaric Medicine Journal

Original articles

Effects of inspiratory muscle training versus high intensity interval training on the recovery capacity after a maximal dynamic apnoea in breath-hold divers. A randomised crossover trial

Francisco de Asís-Fernández[1,2], Tamara del Corral[1,2], Ibai López-de-Uralde-Villanueva[3]

[1] *Departamento de Fisioterapia, Facultad de Ciencias de la Salud. Centro Superior de Estudios Universitarios La Salle, Universidad Autónoma de Madrid, Spain*
[2] *Breatherapy Research Group, Instituto de Neurociencias y Ciencias del Movimiento (INCIMOV), Centro Superior de Estudios Universitarios La Salle, Universidad Autónoma de Madrid, Spain*
[3] *Department of Radiology, Rehabilitation and Physiotherapy, Faculty of Nursing, Physiotherapy and Podiatry, Complutense University of Madrid, Spain*

Corresponding author: *Professor Tamara del Corral, Departamento de Fisioterapia, Facultad de Ciencias de la Salud. Centro Superior de Estudios Universitarios La Salle, Universidad Autónoma de Madrid, Spain*
tamaradelcorral@gmail.com

Key words
Breath-hold diving; Apnea; Exercise; Pulmonary function; Performance; Metabolism

Abstract
(de Asís-Fernández F, del Corral T, López-de-Uralde-Villanueva I. Effects of inspiratory muscle training versus high intensity interval training on the recovery capacity after a maximal dynamic apnoea in breath-hold divers. A randomised crossover trial. Diving and Hyperbaric Medicine. 2020 December 20;50(4):318–324. doi: 10.28920/dhm50.4.318-324. PMID: 33325010.)
Introduction: After a maximal apnoea, breath-hold divers must restore O_2 levels and clear CO_2 and lactic acid produced. High intensity interval training (HIIT) and inspiratory muscle training (IMT) could be employed with the aim of increasing recovery capacity. This study aimed to evaluate the relative effects of IMT versus HIIT on recovery of peripheral oxygen saturation (SpO_2), and also on pulmonary function, inspiratory muscle strength, lactate and heart rate recovery after a maximal dynamic apnoea in breath-hold divers.
Methods: Fifteen breath-hold divers performed two training interventions (IMT and HIIT) for 20 min, three days per week over four weeks in randomised order with a two week washout period.
Results: IMT produced a > 3 s reduction in SpO_2 recovery time compared to HIIT. The forced expiratory volume in the first second (FEV_1) and maximum inspiratory pressure (MIP) were significantly increased in the IMT group compared to HIIT. The magnitude of these differences in favour of IMT was large in both cases. Neither training intervention was superior to the other for heart rate recovery time, nor in peak- and recovery- lactate.
Conclusions: IMT produced a reduction in SpO_2 recovery time compared to HIIT after maximal dynamic apnoea. Even a 3 s improvement in recovery could be important in scenarios like underwater hockey where repetitive apnoeas during high levels of exercise are separated by only seconds. IMT also improved FEV_1 and MIP, but no differences in lactate and heart rate recovery were found post-apnoea between HIIT and IMT.

Introduction

During dynamic apnoea with fins, breath-hold divers compete to dive as deep as possible while oxygen (O_2) and carbon dioxide (CO_2) levels are progressively reduced and increased respectively. A major concern among divers is to surface with a safety margin to avoid hypoxic syncope or blackout; however, hypoxic incidents can be triggered even after the diver has surfaced.[1]

After a maximal apnoea, the diver attempts to recover O_2 levels and clear CO_2 and lactic acid produced. We hypothesised that the speed and success of the recovery depend on respiratory function to some extent; thus, in this study we analysed two types of training that have been shown to improve respiratory and physical function.

High intensity interval training (HIIT)[2] has become popular in recent years, and is characterised by increasing aerobic and anaerobic capacity[3] or increasing skeletal muscle oxidative capacity[4] in a short time period. In addition, inspiratory muscle training (IMT) is an effective method to increase pulmonary gas flow and capacity. IMT produces an increase in the strength and endurance of the specific musculature likely to facilitate optimal exchange of O_2/CO_2.[5] Previous studies suggest that IMT increased lung volumes,

work capacity, and power output in healthy subjects;[6,7] as well as improved physiologic responses in hypoxic exercise.[8] Furthermore, IMT attenuates the human respiratory muscle metaboreflex,[9] leading to a delay in the reduction of blood flow in the limbs, as a consequence of the fatigue of the inspiratory muscles, suggesting better blood flow redistribution after apnoea. HIIT and IMT have beneficial effects on lactate levels and recovery after exercise.[2,10,11]

This study aimed to analyse the effects of IMT versus HIIT on recovery of peripheral oxygen saturation (SpO_2) after maximal dynamic apnoea in breath-hold divers. Our second aim was to investigate the effects of these types of training on pulmonary function, inspiratory muscle strength, lactate recovery and heart rate recovery in the same population.

Methods

The study was approved by the Ethics Committee of La Salle University Centre for Advanced Studies (CSEULS-PI-215/2018) and was conducted following the ethical standards of the Declaration of Helsinki. The study was registered in clinicaltrials.gov, identifier NCT04084535. Divers were informed of the procedures, including benefits and risks, prior to signing the informed consent document, and all provided written informed consent before enrolment.

DESIGN

A single-blind, randomised, crossover trial was conducted. To ensure blinding, an external individual who was not involved in the study allocated participants to each group using GraphPad Software© (1:1 simple randomisation), and the intervention allocations were adequately concealed in sealed envelopes. The participants were not blinded and were allocated into 1 of 2 groups: (1) IMT; or (2) HIIT. The assessor was blinded to the allocation schedule, and the participants were specifically asked not to discuss the intervention with the evaluators. The washout period was two weeks after which the individual began the alternate training mode.

PARTICIPANTS

Participants were recruited from three Spanish freediving centers (Madrid Zaragoza, and Barcelona) from September 2019 to December 2019. Breath-hold divers were eligible to participate if: over 18 years of age; without co-morbidities that limited their ability to participate in exercise programmes or to practice voluntary apnoea; and members of the Spanish Federation of Underwater Activities (FEDAS). The exclusion criteria were participation in another exercise programme during the study period, and inability to attend at least 80% of the intervention sessions.

TRAINING PROCEDURES

The IMT included a four-week home training protocol consisting of 20 minutes (min), three days per week for all sessions. It was performed in a sitting position with a noseclip. Participants were instructed to perform fast and forceful inspirations and were encouraged to achieve maximal inhalation/exhalation with every breath. To provide inspiratory resistance a Powerbreath Classic Competition threshold pressure device (POWERbreathe International Ltd; Southam, Warwickshire, UK) was used. The training load was performed with the percentages of 50% (100 breaths in 10 min) and 80% (30 breathes in 10 min) maximum inspiratory pressure as described in Appendix 1*.

In the other group, the HIIT consisted of a swimming programme of 20 min, three days per week for four weeks. The training was applied under supervision, with the intensity monitored by the participant, who rated the perceived fatigue using the rating scale of perceived effort (RPE).[12,13] The swimming programme consisted of 20 min of interval training: a 1-min high-intensity work interval at about 19 points on the RPE followed by a one-min moderate-intensity work interval at about 12 points on the RPE.

OUTCOMES

All outcome measures were assessed pre-intervention and post-intervention (before and after the four-week programme). The assessments were conducted in a quiet, temperature-regulated, humidity controlled location, close to a swimming pool (24°C (SD 1), relative humidity ~90%).

Baseline measurements including weight, height, spirometry, maximum respiratory pressures, heart rate, SpO_2 and basal end-tidal carbon dioxide (E_TCO_2) were obtained before the maximal dynamic apnoea attempt. Spirometry was assessed with a portable spirometer (Spirobank II Basic, MIR, Rome, Italy) according to the American Thoracic Society/European Respiratory Society task force statement.[14] Maximum respiratory pressures were measured using a device that applies an inspiratory/expiratory load (Micro-RPM™, Care Fusion, San Diego, CA). This measurement was performed in a sitting position with the nose occluded with a nose clip. Divers were asked to perform a forceful and deep inspiration/expiration maintained for longer than 1 s after a complete expiration/inspiration. This was performed at least three times until there was < 20% variability between measurements, and the highest value was recorded.[15] Basal heart rate and SpO_2 were detected by a finger probe pulse oximeter (Nonin® Model 9847, Nonin Medical, Inc.). The basal E_TCO_2 was recorded every 5 seconds (s) over 2 min by the Nonin 9847 series hand-held pulse oximeter/CO_2 detector with semi-quantitative E_TCO_2 bar graph readout using the endotracheal tube adapter placed in the participant's mouth in the supine position.[16]

***Footnote:** Appendices 1 and 2 are available on the DHM journal website for viewing.

Next, the divers were asked to perform maximal dynamic apnoea with bi-fins in a 25 m pool when ready. A safety diver accompanied the divers during the attempt, as is done during competitions. Heart rate, SpO_2 and E_TCO_2 were recorded every 5 s during the 1 min recovery time. The primary outcome was the length of time to return to 95% SpO_2 during the 1 min recovery time after maximal dynamic apnoea. During the measurement, a signal indicated good perfusion with a green light or poor perfusion with a red light. Only data indicating good finger perfusion were analysed. At the same time as pulse oximetry, blood lactate concentrations were measured by analysing capillary blood samples taken from finger pricks using a Lactate Scout point of care analyser (EKF Diagnostics, Cardiff, UK) and at 3 min and 10 min during the passive recovery. The outcome measure to establish lactate recovery was the difference between the maximum value registered and the value at 10 min. Finally, breath-hold divers can also experience diaphragm contractions when they dive owing to the increasing level of CO_2 in the blood and the accompanying urge to breathe. Therefore, we asked participants to count the number diaphragm contractions during the maximal dynamic apnoea in order to evaluate training adaptations.

SAMPLE SIZE

The sample size was designed to detect which training model (IMT or HIIT) produced SpO_2 recovery in less time. For this purpose, in accordance with the recommendations established for crossover designs, a paired Student's *t*-test, with a power of 80% and an alpha error of 5% was chosen. A large effect size (d = 0.8) was used to detect clinically relevant differences.[17] In addition, the sample initially established was increased by 20%, given losses are common in longitudinal studies. Hence, a total sample of at least 15 participants was assessed as being required.

DATA ANALYSIS

A P-value < 0.05 was considered statistically significant. The Shapiro-Wilk test showed a normal distribution of the data except for the number of contractions during apnoea and the lactate assessment (peak and recovery). The statistical analyses were performed according to the procedures described by Wellek and Blettner for crossover designs.[18] The carry-over effects were assessed to confirm they were negligible. Specifically, for the parametric data, a paired Student's *t*-test was used to assess residual and period effects, whereas the Wilcoxon test was used for nonparametric data. The carry over effects were assessed by comparing within-subject sums of the results from both periods through an unpaired Student's *t*-test or the Mann-Whitney U test.

A comparison of the changes between baseline and post-intervention due to IMT versus those produced by HIIT was used to assess treatment effects. Specifically, a paired Student's *t*-test was used for parametric data, and a Wilcoxon test was used for nonparametric data. Effect sizes were established according to Cohen's method (Cohen's d): small (0.20–0.49), medium (0.50–0.79) or large (≥ 0.8).[19]

Furthermore, an intention-to-treat analysis was performed to include missing data and to protect the randomisation. Currently, there is no standardised method to handle missing outcomes.[20] Hence, the average change obtained in the corresponding training intervention was used to replace the missing outcomes. In addition, to carry out the intention-to-treat analysis, the participants were required to perform at least three of the four planned evaluations. Otherwise, the participant's data was not included in the analysis.

Results

Sixteen breath-hold divers were included in the study. Two weeks after starting the study, a participant suffered a trauma that required immobilisation; he was not included in the analysis. Therefore, the sample ultimately analysed consisted of 15 participants (three women and 12 men), of which one was included as intention-to-treat because, for personal reasons, they could not attend the last day of assessments.

The mean age, weight and height of the 15 divers were 36 (SD 9) years, 75 (12) kg and 176 (8) cm. The prior personal best in dynamic apnoea with fins ranged from 60 to 141 m (mean 100 (SD 21) m). At rest and before the dives, all freedivers had a basal SpO_2 above 95% and a basal E_TCO_2 of 30 mmHg; the latter being a function of the measuring device's ability to only provide incremental E_TCO_2 readings of 2, 6, 10, 20, 30, 50, or 75 mmHg. The mean maximal distance during dynamic apnoea recorded in the first attempt was 82 m (SD 20) and the range was 50–120 m. Throughout all study dives individual divers performed the distance recorded in their first attempt.

RESPIRATORY VARIABLES, SPEED, AND NUMBER OF DIAPHRAGM CONTRACTIONS DURING APNOEA

There were no carry-over effects for any of the variables assessed (Table 1). The forced expiratory volume in one second (FEV_1) (mean difference [95% CI] 0.22 L [0.06 to 0.38]) and maximum inspiratory pressure (MIP) (mean difference [95% CI] 13.05 cmH_2O [0.39 to 25.71]) were significantly increased after IMT compared to HIIT (Table 2). The magnitude of these differences in favour of IMT nearly met the threshold classification for 'large' in both cases (FEV_1, d = 0.8; MIP, d = 0.73). Neither training was superior to the other for the rest of the respiratory variables: forced vital capacity (FVC) (mean difference [95% CI] -0.005 L [-0.24 to 0.23]); and maximum expiratory pressure (MEP) (mean difference [95% CI] -2.7 cmH_2O [-16.45 to 11.05]), nor for speed (mean difference [95% CI] -0.03 $m \cdot s^{-1}$ [-0.07 to 0.01]) and number of contractions during apnoea (Z-value = –0.903; P-value = 0.367).

Table 1

Descriptive data for all variables at baseline (Pre) and end (Post) of each training period, as well as assessment of carry-over effects. Data are presented as mean (SD). Note: a) = Residual effects: Pre 1 Total vs. Pre 2 Total; b) = Period effects: Post 1 Total vs. Post 2 Total; c) = Carry-over effects (Post 1 + Post 2): AB vs BA. AB sequence = inspiratory muscle training (IMT) followed by high intensity interval training (HIIT); BA sequence = HIIT followed by IMT; Contract. = diaphragmatic contractions; FEV_1 = forced expiratory volume in the first second; FVC = forced vital capacity; HR-R = recovery time of heart rate; Lactate-M = maximum blood lactate; Lactate-R = blood lactate recovery; MEP = maximum expiratory pressure; MIP = maximum inspiratory pressure; SpO_2-R = recovery time of peripheral oxygen saturation

Parameter		Period 1		Period 2		Mean diff. (95% CI) or Z-value; *P*-value
		Pre	Post	Pre	Post	
Physical recovery after apnoea						
SpO_2-R (s)	AB	13.22 (8.53)	9.71 (5.02)	12.14 (5.87)	11.51 (6.28)	a) -0.96 (-3.7 to 1.78)
	BA	6.00 (3.25)	7.25 (2.44)	8.75 (3.41)	6.75 (4.27)	b) -0.57 (-2.35 to 1.21)
	Total	9.37 (7.1)	8.40 (3.92)	10.33 (4.87)	8.97 (5.66)	c) 7.22 (-2.53 to 16.98)
HR-R (s)	AB	29.14 (15.75)	29.29 (15.62)	32.86 (12.59)	30.53 (12.36)	a) -3.53 (-7.83 to 0.76)
	BA	37.00 (14.40)	38.5 (15.42)	40.38 (13.06)	40.25 (13.41)	b) -1.51 (-7.95 to 4.92)
	Total	33.33 (15.05)	34.2 (15.69)	36.87 (12.97)	35.71 (13.44)	c) -18.94 (-47.89 to 10.02)
Lactate-M ($mmol \cdot L^{-1}$)	AB	4.07 (1.68)	4.03 (2.46)	3.84 (2.69)	3.87 (2.04)	a) Z = -0.786; *P* = 0.432
	BA	3.68 (1.21)	3.63 (1.29)	3.94 (1.70)	3.9 (1.61)	b) Z = -0.346; *P* = 0.729
	Total	3.86 (1.41)	3.81 (1.86)	3.89 (2.13)	3.89 (1.76)	c) Z = -0.463; *P* = 0.643
Lactate-R ($mmol \cdot L^{-1}$)	AB	1.00 (0.61)	0.94 (1.03)	0.97 (0.82)	1.05 (0.65)	a) Z = -0.157; *P* = 0.875
	BA	0.84 (0.52)	0.83 (0.44)	1.06 (0.77)	1.08 (0.84)	b) Z = -1.254; *P* = 0.210
	Total	0.91 (0.55)	0.88 (0.75)	1.02 (0.76)	1.06 (0.73)	c) Z = -0.290; *P* = 0.772
Respiratory assessment						
FVC (L)	AB	5.27 (1.26)	5.36 (1.31)	5.27 (1.35)	5.29 (1.17)	a) 0.09 (-0.15 to 0.33)
	BA	5.97 (0.57)	6.08 (0.64)	5.81 (0.91)	5.86 (0.91)	b) 0.15 (-0.09 to 0.39)
	Total	5.64 (0.99)	5.74 (1.04)	5.56 (1.13)	5.59 (1.04)	c) -1.29 (-3.52 to 0.93)
FEV_1 (L)	AB	4.26 (1.04)	4.45 (1.07)	4.22 (1.17)	4.29 (1.01)	a) 0.14 (-0.05 to 0.33)
	BA	4.96 (0.44)	4.75 (0.29)	4.73 (0.66)	4.82 (0.65)	b) 0.04 (-0.14 to 0.22)
	Total	4.63 (0.83)	4.61 (0.74)	4.49 (0.93)	4.57 (0.85)	c) -0.83 (-2.57 to 0.91)
MIP (cmH_2O)	AB	134.71 (28.22)	161.14 (30.52)	154.14 (30.59)	160.9 (33.88)	a) -8.8 (-19.06 to 1.46)
	BA	161.50 (14.96)	161.75 (22.43)	161.00 (16.85)	168.5 (15.81)	b) -3.49 (-10.1 to 3.13)
	Total	149.00 (25.39)	161.47 (25.51)	157.80 (23.57)	164.95 (25.15)	c) -3.92 (-59.64 to 51.8)
MEP (cmH_2O)	AB	173.71 (32.90)	194.14 (41.11)	180.00 (34.54)	197.07 (38.00)	a) -6.47 (-14.92 to 1.98)
	BA	196.25 (54.10)	216.00 (56.32)	202.88 (52.53)	214.63 (48.12)	b) -0.63 (-11.62 to 10.36)
	Total	185.73 (45.42)	205.80 (49.37)	192.20 (45.06)	206.43 (43.11)	c) -39.41 (-141.8 to 62.96)
Assessment during apnoea						
Speed ($m \cdot s^{-1}$)	AB	0.97 (0.18)	0.99 (0.19)	0.99 (0.20)	1.02 (0.20)	a) -0.03 (-0.08 to 0.01)
	BA	0.89 (0.09)	0.94 (0.11)	0.93 (0.09)	0.96 (0.10)	b) -0.02 (-0.06 to 0.01)
	Total	0.93 (0.14)	0.96 (0.15)	0.96 (0.15)	0.98 (0.15)	c) 0.11 (-0.22 to 0.44)
Contract. (*n*)	AB	16.43 (9.68)	18.57(14.65)	17.00 (9.38)	13.71 (12.05)	a) Z = -0.704; *P* = 0.482
	BA	11.88 (7.68)	10.00 (9.61)	12.13 (9.86)	11.63 (8.14)	b) Z = -0.786; *P* = 0.432
	Total	14.00 (8.67)	14.00 (12.56)	14.4 (9.63)	12.6 (9.83)	c) Z = -0.347; *P* = 0.728

PHYSICAL RECOVERY AFTER APNOEA

Once again, there were no carry-over effects for any of the physical recovery variables assessed (Table 1). The comparison between the interventions for the physical recovery variables is shown in Table 2. The IMT intervention showed a statistically significant reduction in SpO_2 recovery time compared to the HIIT intervention [IMT intervention (SpO_2 recovery = –2.71 (SD 5.04) s) vs HIIT intervention (SpO_2 recovery = 0.37 (3.76) s] (Table 2). Specifically, IMT reduced the SpO_2 recovery time obtained with the HIIT by more than 3 s [mean difference (95% CI) -3.08 s (-5.72 to -0.43)], which implies a difference of moderate-large magnitude (d = 0.69). Neither training was superior to the other in terms of heart rate recovery time [mean difference (95% CI) 0.28 (-5.78 to 6.35) s], nor in peak lactate level (Z-value = 0.683; *P*-value = 0.494) and recovery lactate level (Z-value = –0.369; *P*-value = 0.712).

Table 2

Comparison of the changes between baseline and post-intervention after inspiratory muscle training versus those after high intensity interval training. Data are presented as mean (SD). Contractions = diaphragmatic contractions; FEV_1 = forced expiratory volume in the first second; FVC = forced vital capacity; HIIT = high intensity interval training; HR-R = recovery time of heart rate; IMT = inspiratory muscle training; Lactate-M = maximum blood lactate; Lactate-R = blood lactate recovery; MEP = maximum expiratory pressure; MIP = maximum inspiratory pressure; SpO_2-R = recovery time of peripheral oxygen saturation; * = $P < 0.05$

Parameter	Δ IMT intervention	Δ HIIT intervention	Intervention effects Mean difference (95% CI); d or Z-value; *P*-value
Physical recovery after apnoea			
SpO_2-R (s)	-2.71 (5.04)	0.37 (3.76)	-3.08 (-5.72 to -0.43); d = -0.69*
HR-R (s)	-0.01 (0.66)	-0.29 (10.88)	0.28 (-5.78 to 6.35); d = 0.04
Lactate-M ($mmol \cdot L^{-1}$)	-0.04 (0.60)	-0.01 (0.64)	Z = -0.683; P = 0.494
Lactate-R ($mmol \cdot L^{-1}$)	-0.02 (0.88)	0.03 (0.43)	Z = -0.369; P = 0.712
Respiratory assessment			
FVC (L)	0.07 (0.27)	0.07 (0.24)	-0.005 (-0.25 to 0.23); d = 0
FEV_1 (L)	0.14 (0.28)	-0.08 (0.27)	0.22 (0.06 to 0.38); d = 0.8*
MIP (cmH_2O)	16.33 (21.09)	3.29 (13.76)	13.05 (0.39 to 25.71); d = 0.73*
MEP (cmH_2O)	15.8 (19.20)	18.5 (18.67)	-2.7 (-16.45 to 11.05); d = 0.14
Assessment during apnoea			
Speed ($m \cdot s^{-1}$)	0.02 (0.06)	0.05 (0.04)	-0.03 (-0.07 to 0.01); d = -0.59
Contractions (*n*)	0.73 (7.87)	-2.53 (8.12)	Z = -0.903; P = 0.367

Discussion

This study analysed the effects of IMT versus HIIT on recovery after maximal dynamic apnoea. According to the literature, both interventions could contribute to restoring O_2 levels and clearing the CO_2 and lactic acid produced during apnoea through various mechanisms;[3–5] however, to our knowledge this is the first study comparing IMT versus HIIT in terms of recovery after maximal dynamic apnoea in breath-hold divers. The IMT intervention led to a significant reduction in SpO_2 recovery time compared to the HIIT intervention; in addition, FEV_1 and MIP were significantly increased after the IMT intervention compared to HIIT. The results obtained in our study suggest the superiority of IMT in terms of improved post-apnoea recovery.

Measuring lactate concentrations after maximal apnoea can provide relevant information on the contribution of the anaerobic pathway, lactate clearance, or acidosis tolerance.[21] Previous studies suggested that an effort is considered maximal when it fulfils the following requirements: maximal HR is reached, respiratory quotient (CO_2/O_2) is greater than 1.2, the RPE is close to 20 and blood lactate exceeds 8 $mmol \cdot L^{-1}$;[22,23] but in our study, only two divers reached levels higher than 8 $mmol \cdot L^{-1}$. In previous studies performed with breath-hold divers,[24,25] values of 2.3 $mmol \cdot L^{-1}$ in static apnoea and 7.1 $mmol \cdot L^{-1}$ in dynamic apnoea have been reached. Also, no differences were found in lactate recovery during post apnoea recovery between HIIT and IMT. This outcome could have been due to the low peak lactate concentrations observed in the participants. In previous studies, both HIIT and IMT have demonstrated an influence on post-exercise lactate clearance at high intensity.[26,27] Cited studies suggested that physical training would improve lactate buffering during a 10 min-recovery after exercise; however, in our study (unlike previous studies) lactate recovery was measured after 10-min recovery from maximal voluntary apnoea. It might be that blood flow centralisation (induced by diving reflex or metaborreflex), could modify the metabolic buffering response of the system. Future studies should clarify this controversy. On the other hand, in this study the lactate concentration reached post-apnoea had a stronger association with swimming speed than with hypoxia levels.

Previous studies[28,29] have shown a strong association between apnoea training and vital capacity (VC) increase. This increase was up to 2 L in a trained breath-hold diver versus an untrained diver, for the same height and age; but, in our study, there were no changes in VC after interventions. As suggested by other studies,[30,31] divers (who have significant motor control in their respiratory musculature, thoracic and pleural flexibility, and experience in swimming in hyperbaric conditions) are highly trained, making it difficult to further increase their VC with IMT or HIIT. A 2013 meta-analysis reported that divers and swimmers would

not benefit in respect to VC because they are already close to their optimal condition.[32] Previous studies,[6,7] reported an increase in MIP and VC after IMT; however, in these studies the training duration was doubled (eight weeks vs. four weeks in our study). Nevertheless, similar studies previously demonstrated an increase in MIP after six or four weeks.[8,10] Another conclusion from relevant studies is that only high-intensity IMT (80% of MIP at baseline) increased VC.[6,7] In our study, an increase in MIP and FEV_1 was found after IMT, indicating that IMT is an effective intervention to improve respiratory functionality even in highly trained participants.[33] However, HIIT did not produce improvement in MIP or FEV_1. These results are different when compared to a previous study,[34] which showed no changes for FEV_1 but an increase in MIP after HIIT.

To analyse the recovery after apnoea, the main outcome was monitored by pulse-oximeter to detect the time to reach an $SpO_2 > 95\%$ in divers.[35] In the present study nadir SpO_2 (mean (SD); minimum) values were 70% (15); 32% in HIIT and 72% (16); 33% in IMT. To recover, the breath-hold diver must perform ventilations that allow a rapid and effective restitution of normoxia to reduce risk of a blackout. The present results showed a faster SpO_2 recovery after IMT, suggesting that specific IMT might produce greater ventilation efficiency in the first post-apnoea breaths.

Pulse oximetry is the most common method employed to reflect the first few minutes of oxygenation recovery after submersion; however, this method failed to record the initial 10–15 s after surfacing. This delay was due to the time needed to dry and heat the finger. With the use of pulse oximetry, there is also a delay in nadir O_2 saturation compared to more central measurements. However in our situation, the delay might have been beneficial, given the values we obtained at 20–30 s might represent events that occur at a point closer to the end of the dive. In addition, E_TCO_2 was determinated during the recovery period after the maximal apnoea, but the device only can display the following data: 2, 6, 10, 20, 30, 50 ,75 mmHg CO_2. All divers registered > 75 mmHg during the first breaths, however, it was unable to determine the CO_2 levels precisely after apnoea, suggesting that a more accurate device to measure E_TCO_2 is needed in future research.

Conclusions

IMT showed a decrease in SpO_2 recovery time compared to the HIIT intervention after maximal dynamic apnoea. Although one could question the practical significance of a three-second improvement in recovery of the SpO_2 with IMT compared to HIIT, a difference of this magnitude could be important in extreme performance activities like underwater hockey where heavy apnoeic exercise is performed during repetitive dives separated only by seconds. Regarding secondary outcomes, an improvement in FEV_1 and MIP were achieved, but no differences in lactate and heart rate recovery were found post-apnoea between HIIT and IMT. Thus, IMT appears to be an effective training intervention for divers aiming to improve oxygen recovery after a maximal apnoea.

References

1 Lindholm P, Blogg SL, Gennser M. Pulse oximetry to detect hypoxemia during apnea: comparison of finger and ear probes. Aviat Space Environ Med. 2007;78:770–3. PMID: 17760284.

2 Schoenfeld B, Dawes J. High-intensity interval training: Applications for general fitness training. Strength Cond J. 2009;31:44–6. doi: 10.1519/SSC.0b013e3181c2a844.

3 Hazell TJ, MacPherson REK, Gravelle BMR, Lemon PWR. 10 or 30-s sprint interval training bouts enhance both aerobic and anaerobic performance. Eur J Appl Physiol. 2010;110:153–60. doi: 10.1007/s00421-010-1474-y. PMID: 20424855.

4 Gillen JB, Percival ME, Skelly LE, Martin BJ, Tan RB, Tarnopolsky MA, et al. Three minutes of all-out intermittent exercise per week increases skeletal muscle oxidative capacity and improves cardiometabolic health. PLoS One. 2014;9:e111489. doi: 10.1371/journal.pone.0111489. PMID: 25365337. PMCID: PMC4218754.

5 Kellens I, Cannizzaro F, Gouilly P, Crielaard JM. Entraînement de la force des muscles inspiratoires chez le sujet sportif amateur. Rev Mal Respir. 2011;28:602–8. French. doi: 10.1016/j.rmr.2011.01.008.

6 Enright SJ, Unnithan VB. Effect of inspiratory muscle training intensities on pulmonary function and work capacity in people who are healthy: A randomized controlled trial. Phys Ther. 2011;91:894–905. doi: 10.2522/ptj.20090413. PMID: 21493747.

7 Enright SJ, Unnithan VB, Heward C, Withnall L, Davies DH. Effect of high-intensity inspiratory muscle training on lung volumes, diaphragm thickness, and exercise capacity in subjects who are healthy. Phys Ther. 2006;86:345–54. doi: 10.1093/ptj/86.3.345.

8 Downey AE, Chenoweth LM, Townsend DK, Ranum JD, Ferguson CS, Harms CA. Effects of inspiratory muscle training on exercise responses in normoxia and hypoxia. Respir Physiol Neurobiol. 2007;156:137–46. doi: 10.1016/j.resp.2006.08.006. PMID: 16996322.

9 Witt JD, Guenette JA, Rupert JL, McKenzie DC, Sheel AW. Inspiratory muscle training attenuates the human respiratory muscle metaboreflex. J Physiol. 2007;584:1019–28. doi: 10.1113/jphysiol.2007.140855. PMID: 17855758. PMCID: PMC2277000.

10 Romer LM, McConnell AK, Jones DA. Effects of inspiratory muscle training upon recovery time during high intensity, repetitive sprint activity. Int J Sports Med. 2002;23:353–60. doi: 10.1055/s-2002-33143. PMID: 12165887.

11 Kohn TA, Essén-Gustavsson B, Myburgh KH. Specific muscle adaptations in type II fibers after high-intensity interval training of well-trained runners. Scand J Med Sci Sports. 2011;21:765–72. doi: 10.1111/j.1600-0838.2010.01136.x. PMID: 20492589.

12 Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982;14:377–81. PMID: 7154893.

13 Kurokawa T, Ueda T. Validity of ratings of perceived exertion as an index of exercise intensity in swimming training. Ann Physiol Anthropol. 1992;11:277–88. doi: 10.2114/ahs1983.11.277. PMID: 1642725.

14 Miller MR, Crapo R, Hankinson J, Brusasco V, Burgos F, Casaburi R, et al. General considerations for lung function testing. Eur Respir J. 2005;26:153–61. doi:

10.1183/09031936.05.00034505. PMID: 15994402.
15 American Thoracic Society/European Respiratory Society. ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med. 2002;166:518–624. doi: 10.1164/rccm.166.4.518. PMID: 12186831.
16 George S, MacNab AJ. Evaluation of a semi-quantitative CO_2 monitor with pulse oximetry for prehospital endotracheal tube placement and management. Prehosp Disaster Med. 2002;17:38–41. doi: 10.1017/s1049023x00000108. PMID: 12357564.
17 Angst F, Aeschlimann A, Angst J. The minimal clinically important difference raised the significance of outcome effects above the statistical level, with methodological implications for future studies. J Clin Epidemiol. 2017;82:128–36. doi: 10.1016/j.jclinepi.2016.11.016. PMID: 27986610.
18 Wellek S, Blettner M. On the proper use of the crossover design in clinical trials: part 18 of a series on evaluation of scientific publications. Dtsch Arztebl Int. 2012;109:276–81. doi: 10.3238/arztebl.2012.0276. PMID: 22567063. PMCID: PMC3345345.
19 Cohen J. Statistical power analysis for the behavioural sciences, 2nd ed. Hillsdale (NJ): Lawrence Earlbaum; 1988.
20 Joseph R, Sim J, Ogollah R, Lewis M. A systematic review finds variable use of the intention-to-treat principle in musculoskeletal randomized controlled trials with missing data. J Clin Epidemiol. 2015;68:15–24. doi: 10.1016/j.jclinepi.2014.09.002. PMID: 25304501.
21 Westerblad H, Allen DG, Lännergren J. Muscle fatigue: Lactic acid or inorganic phosphate the major cause? News Physiol Sci. 2002;17:17–21. doi: 10.1152/physiologyonline.2002.17.1.17. PMID: 11821531.
22 Pallarés J, Morán Navarro R. Propuesta metodológica para el entrenamiento de la resistencia cardiorrespiratoria. J Sport Heal Res. 2012;4:119–36.
23 Svedahl K, MacIntosh BR. Anaerobic threshold: The concept and methods of measurement. Can J Appl Physiol. 2003;28:299–323. doi: 10.1139/h03-023. PMID: 12825337.
24 Tagliabue P. Blood lactate accumulation in static and dynamic apneas in humans. In: Human Behaviour and limits in underwater environment: Special conference on breath hold diving. Pisa; 2005. [cited 2020 April 30]. p. 113. Available from: http://apnea.cz/media/products/BLUE_2005_ABSTRACTS.pdf.
25 Schagatay E. Predicting performance in competitive apnea diving, part II: Dynamic apnoea. Diving Hyperb Med. 2010;40:11–22. PMID: 23111834.
26 Brown PI, Sharpe GR, Johnson MA. Loading of trained inspiratory muscles speeds lactate recovery kinetics. Med Sci Sports Exerc. 2010;42:1103–12. doi: 10.1249/MSS.0b013e3181c658ac. PMID: 19997028.
27 Juel C, Klarskov C, Nielsen JJ, Krustrup P, Mohr M, Bangsbo J. Effect of high-intensity intermittent training on lactate and H+ release from human skeletal muscle. Am J Physiol Endocrinol Metab. 2004;286:E245–51. doi: 10.1152/ajpendo.00303.2003. PMID: 14559724.
28 Schagatay E. Predicting performance in competitive apnoea diving. Part I: static apnoea. Diving Hyperb Med. 2009;39:88–99. PMID: 22753202.
29 Whittaker LA, Irvin CG. Going to extremes of lung volume. J Appl Physiol (1985). 2007;102:831–3. doi: 10.1152/japplphysiol.01329.2006. PMID: 17138830.
30 Vašíčková J, Neumannová K, Svozil Z. The effect of respiratory muscle training on fin-swimmers' performance. J Sport Sci Med. 2017;16:521–6. PMID: 29238252. PMCID: PMC5721182.
31 Karsten M, Ribeiro GS, Esquivel MS, Matte DL. The effects of inspiratory muscle training with linear workload devices on the sports performance and cardiopulmonary function of athletes: A systematic review and meta-analysis. Phys Ther Sport. 2018;34:92–104. doi: 10.1016/j.ptsp.2018.09.004. PMID: 30261349.
32 HajGhanbari B, Yamabayashi C, Buna TR, Coelho JD, Freedman KD, Morton TA, et al. Effects of respiratory muscle training on performance in athletes: A systematic review with meta-analyses. J Strength Cond Res. 2013;27:1643–63. doi: 10.1519/JSC.0b013e318269f73f. PMID: 22836606.
33 Henke KG, Sharratt M, Pegelow D, Dempsey JA. Regulation of end-expiratory lung volume during exercise. J Appl Physiol. 1988;64:135–46. doi: 10.1152/jappl.1988.64.1.135. PMID: 3356631.
34 Dunham C, Harms CA. Effects of high-intensity interval training on pulmonary function. Eur J Appl Physiol. 2012;112:3061–8. doi: 10.1007/s00421-011-2285-5. PMID: 22194005.
35 Wood EH. Normal oxygen saturation of arterial blood during inhalation of air and oxygen. J Appl Physiol. 1949;1:567–74. doi: 10.1152/jappl.1949.1.8.567. PMID: 18111529.

Acknowledgements

We thank all the participating breath-hold divers for their contributions and Club Apnea Barcelona, Club Apnea Zaragoza and Apnea Madrid for their assistance.

Conflicts of interest and funding: nil

Submitted: 09 May 2020
Accepted after revision: 04 August 2020

Acute spontaneous spinal cord infarction: Utilisation of hyperbaric oxygen treatment, cerebrospinal fluid drainage and pentoxifylline

Catherine Ashton[1], Neil Banham[2], Merrilee Needham[1,3,4,5]

[1] *Neurology Department, Fiona Stanley Hospital, Murdoch, Australia*
[2] *Department of Hyperbaric Medicine, Fiona Stanley Hospital, Murdoch, Australia*
[3] *Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, Australia*
[4] *Perron Institute for Neurological and Translational Science, Nedlands, Australia*
[5] *University of Notre Dame, Fremantle, Australia*

Corresponding author: *Dr Catherine Ashton, Neurology Department, Fiona Stanley Hospital, 11 Robin Warren Drive, Murdoch, WA 6150, Australia*
catherine.ashton@health.wa.gov.au

Key words
Central nervous system; Hyperbaric oxygen treatment; Infarction; Outcome; Spinal cord; Stroke; Treatment

Abstract
(Ashton C, Banham N, Needham M. Acute spontaneous spinal cord infarction: Utilisation of hyperbaric oxygen treatment, cerebrospinal fluid drainage and pentoxifylline. Diving and Hyperbaric Medicine. 2020 December 20;50(4):325–331. doi: 10.28920/dhm50.4.325-331. PMID: 33325011.)

Introduction: Spinal cord infarction (SCI) is a potentially devastating disorder presenting with an acute anterior spinal artery syndrome, accounting for an estimated 1% of stroke presentations. Aetiologies include aortic surgical complications, systemic hypotension, fibrocartilaginous embolism and vascular malformations. Diagnosis is clinical combined with restriction on diffusion-weighted magnetic resonance imaging (MRI). There are no treatment guidelines for non-perioperative cases although there is limited literature regarding potential therapies, including hyperbaric oxygen treatment (HBOT) and cerebrospinal fluid (CSF) drainage. We describe 13 cases of acute SCI, five receiving HBOT, and three also receiving pentoxifylline and drainage of lumbar CSF.

Methods: Data for all patients with MRI-proven SCI at Fiona Stanley Hospital from 2014–2019 were reviewed.

Results: Thirteen patients, median age 57 years (31–74), 54% female, were identified. Aetiologies: two fibrocartilaginous emboli; seven likely atherosclerotic; two thromboembolic; two cryptogenic. All presented with flaccid paraplegia except one with Brown-Sequard syndrome. Levels ranged from C4 to T11. Five patients received HBOT within a median time of 40 hours from symptom onset, with an average 15 treatments (10–20). Three of these received triple therapy (HBOT, pentoxifylline, CSF drainage) and had median Medical Research Council manual muscle testing power of 5, median modified Rankin Score (mRS) of 1 and American Spinal Injury Association (ASIA) score of D on discharge, compared with 2 power, mRS 3.5 and ASIA B in those who did not.

Conclusions: SCI can be severely disabling. Triple therapy with pentoxifylline, CSF drainage and HBOT may reduce disability and further prospective trials are required.

Introduction

Spinal cord infarction (SCI) is a rare but potentially devastating disorder accounting for an estimated 1% of all stroke presentations.[1] The typical clinical presentation is that of an anterior spinal artery syndrome with acute flaccid paraparesis or quadriparesis, loss of pain and temperature sensation below the level of the lesion and autonomic dysfunction of the bladder and bowel, developing over minutes to hours. There is a broad array of potential aetiologies, with the most common being the peri-operative complication of thoraco-abdominal aortic aneurysm repair. Other causes can be divided into: intrinsic arterial occlusion (secondary to embolism, thrombosis, atherosclerosis), systemic hypo-perfusion, and venous infarction (usually due to arteriovenous malformations). Fibrocartilaginous embolism (FCE) from herniated intervertebral discs is an increasingly recognised cause of embolic spinal cord infarction, although likely under-diagnosed.[2–4] The diagnosis is made clinically, supported by diffusion-weighted magnetic resonance imaging (DW-MRI). Conventional MRI sequences are often not sufficiently sensitive in the acute phase.[5]

Treatment guidelines are available for iatrogenic cases associated with aortic aneurysm repair, and revolve around improving spinal cord perfusion via a combination of blood pressure support and lumbar drainage of cerebrospinal fluid (CSF), but there are no similar treatment guidelines for spontaneous acute spinal cord infarction.[6–8] Animal models mimicking post-operative SCIs have shown neuro-protective effects from various medications, including pentoxifylline, corticosteroids, mannitol and iloprost, although clinical data have not proven their effectiveness.[9–11] Hyperbaric oxygen

treatment (HBOT) has also shown promise in animal models, but there is a paucity of high level evidence to support its use, despite multiple case reports of good outcomes when used in the post-operative infarction population.[10,12,13]

This case series describes 13 cases of spontaneous acute spinal cord infarction at Fiona Stanley Hospital (FSH), five of whom received HBOT, of which three also received pentoxifylline and drainage of lumbar CSF.

Methods

This retrospective audit was approved by the institutional review board of FSH, Murdoch, Western Australia: Quality Activity 33011.

We identified through the hospital database all patients who had been admitted to FSH with a diagnosis of spinal cord infarction from October 2014 to October 2019. Patients with spinal cord infarction secondary to a surgical procedure were excluded as treatment protocols already exist for this cohort. Any patients without DW-MRI evidence of spinal cord infarction were also excluded.

We retrospectively collected data on clinical presentation, treatment and clinical course from the FSH electronic medical record. All clinical details and evaluations were gathered from the notes of the treating neurologists, rehabilitation specialists and physiotherapists. This included demographics and comorbidities, predisposing risk factors including trauma, as well as assessment of neurological deficits on presentation and at discharge using Medical Research Council (MRC) manual muscle testing, the American Spinal Injury Association (ASIA) Score and the modified Rankin Score (mRS). Data regarding investigations performed, treatment received (both pharmacologic and hyperbaric), as well as weeks of rehabilitation required, were also recorded.

Results

A total of 13 patients met the study criteria (see Table 1), with a median age at presentation of 57 years (range 31–74); seven (54%) were female. All but one patient presented with bilateral flaccid lower limb weakness, urinary retention and constipation. One patient presented with a Brown-Sequard syndrome. Eight patients had complete paraplegia with MRC manual muscle testing power of zero out of five (no movement) and ASIA score A, with the remaining patients having incomplete motor deficits of ASIA score C (n = 4) or D (n = 1). Affected spinal cord levels ranged from C4 to T11, with four patients having cervical level involvement.

AETIOLOGY AND RISK FACTORS

Seven patients were thought to have SCI secondary to atherosclerosis. These patients were older with a median age of 68 years (54–74), majority male (n = 5). All had comorbid hypertension and dyslipidaemia, with four also having a previous smoking history. Two patients had type 2 diabetes mellitus and one had a previous internal capsule lacunar stroke.

FCE was the putative aetiology in two patients, with both having performed heavy lifting in the week prior to presentation: Patient 1 had onset of pain and weakness directly after a CrossFit® workout; Patient 2 experienced back pain one week prior to presentation after lifting heavy boxes then had chiropractic manipulation the day before onset of lower limb weakness.

Two patients were considered to have thromboembolic SCIs, with one patient found to have antiphospholipid syndrome on thrombophilia screening, the other patient had a persistent foramen ovale and lower limb deep vein thrombosis, causing paradoxical embolus to the spinal cord.

There were two cases of cryptogenic SCI: one case with negative investigations including transthoracic echocardiogram, 24-h cardiac Holter monitoring, vasculitis and thrombophilia screening; another case with multiple competing aetiologies including FCE from a recent knee meniscal tear or marantic endocarditis with positive anti-nuclear antibodies (20 IU·ml^{-1}) with a homogenous pattern, but no other features suggestive of systemic lupus erythematosus including a negative anti-dsDNA and normal complement levels.

TREATMENT

All patients received standard therapy of initial antiplatelet therapy with 100 mg aspirin and best supportive medical care on the tertiary neurology ward. Four patients also initially received treatment for suspected transverse myelitis with intravenous methylprednisolone without effect. Five patients received HBOT, all commencing within 48 h of symptom onset (mean 32 h, range 10–48) and continuing daily until a plateau in improvement was reached (defined as no further clinical improvement over 48 h): median 15 treatments (range 12–20). All patients were treated initially at 284 kPa (2.8 atmospheres absolute [atm abs]) for at least two treatments then at 243 kPa (2.4 atm abs) or 203 kPa (2 atm abs). Three of these five patients received a 'triple therapy' combination of HBOT, pentoxifylline 400 mg three times per day for five days, and CSF lumbar drainage either from a lumbar spinal drain (n = 1) or recurrent lumbar punctures, draining 20–40 ml of CSF twice (n = 2). Triple therapy was initiated in tandem, as soon as possible, with the initial lumbar punctures performed prior to HBOT.

OUTCOMES

All but one patient undertook a period of inpatient rehabilitation, requiring a median time of 7.5 weeks (range 0–15) to achieve a median mRS of 2 (range 0–5). MRC muscle power grade on discharge from rehabilitation ranged

from 0 to 5 (median 4-). An ASIA score of A (complete motor and sensory deficit) was given in five patients, while six patients had a score of D. The patient who did not receive rehabilitation chose to return to their country of origin after acute therapy was completed and was lost to follow-up.

Patients who recovered to a state of independence (n = 7), defined as an mRS ≤ 2 were more likely to be of younger age (median 46 y, range 31–69), female (five, 71%) and have an aetiology other than atherosclerosis (two FCE, one thromboembolism, two cryptogenic, two atherosclerosis). This group of patients required a median rehabilitation time of three weeks (range 0–14) to achieve a median mRS of 2 (range 0–2) and ASIA D score.

Recipients of HBOT required a median of 3.5 (0–14) weeks rehabilitation to achieve a median mRS of 2 (0–4) and ASIA scores of A (n = 1), D (n = 3) and E (n = 1) on discharge. The patient with the ASIA A score had a SCI secondary to atherosclerosis and was comparatively older at 56 y, compared with a median age of 35 y (31–46) in the remaining four patients.

The patients who received triple therapy appeared to have better outcomes on discharge with a median mRS score of 1 (0–2) and median MRC muscle power of 5- (4+ to 5). These patients were younger (mean age 35, 35–46 y) and had ASIA scores of A (n = 1) and C (n = 2) on presentation (see Table 1 and Figure 1).

Discussion

We present a retrospective case series of spontaneous acute SCI, detailing our experience in treating this relatively uncommon and potentially devastating disorder. The majority of previous cohorts and case studies have included SCI resulting from surgical complications. We excluded these patients from our study to focus on medical presentations, where there are currently no accepted treatment protocols. In this cohort of patients, the initial diagnosis of SCI is not always clear from that of transverse myelitis or other causes of acute flaccid paraparesis, in some part explaining the delay to treatment initiation and why four of the 13 patients also received initial therapy with methylprednisolone.

The cohort was comprised mainly of SCIs associated with vascular risk factors, thought to be secondary to atherosclerosis, consistent with previous reports.[14,15] Interestingly, two out of the 13 cases were of FCE, in keeping with recent evidence that this is an increasingly recognised cause of SCI.[2] In the age of CrossFit® and the rising popularity of heavy weightlifting exercises, it is important for clinicians to be cognisant of the potential for FCE to cause spinal cord ischaemia, as in our patient who performed a CrossFit® workout immediately prior to developing a C6 complete paraplegia.

Post-operative SCI as a complication of aortic surgery has a standardised treatment protocol involving vasopressor support of blood pressure and CSF lumbar drainage to maintain spinal cord perfusion.[6,16] In the present cohort we describe three patients who had excellent outcomes following a combination of recurrent CSF drainage (with a lumbar drain or recurrent high-volume lumbar punctures), pentoxifylline and HBOT; a combination we have named 'triple therapy' for the purposes of this article. This combination is based on case reports showing improved outcomes with HBOT in post-operative SCI, as well as animal models of spinal cord ischaemia showing potential benefit of pentoxifylline, combined with the accepted benefit of CSF drainage in acute post-operative spinal cord infarction. These patients were of younger age and with SCIs of varying aetiologies: FCE, thromboembolism and cryptogenic, and their excellent outcomes returning to independent ambulation and ASIA score D-E emphasises the need for further investigation of this treatment combination in prospective studies.

HBOT is another prospective treatment, used in five of our patients, after multiple case reports have suggested benefit in the mostly post-operative SCI population where treatment can be initiated as soon as symptoms are recognised.[10,12,13] Selecting patients with medical or spontaneous SCI for HBOT provides further challenges as the diagnosis must be suspected on presentation and then access to HBOT must be established. In Western Australia, our centre acts as the sole quaternary referral centre for HBOT, with hyperbaric physicians providing a 24/7 service. Despite this, in these five patients, there was still a median time delay between symptom onset and HBOT initiation of 31 hours (range 10–48), related to delayed diagnosis and referral. Patients were continued on daily HBOT until a plateau of clinical neurological recovery was reached. This treatment protocol is based on the treatment protocols for spinal decompression illness and other acute ischaemic conditions treated with

Figure 1

Patient Subgroup Outcomes. Post-treatment median Medical Research Council (MRC) manual muscle testing power, modified Rankin score, and ASIA scores, across the three subgroups of patients that received HBOT plus standard care, Triple Therapy (of HBOT, CSF drainage and pentoxifylline), or standard care alone. The corresponding numerical ASIA scores are as follows: 1 = A, 2 = B, 3 = C, 4 = D, 5 = E

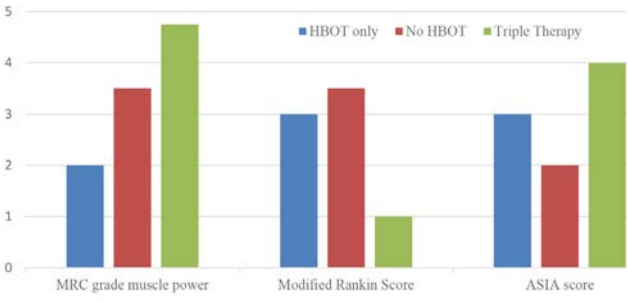


Table 1

Cohort data. HBOT (hyperbaric oxygen treatment) is listed as number of treatments at each pressure, as well as the total time of pressurised treatment in minutes. Patient one completed one 90 min and four 60 min treatments at 284 kPa and twelve 60 min treatments at 243 kPa, for a total duration at pressure of 3,516 minutes. Patient two: two 60 min treatments at 284 kPa and eight 90 min treatments at 243 kPA. Patient three: five 60 min treatments at 284 kPa and fifteen 120 min treatments at 202 kPa. Patient four: One 120 min and twelve 60 min treatments at 284 kPa and three 90 min treatments at 243 kPa. Patient five: three 90 min and five 60 min treatments at 284 kPa and four 90 min treatments at 243 kPa. ANA = anti-nuclear antibodies, ASIA = American Spinal Injury Association score (A = complete motor and sensory deficit, E = normal), bd = twice daily, C = cervical, DVT = deep vein thrombosis, dsDNA = double-stranded deoxyribonucleic acid antibodies, ENA = extractable nuclear antibodies, FCE = fibrocartilaginous embolism. MRC = Medical Research Council manual muscle testing power (out of 5), mRS = modified Rankin Score (out of 6, 0 = no symptoms, 2 = independent, 4 = unable to ambulate independently, 5 = bedridden), T = thoracic

Patient	Age/ Sex	Risk factors	Aetiology of infarct	Spinal level	ASIA on admission	MRC power on admission	Significant results	Treatment	HBOT treatments (total duration)	HBOT: Time delay (hours)	MRC power post-rehabilitation	Duration of rehab (weeks)	mRS on discharge	ASIA on discharge
1	35F	Nil	Thrombo-embolic	C4	A	0	Anti-cardiolipin antibody positive, low C3 and C4	Methyl-prednisolone, aspirin, pentoxifylline, inotropic support to mean arterial pressure > 70, 2 x 40 ml lumbar punctures, anticoagulation from day 14	284 kPa x 5 + 243 kPa x12 (3516 min)	10	4+	6	2	D
2	46F	Knee meniscal tear	Cryptogenic	T3	C	3	ANA strong positive, ENA and dsDNA negative. Marantic endocarditis seen on echocardiogram	Aspirin, pentoxifylline, lumbar drain	284 kPa x 2 + 243 kPa x 8 (2064 min)	40	5-	8	1	D
3	35M	Heavy lifting one week previous, smoker	FCE	T8	C	2		Methyl-prednisolone, aspirin, pentoxifylline, 2 x 20ml lumbar punctures	284 kPa x 5 + 202 kPa x 15 (5280 min)	48	5	0	0	E
4	31F	CrossFit® workout	FCE	C6	A	0	Heterozygous for prothrombin G201210A gene mutation	Aspirin	284 kPa x 13 + 243 kPa x 3 66 (3000 min)	48	1+	14	2	D

Table 1 continued.

5	57M	Hypertension, dyslipidaemia, obesity, obstructive sleep apnoea	Athero-embolic	T1	A	0		Methyl-prednisolone, aspirin	284 kPa x 8 + 243 kPa x 4 (1620 min)	14	2+	12	4	A
6	54M	Previous stroke, dyslipidaemia, insulin resistance	Athero-embolic	T6	C	2.5	Persistent foramen ovale on echocardiogram	Aspirin	0	n/a	3+	15	3	C
7	56M	Dyslipidaemia	Thrombo-embolic	T4	A	0	Persistent foramen ovale on echocardiogram, lower limb DVT	Aspirin, enoxaparin 70 mg bd	0	n/a	0	12	5	A
8	69M	Hypertension, dyslipidaemia, ex-smoker	Athero-embolic	T2	C	3	Heterozygous factor V Leiden, positive cardiolipin IgM, infero-basal hypokinesis on echocardiogram	Aspirin	0	n/a	4+	2.5	1	D
9	76M	Hypertension, dyslipidaemia, T2DM, ex-smoker	Thrombo-embolic	T6	A	0	Atrial fibrillation on cardiac monitoring	Aspirin	0	n/a	0	7	5	A
10	68F	Hypertension, hormone replacement therapy, dyslipidaemia, ex-smoker	Athero-embolic	C5	A	0		Aspirin	0	n/a	4	3	2	D
11	69F	Hypertension, dyslipidaemia, family history of ischaemic heart disease	Athero-embolic	T9	A	0		Aspirin	0	n/a	n/a	n/a	4	A
12	64M	Obesity, hypertension	Athero-embolic	C5	A	0		Aspirin	0	n/a	2	12	4	A
13	61F	Nil	Cryptogenic	T7	D	4		Methyl-prednisolone, aspirin	0	n/a	4	2	2	D

HBOT. Unlike typical post-operative SCI cases, there was a potentially significant delay in treatment initiation in these patients. HBOT is purported to reduce ischaemia by inducing arterial vasoconstriction, thereby reducing tissue oedema whilst maintaining tissue oxygenation and by anti-inflammatory mechanisms reducing ischaemia-reperfusion injury.[17] The potential benefit is seen in preventing secondary neuronal injury and therefore, the earlier the initiation of HBOT, the greater the potential benefit.

Similar antioxidant properties reducing secondary neuronal injury are theorised to be associated with pentoxifylline therapy: improving microcirculation by decreasing blood viscosity and increasing erythrocyte flexibility, while also reducing neutrophil activation and adhesion to reduce ischaemia-reperfusion injury.[11,18] There are no clinical data confirming its effectiveness in patients with acute spontaneous SCI.

As a case series, subgroup analysis is not possible and it is important not to over-interpret the results, but there appears to be a trend towards better outcomes in patients who received 'triple therapy'. We propose that further prospective studies explore this new treatment protocol, particularly that of CSF drainage and HBOT, both of which have case report level data to support use in SCI. It is important to acknowledge that this may not be feasible due to limited access to HBOT at other centres; and that, as per the guidelines written by The International Campaign for Cures of Spinal Cord Injury Paralysis (ICCP) panel in 2007, such studies would require a very large sample size to accurately assess the significance of triple therapy in improving functional outcomes in spontaneous SCI.[19]

Conclusions

Spontaneous SCI can be severely disabling and recovery is often incomplete. Aetiologies across this group are heterogeneous, and fibro-cartilaginous embolism is likely an under-recognised cause. 'Triple therapy' of CSF drainage, HBOT and pentoxifylline may be a promising new treatment protocol for spontaneous SCI and should be prospectively investigated.

References

1 Kramer CL. Vascular disorders of the spinal cord. Continuum (Minneap Minn). 2018;24:407–26. doi: 10.1212/CON.0000000000000595. PMID: 29613893.

2 AbdelRazek MA, Mowla A, Farooq S, Silvestri N, Sawyer R, Wolfe G. Fibrocartilaginous embolism: A comprehensive review of an under-studied cause of spinal cord infarction and proposed diagnostic criteria. J Spinal Cord Med. 2016;39:146–54. doi: 10.1080/10790268.2015.1116726. PMID: 26833287. PMCID: PMC5072491.

3 Mateen FJ, Monrad PA, Leep Hunderfund AN, Robertson CE, Sorenson EJ. Clinically suspected fibrocartilaginous embolism: Clinical characteristics, treatments, and outcomes. Eur J Neurol. 2011;18:218–25. doi: 10.1111/j.1468-1331.2010.03200.x. PMID: 20825469.

4 Nasr DM, Rabinstein A. Spinal cord infarcts: risk factors, management, and prognosis. Curr Treat Options Neurol. 2017;19:28. doi: 10.1007/s11940-017-0464-3. PMID: 28688063.

5 Yadav N, Pendharkar H, Kulkarni GB. Spinal cord infarction: clinical and radiological features. J Stroke Cerebrovasc Dis. 2018;27:2810–21. doi: 10.1016/j.jstrokecerebrovasdis.2018.06.008. PMID: 30093205.

6 Cheung AT, Weiss SJ, McGarvey ML, Stecker MM, Hogan MS, Escherich A, et al. Interventions for reversing delayed-onset postoperative paraplegia after thoracic aortic reconstruction. Ann Thorac Surg. 2002;74:413–9; discussion 420–1. doi: 10.1016/s0003-4975(02)03714-1. PMID: 12173822.

7 McGarvey ML, Mullen MT, Woo EY, Bavaria JE, Augoustides YG, Messé SR, et al. The treatment of spinal cord ischemia following thoracic endovascular aortic repair. Neurocrit Care. 2007;6:35–9. doi: 10.1385/NCC:6:1:35. PMID: 17356189.

8 Shimura S, Cho Y, Aki A, Ueda T. Successful reversal of immediate paraplegia associated with repair of acute Type A aortic dissection using cerebrospinal fluid drainage. Interact Cardiovasc Thorac Surg. 2013;17:1051–3. doi: 10.1093/icvts/ivt389. PMID: 24014618. PMCID: PMC3829504.

9 Wynn MM, Acher CW. A modern theory of spinal cord ischemia/injury in thoracoabdominal aortic surgery and its implications for prevention of paralysis. J Cardiothorac Vasc Anesth. 2014;28:1088–99. doi: 10.1053/j.jvca.2013.12.015. PMID: 25107722.

10 Ilhan G, Aksun M, Ozpak B, Gunes T, Bozok S, Durakoglugil ME, et al. The effect of combined hyperbaric oxygen and iloprost treatment on the prevention of spinal cord ischaemia–reperfusion injury: an experimental study. Eur J Cardiothorac Surg. 2013;44:e332–40. doi: 10.1093/ejcts/ezt398. PMID: 23946499.

11 Savaş S, Delibaş N, Savaş C, Sütçü R, Cindaş A. Pentoxifylline reduces biochemical markers of ischemia-reperfusion induced spinal cord injury in rabbits. Spinal Cord. 2002;40:224–9. doi: 10.1038/sj.sc.3101281. PMID: 11987004.

12 Parotto M, Ouzounian M, Fedorko L, Oreopoulos G, Lindsay T, Katznelson R. Hyperbaric oxygen therapy for spinal cord ischaemia after complex aortic repair – a retrospective review. Anaesthesiol Intensive Ther. 2018;50:103–9. doi: 10.5603/AIT.a2018.0010. PMID: 29882580.

13 Lee K, Strozyk D, Rahman C, Lee LK, Fernandes EM, Claassen J, et al. Acute spinal cord ischemia: Treatment with intravenous and intra-arterial thrombolysis, hyperbaric oxygen and hypothermia. Cerebrovasc Dis. 2010;29:95–8. doi: 10.1159/000259618. PMID: 19923816.

14 Salvador de la Barrera S, Barca-Buyo A, Montoto-Marqués A, Ferreiro-Velasco M, Cidoncha-Dans M, Rodriguez-Sotillo A. Spinal cord infarction: prognosis and recovery in a series of 36 patients. Spinal Cord. 2001;39:520–5. doi: 10.1038/sj.sc.3101201. PMID: 11641795.

15 Rigney L, Cappelen-Smith C, Sebire D, Beran RG, Cordato D. Nontraumatic spinal cord ischaemic syndrome. J Clin Neurosci. 2015;22:1544–9. doi: 10.1016/j.jocn.2015.03.037. PMID: 26154150.

16 McGarvey ML, Cheung AT, Szeto W, Messe SR. Management of neurologic complications of thoracic aortic surgery. J Clin Neurophysiol. 2007;24:336–43. doi: 10.1097/WNP.0b013e31811ec0b0. PMID: 17938602.

17 Thom SR. Hyperbaric oxygen: Its mechanisms and efficacy.

Plast Reconstr Surg. 2011;127(Suppl 1):131S–141S. doi: 10.1097/PRS.0b013e3181fbe2bf. PMID: 21200283. PMCID: PMC3058327.

18 Türköz A, Türköz R, Yörükoğlu K, Onat U, Sağýroğlu E, Sağban M. Evaluation of pentoxifylline in experimental spinal cord ischemia. Eur J Cardiothorac Surg. 1997;12:648–53. doi: 10.1016/s1010-7940(97)00115-2. PMID: 9370412.

19 Fawcett JW, Curt A, Steeves JD, Coleman WP, Tuszynski MH, Lammertse D, et al. Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: Spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. Spinal Cord. 2007;45:190–205. doi: 10.1038/sj.sc.3102007. PMID: 17179973.

Conflicts of interest and funding: nil

Submitted: 15 May 2020
Accepted after revision: 09 August 2020

Reduction of bacterial load with the addition of ultraviolet-C disinfection inside the hyperbaric chamber

Katrina Browne[1], Danielle Wood[2], Kate Clezy[3], Jan Lehm[2], William R Walsh[1]

[1] *Surgical and Orthopaedic Research Laboratory, University of New South Wales, Prince of Wales Hospital, Sydney, Australia*
[2] *Hyperbaric Medicine Unit, Prince of Wales Hospital, Sydney, Australia*
[3] *Infectious Diseases Department, Prince of Wales Hospital, Sydney Australia*

Corresponding author: *Dr Danielle Wood, Hyperbaric Medicine Unit, Prince of Wales Hospital, Nurses Dr, Randwick, NSW 2031, Australia*
danspace@gmail.com

Key words
Hyperbaric research; Hyperbaric facilities; Infectious disease; Bacteriology; Fire; Surveillance; Infection prevention

Abstract
(Browne K, Wood D, Clezy K, Lehm J, Walsh WR. Reduction of bacterial load with the addition of ultraviolet-C disinfection inside the hyperbaric chamber. Diving and Hyperbaric Medicine. 2020 December 20;50(4):332–337. doi: 10.28920/dhm50.4.332-337. PMID: 33325012.)
Introduction: Healthcare acquired infections (HAIs) are associated with increased mortality, morbidity and prolonged hospital stays. Microbiological contamination of the hospital environment directly contributes to HAIs. Optimising environmental cleaning reduces transmission of HAIs. The hyperbaric chamber poses a specific challenge for infection control as certain disinfectants and alcohol-based hand sanitisers are prohibited due to fire risk. Patients often possess multiple risk factors for HAIs. This study compared the bacteria remaining on a surface (bioburden) after a standard clean and after adjunctive disinfection with an ultraviolet-C (UV-C) robot.
Methods: Internal hyperbaric chamber surfaces were first manually cleaned with Clinell® universal wipes and the floor was mopped with Whiteley neutral detergent. Allocated surfaces were swabbed using sterile cotton swabs and processed using a standard microbial culture and a bacteria-specific rapid metabolic assay. Bacterial contamination was also measured by direct contact plating on flat surfaces. The plexiglass ports were covered to protect from potential UV-C mediated damage and used as a negative control. A UV-C disinfection robot was then used to disinfect the chamber for 30 min, whereafter surfaces were swabbed again.
Results: There was a significantly greater mean reduction in bioburden following adjunctive UV-C disinfection than with standard cleaning alone. The surfaces not routinely manually cleaned (e.g., bench, phone) showed greatest reduction in bacterial load following UV-C cleaning.
Conclusions: There was a significant reduction in the bacterial load in the chamber following an adjunctive UV-C clean compared with that of a standard clean. Adjunctive cleaning of the hyperbaric chamber environment with a non-touch UV-C device shows promise as a method to reduce HAIs.

Introduction

Healthcare-associated infections (HAIs) are an ongoing concern in hospital settings and are a well-recognised contributor to morbidity, mortality and hospital length of stay.[1] Environmental contamination (bacteria remaining on surfaces and equipment following patient use) has been shown to directly contribute to the transmission of HAIs.[2,3] Consequently, enhanced environmental cleaning has shown to be an effective strategy to reduce the transmission of infectious pathogens in hospital settings, especially that of multidrug-resistant organisms.[4–6]

The hyperbaric unit presents a specific challenge when it comes to infection control as alcohol and other potentially flammable cleaning products and hand sanitisers are prohibited in the chamber and its surrounds. Whilst we found only one record of an adverse event related to alcohol-based hand sanitiser use in the chamber,[7] strict adherence to guidelines from the National Fire Prevention Association and other similar bodies, prevents the use of flammable materials in the chamber.

There are no published studies monitoring infection rates in hyperbaric units. Routine screening of patients for multidrug-resistant organisms (MDROs) is not standard practice in most units, despite high turnover and the patient cohort often possessing at least one risk factor for infection.[8] These include, but are not limited to, frequent hospitalisations, intensive care stays, prior antibiotic treatment, chronic non-healing wounds and having invasive medical devices.[8]

An under appreciated route of disease transmission is the contamination of medical equipment and/or the healthcare

environment.[9] In all units there are environmental reservoirs of pathogens that remain viable.[10] Contact with the contaminated environment by healthcare workers or patients may result in the transmission of these pathogens throughout the healthcare facility.[11] While hand hygiene is currently the most effective measure to prevent cross-transmission of infectious pathogens, compliance is extremely low and only transiently effective.[12] Alcohol-based hand rubs have shown to improve compliance rates;[12] however, these products are prohibited in hyperbaric units due to the fire risk.

Previous studies have demonstrated that enhanced environmental cleaning protocols resulted in lower overall contamination;[13–15] and that a decreased bioburden resulted in reduced infection rates.[4,16,17] Therefore, it is essential to consider enhanced environmental cleaning to prevent the transmission of HAIs in the hyperbaric medicine unit.

Ultraviolet-C (UV-C) is a high-energy, low-wavelength form of light that has germicidal properties.[18] It is absorbed by nucleic acids in microorganisms, resulting in irreversible cell damage, and rapid cell death. UV-C can effectively kill a broad range of pathogens, including viruses, fungi, moulds, multi-drug resistant bacteria (methicillin-resistant *Staphylococcus aureus*) and bacterial spores (*Clostridium difficile*).[18] UV-C has been utilised for its germicidal properties for decades, particularly for food and beverage processing, as well as air, water and surface disinfection.[18] More recently, UV-C technologies have been developed to disinfect the clinical environment.

It is in this setting that we chose to compare cleaning protocols by looking at the environmental bioburden (bacterial load on surfaces) following a standard clean with Clinell® universal wipes and Whiteley neutral detergent surface cleaner, to that following additional treatment with an automated UV-C disinfection robot. This study aimed to assess the efficacy of an automated UV-C disinfection robot to reduce the environmental bioburden in the hyperbaric chamber beyond that achieved with a standard clean.

Methods

The study was conducted in the routine patient treatment compartment of a large multiplace hyperbaric chamber after a single busy treatment day.

ROUTINE CLEANING

The compartment was cleaned at the end of a treatment day. Visually soiled surfaces and patient chairs were cleaned with Clinell® universal wipes (benzalkonium chloride 0.45%, didecyl dimethyl ammonium chloride 0.4% and polyhexamethylene biguanide 0.1%). Additionally, the floor was mopped with Whiteley neutral detergent (ethoxylated nonylphenol and dipentene) surface cleaner.

UV-C DISINFECTION

An automated UV-C disinfection robot (ThorUVC®, Finsen Tech, London, UK) was used as an adjunct cleaning method in the chamber. Following routine chamber cleaning, the UV-C robot was placed in the centre of the room and operated remotely with an accompanying tablet. As UV-C is potentially damaging to acrylic surfaces, the plexiglass ports in the chamber were covered prior to activation of the robot. At 254 nm, UV-C light cannot penetrate past the superficial surface layer of materials, thus the plexiglass ports were adequately protected with thin rubber covers. Once activated, the robot extended up to 2.25 m (depending on ceiling height) and conducted a 3-dimensional room scan to detect parameters such as room size and surface area. Large objects that created shadows were depicted in the room scan generated. Once the disinfection cycle was initiated, UV-C light (254 nm) was used to irradiate the chamber for a treatment time of 30 min. This treatment time was calculated automatically using an algorithm based on the inverse square law: that disinfection time is inversely proportional to the square of the distance from the UV-C source.

SAMPLE COLLECTION

Samples from ten surfaces, nine of which could be regarded as high-touch clinical surfaces (the exception being the acrylic port) inside the chamber were taken at three times: prior to routine cleaning, post-routine cleaning and post-UV-C treatment. All equipment, including patient chairs, were kept in the chamber during disinfection. The designated surfaces, each with an approximate area of 10 cm x 10 cm (100 cm^2), were swabbed. If the clinical surface was less than 100 cm^2, the entire surface was swabbed (e.g., door handle). Surfaces were uniformly swabbed to avoid collection error. Swabs were then immersed in 500 µL sterile collection fluid.

In addition to surface swabbing, five of the ten clinical surfaces were suitable for direct-contact plating (flat sample surface). RODAC-style plates (surface area 21.5 cm^2) were prepared using enough trypticase-soy agar (TSA) to achieve a convex meniscus. Plates were then air-dried for 1 h and exposed to UV-C light for 10 min. Plates were then covered and stored at 4°C until required. Direct-contact plates were pressed against clinical surfaces with a uniform downward pressure to ensure the whole agar surface contacted the clinical surface.

BACTERIAL MEASUREMENTS

Conventional microbial culture

A 450 µL aliquot of each sample fluid was inoculated onto a TSA plate and aerobically cultured at 37°C. Viable bacterial colonies were enumerated after 24 h and recorded as colony forming units (CFU). If individual colonies could not be distinguished (entire surface area covered) the CFU

was recorded as 100 (100%). Quality control plates were included to ensure no bacterial contamination prior to surface inoculation. The acrylic port in the chamber was used as an additional negative control as it was covered and hence not exposed to UV-C light, or cleaning chemicals.

Bacteria-specific rapid metabolic assay

A 50 µL aliquot of sample fluid was processed through a bacteria-specific, rapid metabolic assay (BSRMA) (Profile 1, Q Biotechnologies, London, UK). This assay was used as a 'real-time' test to assess the bacterial contamination of surfaces. The assay was performed according to manufacturer's instructions. Briefly, the sample fluid was filtered (0.45 µm) to remove somatic cells and non-bacterial adenosine triphosphate (ATP). Bacterial cells were then lysed to release ATP and combined with 50 µL luciferin/luciferase to initiate an ATP-dependent, light-producing reaction. This reaction was quantified with a luminometer and the output was recorded in relative light units (RLU). The amount of fluorescence detected by the luminometer is proportional to the number of viable bacteria present, where 1 RLU is proportional a single bacterium in the sample.[19]

Direct contact plating

The plates obtained using direct contact plating were covered and aerobically incubated at 37°C. CFUs were enumerated following 24 h incubation.

Results

Conventional microbiological culture data show that prior to manual cleaning, all nine high touch surface samples were positive for bacterial growth (Table 1). Following routine cleaning, the mean reduction in bioburden was 47% (SD 61). Following an additional UV-C disinfection, the mean reduction in bioburden was 62%. Statistical analysis, using a Wilcoxon signed rank test with continuity correction, demonstrates there was a significant difference between post-clean and post-UV-C bioburdens ($P = 0.049$). No change was seen in the acrylic port negative control.

Similarly, the BSRMA data shows that prior to routine cleaning, all nine surfaces were positive for bacterial growth. Following routine cleaning, the mean reduction in bioburden was 42% (SD 36). Following an additional UV-C disinfection, the mean reduction in bioburden was 92% (SD 9). Statistical analysis, using a Wilcoxon signed rank test with continuity correction, demonstrates there was a significant difference between post-clean and post-UV-C bioburdens ($P = 0.001$). No significant difference was seen in the acrylic port negative control.

Again, direct-contact plate sampling demonstrated that prior to routine cleaning, all five suitable surfaces were positive for bacterial growth. Following routine cleaning, the mean reduction in bioburden was 47% (SD 43). Following an additional UV-C disinfection, the mean reduction in bioburden was 95% (SD 11). Statistical analysis, using a Wilcoxon signed rank test with continuity correction, demonstrates there was a significant difference between post-clean and post-UV-C bioburdens ($P = 0.001$).

Discussion

This study assessed the ability of a UV-C disinfection robot to decrease the bioburden of clinical surfaces in the multiplace hyperbaric chamber. Following routine manual cleaning, viable bacteria were detected on all surfaces (Tables 1–3). Adjunctive UV-C disinfection significantly reduced this bioburden. Additionally, we compared three

Table 1

Conventional microbiological cultures. The bioburden (colony forming units) on clinical surfaces is reduced when exposed to UV-C treatment, compared to manual room cleaning only*. *P*-value derived from Wilcoxon signed rank test with continuity correction

Clinical Surface	Pre-clean	Post-clean	Post-UVC*
Bench	8	11	1
Chair (arm rest)	100	2	0
Chair (seat)	2	0	0
Door handle	100	1	1
Floor (doorway)	20	3	1
Floor (shadow)	9	13	1
Phone	3	2	3
Station oxygen supply	12	1	0
Tap	1	1	0
Acrylic port (negative control)	2	2	2
P-value		0.049*	

Table 2

Bacteria-specific rapid metabolic assay. The bioburden (relative light units detected by the luminometer, proportional to the number of individual bacteria) on clinical surfaces is reduced when exposed to UV-C treatment, compared to manual room cleaning only*. *P*-value derived from Wilcoxon signed rank test with continuity correction

Surface	Pre-clean	Post-clean	Post-UVC*
Bench	170	192	4
Chair (arm rest)	322	107	3
Chair (seat)	627	214	13
Door handle	333	102	4
Floor (doorway)	93	29	9
Floor (shadow)	61	58	5
Phone	269	240	27
Station oxygen supply	158	130	4
Tap	886	136	7
Acrylic port (negative control)	278	297	354
P-value		0.001*	

Table 3

Direct-contact plating for surface contamination. The bioburden (colony forming units) on clinical surfaces is reduced when exposed to UV-C treatment, compared to manual room cleaning only*. *P*-value derived from Wilcoxon signed rank test with continuity correction

Surface	Pre-clean	Post-clean	Post-UVC*
Chair (arm rest)	4	1	0
Chair (seat)	1	1	0
Door handle	30	4	1
Floor	100	100	0
Phone	4	1	0
P-value		0.001*	

different surface-testing methods to quantify the bioburden. As each testing method varies greatly in its methodology, sensitivity and specificity, the three methods cannot be compared within each other. Instead, we used the post-manual clean and post-UV-C data in each method to assess the efficacy of adjunctive UV-C disinfection. The most sensitive detection method was the BSRMA (Table 2), with an overall mean reduction in bioburden of 92%.

The sensitivity of surface-testing methods is particularly important when considering infectious pathogens with low minimum infectious doses (e.g., *Escherichia coli*). Detectable CFUs ranged between 1–100, whereas RLUs ranged between 3–886. The BSRMA detected viable but non-culturable bacteria on the chair (arm rest and seat), oxygen inlet, tap and phone (Table 2), where bacterial growth on agar was negative. Conventional microbial testing relies on aerobic culture on agar plates, yet the sensitivity of this method is extremely low. Less than 1% of bacteria found in water and soil grow into visibly detectable colonies (CFU) on 2-dimentional surfaces such as agar.[20] Bacteria present in clinical surface samples often have slower metabolic turnover and may require different growth nutrients and/or conditions in order to replicate.[20]

Real-time metabolic testing has shown to be more sensitive and reliable than microbial culture. Due to the evolutionarily conserved ATP production in bacteria, the BSRMA is highly sensitive to the viable but non-culturable bacteria present in the sample. In this study the floor was mopped with a detergent solution and allowed to dry before surface testing. After routine cleaning, direct-contact plates showed 100 CFUs on the floor (Table 3). After UV-C disinfection, no CFUs were detected. While a reduction was still seen using the BSRMA, viable bacteria were still detected. This is why the study included the BSRMA as an additional method, as it is more sensitive to enumerating individual bacteria present in the sample.

One limitation of the BSRMA is that while it is highly sensitive, there is no specificity towards the species of bacteria and microbial culture is required to identify individual pathogens. The agar-cultured samples were only quantitively analysed for bacteria and individual species were not identified. While the characterisation of environmental pathogens is of interest to infection prevention personnel, it is not essential given the aim of this study. It is known that while some MDROs are less sensitive to detergents and disinfectants than their sensitive counterparts,[21] both populations are equally susceptible to UV-C disinfection.[18] The sporicidal setting of the ThorUVC® device calculates treatment time to ensure correct exposure time in order to kill the most persistent pathogens (e.g., *C. difficile* spores).[18]

Unlike other cleaning methods, bacteria are not known to acquire resistance to UV-C light. As UV-C causes molecular lesions in DNA, it is thought that neighbouring bacteria cannot acquire resistance genes via horizontal gene transfer if the genetic material is damaged by UV-C.[22] Further research into the benefit of UV-C disinfection on the reduction of MDRO-related HAIs would provide an excellent case for integration of this technology into the terminal cleaning protocol.

Measuring any reduction in HAI rates and associated costs was beyond the scope of this study. Yet it was clearly demonstrated that standard manual cleaning does not efficiently disinfect all surfaces (door handles, phones, bench tops), and surfaces that were manually cleaned demonstrated large variability in their cleaning efficacy (floors, chairs). There is an inherent limitation with manual cleaning in that not all surfaces may be reached (e.g., ceilings, walls) and other surfaces may simply be missed due to human error or time constraints. Paradoxically, surfaces may become contaminated during the cleaning process.[23] Dirty cleaning cloths, mops and contaminated cleaning chemicals have been shown to cross-contaminate surfaces.[24]

It is important to consider the benefits of automated disinfection technology, compared to enhanced manual cleaning protocols. It is repeatedly presented in the literature that the efficacy of manual cleaning is highly variable. For example, only 50% of high-touch hospital surfaces were appropriately disinfected by cleaning staff.[14] As healthcare facilities are increasingly looking for cost saving measures, the high cost of manual labour is an important consideration. Additionally, it should be acknowledged that adjunct UV-C disinfection resulted in an overall reduction in bioburden, of ~90%, in 30 min. The duration of manual cleaning required to achieve the same result is unknown.

These data do highlight one acknowledged limitation of UV-C disinfection; that shadowed surfaces demonstrate less efficient disinfection than direct line-of-sight surfaces. The lowest reductions were seen on partially shadowed surfaces such as the door handle (Table 1, Table 3) and the phone (Table 1, Table 2). Additionally, this study was conducted in a large rectangular multiplace chamber where the acrylic ports were covered from UV-C light. Given the potential for ultraviolet light to degrade acrylic, we would not recommend UV-C cleaning in monoplace chambers or in chambers where acrylic components could not be covered. In addition, as the 'shadowed' areas are dependent on light reflection, the results would be likely to be different in a cylindrical chamber.

While this study did not directly measure the effect of bioburden reduction on the rate of HAI, several other papers have assessed the clinical impact of enhanced environmental disinfection on HAI. Hayden et al. studied the role of environmental contamination in the cross-transmission of antibiotic-resistant bacteria.[4] They determined that enhanced cleaning resulted in a decreased bioburden, which resulted in reduced acquisition of vancomycin-resistant *Enterococcus*. McMullen et al. showed that enhanced cleaning protocols reduced the *Clostridium difficile* infection rate, which was maintained for two years following the enhanced cleaning regimen.[17] Furthermore, Dancer et al. suggested that employing one extra, full time cleaner had a profound impact on HAI rates.[16] In their study, enhanced cleaning of high-touch areas significantly lowered the overall bioburden and resulted in reduced methicillin-resistant *Staphylococcus aureus* infection rates over a 12-month study.[16]

Conclusions

This study suggests that adjunctive UV-C disinfection technology can significantly reduce the environmental bioburden in the multiplace hyperbaric oxygen chamber. Further studies on the baseline rates of HAI in the hyperbaric unit would be required to understand the clinical relevance of the bioburden reduction, especially with respect to reduction of multidrug-resistant organisms.

References

1 Revelas A. Healthcare-associated infections: A public health problem. Niger Med J. 2012;53:59–64. doi: 10.4103/0300-1652.103543. PMID: 23271847. PMCID: PMC3530249.

2 Cohen B, Liu J, Cohen AR, Larson E. Association between healthcare-associated infection and exposure to hospital roommates and previous bed occupants with the same organism. Infect Control Hosp Epidemiol. 2018;39:541–6. doi: 10.1017/ice.2018.22. PMID: 29486805. PMCID: PMC5935247.

3 Otter JA, Yezli S, Salkeld JAG, French GL. Evidence that contaminated surfaces contribute to the transmission of hospital pathogens and an overview of strategies to address contaminated surfaces in hospital settings. Am J Infect Control. 2013;41(5 Suppl):S6–S11. doi: 10.1016/j.ajic.2012.12.004. PMID: 23622751.

4 Hayden MK, Bonten MJM, Blom DW, Lyle EA, van de Vijver DAMC, Weinstein RA. Reduction in acquisition of vancomycin-resistant enterococcus after enforcement of routine environmental cleaning measures. Clin Infect Dis. 2006;42:1552–60. doi: 10.1086/503845. PMID: 16652312.

5 Weber DJ, Rutala WA, Miller MB, Huslage K, Sickbert-Bennett E. Role of hospital surfaces in the transmission of emerging health care-associated pathogens: Norovirus, Clostridium difficile, and Acinetobacter species. Am J Infect Control. 2010;38:S25–33. doi: 10.1016/j.ajic.2010.04.196. PMID: 20569853.

6 Anderson DJ, Moehring RW, Weber DJ, Lewis SS, Chen LF, Schwab JC, et al. Effectiveness of targeted enhanced terminal room disinfection on hospital-wide acquisition and infection with multidrug-resistant organisms and Clostridium difficile: A secondary analysis of a multicentre cluster randomised controlled trial with crossover design (BETR Disinfection). Lancet Infect Dis. 2018;18:845–53. doi: 10.1016/S1473-3099(18)30278-0. PMID: 29880301. PMCID: PMC6487496.

7 Bryant KA, Pearce J, Stover B. Flash fire associated with the

use of alcohol-based antiseptic agent. Am J Infect Control. 2002;30:256–7. doi: 10.1067/mic.2002.125395. PMID: 12032505.

8 Safdar N, Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobial-resistant Staphylococcus aureus, enterococcus, gram-negative bacilli, Clostridium difficile, and Candida. Annals Intern Med. 2002;136:834–44. doi: 10.7326/0003-4819-136-11-200206040-00013. PMID: 12044132.

9 Boyce JM. Environmental contamination makes an important contribution to hospital infection. J Hosp Infect. 2007;65:50–4. doi: 10.1016/S0195-6701(07)60015-2. PMID: 17540242.

10 Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC Infect Dis. 2006;6:130. doi: 10.1186/1471-2334-6-130. PMID: 16914034. PMCID: PMC1564025.

11 Bhalla A, Pultz NJ, Gries DM, Ray AJ, Eckstein EC, Aron DC, et al. Acquisition of nosocomial pathogens on hands after contact with environmental surfaces near hospitalized patients. Infect Control Hosp Epidemiol. 2004;25(2):164–7. doi: 10.1086/502369. PMID: 14994944.

12 Allegranzi B, Pittet D. Role of hand hygiene in healthcare-associated infection prevention. J Hosp Infect. 2009;73:305–15. doi: 10.1016/j.jhin.2009.04.019. PMID: 19720430.

13 Goodman ER, Platt R, Bass R, Onderdonk AB, Yokoe DS, Huang SS. Impact of an environmental cleaning intervention on the presence of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci on surfaces in intensive care unit rooms. Infect Control Hosp Epidemiol. 2008;29:593–9. doi: 10.1086/588566. PMID: 18624666. PMCID: PMC2670228.

14 Carling PC, Parry MF, Bruno-Murtha LA, Dick B. Improving environmental hygiene in 27 intensive care units to decrease multidrug-resistant bacterial transmission. Crit Care Med. 2010;38:1054–9. doi: 10.1097/CCM.0b013e3181cdf705. PMID: 20081531.

15 Otter JA, Yezli S, French GL. The role played by contaminated surfaces in the transmission of nosocomial pathogens. Infect Control Hosp Epidemiol. 2011;32:687–99. doi: 10.1086/660363. PMID: 21666400.

16 Dancer SJ, White LF, Lamb J, Girvan EK, Robertson C. Measuring the effect of enhanced cleaning in a UK hospital: a prospective cross-over study. BMC Med. 2009;7:28. doi: 10.1186/1741-7015-7-28. PMID: 19505316. PMCID: PMC2700808.

17 McMullen KM, Zack J, Coopersmith CM, Kollef M, Dubberke E, Warren DK. Use of hypochlorite solution to decrease rates of Clostridium difficile-associated diarrhea. Infect Control Hosp Epidemiol. 2007;28:205–7. doi: 10.1086/511791. PMID: 17265404.

18 Kowalski W. Ultraviolet Germicidal Irradiation Handbook UVGI for air and surface disinfection introduction. Ultraviolet Germicidal Irradiation Handbook. 2009:1–16. doi: 10.1007/978-3-642-01999-9_1.

19 Siragusa GR, Cutter CN. Microbial ATP bioluminescence as a means to detect contamination on artificially contaminated beef carcass tissue. J Food Prot. 1995;58:764–9. doi: 10.4315/0362-028X-58.7.764. PMID: 31137335.

20 Fakruddin M, Mannan KS, Andrews S. Viable but nonculturable bacteria: Food safety and public health perspective. ISRN Microbiol. 2013;2013:703813. doi: 10.1155/2013/703813. PMID: 24191231. PMCID: PMC3804398.

21 Russell AD. Bacterial resistance to disinfectants: Present knowledge and future problems. J Hosp Infect. 1999;43:S57–68. doi: 10.1016/s0195-6701(99)90066-x. PMID: 10658759.

22 Dunlop PSM, Ciavola M, Rizzo L, McDowell DA, Byrne JA. Effect of photocatalysis on the transfer of antibiotic resistance genes in urban wastewater. Catalysis Today. 2015;240:55–60. doi: 10.1016/j.cattod.2014.03.049.

23 Nigam Y, Cutter J. A preliminary investigation into bacterial contamination of Welsh emergency ambulances. Emerg Med J. 2003;20:479–82. doi: 10.1136/emj.20.5.479. PMID: 12954699. PMCID: PMC1726203.

24 Dharan S, Mourouga P, Copin P, Bessmer G, Tschanz B, Pittet D. Routine disinfection of patients' environmental surfaces. Myth or reality? J Hosp Infect. 1999;42:113–7. doi: 10.1053/jhin.1999.0567. PMID: 10389060.

Acknowledgements

The authors would like to thank the friendly staff at the Hyperbaric Medicine Unit, Prince of Wales Hospital for their assistance in this study.

Conflicts of interest and funding: nil

Submitted: 23April 2020
Accepted after revision: 09 August 2020

Effect of antiplatelet and/or anticoagulation medication on the risk of tympanic barotrauma in hyperbaric oxygen treatment patients, and development of a predictive model

Adam E Howard[1], Peter Buzzacott[2], Ian C Gawthrope[1,3], Neil D Banham[1]

[1] *Department of Hyperbaric Medicine, Fiona Stanley Hospital, Western Australia*
[2] *Pre-Hospital, Resuscitation and Emergency Care Research Unit, School of Nursing, Midwifery and Paramedicine, Curtin University, Western Australia*
[3] *University of Notre Dame, Fremantle, Western Australia*

Corresponding author: *Dr Adam Howard, Department of Hyperbaric Medicine, Fiona Stanley Hospital, 11 Robin Warren Drive, Murdoch, WA 6150, Australia*
adam.howard@health.wa.gov.au

Key words:
Middle ear; Risk factors; Haematology; Women; Age; Data

Abstract
(Howard AE, Buzzacott P, Gawthrope IC, Banham ND. Effect of antiplatelet and/or anticoagulation medication on the risk of tympanic barotrauma in hyperbaric oxygen therapy patients, and development of a predictive model. Diving and Hyperbaric Medicine. 2020 December 20;50(4):338–342. doi: 10.28920/dhm50.4.338-342. PMID: 33325013.)
Introduction: Middle ear barotrauma (MEBt) is a common side effect of hyperbaric oxygen treatment (HBOT) and can result in pain, hearing loss, tinnitus and otorrhagia. The use of antiplatelet/anticoagulant drugs is thought to increase the risk and severity of MEBt during HBOT.
Methods: Single centre, retrospective observational cohort study of all patients treated with HBOT over a 4-year period (between 01 January 2015 to 31 December 2018) looking at the incidence of MEBt and the concurrent use of antiplatelet and/or anticoagulant drugs. MEBt was assessed by direct otoscopy of the tympanic membrane post-HBOT and scored using the modified Teed classification. Multivariate modelling assessed the relationship between antiplatelet and/or anticoagulation drug use, age, sex, and MEBt during HBOT.
Results: There was no evidence that antiplatelet and/or anticoagulation drugs increase the risk of tympanic barotrauma in HBOT patients. The prevalence of MEBt was higher in female patients than in males (χ^2 $P = 0.004$), and increased with age (χ^2 $P = 0.048$). No MEBt was recorded in patients undergoing recompression therapy for decompression sickness or cerebral arterial gas embolism.
Conclusions: In this retrospective single-centre study, antiplatelet and/or anticoagulation drugs did not affect the risk of MEBt, but both age and sex did, with greater prevalence of MEBt among older patients and females compared with younger patients and males. A predictive model, requiring further validation, may be helpful in assessing the likelihood of MEBt in patients undergoing HBOT.

Introduction

Hyperbaric oxygen treatment (HBOT) is a frequently used medical treatment with multiple indications outside of decompression illness. This has resulted in non-diving patients being administered HBOT with little or no experience in middle ear equalisation techniques. Middle ear barotrauma (MEBt) is a common side effect of HBOT. In the hyperbaric environment, rapidly increasing pressure during compression can "*overwhelm the ability of pressure regulation of the middle ear if active equalization is not often practiced*".[1] The unequal pressure gradient between the middle ear and external canal can lead to damage of the tympanic membrane and its structures, resulting in stretching, tearing and haemorrhage. Patients can experience symptoms ranging from mild discomfort, to ear pain, hearing loss, tinnitus and otorrhagia.

The incidence of MEBt is reported between 4.1–91% of patients.[2–7] The risk can be mitigated by assessment of patients with tympanometry, education around equalisation techniques and slow chamber compression (14–21 kPa·min^{-1} or less).

The use of antiplatelets/anticoagulants (AP/ACs) increase the risk of bleeding,[8,9] and are thought to increase the risk and severity of MEBt. A previous study looked at the risk of MEBt with the use of AP/ACs. It prospectively compared 73 patients from four hyperbaric centres: 34 participants on antiplatelet/anticoagulation therapy (treatment arm) versus 39 control patients who were not.[10] They reported no increase in MEBt-associated haemorrhagic complications between the two groups.

Methods

This retrospective, single centre observational study included all patients treated with HBOT between 01 January 2015 and 31 December 2018 at Fiona Stanley Hospital (FSH) Hyperbaric Medicine Unit (HMU). Approval was obtained via the FSH Clinical Audit Process (Activity number 28442). Data was collected via the BOSSnet (Core Medical Solutions, Adelaide, SA 5000) electronic medical record (EMR) system and the HMU's patient demographic cover sheet folder (Appendix 1*). This divided patients into their year of treatment and HMU identifying number. Information accessed included the HMU assessment and data form, referral letters and discharge letters. Patients receiving AP/ACs during their course of HBOT were included in the treatment group while all other patients constituted the control group.

Otoscopy was performed on all patients after their initial treatment and then in those who reported ear discomfort during a HBOT session as per the HMU's usual practice. Grading of MEBt was according to the modified Teed classification of MEBt (Table 1) and was documented in the patient's EMR and cover sheet (Appendix 1*).[11] HBOT was administered in either the multi-place chamber (Fink FETL-181, Fink Engineering Pty Ltd**,** Warana, Australia) or a mono-place chamber (Sechrist 3200 or 3600ER, Sechrist Industries Inc, Anaheim CA). Patients treated inside the multi-chamber were accompanied by a trained hyperbaric nurse. Assistance was offered if difficulty with equalisation occurred and compression was immediately halted and adjusted by the outside technician. Treatment tables and pressures used depended on the clinical indication for treatment (203–284 kPa). Compression rates for the multi-chamber were routinely 14 kPa·min^{-1} and in the mono-place chambers were set at 20.7 kPa·min^{-1} unless slowed on the advice of a hyperbaric physician.

All awake patients were educated in the techniques used to equalise as well as being supplied with water bottles to assist in swallowing during compression and decompression. At the FSH HMU the multiplace chamber inside nurse attendant is mobile and vigilant, and the technician is on constant audio and visual contact with the patients inside the monoplace chamber. The unit policy during the study period stated "*as soon as ear pain or difficulty in equalisation is flagged, compression is to be halted, with the potential for decompression to 5–10 kPa below the ceased pressure prior to either abandoning or recommencing at a slower compression rate*".

STATISTICAL ANALYSIS

Data were compiled using MS Excel® and imported into SAS (Statistical Analysis System, Cary, NC version 9.4) for analysis. Differences in mean age between sub-groups were tested using Student's *t*-test with pooled standard deviation.

Table 1
Modified Teed classification of MEBt

Grade	Manifestations
0	Symptoms without signs
I	Injection of the tympanic membrane, especially along the handle of the malleus
II	Injection plus slight haemorrhage within the substance of the tympanic membrane
III	Gross haemorrhage within the substance of the tympanic membrane
IV	Free blood in the middle ear as evidenced by blueness and bulging
V	Perforation of the tympanic membrane

Unweighted Chi-square tests assessed proportions in binary variables (e.g., AP/AC use by sex). To assess the potential association between AP/AC use and MEBt, MEBt was collapsed to three levels; none, mild (Grade I), or involving haemorrhage (Grad II or above). An ordered (ternary) logistic regression model was weighted according to the number of HBOT treatments each patient (i) had completed and these weights (w_i) were normalised (w'_i) by multiplying them by the sample size ($n = 642$) divided by the sum of the weights (the total number of treatments) (Eq. 1).

$$w_i' = \frac{n.w_i}{\sum_{i=1}^{n} w_i} \quad \text{(Eq. 1)}$$

This ensured the covariance matrix of the parameter estimates was not disproportionately affected by the scale of the weighting variable (number of HBOT treatments). The initial model, which also considered potential interactions, is shown in Equation 2. The model was optimised through backwards elimination with least significant variables and interactions (identified by joint tests and conforming to the hierarchical principle) removed until all remaining variables were significant at $P \leq 0.05$

$$ln\left[\frac{P_{MEBt_i'}}{1-P_{MEBt_i'}}\right] = \alpha_j + ß_1 Sex_i + ß_2 Age_i + ß_3 Med_i + ß_4 Sex_i * Age_i + ß_5 Sex_i * Meds_i + Age_i * Meds_i + ß_7 Age_i * Sex_i * Meds_i \quad \text{(Eq. 2)}$$

Where MEBt' = the outcome MEBt (0, 1 or 2) scaled by w', α_j = the intercept for outcome *j*, β_{1-7} = the respective estimates for each independent variable, Sex = male (0) or female (1), Age is in whole years, and Meds = 1 for AP/AC medication use and 0 = no AP/AC medications. A Hosmer and Lemeshow goodness of fit test assessed if the expected outcomes significantly differed from the observed outcomes. $P \leq 0.05$ was accepted as significant, when deciding whether to reject the null hypothesis (that the expected outcomes significantly differ from the observed outcomes).

***Footnote:** Appendices 1 and 2 are available on the DHM journal website for viewing.

Table 2
Indications for hyperbaric oxygen therapy for patient included in the present study. ISSHL = idiopathic sudden sensorineural hearing loss

Pathology	Frequency *n* (%)
Non-healing wounds	145 (23)
Pre/post dental clearance	109 (17)
Radiation cystitis/proctitis	89 (14)
Osteoradionecrosis	77 (12)
Decompression illness	70 (11)
Necrotising fasciitis	32 (5)
Carbon monoxide poisoning	26 (4)
Radiation tissue injury	26 (4)
Retinal artery occlusion	14 (2)
Cerebral arterial gas embolism	13 (2)
ISSHL	9 (1)
Burns	6 (1)
Osteomyelitis	6 (1)
Acute spinal infarction	6 (1)
Calciphylaxis	5 (1)
Avascular necrosis	2 (< 1)
Disseminated fungal disease	2 (< 1)
Crush injury	2 (< 1)
Pyoderma gangrenosum	1 (< 1)
Supranuclear palsy	1 (< 1)
Bell's palsy	1 (< 1)
Total	642

Results

There were 642 patients treated at FSH HMU over the four years, receiving a total of 13,989 HBOT treatments (median 27, IQR 25). There was a greater proportion of males (n = 450, 70%) treated compared with females and their mean age was greater (58 y vs. 53 y, SD 17.2, t = -3.16, P = 0.002). The prevalence of indications for HBOT are shown in Table 2.

AP/AC use was reported by 180 patients (28%). The most common prescription was aspirin alone (n = 88, 14%) with a further 11 patients prescribed AP/AC simultaneously. Other types of AP/ACs included clopidogrel, dipyridamole, warfarin, unfractionated heparin infusion (inpatients), low molecular weight heparin and the newer direct acting oral anticoagulants (DOACs). Males were more commonly prescribed AP/ACs than females (30% vs. 23%, χ^2 P = 0.059).

MEBt occurred in 84 patients (11% males vs. 19% females) with the majority consisting of grade I or II according to the modified Teed criteria (87%). Two patients experienced grade IV or V MEBt. One patient twice had documented barotrauma during their course of treatment with bilateral MEBt on one of those events. The higher Teed grade from this patient was put into our analysis, while the other 83 patients with MEBt had a single documented barotrauma each. All grade III MEBt and above with evidence of gross haemorrhage or perforation occurred in the control group. Mean age was greater among patients with MEBt (63 vs. 56, SD 17.2, t = -3.48, P = 0.0005). No other bleeding complications were recorded for any patients that were unrelated to their current hyperbaric indication. No MEBt was recorded in patients undergoing recompression therapy for decompression sickness or cerebral arterial gas embolism (CAGE). Patients undertaking HBOT for osteoradionecrosis (ORN) prophylaxis pre/post dental treatment or established ORN were assessed for increased prevalence of MEBt, compared with the remainder of the cohort. There was no association with increased MEBt in the pre/post dental group (16% vs. 13%%, χ^2 P = 0.402), nor in the ORN group (14% vs. 13%%, χ^2 P = 0.475), or when the two groups were combined (15% vs. 12%%, χ^2 P = 0.355).

Ultimately, the model (Eq. 2) was optimised and the following variables were removed, in order: Age*Sex*Meds (χ^2 P = 0.208), Sex*Meds (χ^2 P = 0.727), Age*Sex (χ^2 P = 0.180), Age*Meds (χ^2 P = 0.187), then finally Meds (χ^2 P = 0.736). The resulting model is shown in Equation 3. Sex and age were significantly associated with MEBt (χ^2 P = 0.004, OR 2.0, 95% CI 1.2, 3.2) and (χ^2 P = 0.048, OR[10] 1.2, 95% CI 1.0, 1.3) respectively. The Hosmer and Lemeshow goodness of fit test showed P = 0.36 therefore, the null hypothesis was rejected and model fit accepted.

$$ln\left[\frac{P_{MEBt_i'}}{1-P_{MEBt_i'}}\right] = \alpha_j - [0.3421 * Sex_i\ (M = 0,\ F = 1) - [0.0148 * Age_i\ (yrs)] \quad \text{(Eq. 3)}$$

The estimate for the intercept (α_1) comparing no MEBt with (MEBt I or ≥ II) was 2.5246 (SE 0.4752), and for comparing (no MEBt or MEBt I) with MEBt ≥ II the (α_2) intercept was 3.2009 (SE 0.4853). Confidence intervals for parameter estimates were 0.000–0.030 for age and 0.109–0.576 for sex. Examples of translating Equation 2 into odds and probabilities are given in Appendix 2*. The percentage of patients in the three older age groups is shown in Table 3, by MEBt status. These percentages are weighted by number of treatments, to account for differences in exposure and MEBt in different age groups and sexes, but the unweighted percentages showed the same trend, (to an even greater degree). Patients aged ≥ 50 y accounted for 11,210 (80%) of the 13,989 HBOT treatments in this study.

Discussion

The most common complication of HBOT is myopic ocular changes, occurring in 25–100% of patients and dependent on the number of treatments and method of oxygen delivery.[12,13] MEBt is the second most frequent complication, with less common side effects including sinus and dental barotrauma, anxiety, cataracts, hypoglycaemic events during treatment and oxygen toxicity seizures (1/3,000–1/10,000 treatments).[2,4-7,12–16] The present study, looking at the largest cohort of patients, supports previous findings that MEBt is a common complication of HBOT.

Our unit cohort experienced a relatively low prevalence of MEBt compared with previous reports.[2–7] All of our patients underwent a thorough health check prior to commencing HBOT and education on equalising techniques. This included assessment of tympanic membrane movement under direct vision during Valsalva, as well as tympanometry. Several patients including intubated patients had myringotomies performed prior to commencing HBOT.[17] This may have slightly reduced the incidence of MEBt, but with 558 no-MEBt patients their effect upon the results would have been negligible, and non-directional regarding AP/AC use. A French unit treating a majority of acute cases reported a 13.6% incidence of MEBt with no influence of age, sex or mechanical ventilation.[18]

No patients treated for decompression illness suffered MEBt or had pre-existing evidence of MEBt prior to HBOT. Although speculative, this could be assumed to be from prior experience at equalising. The results reported remain valid even when patients treated for DCI were excluded. Another potential confounder for our observed prevalence could have arisen when patients asked for equalisation support prior to notifying of pain, which may have resulted in otoscopy not being performed post treatment. This could have reduced the actual total MEBt numbers and could explain why modified Teed scores of 0 were not recorded. A comparable HBOT unit in Australia experienced a 43.4% incidence of MEBT over the study period with similar characteristics of patient demographics and indications.[19] Grade 0 was reported in that study, although exact numbers were not stated.

ANTIPLATELET/ANTICOAGULATION USAGE

A small study of the prevalence of AP/AC usage in general practice patients showed 11.3% (95% CI 9.5, 13.1%) were prescribed AP/AC medication.[20] Indications for antiplatelets include coronary artery disease, cerebrovascular disease, arterio-venous shunt thrombosis, peripheral vascular disease with or without grafts.[21] Indications for anticoagulants include deep vein thrombosis, pulmonary embolism, atrial fibrillation, valvular disease or replacement and cardiomyopathy. Both AP and AC increase the risk of bleeding and are included in the bleeding risk stratification scoring of HAS-BLED and HEMORR2HAGES.[8,9] Our study showed no increased risk of MEBt associated with the use of AP and/or AC.

Table 3
Percentage of patients in three older age groups, by MEBt status and sex (and weighted by number of treatments)

Age group	No MEBt (%)	MEBt (%)	Males (% MEBt)	Females (% MEBt)
≥50 yrs	84	16	14	22
≥60 yrs	83	17	15	24
≥70 yrs	82	18	15	31

This observational study is the largest published cohort looking at the use of AP/AC and risk of MEBt in patients receiving HBOT. As reported in a previous study, males were more commonly prescribed AP/AC medication (30% vs. 23%) and this may be due to the higher incidence of MI and stroke seen in the aging male population compared with females.[22] In our study, males were more commonly prescribed AP/AC but it was statistically non-significant compared with females (30% vs 23%, χ^2 $P = 0.059$). Even so, the percentage of females in the three older age groups that suffered MEBt increased with age (Table 3). Sex and age have not been shown to influence prevalence of MEBt in other studies.[18] With the large number of patients included in the observation period, we were able to develop a statistical model to assess the likelihood of MEBt. This equation may be used to help assess an individual patient's risk of MEBt and thus develop strategies to prevent it. Sex and age were a secondary finding not included in the null hypothesis, so when using the above equation to estimate probability of MEBt, it should be remembered that the cohort described in this study may not be representative of patients at hyperbaric chambers in other locations. Furthermore, the probabilities generated assume patients will receive the same types and number of treatments as those patients upon whom the model was calibrated. We plan to look at validation of this statistical model involving a more heterogeneous patient mix.

AGE AND SEX

The tympanic membrane (TM) changes with age, with thinning, reduced vascularity, cellular atrophy and increasing TM stiffness.[23] The resultant decrease in compliance could account for the increasing risk of MEBt seen with age. Eustachian tube (ET) function is also affected by age-related atrophy. The tensor veli palatini muscle shows increasing fat tissue replacement with age and increasing ET cartilage calcification.[24–26] These two factors could represent increasing ET dysfunction leading to a higher MEBt risk due to pressure dysequilibrium. What is difficult to explain is why females are at a higher risk than males. There are no studies that differentiate the ageing subjects into sex.

Conclusions

In this single-centre study, AP/ACs did not affect the risk of MEBt, but both age and sex did, with greater prevalence

of MEBt among older patients and females, compared with younger patients and males. A large, multi-centre trial would be required to validate the above findings and the use of a predictive model to determine risk. A predictive model, requiring further validation, may be helpful in assessing the likelihood of MEBt in patients undergoing HBOT.

References

1 Lima MAR, Farage L, Cury MCL, Júnior FB. Update on middle ear barotrauma after hyperbaric oxygen therapy – insights on pathophysiology. Int Arch Otorhinolaryngol. 2014;18:204–9. doi: 10.1055/s-0034-1366974. PMID: 25992091. PMCID: PMC4297009.

2 Beuerlein M, Nelson RN, Welling DB. Inner and middle ear hyperbaric oxygen-induced barotrauma. Laryngoscope. 1997;107:1350–6. doi: 10.1097/00005537-199710000-00011. PMID: 9331312.

3 Goplen FK, Grønning M, Aasen T, Nordahl SHG. Vestibular effects of diving – a 6-year prospective study. Occup Med. 2010;60:43–8. doi: 10.1093/occmed/kqp148. PMID: 19854795.

4 Ng AWA, Muller R, Orton J. Incidence of middle ear barotrauma in staged versus linear chamber compression during hyperbaric oxygen therapy: A double blinded, randomized controlled trial. Undersea Hyperb Med. 2017;44:101–7. doi: 10.22462/3.4.2017.3. PMID: 28777900.

5 Igarashi Y, Watanabe Y, Mizukoshi K. Middle ear barotrauma associated with hyperbaric oxygenation treatment. Acta Otolaryngol Suppl. 1993;504:143–5. doi: 10.3109/00016489309128142. PMID: 8470522.

6 Blanshard J, Toma A, Bryson P, Williamson P. Middle ear barotrauma in patients undergoing hyperbaric oxygen therapy. Clin Otolaryngol Allied Sci. 1996;21:400–3. doi: 10.1046/j.1365-2273.1996.00813.x. PMID: 8932942.

7 Nasole E, Zanon V, Marcolin P, Bosco G. Middle ear barotrauma during hyperbaric oxygen therapy; a review of occurrences in 5,962 patients. Undersea Hyperb Med. 2019;46:101–6. PMID: 31051054.

8 Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJGM, Lip GYH. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest. 2010;138:1093–100. doi: 10.1378/chest.10-0134. PMID: 20299623.

9 Gage BF, Yan Y, Milligan PE, Waterman AD, Culverhouse R, Rich MW, et al. Clinical classification schemes for predicting hemorrhage: Results from the National Registry of Atrial Fibrillation (NRAF). Am Heart J. 2006;151:713–9. doi: 10.1016/j.ahj.2005.04.017. PMID: 16504638.

10 Fijen VA, Westerweel PE, van Ooij P-J, van Hulst RA. Tympanic membrane bleeding complications during hyperbaric oxygen treatment in patients with or without antiplatelet and anticoagulant drug treatment. Diving Hyperb Med. 2016;46:22–5. PMID: 27044458.

11 Edmonds C, Bennett M, Lippmann J, Mitchell SJ. Diving and Subaquatic Medicine, 5th ed. Boca Raton (FL): CRC Press; 2016. p. 87.

12 Heyboer M 3rd, Sharma D, Santiago W, McCulloch N. Hyperbaric oxygen therapy: Side effects defined and quantified. Adv Wound Care. 2017;6:210–24. doi: 10.1089/wound.2016.0718. PMID: 28616361. PMCID: PMC5467109.

13 Bennett MH, Hui CFb, See HG, Au-Yeung KL, Tan C, Watson S. The myopic shift associated with hyperbaric oxygen administration is reduced when using a mask delivery system compared to a hood – a randomised controlled trial. Diving Hyperb Med. 2019;49:245–52. doi: 10.28920/dhm49.4.245-252. PMID: 31828742. PMCID: PMC7039782.

14 Davis JC. Hyperbaric oxygen therapy. J Intensive Care Med. 1989;4:55–7.

15 Costa DA, Ganilha JS, Barata PC, Guerreiro FG. Seizure frequency in more than 180,000 treatment sessions with hyperbaric oxygen therapy – a single centre 20-year analysis. Diving Hyperb Med. 2019;49:167–74. doi: 10.28920/dhm49.3.167-174. PMID: 31523791. PMCID: PMC6884101.

16 Banham ND. Oxygen toxicity seizures: 20 years' experience from a single hyperbaric unit. Diving Hyperb Med. 2011;41:202–10. PMID: 22183697.

17 Presswood G, Zamboni WA, Stephenson LL, Santos PM. Effect of artificial airway on ear complications from hyperbaric oxygen. Laryngoscope. 1994;104:1383–4. doi: 10.1288/00005537-199411000-00011. PMID: 7968168.

18 Bessereau J, Tabah A, Genotelle N, Français A, Coulange M, Annane D. Middle-ear barotrauma after hyperbaric oxygen therapy. Undersea Hyperb Med. 2010;37:203–8. PMID: 20737927.

19 Commons KH, Blake DF, Brown LH. A prospective analysis of independent patient risk factors for middle ear barotrauma in a multiplace hyperbaric chamber. Diving Hyperb Med. 2013;43:143–7. PMID: 24122189.

20 Anticoagulant and antiplatelet use in general practice patients. SAND abstract no.199 from the BEACH program. Sydney: Family Medicine Research Centre, University of Sydney; 2013. p. 149. Available from: https://www.sydney.edu.au/content/dam/corporate/documents/faculty-of-medicine-and-health/research/research-collaborations,-networks-and-groups/33-general-practice-activity-in-australia-2012%E2%80%9313.pdf. [cited 2020 February 06].

21 Baker RI, Hankey GJ. Antiplatelet drugs. Med J Aust. 1999;170:379–82. PMID: 10327952.

22 Carandang R, Seshadri S, Beiser A, Kelly-Hayes M, Kase CS, Kannel WB, et al. Trends in incidence, lifetime risk, severity, and 30-day mortality of stroke over the past 50 years. JAMA. 2006;296:2939–46. doi: 10.1001/jama.296.24.2939. PMID: 17190894.

23 Liu TC, Chen YS. Aging and external ear resonance. Audiology. 2000;39:235–7. PMID: 11093606.

24 Takasaki K, Sando I, Balaban CD, Haginomori S, Ishijima K, Kitagawa M. Histopathological changes of the eustachian tube cartilage and the tensor veli palatini muscle with aging. Laryngoscope. 1999;109:1679–83. doi: 10.1097/00005537-199910000-00024. PMID: 10522942.

25 Oswal V, Remacle M. Principles and practice of lasers in otorhinolaryngology and head and neck, 2nd ed. Amsterdam: Kugler Publications; 2014. p. 513.

26 Ruah CB, Schachern PA, Zelterman D, Paparella MM, Yoon TH. Age-related morphologic changes in the human tympanic membrane. A light and electron microscopic study. Arch Otolaryngol Head Neck Surg. 1991;117:627–34. doi: 10.1001/archotol.1991.01870180063013. PMID: 2036184.

Conflicts of interest and funding: nil

Submitted: 06 February 2020
Accepted after revision: 16 August 2020

Xuebijing attenuates decompression-induced lung injuries

Wen-tao Meng[1,2], Long Qing[3], Quan Zhou[1], Wei-gang Xu[1]

[1] *Department of Diving and Hyperbaric Medicine, Naval Special Medicine Center, Naval Medical University, Shanghai, China*
[2] *Discipline of Military and Special Medicine, The 92493 Military Hospital of PLA, Huludao, China*
[3] *Naval Diving Medical Discipline, Naval Special Medicine Center, Naval Medical University, Shanghai, China*

Corresponding author: *Professor Wei-gang Xu, Department of Diving and Hyperbaric Medicine, Naval Special Medicine Center, Naval Medical University, Shanghai, China*
wg_hsu@163.com

Key words
Decompression sickness; Decompression illness; Inflammation; Pulmonary oedema

Abstract
(Meng W, Qing L, Zhou Q, Xu W. Xuebijing attenuates decompression-induced lung injuries. Diving and Hyperbaric Medicine. 2020 December 20;50(4):343–349. doi: 10.28920/dhm50.4.343-349. PMID: 33325014.)
Introduction: The lung is among the primary organs involved in decompression sickness (DCS). Xuebijing (XBJ), a traditional Chinese medicine, has been widely used in the treatment of various acute lung diseases. This study aimed to explore potential benefit of XBJ on lung injuries induced by DCS in a rabbit model.
Methods: Twenty-four male New Zealand white rabbits underwent a simulated air dive to 50 meters' sea water for 60 min with 2.5 min decompression, and received an intravenous injection of XBJ (5 ml·kg^{-1}) or an equal volume of saline immediately following decompression. DCS signs were monitored for 24 h, and blood was sampled before simulated diving and at 6 h and 12 h following decompression for determination of inflammatory indices. Lung tissues were sampled after euthanasia for histology analysis and lung water content, as well as tumour necrosis factor-α level. Another six rabbits were used as control.
Results: XBJ significantly ameliorated lung injuries (lung wet/dry ratio and total protein content in bronchoalveolar lavage fluid), and notably inhibited systemic (serum level of interleukin-1β) and local (tumour necrosis factor-α in bronchoalveolar lavage fluid) inflammation responses.
Conclusions: The results strongly suggest the benefits of XBJ on ameliorating DCS lung injuries, which is possibly via inhibiting systemic and local inflammation. XBJ may be a potential candidate for the treatment of decompression-induced lung injuries.

Introduction

Decompression sickness (DCS) is a major concern for scuba divers, compressed air workers and other personnel exposed to hyperbaric environments.[1] It has been well demonstrated that the severity of DCS is related to circulating bubbles induced by decompression, which may lead to mechanical obstruction, venous congestion, endothelial dysfunction, inflammation and coagulation activation.[2,3] The lung is a pivotal organ involved in DCS, in which the pulmonary capillary network bears the brunt of venous bubble formation as a superb filter,[4] and prevents bubbles flowing into the systemic circulation by trapping and excreting venous bubbles.[5] Bubbles could induce inflammation cascades, as well as mechanical injury of the endothelial cells, giving rise to increased permeability of the blood-lung barrier,[6] and leading to interstitial lung oedema as a result.[7] When overloaded with large numbers of bubbles pulmonary vascular obstruction occurs producing symptoms including chest pain, cough, dyspnoea and even death.[8] It has been suggested that the early death following decompression may be associated with pulmonary DCS.[9] Studies have confirmed lung injury, such as pulmonary oedema, induced by decompression.[7,10] Hence, protection from lung injury caused by bubbles may be of great importance for the prognosis of DCS. Although hyperbaric oxygen treatment (HBOT) is the primary intervention for DCS, there is frequently a time delay for DCS patients to receive HBOT, and potential for drugs targeting DCS pathophysiology to improve its prognosis.

Xuebijing (XBJ) is a traditional Chinese medicine, which is composed of *Carthamus tinctorius*, *Radix paeoniae rubra*, *Ligusticum wallichii*, *Radix salviae miltiorrhizae* and *Radix angelicae sinensis*.[11] Properties of inflammation inhibition, immune function enhancement and microcirculation improvement have been confirmed in animal and clinical trials.[11,12] XBJ was approved for the treatment of sepsis and multiple organ dysfunction syndromes (MODS) by the China Food and Drug Administration in 2004. Clinical studies indicate that addition of XBJ to standard treatment for severe community-acquired pneumonia significantly improves prognosis, reduces 28-day mortality and shortens duration of intensive care stay with a low incidence of adverse effects.[13,14] Other experimental and clinical studies suggest significant benefits for treating acute lung

injuries,[13,15,16] and it is also recommended for the treatment of COVID-19 in China.[17] Considering that DCS is a systemic disease accompanied with inflammation, oxidative responses, coagulation and endothelial dysfunction,[1,18,19] we explored potential effects of XBJ on lung injury in a rabbit DCS model.

Methods

ANIMALS

The experimental protocol was approved by the Ethics Committee for Animal Experiments of the Naval Medical University (Approved number: 20180820060), and all the procedures were performed in line with related guidelines and regulations. A total of 30 male New Zealand White rabbits with weights varying from 2.0 to 2.3 kg were obtained from Shanghai Shengwang Laboratory Animal Co. Ltd. The rabbits were housed individually in metal cages with controlled humidity (50–60%), temperature (24–26°C) and a natural light/dark cycle. Food and water were provided *ad libitum*. Prior to experimental procedures, rabbits were acclimatised to the laboratory environment for one week.

PROCEDURE AND DESIGN

The rabbits were randomly divided into three groups: 12 each for XBJ and saline groups, and six for the normal control group to acquire normal values, which were in line with animal ethics. Our previous research showed that the simulated diving profile could yield an incidence of DCS in rabbits around 75%, and 12 rabbits in each group would produce approximately nine cases with DCS, which were enough to compare biomedical indices between groups. Rabbits in the former two groups were subjected to simulated diving and rapid decompression to induce DCS. In the XBJ group, rabbits received an intravenous injection of XBJ (Tianjin Chase Sun Pharmaceutical Co., Tianjin, China) 5 ml·kg^{-1} body weight immediately after decompression. Rabbits in the saline group were given the equal volume of saline in the same way. Normal rabbits were sham exposed (normobaric air) in order to acquire normal values of the indices. After rapid decompression, the rabbits were under continuous observation for 24 h by a member of staff blinded to the treatments. Blood was sampled before simulated diving and at 6 and 12 h following decompression for determination of inflammatory indices. Surviving rabbits were euthanised at 24 h after decompression with an intraperitoneal injection of pentobarbital (200 mg·kg^{-1}), and then lung tissues and bronchoalveolar lavage fluid (BALF) were sampled. Normal controls were sham exposed (normobaric air) and sampled similarly.

SIMULATED DIVING

The rabbits were subjected to simulated diving in an animal hyperbaric chamber (DWC150, Yangyuan, Shanghai, China) in pairs, each time with one in the XBJ group and the other one in the saline group. The pressure was increased to 600 kPa (absolute pressure) in 5 min and maintained for 60 min using compressed air. Compression began slowly and was completed in 5 min to minimise any possible discomfort. Thereafter, decompression procedure was conducted linearly to ambient pressure at a rate of 200 kPa·min^{-1}. The chamber underwent continuous ventilation to avoid accumulation of carbon dioxide (CO_2).

DCS SYMPTOM OBSERVATION

After surfacing, rabbits were under continuous observation to evaluate DCS by one observer blinded to the treatments. DCS was diagnosed as individuals with at least one symptom including abnormal biting, respiratory or motor dysfunction, seizure and death. When individuals exhibited paralysis, dyspnoea, seizure or death, then severe DCS was diagnosed. Respiratory function was monitored and scored at 10, 20, 30, 40, 60, 90 and 120 min following decompression using a 0-4 grading scale as follows: 0 = normal breathing; 1 = mild laboured breathing; 2 = restlessness and laboured breathing; 3 = severely laboured breathing, recumbent posture; 4 = collapse, stupor and death.[20] As respiratory changes progressed rapidly and usually recovered within 2 h of decompression, the maximal score observed during the 2 h period was deemed the respiratory score of each rabbit.

DETERMINATION OF SERUM INFLAMMATORY FACTORS

One millilitre of venous blood was sampled and centrifuged at 4°C and 2,500 rpm for 10 min. Serum levels of interleukin-1beta (IL-1β) and macrophage chemokine-1 (MCP-1) were determined by enzyme-linked immunosorbent assay (ELISA) kits (Jiancheng Bioengineering Institute, Nanjing, China). The coefficient of variation of inter-assay and intra-assay was less than 10% and 12%, respectively. The accuracy and precision were ± 1% and ≤ 0.2%, respectively. All assays were conducted according to the manufacturer's instructions.

BALF ANALYSIS

After euthanasia at 24 h following decompression, the right main bronchus was clipped, and 10 ml 0.9% saline was slowly infused in and out three times through a special plastic tube inserted into the trachea. The procedure was repeated for a total of three washes (30 ml), and BALF recovery was approximately 80%. Total BALF protein was measured by bicinchoninic acid (BCA) using enhanced BCA protein assay kits (Beyotime Institute of Biotechology, Nantong, China). Tumour necrosis factor-α (TNF-α) was determined by ELISA kits (Jiancheng Bioengineering Institute, Nanjing, China).

LUNG WET/DRY WEIGHT RATIO ASSAY

Lung water content can reflect the severity of pulmonary oedema, which was assayed by lung wet/dry (W/D) weight

ratio. Right lower lung lobes were taken and weighed as wet weight, and then incubated in an oven at 60°C for 72 h to obtain the dry weight.

HISTOLOGICAL EXAMINATION

Right upper lung lobes were incised and fixed in 10% buffered formalin solution, and embedded in paraffin, which were then sectioned at 5 μm thickness and stained with haematoxylin and eosin (H&E). Sections were examined using a light microscope (DMi8, Leica, Germany) and scanned using an automatic digital slide scanner (Pannoramic MIDI, 3DHISTECH, Hungary). Each section was identified for alveolar congestion, haemorrhage, inflammatory infiltration and thickened alveolar walls, and scored for each item using a histologic scoring system as follows: 0 = normal lungs; 1 = < 25% lung involvement; 2 = 25–50% lung involvement; 3 = 50–75% lung involvement; 4 = > 75% lung involvement. The average score of each section was determined to represent the histopathology score.[21,22]

STATISTICAL ANALYSIS

Where applicable, values were expressed as mean (standard deviation [SD]) or median (interquartile range) except for incidence and death rate of DCS, which were compared between the XBJ and saline group by Chi-square test. Normal distribution of data was determined using the Shapiro-Wilk test. An independent-samples *t*-test was used to compare blood indices between the two groups. Lung W/D weight ratio, BALF TNF-α and protein content were compared using one-way ANOVA followed by Dunnett's test among the XBJ, saline and normal control groups. Respiratory and histological scores were compared between XBJ and saline groups using a Mann-Whitney U test. *P*-values less than 0.05 were considered statistically significant.

Results

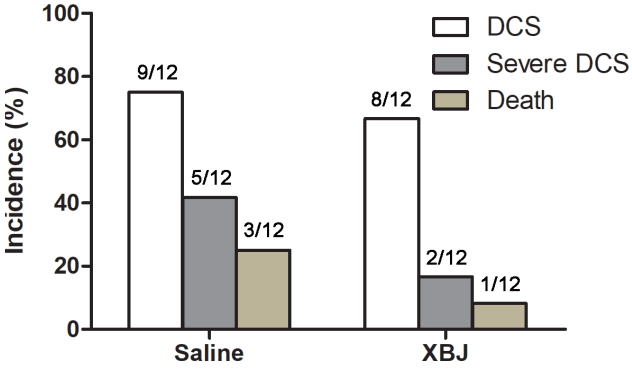
INCIDENCE OF DCS AND DEATH RATE

All DCS cases occurred within 30 min following decompression. Three rabbits died in the saline group within 1 h following decompression after a short period of severe dyspnea and convulsions, and one died in the XBJ group at 6 h following decompression with circulatory dysfunction. There was no significant difference in incidence of severe DCS (2/12 vs. 5/12, χ^2= 0.807, P = 0.369) and death rate (1/12 vs. 3/12, χ^2=0.300, P = 0.584) between XBJ and saline groups respectively (Figure 1).

DECOMPRESSION-INDUCED LUNG INJURIES

After surfacing, 42% of the rabbits exhibited transient tachypnoea. XBJ did not decrease respiratory scores significantly (Z = -1.812, P = 0.070, Figure 2A). Lung water content evaluated by lung W/D weight ratio was significantly decreased by XBJ (4.71 (SD 0.07) vs. 4.81 (0.12), t = 2.335,

Figure 1
Effects of XBJ on the incidence and death rate of DCS in rabbits. There were no statistically significant differences between groups in the incidence of severe DCS and deaths



P = 0.031, Figure 2B). At 24 h following decompression, levels of TNF-α and total BALF protein in the saline group increased significantly (89.2 (10.0) vs. 53.5 (11.5); 0.34 (0.06) vs. 0.21 (0.04), P < 0.05), and were notably inhibited by XBJ (66.6 (19.3) vs. 89.2 (10.0); 0.28 (0.04) vs. 0.34 (0.06), P < 0.05, Figure 2C and 2D).

LUNG HISTOPATHOLOGY

Representative histologic examination findings are shown in Figure 3. Rupture of normal alveolar structure, thickened alveoli septum, haemorrhage and infiltration of neutrophils were present in DCS rabbits (Panels B1 and B2) when compared with normal controls (Panels A1 and A2), which were notably ameliorated by XBJ treatment (Panels C1 and C2). Lung injury scores in detail are shown in Panel E, and XBJ significantly decreased histopathology score (1.16 (0.57) vs. 1.89 (0.71), Z = -2.041, P = 0.041, Panel D).

SYSTEMIC INFLAMMATION

Levels of serum IL-1β and MCP-1 significantly increased following decompression, with an average increase of approximately 20% (Panels A and B). XBJ significantly inhibited the increase of IL-1β (0.13 (0.08) vs. 0.21 (0.09), P = 0.040, Panel C). There was no statistical difference in rate of change in MCP-1 between the two groups (Figure 4).

Discussion

Decompression-induced circulating bubbles of >20 μm in diameter are often trapped in the lung capillaries and then dissolve during expiration.[23] Formation of a small number of venous bubbles is common in diving and typically do not cause symptoms because they are usually filtered out by the pulmonary circulation. However, a large number or volume of bubbles might compromise the capability of the lungs to filter them,[24] and cause symptoms including chest pain, cough, dyspnoea and even death.[8] Although HBOT is the most efficient treatment, exploration of potential drugs

Figure 2

XBJ ameliorated DCS induced lung injuries. Numerical values in the bars denote the number of rabbits in each group. # = $P < 0.05$ vs. normal control, * = $P < 0.05$ and ** = $P < 0.01$ vs. saline group

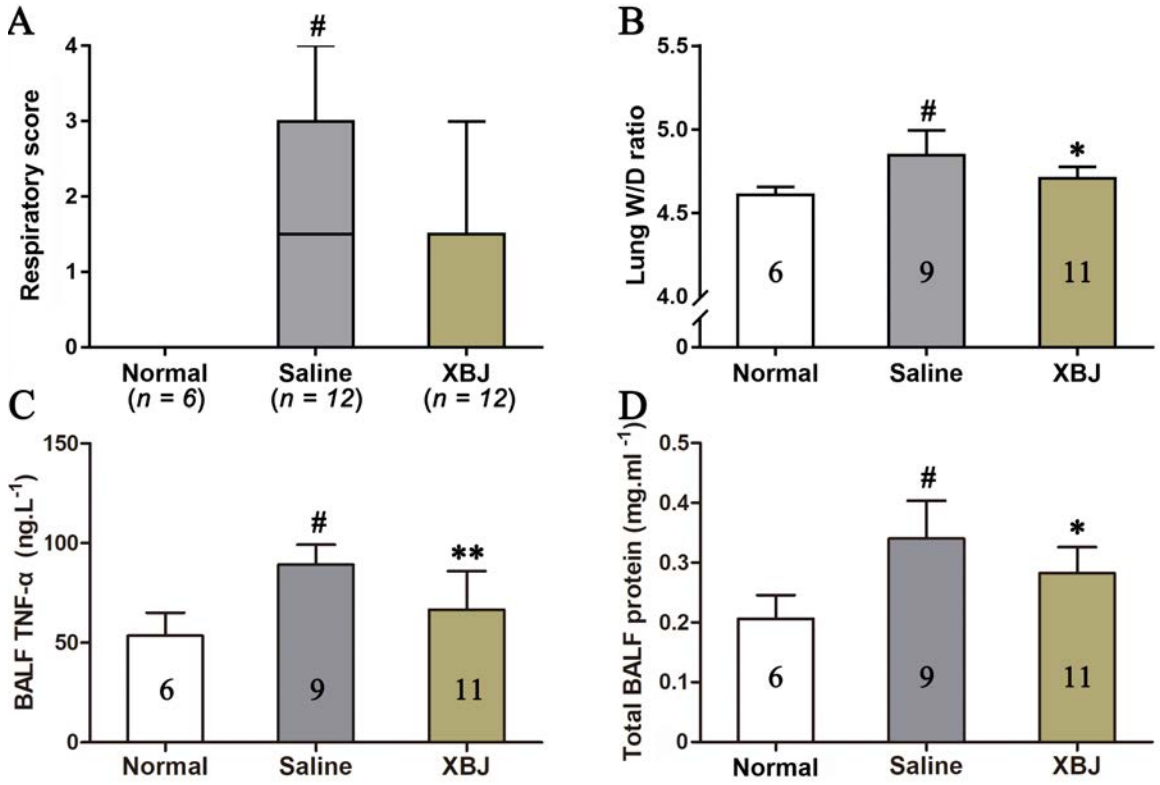
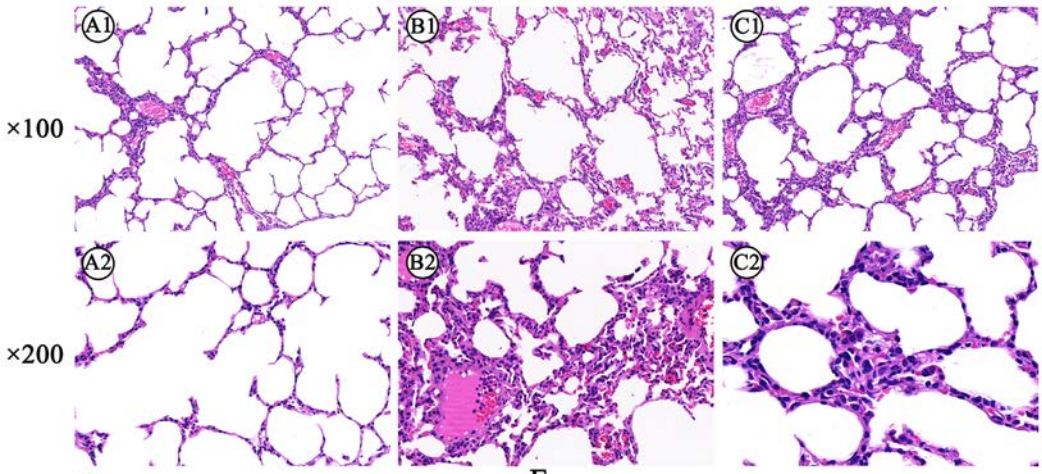


Figure 3

Representative photomicrographs and scores of the lung histopathology of DCS rabbits. A panels = normal histopathology of lung parenchyma. B panels = saline group showing disruption of alveolar structure, haemorrhage, infiltration of neutrophils and thickened alveoli septa. C panels = XBJ group showing ameliorated histopathology. D and E panels show lung histopathology score distribution and differences. * = $P < 0.05$ vs. saline group



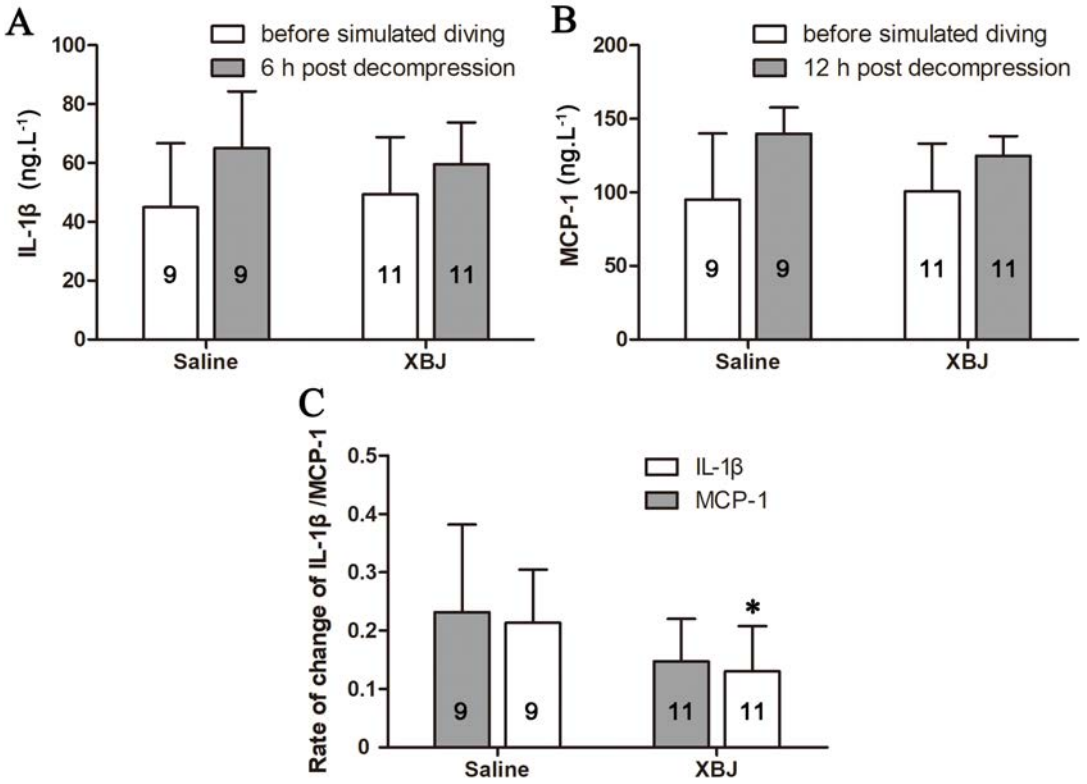
E

Lung histopathology score distribution

Score	Incidence *n* (%)		
	Normal	Saline group	XBJ group
0~1	6 (100)	1 (11.1)	4 (36.4)
1~2	0 (0.0)	4 (44.5)	6 (54.5)
2~3	0 (0.0)	3 (33.3)	1 (9.1)
3~4	0 (0.0)	1 (11.1)	0 (0.0)

Figure 4

Comparison of XBJ and saline groups in respect of plasma inflammatory markers: panel A = IL-1β; panel B = MCP-1; panel C = rate of change in markers. * = $P < 0.05$ vs. saline group



targeting lung injuries induced by DCS are still areas of research focus.

In this study, potential benefits of XBJ were investigated in a rabbit DCS model. Among the indices studied, increased lung W/D weight ratio and BALF protein content following decompression were inhibited by XBJ, indicating amelioration of pulmonary oedema. As DCS is also an inflammatory process, TNF-α, IL-1β and MCP-1 were selected as indices for determining severity of inflammatory responses. In a previous study, IL-1β and MCP-1 peaked at 6 and 12 h following decompression, respectively.[25] XBJ notably decreased the elevated serum levels of IL-1β following decompression. IL-1β is an important pro-inflammatory cytokine mediating other cytokine production and vascular injuries related to decompression.[26] Though no statistical difference existed in rate of change in MCP-1 between groups, XBJ treatment showed a trend toward decreased MCP-1 levels. XBJ significantly decreased TNF-α level in BALF. The alleviated systemic and local lung inflammatory responses may in turn reduce lung injury induced by circulating bubbles.

It is reported that pulmonary pathophysiologic changes caused by DCS include pulmonary hypertension, which is due to either vascular obstruction by bubbles or inflammatory cell accumulation.[27] Accompanied pulmonary hypertension, the permeability of pulmonary micro-vascular and epithelial membranes induces interstitial and alveolar oedema.[28] Although clinical symptoms are typically not present in divers, there is ultrasonic evidence showing subclinical pulmonary oedema following decompression.[7] XBJ has been shown to be effective in attenuating acute lung injury via inhibition of the activity of Toll-like receptor 4 (TLR4) and nuclear factor kappa B (NF-κB) and decreasing lung permeability.[29] As confirmed in the present study, increased levels of BALF protein and lung W/D ratio were significantly inhibited by XBJ when compared with the saline group. XBJ treatment significantly ameliorated pulmonary oedema and showed a tendency to improve respiratory function following decompression. These findings are consistent with other studies of XBJ on acute lung injury caused by dichlorvos poisoning and sepsis.[15,30]

The presence of bubbles is also accompanied by activation of inflammatory cascades, capillary leakage and haemconcentration,[31] which make it more difficult to treat DCS by HBOT alone.[23] As an extraction from many herbs, XBJ exerts powerful anti-inflammatory properties via many pathways including NF-κB inhibition and IκB kinase enzyme activation,[32,33] and it has been found efficient in suppressing uncontrolled release of inflammatory factors.[34] The present results suggest that XBJ ameliorated systemic and local inflammation responses following decompression, and notably attenuated lung injuries as a result, which is in accord with previous studies.[15] XBJ is also reported to reduce lung injuries via ameliorating apoptosis.[16] This alleviation of biochemical indices provides support for the

use of XBJ in treating lung injuries caused by decompression bubbles.

XBJ consists of five Chinese herbs. Though it is unclear which component(s) contribute to its (their) anti-inflammatory effects, XBJ exhibits good batch-to-batch quality consistency (with lot-to-lot variability of 9.6% for the level I pathalide),[33] and no serious side effects were found in 31,913 participants in a clinical study.[35] It has been widely adopted for the treatment of sepsis and MODS, as well as COVID-19 in China.[17,36] The present study explored potential benefits of XBJ in DCS for the first time, and confirmed its potential in treating decompression-induced lung injuries. However, this study has limitations. The current sample size may be too small to detect differences in DCS incidence and death rate, and it was calculated that a sample size of 40 for the two groups would be required to provide 80% power to reach statistical significance. Although XBJ has been adopted clinically in treating various diseases, more animal studies are still needed before using XBJ on divers.

Conclusions

XBJ significantly attenuated decompression-induced lung injuries in this animal model; an effect mainly attributed to its anti-inflammatory properties. XBJ has been widely used clinically with few side effects, and it may be a promising candidate for DCS treatment.

References

1 Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. Lancet. 2011;377(9760):153–64. doi: 10.1016/S0140-6736(10)61085-9. PMID: 21215883.

2 Mazur A, Lambrechts K, Buzzacott P, Wang Q, Belhomme M, Theron M, et al. Influence of decompression sickness on vasomotion of isolated rat vessels. Int J Sports Med. 2014;35:551–58. doi: 10.1055/s-0033-1358472. PMID: 24258471.

3 Barak M, Katz Y. Microbubbles: Pathophysiology and clinical implications. Chest. 2005;128:2918–32. doi: 10.1378/chest.128.4.2918. PMID: 16236969.

4 Pontier J-M, Gempp E, Ignatescu M. Blood platelet-derived microparticles release and bubble formation after an open-sea air dive. Appl Physiol Nutr Metab. 2012;37:888–92. doi: 10.1139/h2012-067. PMID: 22735037.

5 Levett DZH, Millar IL. Bubble trouble: A review of diving physiology and disease. Postgrad Med J. 2008;84(997):571–8. doi: 10.1136/pgmj.2008.068320. PMID: 19103814.

6 Hjelde A, Brubakk AO, Bergh K, Videm V, Ustad AL. Effect of anti-C5a antibody on blood-lung and blood-brain barrier in rabbits after decompression. Undersea Hyperb Med. 1999;26:249–56. PMID: 10642072.

7 Ljubkovic M, Gaustad SE, Marinovic J, Obad A, Ivancev V, Bilopavlovic N, et al. Ultrasonic evidence of acute interstitial lung edema after SCUBA diving is resolved within 2–3h. Respir Physiol Neurobiol. 2010;171(2):165–70. doi: 10.1016/j.resp.2010.02.008. PMID: 20188217.

8 Neuman TS, Spragg RG, Wagner PD, Moser KM. Cardiopulmonary consequences of decompression stress. Respir Physiol. 1980;41:143–53. doi:10.1016/0034-5687(80)90048-1. PMID: 6776599.

9 Geng M, Zhou L, Liu X, Li P. Hyperbaric oxygen treatment reduced the lung injury of type II decompression sickness. Int J Clin Exp Pathol. 2015;8:1797–803. PMID: 25973070. PMCID: PMC4396314.

10 Han C, Zhang P, Liu W. Macrophage polarization is related to the pathogenesis of decompression induced lung injury. Med Gas Res, 2017;7:220–3. doi: 10.4103/2045-9912.215753. PMID: 29152216. PMCID: PMC5674661.

11 Jiang M, Zhou M, Han Y, Xing L, Zhao H, Dong L, et al. Identification of NF-κB inhibitors in Xuebijing injection for sepsis treatment based on bioactivity-integrated UPLC-Q/TOF. J Ethnopharmacol. 2013;147:426–33. doi: 10.1016/j.jep.2013.03.032. PMID: 23524166.

12 He J, Tan Z, Zhang M, Guo L. Effect of Xuebijing injection on hemodynamics and endothelial function in patients with severe sepsis: a prospective study. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2015;27:127–32. doi: 10.3760/cma.j.issn.2095-4352.2015.02.010. PMID: 25665612.

13 Song Y, Yao C, Yao Y, Han H, Zhao X, Yu K, et al. XueBiJing injection versus placebo for critically ill patients with severe community-acquired pneumonia: A randomized controlled trial. Crit Care Med. 2019;47(9):e735–e743. doi: 10.1097/CCM.0000000000003842. PMID: 31162191. PMCID: PMC6727951.

14 Gao J, Kong L, Liu S, Feng Z, Shen H, Liu Q, et al. A prospective multicenter clinical study of Xuebijing injection in the treatment of sepsis and multiple organ dysfunction syndrome. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2015;27:465–70. doi: 10.3760/cma.j.issn.2095-4352.2015.06.010. PMID: 26049185. Chinese.

15 He F, Wang J, Liu Y, Wang X, Cai N, Wu C, et al. Xuebijing injection induces anti-inflammatory-like effects and downregulates the expression of TLR4 and NF-κB in lung injury caused by dichlorvos poisoning. Biomed Pharmacother. 2018;106:1404–11. doi: 10.1016/j.biopha.2018.07.111. PMID: 30119213.

16 Chen Y, Tong H, Pan Z, Jiang D, Zhang X, Qiu J, et al. Xuebijing injection attenuates pulmonary injury by reducing oxidative stress and proinflammatory damage in rats with heat stroke. Exp Ther Med. 2017;13:3408–16. doi: 10.3892/etm.2017.4444. PMID: 28588676. PMCID: PMC5450780.

17 Jin Y, Cai L, Cheng Z, Cheng H, Deng T, Fan Y, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res. 2020;7(1):4. doi: 10.1186/s40779-020-0233-6. PMID: 32029004. PMCID: PMC7003341.

18 Zhang K, Wang M, Wang H, Liu Y, Buzzacott P, Xu W. Time course of endothelial dysfunction induced by decompression bubbles in rats. Front Physiol. 2017;8:181. doi: 10.3389/fphys.2017.00181. PMID: 28386238. PMCID: PMC5362629.

19 Bosco G, Rizzato A, Quartesan S, Camporesi E, Mrakic-Sposta S, Moretti S, et al. Spirometry and oxidative stress after rebreather diving in warm water. Undersea Hyperb Med. 2018;45:191–8. PMID: 29734571.

20 Atkins CE, Lehner CE, Beck KA, Dubielzig RR, Nordheim EV, Lanphier EH. Experimental respiratory decompression sickness in sheep. J Appl Physiol (1985). 1988;65:1163–71. doi: 10.1152/jappl.1988.65.3.1163. PMID: 3182487.

21 Belperio JA, Keane MP, Burdick MD, Londhe V, Xue YY, Li K, et al. Critical role for CXCR2 and CXCR2 ligands during the pathogenesis of ventilator-induced lung injury. J Clin Invest. 2002;110:1703–16. doi: 10.1172/JCI15849. PMID: 12464676. PMCID: PMC151632.

22 Nishina K, Mikawa K, Takao Y, Shiga M, Maekawa N, Obara H. Intravenous lidocaine attenuates acute lung injury induced by hydrochloric acid aspiration in rabbits. Anesthesiology. 1998;88:1300–9. doi: 10.1097/00000542-199805000-00022. PMID: 9605691.

23 Papadopoulou V, Tang M-X, Balestra C, Eckersley RJ, Karapantsios TD. Circulatory bubble dynamics: from physical to biological aspects. Adv Colloid Interface Sci. 2014;206:239–49. doi: 10.1016/j.cis.2014.01.017. PMID: 24534474.

24 Butler BD, Hills BA. The lung as a filter for microbubbles. J Appl Physiol Respir Environ Exerc Physiol. 1979;47:537–43. doi: 10.1152/jappl.1979.47.3.537. PMID: 533747.

25 Meng WT, Qing L, Li CZ, Zhang K, Yi HJ, Zhao XP, et al. Ulinastatin: A potential alternative to glucocorticoid in the treatment of severe decompression sickness. Front Physiol. 2020;11:273. doi: 10.3389/fphys.2020.00273. PMID: 32273851. PMCID: PMC7113395.

26 Thom SR, Bhopale VM, Yang M. Microparticle-induced vascular injury in mice following decompression is inhibited by hyperbaric oxygen: Effects on microparticles and interleukin-1β. J Appl Physiol (1985). 2019;126:1006–14. doi: 10.1152/japplphysiol.01109.2018. PMID: 30763157.

27 Little TM, Butler BD. Dibutyryl cAMP effects on thromboxane and leukotriene production in decompression-induced lung injury. Undersea Hyperb Med. 1997;24:185–91. PMID: 9308142.

28 Marinovic J, Ljubkovic M, Obad A, Breskovic T, Salamunic I, Denoble PJ, et al. Assessment of extravascular lung water and cardiac function in trimix SCUBA diving. Med Sci Sports Exerc. 2010;42:1054–61. doi: 10.1249/MSS.0b013e3181c5b8a8. PMID: 19997032.

29 Liu MW, Su MX, Zhang W, Wang YQ, Chen M, Wang L, et al. Protective effect of Xuebijing injection on paraquat-induced pulmonary injury via down-regulating the expression of p38 MAPK in rats. BMC Complement Altern Med. 2014;14:498. doi: 10.1186/1472-6882-14-498. PMID: 25511395. PMCID: PMC4301062.

30 Shi X, Chen G, Wei J, Feng D, Chen Y, Zhou H, et al. UHPLC-Q-TOF MS-based metabolic analysis for the therapeutic efficacy of "xuebijing injection" against sepsis-induced acute lung injury. Evid Based Complement Alternat Med. 2018;2018:8514619. doi: 10.1155/2018/8514619. PMID: 30344613. PMCID: PMC6174773.

31 Boussuges A, Blanc P, Molenat F, Bergmann E, Sainty JM. Haemoconcentration in neurological decompression illness. Int J Sports Med. 1996;17:351–5. doi: 10.1055/s-2007-972859. PMID: 8858406.

32 Xu Y, Jiang WL, Zhang SP, Zhu HB, Hou J. Protocatechuic aldehyde protects against experimental sepsis in vitro and in vivo. Basic Clin Pharmacol Toxicol. 2012;110:384–9. doi: 10.1111/j.1742-7843.2011.00827.x. PMID: 22050905.

33 Zhou H, Bian D, Jiao X, Wei Z, Zhang H, Xia Y, et al. Paeoniflorin protects against lipopolysaccharide-induced acute lung injury in mice by alleviating inflammatory cell infiltration and microvascular permeability. Inflamm Res. 2011;60:981–90. doi: 10.1007/s00011-011-0359-9. PMID: 21744312.

34 Zhang N, Cheng C, Olaleye OE, Sun Y, Li L, Huang Y, et al. Pharmacokinetics-based identification of potential therapeutic phthalides from xuebijing, a Chinese herbal injection used in sepsis management. Drug Metab Dispos. 2018;46:823–34. doi: 10.1124/dmd.117.079673. PMID: 29523601.

35 Zheng R, Wang H, Liu Z, Wang X, Li J, Lei X, et al. A real-world study on adverse drug reactions to Xuebijing injection: hospital intensive monitoring based on 93 hospitals (31,913 cases). Ann Transl Med. 2019;7:117. doi: 10.21037/atm.2018.09.26. PMID: 31032272. PMCID: PMC6465439.

36 Li C, Wang P, Zhang L, Li M, Lei X, Liu S, et al. Efficacy and safety of Xuebijing injection (a Chinese patent) for sepsis: A meta-analysis of randomized controlled trials. J Ethnopharmacol. 2018;224:512–21. doi: 10.1016/j.jep.2018.05.043. PMID: 29860133.

Conflicts of interest and funding: nil

Submitted: 30 March 2020
Accepted after revision: 30 June 2020

Effects of freediving on middle ear and eustachian tube function

Moritz F Meyer[1,2], Kristijana Knezic[1], Stefanie Jansen[1], Heinz D Klünter[1], Eberhard D Pracht[3], Maria Grosheva[1]

[1] *Department of Otorhinolaryngology, Head and Neck Surgery, University of Cologne, Germany*
[2] *Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Essen, University Duisburg-Essen, Essen, Germany*
[3] *German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany*

Corresponding author: *Dr Moritz F Meyer, Department of Otorhinolaryngology, Head and Neck Surgery, Faculty of Medicine, University Hospital of Essen, Hufelandstraße 55, 45122 Essen, Germany*
moritz.meyer@uk-essen.de

Key words
Tympanometry; Repetitive diving; Ear barotrauma; ENT; Risk factors; Valsalva manoeuvre

Abstract
(Meyer MF, Knezic K, Jansen S, Klünter HD, Pracht ED, Grosheva M. Effects of freediving on middle ear and eustachian tube function. Diving and Hyperbaric Medicine. 2020 December 20;50(4):350–355. doi: 10.28920/dhm50.4.350-355. PMID: 33325015.)
Introduction: During descent in freediving there is exposure to rapidly increasing pressure. Inability to quickly equalise middle ear pressure may cause trauma to the ear. This study aimed to evaluate the occurrence of pressure-related damage to the middle ear and the Eustachian tube during freediving and to identify possible risk factors.
Methods: Sixteen free divers performed diving sessions in an indoor pool 20 metres' freshwater (mfw) deep. During each session, each diver performed four own free dives and up to four safety dives. Naso- and oto-endoscopy and Eustachian tube function tests were performed on the right and left ears before diving, between each session and after the last session. The otoscopic findings were classified according to the Teed classification (0 = normal tympanic membrane to 4 = perforation). Additionally, ENT-related complaints were assessed using a questionnaire.
Results: Participants performed 317 dives (on average 20 dives per diver, six per session). The average depth was 13.3 mfw. Pressure-related changes (Teed 1 and 2) were detected in 48 % of ears. Teed level increased significantly with an increasing number of completed sessions ($P < 0.0001$). Higher pressure-related damage (Teed 2) occurred in less experienced divers, was associated with significantly lower peak pressures in the middle ear and led to more ear-related symptoms. A preference for the Frenzel technique for middle ear pressure equalisation during freediving was shown.
Conclusions: Pressure exposure during freediving had a cumulative effect on the middle ear. Factors such as diving depth, diving experience and number of diving sessions correlated with the occurrence of higher Teed levels.

Introduction

Freediving is the oldest form of diving. In the past, free divers collected shells, sponges and pearls or went spear fishing. Several indigenous sea harvesting groups, like Japanese Ama divers, still practice freediving today.[1,2]

Freediving is also common among military and recreational divers. In the leisure sector, the main focus of freediving is on exploring the underwater world with minimal equipment. In competitive forms, longer apnoea times or distance and depth performance are targeted.

During descent in freediving, the body is exposed to rapid pressure increase over a short period of time. More than in any other sport, proper function of the Eustachian tube, the tympanic cavity and the mastoid, and use of an efficient equalisation technique are essential for prevention of middle and inner ear barotrauma.[3–11] Although learning the most appropriate pressure equalisation technique is an essential step in education of free divers, there is little or no research on pressure equalisation or pressure related changes in the middle ear. Besides the common techniques such as the Toynbee and Valsalva manoeuvres, there are less common mechanisms like the Frenzel and Delonca manoeuvres. Frenzel, which was developed in the German Air Force, is based on a pressure increase in the nasopharynx, created by compression of the tongue on the palate. The Delonca technique (also called 'hands-free' technique) is based on voluntary control of the tensor veli palatine muscle or moving the jaw to open the Eustachian tube. Another description of the procedure is to tense the muscles of the soft palate and the throat while pushing the lower jaw forward and down as if to start yawning. This should pull the Eustachian tube open.

The available literature on middle ear barotrauma includes mainly retrospective reviews or studies using subjective questionnaires.[5,6,9–11] Only a few studies have prospectively examined scuba divers for ear-related complaints and

ear examination findings immediately before and after diving.[3,12–16] Several investigations have suggested that cases of ear barotrauma in commercial and recreational divers are likely under-reported.[9,10]

The aim of this study was to evaluate the occurrence of pressure-related damage to of the middle ear and the Eustachian tube during freediving and to identify possible risk factors.

Methods

The Ethics Committee of the University of Cologne, Germany, approved this observational prospective cohort study. The study (local register code 17-461) was registered in the German Register for Clinical Studies (DRKS: DRKS00013946). All participants signed a written consent before participation.

INCLUSION CRITERIA

Only divers with experience in freediving were included. None had been diving (freediving or scuba diving) for at least 24 hours prior to the study. Every participant presented a medical certificate confirming his or her physical fitness to dive.

DIVING SETTING AND ASSESSMENT

The study, including all examinations and dives, was carried out in one day.

Before diving, ear nose and throat (ENT) endoscopy and a Eustachian tube function test (ETFT) (tympanometry) were conducted. The endoscopy included the examination of the nasopharynx, the nose and both ears with a rigid 0 endoscope (Storz, Tuttlingen, Germany). Additionally, each participant filled in a questionnaire about their freediving experience (number of sessions, time period of freediving, maximum diving depth, last freediving session), preferred pressure equalisation technique and their diving complaints during past descents (ENT/non-ENT-related).

All dives were carried out in an indoor freshwater pool with a maximum depth of 20 metres' fresh water (mfw) (Dive4Life, Siegburg, Germany). Sixteen free divers participated in the study. The descending position (e.g., prone, head first), as well as the diving depth was not predetermined. Diving sessions were performed in groups of four.

The maximum number of dives per session per diver was set to four. Additionally, each diver could perform up to four safety dives for a group partner. The objective for the safety diver was to meet the free diver at a depth of 10 mfw and escort him to the surface.

For inclusion, each diver had to complete each full session and at least two sessions, but could drop out between any further sessions. In this setting, each diving session consisted of a minimum of four dives and maximum of eight dives (four regular + four safety dives). Participants recorded the depth of each dive directly after the ascent on a board, which was attached to a buoy in the pool.

Before the first session and at the end of each further session, divers were examined and interviewed on the surface. Examinations included endoscopic otoscopy, ETFT of both ears, and completion of a questionnaire.

OTOSCOPY

The endoscopic otoscopic findings were classified using the Teed scale for scoring barotrauma,[17] modified by Edmonds,[18] for the right and left ears separately. Teed level 0 defined a normal tympanic membrane, Teed 1 a retraction and increased vascularisation of the manubrium and shrapnel's membrane, Teed 2 retraction and hyperaemia of the entire tympanic membrane, Teed 3 fluid or blood in the middle ear, and Teed 4 a perforated tympanic membrane.

EUSTACHIAN TUBE FUNCTION TEST

ETFT was carried out using a Titan tympanometer according to the manufacturer's guidelines (Titan, Interacoustics A/S, Denmark) in sitting position for each ear separately. The frequency setting for tympanometry was 226 Hz. Baseline tympanometry was performed first (R-tymp), a second measurement was made after a Valsalva manoeuvre (V-tymp) and a third after swallowing (S-tymp). We refer to a previous publication for details.[16]

QUESTIONNAIRES

After each diving session, the following questions were asked:
1. Have you had problems with pressure equalisation or pain during the session? Options: yes or no.
2. Which pressure equalisation method was preferably used during the session? Options: Frenzel, Valsalva, Toynbee, Delonca. Multiple answers were allowed.

After completing all dives, all participants additionally rated the ease of the pressure equalisation during the sessions in response to the following question: "*Have you experienced changes in pressure equalisation during the training*? If yes, "*Did it get easier or worse during the training*?" and "*Have you skipped a dive because of equalisation problems*?"

STATISTICAL ANALYSIS

All data were anonymised. Findings for the right and the left ear were analysed separately. We used SPSS software, version 23.0.0.0 (IBM Corporation, USA) for statistical evaluation. Continuous variable data were presented as mean (SD) or median and 95% confidence intervals. Categorical variables are presented as absolute numbers

and percentages. We applied the Kruskall-Wallis test for analysis of non-parametric continuous data and Pearson´s Chi-squared test for analysis of categorical data. A P-value < 0.05 was considered statistically significant. No corrections were made for multiple testing. All reported P-values are two-sided.

Results

DIVER CHARACTERISTICS

Sixteen free divers (five female) participated in the study. Their mean age was 51 y (range 27 to 67). The divers had a mean diving experience of 7 y (95% CI 4 to 9 y) with a mean number of 105 freediving sessions (95% CI 16 to 193) and a mean maximum depth of 28 metres (95% CI 20 to 36). The last dive was carried out on average two months (95% CI 1 to 3 months) before the study.

We defined three participants with ≥ 100 completed freediving sessions as experienced divers and two participants with ≤ 10 freediving sessions as inexperienced. The remaining 11 divers were defined as intermediate. Twelve participants (12/16; 75%) had confirmed ENT-specific problems in the past. Six participants reported problems with pressure equalisation before the study.

DIVES

During the study, 16 participants completed 317 dives; an average of 20 dives per participant. The mean number of dives per participant per session was six (95% CI 5 to 7 dives) with an average depth of 13.3 mfw (95% CI 9.9 to 16.8).

OTOSCOPIC FINDINGS

Initially, 28 ears (87.5%) were characterised as Teed 0 and 4 (12.5%) as Teed 1 (Table 1). Teed grading changed during the study to a higher level in 48% of the ears. Of these, Teed 1 was found in 40% and Teed 2 in 8% (Table 1). No ears received a Teed 3 or 4 score. Increased Teed score was associated with an increasing number of completed freediving sessions (P < 0.0001, chi-square test) (see Figure 1).

Correlation of otoscopic findings and diving experience

The experience of participants did not significantly influence the Teed level (P = 0.145, Chi-square test) though the study was underpowered to demonstrate this. Teed level 2 was evident only in less experienced divers (data not shown).

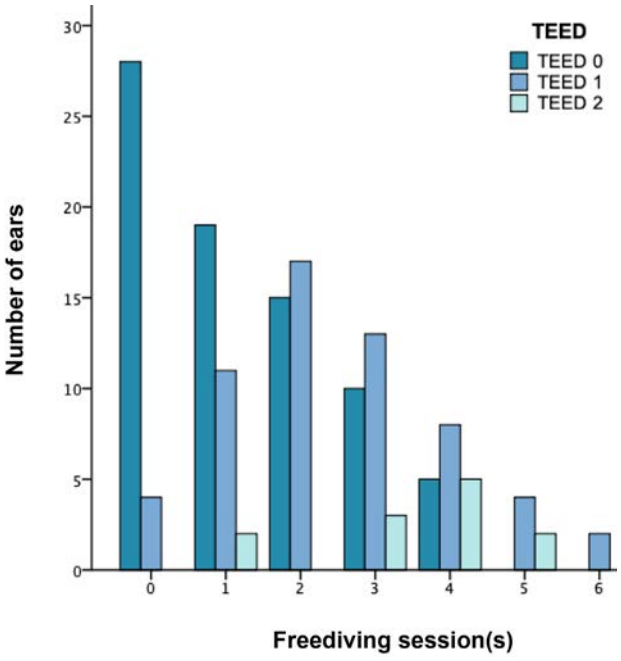
Correlation of otoscopic findings and diving depth

Participants with Teed 2 barotrauma performed significantly shallower dives than divers with Teed 1 or 0 (pair-wise comparison, Teed 2 vs. 1 P = 0.020, Teed 2 vs. 0 P = 0.025, respectively, Mann-Whitney U test) (Figure 2).

Table 1
Summary of all ear findings collected in the study according to the Teed classification. Two sessions were performed by all divers. After the second session, there were divers who did not perform any further sessions. Accordingly, the number of ear findings after session two decreased

Session	Number of ears			
	Teed 0	Teed 1	Teed 2	Sum
0	28	4	0	32
1	19	11	2	32
2	15	17	0	32
3	10	13	3	26
4	5	8	5	18
5	0	4	2	6
6	0	2	0	2

Figure 1
Change of otoscopic findings during the freediving sessions on both sides. The absolute number of findings with Teed 0, 1 and 2 scores is shown. The number of findings with Teed > 0 increases significantly with the consecutive number of sessions (P < 0.0001, Chi-square test)



Correlation of otoscopic findings and ETFT

Initially, all participants showed a type-A tympanogram in the ETFT. The peak pressure (R-tymp) in the middle ear remained stable during the consecutive sessions without significant changes in those divers with Teed score 0 and 1. However, participants with higher Teed level (Teed 2 vs. 0 and vs. 1), showed a significant negative shift of the peak pressure (P < 0.0001, Figure 3).

Figure 2

Average diving depth of all dives in participants with Teed 0, 1 and 2 scores. Participants with Teed 2 scores performed significantly shallower dives than divers with Teed 1 or 0 scores (pair-wise comparison, Teed 2 vs. 1 $P = 0.020$, Teed 2 vs. 0 $P = 0.025$ respectively, Mann-Whitney U test). The circles and asterisks represent outliers. mfw = metres' fresh water

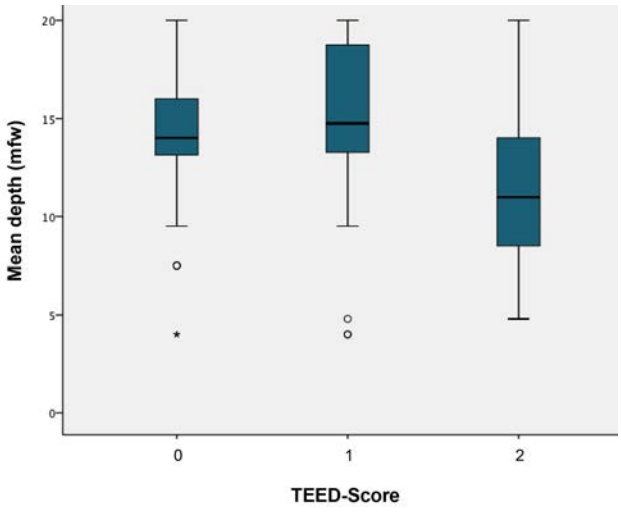
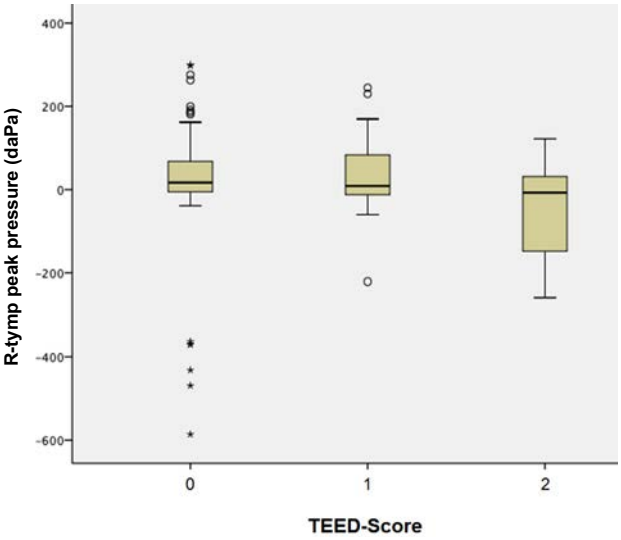


Figure 3

Correlation of the peak pressure (R-tymp, in deka Pascals [daPa]) and Teed score (Teed 0, 1 and 2). Participants with Teed 2 barotrauma showed a significantly lower peak pressure than those with Teed 0 and Teed 1, respectively ($P < .0001$). The circles and asterisks represent outliers



Correlation of otoscopic findings and equalisation technique

Most of the divers used more than one technique during the training. The techniques were the Frenzel manoeuvre in (56%), Valsalva (47%) and Toynbee (24%). Only 10% performed the Delonca technique during the diving sessions.

Participants with Teed 2 barotrauma more often employed the Valsalva manoeuvre than the Frenzel technique in comparison to divers with Teed 0 or 1 scores ($P < 0.0001$, chi-square test). Participants with high experience only used the Frenzel technique for pressure equalisation, whereas six of 11 intermediate divers and one of the two beginners applied the Frenzel manoeuvre ($P < 0.002$; chi-square test).

Correlation of otoscopic findings and pressure equalisation-related complaints

Divers with Teed 0 and Teed 1 scores did not report problems with pressure equalisation or pain during diving in 81% and 73% of cases respectively. Complaints of pressure equalisation were reported by 19%, 27% and 67% of divers with Teed 0, 1 and 2 scores respectively. Participants with Teed level 2 barotrauma reported significantly more complaints and pain during diving ($P = 0.003$, Chi-square test).

Regarding pressure equalisation, 6 of 16 (38%) participants affirmed that they had problems with equalisation during descent. Three of them reported that equalisation improved, two reported that it became worse. The one remaining diver reported no changes in equalisation. Three participants had to discontinue the dive because of the equalisation problems.

Discussion

Both scuba divers and free divers are exposed to pressure differences during diving. In scuba diving, a 'typical' dive lasts up to an hour, reaching the deepest depth relatively quickly and moving to a shallower depth toward the end of the dive. The special aspect of freediving is that the descent and ascent must take place within one breath. The depth of the dive is therefore, the dependent on the diver's apnoea time and the ability to easily equalise middle ear pressure. Thus, due to the nature of the sport, typical free divers make many more descents and ascents than scuba divers during a day of diving.

During the present study, 16 free divers were observed during training sessions and the pressure-related changes in the middle ear and the function of the Eustachian tube were evaluated in real time. The number of otoscopic findings with higher Teed scores increased significantly with an increasing number of completed diving sessions (Figure 1, Table 1). In 52% of the examined ears, no changes of Teed score were seen. In similar studies in scuba divers, the incidence of a Teed score > 0 was 58% and 74% after repetitive multiple-level dives in saltwater and freshwater respectively.[3,14] However, the scuba dives were carried out over several days and might be associated with a higher total pressure-related stress than the freediving sessions in the current study. Most otoscopic changes in freedivers were mild (Teed 1) and severe changes (such as Teed 3), were not present. This indicates that freedivers might cope with pressure exposure differently than scuba divers.

The experience of the participants might also influence the results. In the current study, most participants were

intermediate in terms of freediving experience (number of sessions 11–99). Two were beginners with < 10 sessions and three divers reported ≥ 100 sessions. Teed 2 barotrauma was only present in divers with less than 100 sessions. Interestingly, several of them (6/16), independent of their level of experience, affirmed problems with pressure equalisation during previous diving.

Most of the participants used several techniques for pressure equalisation. The Frenzel technique was most preferred, followed by the Valsalva and Toynbee manoeuvres respectively. It is noticeable that experienced divers only used the Frenzel manoeuvre, while the less experienced also used other techniques. We may assume, that more experienced divers equalised differently (Frenzel) and more efficiently, thus showing less barotrauma. However, the mechanism of this manoeuvre should be further investigated under standardised conditions (i.e., in a pressure chamber). In further studies it should be investigated whether training in the correct execution of effective pressure equalisation mechanisms (e.g., the Frenzel manoeuvre) can lead to a reduction of barotrauma.

Our results further show, that shallower dives and use of Valsalva manoeuvre were associated with a higher incidence of Teed level 2 barotrauma and negative pressure in the middle ear (Figure 2). The association with shallow dives seems paradoxical at first, since these divers must have had a lower pressure load on the middle ear than divers with greater diving depths. But a similar association with the diving depths was shown during a study in freshwater scuba divers.[14] It should be remembered that as pressure increases, the greatest proportional changes in volume occur over the first 10 m of descent, thus this depth is clearly sufficient to cause changes in the middle ear. These findings suggest that beginners might be more susceptible to barotrauma than experienced free divers, who may transition through the first 10 m of descent more efficiently from an equalisation perspective. However, the small number of participants does not allow firm conclusions on the effect of divers' experience on pressure equalisation.

In relation to pressure change in the tympanic cavity, the R-tymp peak pressure did not change significantly after each diving session except in divers who developed Teed 2 barotrauma (see below). This contrasts with investigations in scuba divers which revealed a negative shift of peak pressure during repetitive dives; however these were carried out over several consecutive days.[15,16] A similar effect might also occur in freediving after diving over several consecutive days. Further studies are needed to evaluate this. The results of the current study show that the high-pressure load during freediving does not cause a significant change in Eustachian tube function – at least not more than in scuba diving.

In contrast to ears with Teed 0 and 1 scores, a significant negative shift of the middle ear pressure was present in ears with Teed level 2 barotrauma (Figure 3). Although higher Teed levels (Teed > 2) were not seen in the current group, Teed 2 was symptomatic in most of the divers. The more symptomatic pressure-related changes of the tympanic membrane and the middle ear correlated to previous publications in which scuba divers also revealed more symptoms in relation to higher Teed levels with the maximum of complaints (35%) if Teed 2 barotrauma occurred.[3,14] As this level of barotrauma is both relatively common and symptomatic in free divers and scuba divers,[3,14] this degree of pressure damage might be considered 'clinically relevant' barotrauma and should be communicated to the diver.

Altogether, participants reported ear-related complaints after 27% of the dives. This number is higher than in studies with scuba divers (19% in scuba divers in saltwater and 10% in freshwater).[3,14] This aspect is ultimately a logical consequence of the more rapidly changing pressure differentials in freediving and the consequent need for optimal Eustachian tube function.

The present study certainly has its limitations. The low number of participants limits generalisation and drawing of firm conclusions. In addition, only one day of freediving was analysed. Free divers should be examined over several consecutive days to assess the cumulative effect of pressure exposure. In addition, the divers were free to choose their diving profile and diving behaviour, so there was no standardised test set-up. The dives undertaken were sufficient to show some significant effects; however, the lack of standardisation reduced comparability. In addition, other factors not explored here might also play a role in Eustachian tube function. For example, neither the temperature of the water nor the chlorination were considered for this evaluation. Furthermore, the limitation of the ETFT has to be mentioned. The ETFT tympanometer offered the advantage of being easily operated and providing dynamic tympanometry during the pressure equalisation manoeuvres. However, no standardised values are available for this test.

Conclusions

In this prospective, observational cohort trial, repeated pressure exposure during freediving had a cumulative effect on the middle ear. Increasing number of diving sessions was associated with a higher number of pathologic Teed scores (Teed 1 and 2). Factors such as diving depth, diving experience and number of diving sessions correlated with the occurrence of higher Teed levels.

References

1 Mohri M, Torii R, Nagaya K, Shiraki K, Elsner R, Takeuchi H, et al. Diving patterns of Ama divers of Hegura Island, Japan. Undersea Hyperb Med. 1995;22:137–43. PMID: 7633275.

2 Yanagawa Y, Omori K, Takeuchi I, Jitsuiki K, Ohsaka H, Ishikawa K. The on-site differential diagnosis of decompression sickness from endogenous cerebral ischaemia

in an elderly Ama diver using ultrasound. Diving Hyperb Med. 2018;48:262–3. doi: 10.28920/dhm48.4.262-263. PMID: 30517960. PMCID: PMC6355307.
3 Jansen S, Meyer MF, Boor M, Felsch M, Klünter HD, Pracht ED, et al. Prevalence and risk factors of barotrauma in recreational scuba divers after repetitive dives in salt water. Otol Neurotol. 2016;37:1325–31. doi: 10.1097/MAO.0000000000001158. PMID: 27636390.
4 Molvaer OI, Natrud E. Ear damage due to diving. Acta Otolaryngol Suppl. 1979;360:187–9. PMID: 287337.
5 Elliott EJ, Smart DR. The assessment and management of inner ear barotrauma in divers and recommendations for returning to diving. Diving Hyperb Med. 2014;44:208–22. PMID: 25596834.
6 Klingmann C, Praetorius M, Baumann I, Plinkert PK. Otorhinolaryngologic disorders and diving accidents: an analysis of 306 divers. Eur Arch Otorhinolaryngol. 2007;264:1243–51. PMID: 17639445.
7 Fitz-Clarke JR. Breath-hold diving. Compr Physiol. 2018;8:585–630. doi: 10.1002/cphy.c160008. PMID: 29687909.
8 Azizi MH. Ear disorders in scuba divers. Int J Occup Environ Med. 2011;2:20–6. PMID: 23022815.
9 Hubbard M, Davis FM, Malcolm K, Mitchell SJ. Decompression illness and other injuries in a recreational dive charter operation. Diving Hyperb Med. 2018;48:218–23. doi: 10.28920/dhm48.4.218-223. PMID: 30517953. PMCID: PMC6355312.
10 Ranapurwala SI, Bird N, Vaithiyanathan P, Denoble PJ. Scuba diving injuries among Divers Alert Network members 2010–2011. Diving Hyperb Med. 2014;44:79–85. PMID: 24986725.
11 Monnot D, Michot T, Dugrenot E, Guerrero F, Lafère P. A survey of scuba diving-related injuries and outcomes among French recreational divers. Diving Hyperb Med. 2019;49:96–106. doi: 10.28920/dhm49.2.96-106. PMID: 31177515. PMCID: PMC6704004.
12 Ramos CC, Rapoport PB, Brito Neto RV. Clinical and tympanometric findings in repeated recreational scuba diving. Travel Med Infect Dis. 2005;3:19–25. doi: 10.1016/j.tmaid.2004.06.002. PMID: 17292000.
13 Green SM, Rothrock SG, Green EA. Tympanometric evaluation of middle ear barotrauma during recreational scuba diving. Int J Sports Med. 1993;14:411–5. doi: 10.1055/s-2007-1021201. PMID: 8244609.
14 Jansen S, Meyer MF, Boor M, Felsch M, Klünter HD, Pracht ED, et al. Repetitive freshwater diving: Risk factors and prevalence of barotrauma. Undersea Hyperb Med. 2017;44:407–14. PMID: 29116695.
15 Jansen S, Boor M, Meyer MF, Pracht ED, Volland R, Klünter HD, et al. Influence of repetitive diving in freshwater on pressure equalization and Eustachian tube function in recreational scuba divers. Diving Hyperb Med. 2017;47:223–7. doi: 10.28920/dhm47.4.223-227. PMID: 29241231. PMCID: PMC6706342.
16 Meyer MF, Boor M, Jansen S, Pracht ED, Felsch M, Klünter HD, et al. Influence of repetitive diving in saltwater on pressure equalization and Eustachian tube function in recreational scuba divers. Diving Hyperb Med. 2017;47:214–5. doi: 10.28920/dhm47.4.216-222. PMID: 29241230. PMCID: PMC6706334.
17 Teed RW. Factors producing obstruction of the auditory tube in submarine personnel. United States Naval Medical Bulletin. 1944;42:293–306.
18 Edmonds C. Otological aspects of diving. Australasian Medical Publishing Company; 1973.

Conflicts of interest and funding: nil

Submitted: 16 March 2020
Accepted after revision: 07 July 2020

Safety proposals for freediving time limits should consider the metabolic-rate dependence of oxygen stores depletion

Charlotte Sadler[1], Kaighley Brett[1], Aaron Heerboth[1], Austin R Swisher[2], Nader Mehregani[2], Ross Touriel[1], Daniel T Cannon[2]

[1] *Department of Emergency Medicine, University of California, San Diego, USA*
[2] *School of Exercise and Nutritional Sciences, San Diego State University, San Diego, USA*

Corresponding author: *Dr Charlotte Sadler, Department of Emergency Medicine, University of California, San Diego, USA*
csadler@ucsd.edu

Key words
Hypoxia; Breath-hold diving; Diving research; Hyperventilation; Metabolism; Apnoea; Apnea

Abstract
(Sadler C, Brett K, Heerboth A, Swisher AR, Mehregani N, Touriel R, Cannon DT. Safety proposals for freediving time limits should consider the metabolic-rate dependence of oxygen stores depletion. Diving and Hyperbaric Medicine. 2020 December 20;50(4):356–362. doi: 10.28920/dhm50.4.356-362. PMID: 33325016.)
Introduction: There is no required training for breath-hold diving, making dissemination of safety protocols difficult. A recommended breath-hold dive time limit of 60 s was proposed for amateur divers. However, this does not consider the metabolic-rate dependence of oxygen stores depletion. We aimed to measure the effect of apnoea time and metabolic rate on arterial and tissue oxygenation.
Methods: Fifty healthy participants (23 (SD 3) y, 22 women) completed four periods of apnoea for 60 s (or to tolerable limit) during rest and cycle ergometry at 20, 40, and 60 W. Apnoea was initiated after hyperventilation to achieve $P_{ET}CO_2$ of approximately 25 mmHg. Pulse oximetry, frontal lobe oxygenation, and pulmonary gas exchange were measured throughout. We defined hypoxia as $SpO_2 < 88\%$.
Results: Static and exercise (20, 40, 60 W) breath-hold break times were 57 (SD 7), 50 (11), 48 (11), and 46 (11) s ($F[2.432, 119.2] = 32.0$, $P < 0.01$). The rise in $P_{ET}CO_2$ from initiation to breaking of apnoea was dependent on metabolic rate (time × metabolic rate interaction; $F[3,147] = 38.6$, $P < 0.0001$). The same was true for the fall in SpO_2 ($F[3,147] = 2.9$, $P = 0.03$). SpO_2 fell to < 88% on 14 occasions in eight participants, all of whom were asymptomatic.
Conclusions: Independent of the added complexities of a fall in ambient pressure on ascent, the effect of apnoea time on hypoxia depends on the metabolic rate and is highly variable among individuals. Therefore, we contend that a universally recommended time limit for breath-hold diving or swimming is not useful to guarantee safety.

Introduction

Breath-hold diving, also known as freediving, is a popular recreational and competitive sport. Freediving is all diving done between two breaths of air and without the use of any breathing apparatus or external gas supply.[1] In addition to a stand-alone competitive sport, breath-hold diving is also done as a part of snorkelling, spearfishing, and swimming. Breath-hold divers may compete in various disciplines, including maximum time and depth. Outside of recreational and competitive sport, breath-hold diving is common across all ages in a variety of leisure time activities taking place in swimming pools, lakes, and oceans.

Loss of consciousness and death from hypoxia is a concern during breath-hold diving and swimming and occurs due to low brain tissue oxygen partial pressure (PO_2). At depth, the increased hydrostatic pressure results in an elevated alveolar PO_2 sufficient to maintain consciousness, at least for a limited period of time. However, during ascent the alveolar PO_2 falls with the reduction in hydrostatic pressure in addition to the reduction from normal O_2 consumption. The arterial PO_2 follows suit and unconsciousness may result prior to or just after reaching the surface, which may result in drowning. This is compounded by depletion of O_2 stores due to muscular activity and suppression of the drive to breathe due to low arterial partial pressure of carbon dioxide (PCO_2) following hyperventilation. Hypoxic syncope may occur even in very shallow breath holds, such as in a pool.

Unlike scuba diving, which is regulated and requires training and certification for participation, there is no such prerequisite for participation in breath-hold diving. Although there are many organisations that provide courses and certifications in breath-hold diving, they are not mandatory. As a consequence, it is difficult to disseminate safety rules or protocols to the public, unless they choose to take a formal breath-hold diving class. Thus, any rule that is proposed must be fairly simple to disseminate and implement. At a joint meeting of the Undersea and Hyperbaric Medical Society (UHMS) and the Divers Alert Network (DAN) in 2006, one presenter proposed to set a limit of 60 seconds (s) duration as a safety measure for amateur breath-hold diving.[2]

Although this was not officially adopted or recommended by the aforementioned organisations, we wanted to further investigate this proposition, as a simple, widely applicable safety rule could potentially be very useful. However, a fixed time limit recommendation likely cannot account for variable metabolic rate and oxygen store depletion. For example, hypoxia may not set in during 120 s of static apnoea, yet < 40 s of apnoeic exercise may be sufficient to elicit dangerous hypoxia.[3–5] We aimed to measure the effect of work rate on arterial and tissue oxygenation during apnoeic exercise. We hypothesised that the effects of apnoea on arterial and tissue oxygenation are dependent on metabolic rate.

Methods

The protocol was approved by the Institutional Review Boards at San Diego State University and University of California, San Diego and complied with the Declaration of Helsinki.

PARTICIPANTS

Fifty healthy volunteers were recruited: 22 women; age 23 (SD 2) years (y); body mass index (BMI) 23.5 (2.8) $kg \cdot m^{-2}$; height 163 (7) cm; weight 62.0 (9.1) kg, and 28 men: 23 (3) y; 23.9 (3.9) $kg \cdot m^{-2}$; 179 (8) cm; 76.2 (13.7) kg. Inclusion criteria included age 18–30 y, non-pregnant, non-smokers and ability to participate in physical activity. Exclusion criteria included a history of heart disease, syncope, asthma, vertigo, or exertional chest pain or shortness of breath. Volunteers provided written informed consent and were screened for cardiovascular risks with the Physical Activity Readiness Questionnaire (PAR-Q) prior to beginning any physical activity. A brief intake form was also filled out by the participants to collect information on their prior dive experience and exercise habits. Of the 50 volunteers, one participant had previous free dive experience. Freediving was not formally defined, but instead the responses reflected the participants' own opinion of their activities. However, it was likely that most had engaged in breath-hold swimming and diving during recreational activities. Forty-eight out of 50 participants exercised at least once a week and reported 3.2 (SD 1.6) sessions of exercise per week. There were no differences between the sexes in age, BMI, or reported frequency of exercise sessions per week.

PROTOCOL

Volunteers completed four periods of apnoea for 60 s (or to their tolerable limit if < 60 s) sequentially during seated rest and cycle ergometry at 20, 40, and 60 W (Excalibur Sport PFM, Lode BV, Groningen, NL). Each apnoea was preceded by hyperventilation and subjects were instructed to begin breath-holding when they achieved an end tidal PCO_2 ($P_{ET}CO_2$) of 25 mmHg. This practice is commonly used to extend apnoea duration and was done in an attempt to mimic real world conditions, as well as increase the likelihood that the participants would be able to complete the full 60 s of apnoea. At the initiation of the apnoeic period, participants were instructed to complete a near maximal inspiration and also encouraged to close their glottis. They had been instructed on this technique during the orientation to the experiment. The volunteers were fitted with a nose-clip and remained on the mouthpiece (80 mL dead space) for the duration of the apnoea. At 60 s, or at the limit of tolerance, the participants were encouraged to perform a deep expiration nearly to residual volume as this aided in a confident single-breath measurement of the end tidal gas fractions. Each trial (including the static trial) was preceded and separated by a 3 min period of cycling at 20 W while breathing normally, which we considered active recovery. Pulse oximetry, frontal lobe oxygenation, and pulmonary gas exchange were measured throughout the hyperventilation and apnoeic periods. Based on clinical experience, and for the sake of safety, we chose to define hypoxia as a peripheral oxygen saturation (SpO_2) of < 88% and trials were stopped if SpO_2 dropped below this value. The mouthpiece was removed during the rest periods for comfort.

MEASUREMENTS

Respired gases and ventilation were measured breath-by-breath with a commercial metabolic measurement system (VMAX Encore, Vyaire, Yorba Linda, CA, USA). The system was calibrated immediately prior to each experiment. A 3 L syringe (Hans Rudolph Inc., Shawnee, KS, USA) was used to calibrate the mass flow sensor from ~0.2 to 8.0 $L \cdot s^{-1}$, mimicking flow rates expected at rest and during exercise. The CO_2 and O_2 analysers were calibrated using gases of known concentrations (O_2 26.0 and 16.0%; CO_2 0.0 and 4.0%). Cardiac function was monitored continuously using a 12-lead ECG (GE Cardiosoft, GE Healthcare, Chicago, IL, USA) and a pulse oximeter to measure SpO_2 was applied to the middle or ring finger (Nonin Medica Inc, Plymouth, MN, USA). While SpO_2 was monitored throughout the apnoea, the baseline and nadir of SpO_2 was used for analysis.

NEAR-INFRARED SPECTROSCOPY

Near-infrared spectroscopy (NIRS) was used to measure frontal lobe oxygenation during static and exercising apnoea. The measurement technique relies on the known absorption characteristics of oxygenated haemoglobin (HbO_2) and deoxygenated haemoglobin (HHb) when NIR light is directed into tissue.[6,7] The NIRS device (NIRO-200, Hamamatsu Photonics KK, Hamamatsu, Japan) consisted of a laser diode light source, and a photodiode to detect the returned NIR light after passing through the tissue under interrogation. The NIRS probe (consisting of one fiber optic emission optode and two detection optodes) was secured over the frontal lobe with care to avoid the sinus cavities. The probe was affixed using double-sided adhesive tape and an elastic bandage to minimise ambient light contamination and movement of the probes. The

probes were enclosed in a black rubber housing with a fixed emission/detection distance (detectors were 4 and 5 cm from the emitter) for measurement of the relative absorbance of each chromophore by spatially resolved spectroscopy (SRS). Source light was provided at three wavelengths (775, 810 and 850 nm) and detection sampled at 2 Hz to calculate the tissue oxygenation index (TOI). The SRS method is thought to allow signal loss, due to light scatter, to be better accounted for in calculation of TOI ($[HbO_2]/[HbO_2+HHb]$, expressed as a percentage) and the signal is therefore proportional to chromophore concentration.[6,7]

STATISTICAL ANALYSES

A two-factor repeated measures analysis of variance (ANOVA) was used to test the effect of apnoea duration (time, 2 levels: pre/post apnoea) and metabolic rate (condition, 4 levels: 0, 20, 40, 60 W). A one-factor repeated measures ANOVA was used to test difference in apnoea duration across the static and exercise conditions. Bonferroni-corrected *post hoc t*-tests were used in case of a main effect in the omnibus test. All data were analysed using the Prism v7, GraphPad (GraphPad Software Inc., San Diego, CA, USA). Results are reported as mean (SD).

Results

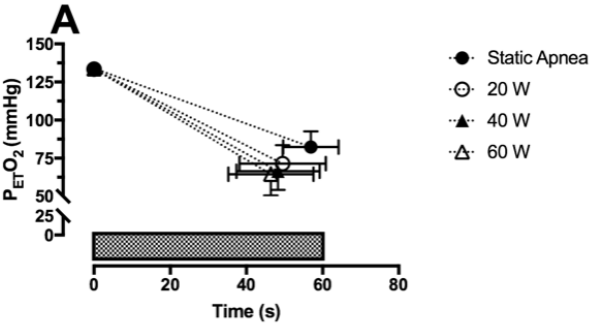
All of the participants completed the protocol, though not every participant was able to complete a full 60 s of apnoea. Static and exercise (20, 40, and 60 W) breath-hold break times were 57 (7), 50 (11), 48 (11), and 46 (11) s ($F [2.432, 119.2] = 32.0$, $P < 0.01$). Mean $P_{ET}CO_2$ at the initiation of apnoea was identical across the four conditions (all at 23 [2] mmHg). No trials were discontinued due to $SpO_2 < 88\%$, and all of the apnoeas < 60 s were ended voluntarily by the participant.

The effect of apnoea time on end tidal PO_2 ($P_{ET}O_2$), $P_{ET}CO_2$, SpO_2, and heart rate was dependent upon the power output (Figure 1A–C, $P_{ET}O_2$ $F [3,147] = 35.01$, $P < 0.0001$, $P_{ET}CO_2$ $F [3,147] = 38.6$, $P < 0.0001$, HR $F [3,147] = 9.6$, $P < 0.0001$; Figure 2A, SpO_2 $F [3,147] = 6.36$, $P = 0.0004$). Frontal lobe TOI was not affected during the apnoeic period (Figure 2B).

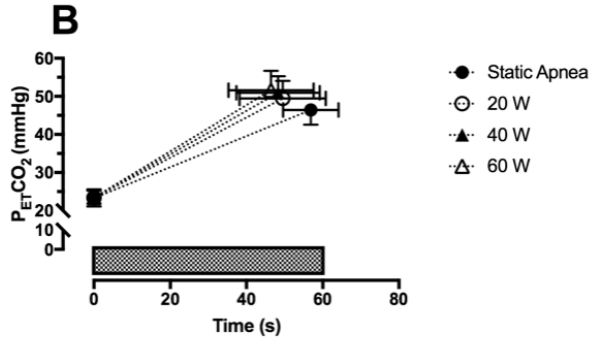
In total, there were 14 episodes of hypoxia (defined as $SpO_2 \leq 88\%$): six in the 20 W trial; five in the 40 W trial; and three in the 60 W trial. No episodes of hypoxia were recorded during the static apnoea. These 14 episodes occurred in eight participants. No oxygen saturations ≤ 88% were observed during the apnoea, rather they occurred in the 30 s period after the apnoea ended. The lowest oxygen saturation observed was 82%. The lowest saturation values occurring after completion of apnoea is due to transit delay to capillary bed in the finger. These nadir SpO_2 values are what appear in the analysis and in Figure 2A. Similar phenomena were present in other breath-hold studies.[4] No participants experienced loss of consciousness or any neurologic signs

Figure 1

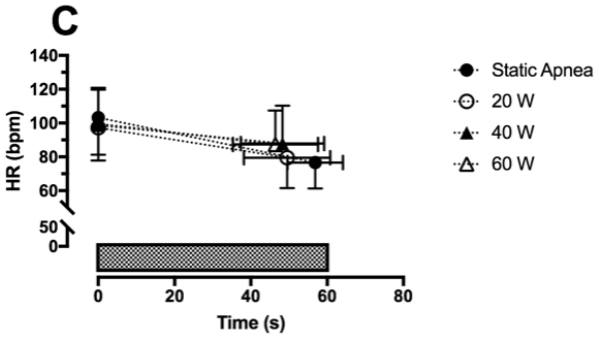
Gas exchange and heart rate during static and exercising apnoea. Shaded rectangle along the x-axis represents the target breath-hold duration of 60 s. Panel A: $P_{ET}O_2$ measured immediately prior to, and at the first expiration following apnoea. A condition x time interaction was present ($F [3,147] = 35.01$, $P < 0.0001$), thus the effect of apnoeic time on $P_{ET}O_2$ depended on the power output. Panel B: $P_{ET}CO_2$ measured immediately prior to, and at the first expiration following apnoea. A condition x time interaction was present ($F [3,147] = 38.6$, $P < 0.0001$), thus the effect of apnoeic time on $P_{ET}CO_2$ depended on the power output. Panel C: Heart rate (HR) measured at initiation and completion of the apnoeic period. A condition x time interaction was present ($F [3,147] = 9.6$, $P < 0.0001$), thus the effect of apnoeic time on heart rate depended on the power output



Condition x Time interaction present
F (3, 147) = 35.01 *p<0.0001*
The effect of apneic period on $P_{ET}O_2$ depends on the power output

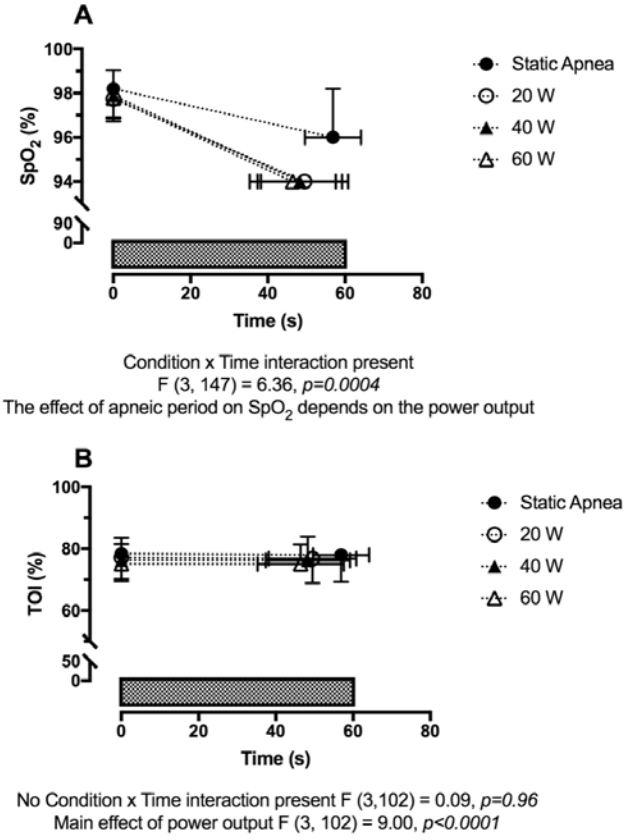


Condition x Time interaction present
F (3, 147) = 38.64, *p<0.0001*
The effect of apneic period on $P_{ET}CO_2$ depends on the power output



Condition x Time interaction present
F (3, 147) = 9.595, *p<0.0001*
The effect of apneic period on HR depends on the power output

Figure 2
Pulse oximetry and near-infrared spectroscopy data during static and exercising apnoea. Shaded rectangle along the x-axis represents the target breath-hold duration of 60 s. Panel A: SpO_2 at initiation and SpO_2 following the apnoeic period. A condition x time interaction was present (F [3,147] = 6.4, P = 0.0004), thus the effect of apnoeic time on S_pO_2 depended on the power output. Panel B: Tissue oxygenation index (TOI), as measured with near-infrared spectroscopy, was not affected by apnea duration (F [1,34] = 0.7, P = 0.4)



or symptoms and the only subjective symptoms reported were presyncope ('seeing stars' as described by one subject).

Discussion

The study aimed to measure the effect of work rate on arterial and tissue oxygenation during apnoeic exercise. Unsurprisingly, the effects of apnoea on $P_{ET}O_2$, $P_{ET}CO_2$, SpO_2, and heart rate were dependent upon the power output and, therefore, the metabolic rate. While it is not advised to interpret main effects in the presence of an interaction, there does appear to be a dose response in most variables to that of work rate (Figure 1). SpO_2 appears to be the exception (Figure 2A) and this may be due to the relatively narrow range of work rates included in our study design. All power outputs were in the moderate intensity domain and this was intentional seeing as heavy and very-heavy intensity work is rather difficult to sustain during apnoea. However, we want to reiterate that making interpretations for dose-response across the main effect of metabolic rate is speculative.

Brain oxygenation was unaffected by apnoea or work rate, owing to apparently robust autoregulation of brain perfusion. Apnoea duration was reduced in a step-wise manner to increasing power output – also not a surprising finding. While not all participants were able to complete the desired 60 s apnoea across the exercise conditions, there were no instances of loss of consciousness or dangerously low SpO_2.

The primary finding reinforces the concept that depletion of O_2 stores during apnoea is dependent on metabolic rate. This argues against the rationale for assigning a fixed time limit for apnoeic swimming or diving. The problem becomes much more complex when hydrostatic pressure changes are considered, such as when a diver descends and ascends during the activity.

THE PUBLIC HEALTH PROBLEM

According to the most recent DAN incidence report, there were 300 breath-hold diving accidents reported between 2010–2013 and 243 (81%) were fatalities. It is unlikely that this represents the true number of incidents, as there is significant under reporting and other obstacles to collecting these data. Nevertheless, there are a substantial number of accidents. It is probable that near-fatalities and accidents are even further under reported than deaths. In the cases reported, the activities described were snorkelling (56%), spear fishing (18%), freediving (16%) and collecting (10%). In a detailed subset of 162 cases, the disabling injury most commonly reported was hypoxic blackout (40 cases, 25%).[8] While there is no national surveillance programme for hypoxic loss of consciousness in water, these events are common even in community pools.[9] These cases occur even in guarded swimming pools, with dangerous underwater breath-holding behaviours cited as a common factor in these incidents.[10] The behaviours cited included: hyperventilation prior to breath-hold and training for static (motionless or still) apnoea and dynamic (swimming or diving) apnoea.[9] Men 16–20 yr of age are at particularly high risk for these behaviours.[10]

OBSTACLES FOR SAFETY RECOMMENDATIONS

An obstacle to developing recommendations or rules for breath hold diving is the wide variability in work rate and duration when complications arise. For example, breath holds longer than 79 s were associated with increased likelihood of blackouts in Hawaiian fisherman[11] whereas people at rest may not become hypoxic even with a breath-hold of up to 120 s.[4]

Next, measures of arterial oxygen saturation (SaO_2) when complications arise is also variable.[5,12] Based upon blood gas measurements from competitive breath-hold divers, a PaO_2 of approximately 30 mmHg is needed to maintain consciousness on the surface after a dive.[13,14] A PaO_2 of 30 mmHg typically corresponds to an SaO_2 of 55–60%. The value is dependent on the allosteric modifiers present

in the blood. Arterial desaturation of 20–50% is possible following 40 s of apnoea while exercising at 100 watts.[5] In another example, 80 s breath hold at two atmospheres absolute pressure with exercise resulted in SaO_2 of 58% with notable impairment.[12] Power to 60 W was constrained at maximum and did not have any incidences of SpO_2 < 88% during the apnoeas. Yet, swimming and diving can require higher power and greater deoxygenation.[15] For example, greater oxygen desaturations are present with higher output (120 W) corresponding to swimming speeds of ~0.5 $m \cdot s^{-1}$.[16] This is not a surprising result and is in agreement with our demonstration that O_2 stores depletion is metabolic rate-dependent. Without carefully defining the metabolic work and O_2 demands, a dive time limit alone, is unlikely to be useful.

A final barrier for safety recommendations is the variability in hydrostatic pressure effects. As in the example above, critical PO_2 in diving studies is that value necessary to maintain consciousness until surfacing. However, this is only the value upon reaching the surface – the PaO_2 at depth is hydrostatic-pressure dependent. Hypoxia of ascent is the primary threat and occurs as alveolar PO_2 is reduced due to the steep fall in hydrostatic pressure.[13] The present study was conducted at 1 atmosphere pressure and could not take account of the effects of hydrostatic pressure change on alveolar, arterial, and tissue PO_2 and PCO_2. Biological variation also complicates critical blood gases. Breath-hold divers' blood gases at a depth of 40 m show expected hyperoxia followed by hypoxia upon surfacing.[17] However, even this behaviour was not uniform. Compression atelectasis and V/Q mismatch at depth followed by subsequent reversal of this phenomenon while ascending may be responsible for the variability in blood gas measurements.[17] Loss of consciousness may also occur just after reaching the surface due to the circulatory delay in the oxygen reaching the brain tissue. Without considering the hydrostatic pressure changes involved in a dive, a time limit may be of limited utility.

ABSENCE OF ADVERSE EVENTS IN THIS EXPERIMENT

An important limitation in the design of this study is that of a sample not powered or designed to test safety. While we did not measure any instances of hypoxia within the 60 s apnoeic period, hypoxia was observed in 14 trials after the cessation of apnoea. The hypoxia definition of SaO_2 88% is, by definition, an arbitrary cutoff and it is not suggested that this be universally used as a definition of hypoxia or danger.

In this study, brain tissue oxygenation was consistently maintained across apnoeic time and metabolic rate. Further, brain oxygenation did not change in proportion to SpO_2 across the range of values achieved. The disparity is due to the superb autoregulation for perfusion in the brain.[18] Whilst there was a main effect of metabolic rate on brain oxygenation, the differences were of no physiologic consequence. These findings are in contrast to trained breath-hold divers performing maximal breath-hold in which cerebral oxygenation is challenged due to the extreme duration of apnoea (> 240 s).[19] Oxygen consumption in trained divers is also decreased, likely due to the development of a more pronounced diving reflex (and subsequent bradycardia).[20] Training prolongs the physiologic break point (onset of involuntary ventilatory activity), secondary to a decreased ventilatory response to increased $PaCO_2$.[21] Clearly, the risk for hypoxia is much greater in divers capable (on average) of > 240 s breath-hold.[19] This is, again, independent of any additional complexities from hypoxia of ascent.

SAFETY RECOMMENDATIONS FOR THE FUTURE

It may not be feasible to recommend an apnoeic time limit for amateur breath hold divers in a recreational setting. Guidance, tools or training are needed to make freediving safer. For example, in the setting of underwater rescue, a 40 s maximal breath hold time was recommended.[1] The limit was based on a study of repeated breath-hold dives (divers were recreational freediving instructors) to 5 m and 8 m for varying durations (maximum of 45 s). This recommendation relies on the mean nadir oxygen saturation of 89% for 45 s dives, with the lowest recorded saturation of 71%.[1] A conservative time limit such as this one could be imposed that would mitigate most of the dangers discussed above. However, apnoea time should not be a primary prescribed safety variable. The depletion of O_2 stores during apnoea is dependent on the metabolic rate (therefore, work rate) and may be highly variable amongst individuals. It seems an impossible task to develop multiple sets of rules or time limits based on different theoretical scenarios with many variables.

LIMITATIONS

Order effect is a serious limitation of our study design. Each volunteer performed the trials in the same order (i.e., static, 20 W, 40 W, and 60 W) with a 3 min active recovery period between each trial. This may have affected the volunteers' success in completing the 60 s of apnoea. It is not possible to speculate whether the order effect increased or decreased the apnoea time. While VO_2 gain (VO_2 per unit power: ~10 $mL \cdot min^{-1} \cdot W^{-1}$ for cycling) is surprisingly rigid[22] an order effect on apnoea durations may have underestimated the strength of the metabolic-rate dependence in the studied variables. That is, high power output trials resulted in shorter breath hold times and, if anything, this may have constrained the magnitude of disturbances to O_2 stores, end tidal measurements, etc. Finally, order effect does present a small risk for a priming effect on the metabolism. However, there is strong evidence that this priming effect is only present when including the heavy and very-heavy intensity domains and is thus unlikely in this study design.[23–25]

Finally, it was not possible to account for the effects of immersion and the diving reflex, which could potentially mitigate some of the effects of pressure on oxygen consumption referenced above. The diving reflex slows the heart rate and decreases myocardial oxygen demand, thereby reducing whole body $\dot{V}O_2$ and slowing time to hypoxia. Thus, oxygen saturation during apnoea decreases less with facial immersion, which could have a protective effect against hypoxia in the water. Facial immersion alone slows oxygen consumption to a greater degree than apnoea alone.[26] There are additional effects of immersion and temperature, such as peripheral vasoconstriction, that were not accounted for in this study.

Conclusions

The effect of apnoea on O_2 stores depletion was, as expected, dependent on metabolic rate, independent from the added complexities of a fall in static pressure on ascent. Therefore, it is contended that a time limit for amateur, recreational breath-hold diving may not guarantee safety.

References

1 Schagatay E, Åman PA. Repeated freediving – An efficient and safe method to rescue subjects trapped in cars underwater. Safety Science. 2019;118:752–6. doi: 10.1016/j.ssci.2019.05.023.

2 Butler FK. A proposed 60 second limit for breath-hold diving. In: Lindholm P, Pollock NW, Lundgren CEG, editors. Breath-hold Diving. Proceedings of the Undersea Hyperbaric Medical Society/Divers Alert Network 2006 June 20-21 workshop. Durham (NC): Divers Alert Network; 2006. [cited 2020 July 19]. p. 64–74. Available from: https://www.diversalertnetwork.org/files/UHMS_DAN_2006_Breath-hold_Workshop_Proceedings.pdf.

3 Andersson J, Schagatay E. Arterial oxygen desaturation during apnea in humans. Undersea Hyperb Med. 1998;25:21–5. PMID: 9566083.

4 Andersson JPA, Linér MH, Rünow E, Schagatay EKA. Diving response and arterial oxygen saturation during apnea and exercise in breath-hold divers. J Appl Physiol (1985). 2002;93:882–6. doi: 10.1152/japplphysiol.00863.2001. PMID: 12183481.

5 Lindholm P, Nordh J, Linnarsson D. Role of hypoxemia for the cardiovascular responses to apnea during exercise. Am J Physiol Regul Integr Comp Physiol. 2002;283:R1227–35. doi: 10.1152/ajpregu.00036.2002. PMID: 12376417.

6 Ferrari M, Mottola L, Quaresima V. Principles, techniques, and limitations of near infrared spectroscopy. Can J Appl Physiol. 2004;29:463–87. doi: 10.1139/h04-031. PMID: 15328595.

7 Wolf M, Ferrari M, Quaresima V. Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications. J Biomed Opt. 2007;12:062104. doi: 10.1117/1.2804899. PMID: 18163807.

8 Pollock NW. Breath-hold dive incidents. In: Buzzacott P, editors. DAN Annual Diving Report 2012–2015 ed. Durham (NC): Divers Alert Network; 2015. [cited 2020 July 19]. p. 79–92. Available from: https://www.ncbi.nlm.nih.gov/books/NBK344435/pdf/Bookshelf_NBK344435.pdf.

9 Boyd C, Levy A, McProud T, Huang L, Raneses E, Olson C, et al. Fatal and nonfatal drowning outcomes related to dangerous underwater breath-holding behaviors — New York State, 1988–2011. MMWR Morb Mortal Wkly Rep. 2015;64:518–21. PMID: 25996093. PMCID: PMC4584570.

10 Craig AB Jr. Summary of 58 cases of loss of consciousness during underwater swimming and diving. Med Sci Sports. 1976;8:171–5. doi: 10.1249/00005768-197600830-00007. PMID: 979564.

11 Smerz R, Farm F. Diving habits historically associated with 'shallow water blackout' in Hawaiian free-divers. In: Lindholm P, Pollock NW, Lundgren CEG, editors. Breath-hold diving. Proceedings of the Undersea Hyperbaric Medical Society/Divers Alert Network, 2006 June 20–21 workshop. Durham (NC): Divers Alert Network; 2006. [cited 2020 July 19]. p. 60–3. Available from: https://www.diversalertnetwork.org/files/UHMS_DAN_2006_Breath-hold_Workshop_Proceedings.pdf.

12 Lanphier EH, Rahn H. Alveolar gas exchange during breath-hold diving. J Appl Physiol (1985). 1963;18:471–7. doi: 10.1152/jappl.1963.18.3.471. PMID: 31083864.

13 Lindholm P. Physiological mechanisms involved in the risk of loss of consciousness during breath-hold diving. In: Lindholm P, Pollock NW, Lundgren CEG, editors. Breath-hold diving. Proceedings of the Undersea Hyperbaric Medical Society/Divers Alert Network, 2006 June 20-21 workshop. Durham (NC): Divers Alert Network; 2006. [cited 2020 July 19]. p. 26–31. Available from: https://www.diversalertnetwork.org/files/UHMS_DAN_2006_Breath-hold_Workshop_Proceedings.pdf.

14 Lindholm P, Lundgren CEG. Alveolar gas composition before and after maximal breath-holds in competitive divers. Undersea Hyperb Med. 2006;33:463–7. PMID: 17274316.

15 Smith DJ, Norris SR, Hogg JM. Performance evaluation of swimmers: Scientific tools. Sports Med. 2002;32:539–54. doi: 10.2165/00007256-200232090-00001. PMID: 12096928.

16 Lindholm P, Sundblad P, Linnarsson D. Oxygen-conserving effects of apnea in exercising men. J Appl Physiol (1985). 1999;87:2122–7. doi: 10.1152/jappl.1999.87.6.2122. PMID: 10601158.

17 Bosco G, Rizzato A, Martani L, Schiavo S, Talamonti E, Garetto G, et al. Arterial blood gas analysis in breath-hold divers at depth. Front Physiol. 2018;9:1558. doi: 10.3389/fphys.2018.01558. PMID: 30455649. PMCID: PMC6230561.

18 Aaslid R, Lindegaard KF, Sorteberg W, Nornes H. Cerebral autoregulation dynamics in humans. Stroke. 1989;20:45–52. doi: 10.1161/01.str.20.1.45. PMID: 2492126.

19 Palada I, Obad A, Bakovic D, Valic Z, Ivancev V, Dujic Z. Cerebral and peripheral hemodynamics and oxygenation during maximal dry breath-holds. Respir Physiol Neurobiol. 2007;157:374–81. doi: 10.1016/j.resp.2007.02.002. PMID: 17363344.

20 Engan H, Richardson M, Lodin-Sundström A, van Beekvelt M, Schagatay E. Effects of two weeks of daily apnea training on diving response, spleen contraction, and erythropoiesis in novel subjects. Scand J Med Sci Sports. 2013;23:340–8. doi: 10.1111/j.1600-0838.2011.01391.x. PMID: 23802288.

21 Schagatay E, van Kampen M, Emanuelsson S, Holm B. Effects of physical and apnea training on apneic time and the diving response in humans. Eur J Appl Physiol. 2000;82:161–9. doi: 10.1007/s004210050668. PMID: 10929209.

22 Wilcox SL, Broxterman RM, Barstow TJ. Constructing quasi-linear $\dot{V}O2$ responses from nonlinear parameters. J Appl Physiol (1985). 2016;120:121–9. doi: 10.1152/

japplphysiol.00507.2015. PMID: 26565018.
23 DiMenna FJ, Wilkerson DP, Burnley M, Jones AM. Influence of priming exercise on pulmonary O_2 uptake kinetics during transitions to high-intensity exercise from an elevated baseline. J Appl Physiol (1985). 2008;105:538–46. doi: 10.1152/japplphysiol.90357.2008. PMID: 18511522.
24 Murias JM, Spencer MD, Delorey DS, Gurd BJ, Kowalchuk JM, Paterson DH. Speeding of VO_2 kinetics during moderate-intensity exercise subsequent to heavy-intensity exercise is associated with improved local O_2 distribution. J Appl Physiol (1985). 2011;111:1410–5. doi: 10.1152/japplphysiol.00607.2011. PMID: 21836042.
25 Endo M, Usui S, Fukuoka Y, Miura A, Rossiter HB, Fukuba Y. Effects of priming exercise intensity on the dynamic linearity of the pulmonary VO(2) response during heavy exercise. Eur J Appl Physiol. 2004;91:545–54. doi: 10.1007/s00421-003-1005-1. PMID: 14648126.
26 Andersson JPA, Linér MH, Fredsted A, Schagatay EKA. Cardiovascular and respiratory responses to apneas with and without face immersion in exercising humans. J Appl Physiol (1985). 2004;96:1005–10. doi: 10.1152/japplphysiol.01057.2002. Epub 2003 Oct 24. PMID: 14578373.

Acknowledgements

We wish to thank our volunteers for their time and dedication. We thank Jesse Brennan for his assistance with data analysis.

Conflicts of interest and funding

No conflicts of interest were disclosed. This research was supported by the Nate Upton Foundation.

Submitted: 31 July 2019
Accepted after revision: 19 July 2020

A review of diving practices and outcomes following the diagnosis of a persistent (patent) foramen ovale in compressed air divers with a documented episode of decompression sickness

Christopher W Scarff[1], John Lippmann[2,3], Andrew W Fock[1,3]

[1] *Department of Intensive Care and Hyperbaric Medicine, Alfred Hospital, Melbourne, Australia*
[2] *Australasian Diving Safety Foundation, Melbourne, Australia*
[3] *Department of Public Health and Preventive Medicine, Monash University, Melbourne, Australia*

Corresponding author: *Dr Christopher W Scarff, The Alfred, PO Box 315, Prahran 3181, VIC, Australia*
c.scarff@alfred.org.au

Key words
Decompression illness; Persistent (patent) foramen ovale (PFO); Safety; Education; Diving research

Abstract
(Scarff CW, Lippmann J, Fock AW. A review of diving practices and outcomes following the diagnosis of a persistent (patent) foramen ovale in compressed air divers with a documented episode of decompression sickness. Diving and Hyperbaric Medicine. 2020 December 20;50(4):363–369. doi: 10.28920/dhm50.4.363-369. PMID: 33325017.)
Introduction: The presence of a persistent (patent) foramen ovale (PFO) increases the risk of decompression sickness (DCS) whilst diving with pressurised air. After the diagnosis of a PFO, divers will be offered a number of options for risk mitigation. The aim of this study was to review the management choices and modifications to diving practices following PFO diagnosis in the era preceding the 2015 joint position statement (JPS) on PFO and diving.
Methods: A retrospective study was conducted of divers sourced from both the Alfred Hospital, Melbourne and the Divers Alert Network Asia-Pacific during the period 2005–2015. Divers were contacted via a combination of phone, text, mail and email. Data collected included: diving habits (years, style and depths); DCS symptoms, signs and treatment; return to diving and modifications of dive practices; history of migraine and echocardiography (ECHO) pre- and post-intervention; ECHO technique(s) used, and success or failure of PFO closure (PFOC). Analyses were performed to compare the incidence of DCS pre- and post-PFO diagnosis.
Results: Seventy-three divers were interviewed. Sixty-eight of these returned to diving following the diagnosis of PFO. Thirty-eight underwent PFOC and chose to adopt conservative diving practices (CDPs); 15 chose PFOC with no modification to practices; 15 adopted CDPs alone; and five have discontinued diving. The incidence of DCS decreased significantly following PFOC and/or adoption of conservative diving practices. Of interest, migraine with aura resolved in almost all those who underwent PFOC.
Conclusions: Many divers had already adopted practices consistent with the 2015 JPS permitting the resumption of scuba diving with a lowering of the incidence of DCS to that of the general diving population. These results support the recommendations of the JPS.

Introduction

Decompression sickness (DCS) was first described in the latter part of the 19th century by Paul Bert, though it was not until almost 150 years later that the patterns of cutaneous, inner ear and neurological DCS were associated with intracardiac right-to-left shunts.[1,2] The incidence of right-to-left shunt was higher in a cohort of divers with a history of DCS (especially with severe symptoms), than in some cohorts of healthy individuals (although the methods for shunt detection differed).[3] The majority of these shunts were found to be due to a patent (sic) foramen ovale. Persistent (patent) foramen ovale (PFO) can be identified in 25–33% in the population[4] but, owing to non-specific symptoms and signs, there is a reliance on echocardiographic examination for definitive diagnosis upon clinical suspicion raised by family history, migraine with aura,[5] transient ischaemic attack, cryptogenic stroke,[6] shunt-induced cyanosis[4] and DCS suggestive of PFO.

The risk of DCS in association with scuba diving is in the order of 1.9:10,000 with the presence of PFO potentially increasing that risk almost fivefold.[7–9] This makes affected divers more susceptible to DCS even on dives that would normally not be considered provocative in accordance with commonly used decompression recommendations and accepted conservative diving practices (CDP).[8] PFO closure (PFOC) is not a guarantee against further DCS, nor is it a risk-free procedure. However, as well as reducing the likelihood of DCS, it may have benefits in conditions such as migraine with aura[5] and cryptogenic stroke.[10,11] Thus, the decision matrix can be complex.

In light of this, the South Pacific Underwater Medical Society (SPUMS) conducted a symposium on the topic, resulting in a consensus statement in 2015.[12] This included recommendations made on the basis of both evidence and expert opinion, aiming to provide guidance for diving physicians when offering advice to divers to reduce the risk of DCS in the presence of a PFO. The recommendations include measures such as diving cessation, adoption of (more) conservative practices and/or PFOC.

The aim of this study was to review closure procedures undertaken and any changes in the diving practices and outcomes of divers who presented with documented PFO following DCS over the period 2005 to 2015 prior to the publication of the Joint Position Statement of 2015. We enlisted two cohorts: divers who presented to the Hyperbaric Unit of the Alfred Hospital, Melbourne for treatment or advice for DCS, and divers who reported to the Divers Alert Network Asia-Pacific (DAN AP) that they had been diagnosed with an intracardiac shunt following a presentation for DCS.

Methods

Approval for this retrospective cohort study was obtained from the Alfred Hospital Ethics Committee 07/05/2015 (Number 236/15).

Patient histories from the Hyperbaric Unit at the Alfred Hospital, Melbourne and cases involving Australian residents reported to the DAN AP over a ten-year period (2005–2015) were reviewed for the following diagnoses: dermatological, vestibular, central neurological or spinal DCS. These histories were then examined for the presence of documented or suspected PFO. Patients without documented evidence of PFO were excluded from further assessment and analysis.

All patients were contacted via mail and/or email prior to subsequent telephone interview(s) and/or receipt of a written questionnaire. Informed consent for collection of data was obtained from participants who supplied relevant diving history and medical information. Data collected included: demographics; history of migraine pre- and post-PFOC; diving habits (years, style number of dives and depths); DCS symptoms, signs and treatment; return to diving and practice modifications; echocardiography reports pre- and post- closure, where available; success or failure of PFOC, and technique for closure.

Defects noted at echocardiography as 'large', 'significant', requiring a 25 mm device or having bubble transit at rest were allocated to the 'large' group. Defects noted to be 'small', requiring a device less than 25 mm or only demonstrating bubbles upon provocation were allocated to the 'small' group. Information on device type was not always available.

Descriptive statistical analyses (Microsoft Word 15.25) were performed. The incidence of DCS was calculated pre- and post-diagnosis of PFO. Difference in incidence rates between pre- vs post-diagnosis periods and the corresponding 95% confidence intervals were determined using the incidence rate procedure available in Stata software version 15 (StataCorp, Texas, USA).

Results

Two hundred and fifteen presentations to the Alfred during 2005–2015 resulted in 24 eligible subjects: 50 patient histories satisfied the original research criteria; 14 patients were lost to follow-up and 12 had a history consistent with PFO but had either a normal echocardiogram or had not been investigated. Over the same period, 77 DAN AP members or prospective members declared having been diagnosed with a right-to-left shunt, resulting in 49 subjects: 24 declined enrolment, two were lost to follow-up, and the two divers common to both cohorts were counted amongst the Alfred cohort. The combined population of 73 had a mean age of 47.6 (SD 11.2) and comprised 51% males. Fifty-five (75%) patients had undergone one or more procedures to close a PFO and/or other septal defects and 18/73 (25%) did not undergo closure. At the time of interview, 68/73 (93%) had returned to diving, four had ceased compressed air diving and one was planning to resume diving once lifestyle and family commitments had improved.

DCS SYMPTOMS AND SIGNS

The symptoms and signs reported (total numbers of the 73 divers) were typical for a cohort suffering DCS related to PFO: rash (46), headache (35), altered balance (32), paraesthesia (31), altered vision (29), swelling (26), fatigue (17), altered hearing (14), vertigo (13), nausea/vomiting/diarrhoea (12), confusion (11), pain-other (7), collapse (3), and tinnitus (2). Multiple divers reported multiple symptoms and/or signs.

DIVING HISTORY AND SEQUELAE

Based on self-reported diving history, the median (interquartile range, IQR) number of dives prior to assessment was 345 (153, 800) over a median (IQR) of 14 (8, 25) years; giving an average of approximately 38 (21, 68) dives per year. The median (IQR) number of dives that were conducted after the DCS event that had precipitated the assessment with or without PFO closure was 130 (50, 250).

Prior to assessment, there were 80 reported cases of DCS in the 73 divers during 50,107 dives giving an incidence of 16.0 cases per 10,000 dives. There were three reported cases after PFO management that were consistent with DCS during 19,118 dives, giving an incidence of 1.6 cases per 10,000 dives. The rate of DCS differed significantly from

Table 1
Diving style before and after PFO diagnosis. Data are *n* (%). msw = metres' seawater

Phase	Not diving	Recreational 0–30 msw	Deeper > 30 msw	Technical	Commercial
Pre-intervention	–	8 (11.0)	31 (42.5)	31 (42.5)	3 (4.1)
Post-intervention	5 (6.8)	25 (34.2)	14 (19.2)	25 (34.2)	4 (5.5)

Table 2
Comparison of PFO repair status and change in diving practice

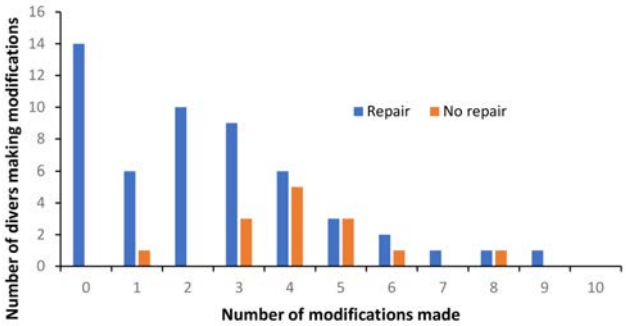
PFO status	*n* (%)
Closure and no change	15 (20.1)
Closure and CDP	38 (52.1)
Closure and no diving	2 (2.7)
Not closed and CDP	15 (20.1)
Not closed and no diving	3 (4.1)
Total	73 (100)

pre- to post-: 14.4 cases per 10,000 dives (95% CI 10.5 to 18.3 ($P < 0.0001$).

Six divers reported that, on multiple occasions, they had symptoms consistent with DCS, but these were unconfirmed so are not included for the calculation of incidence. Examples of their reports include 'symptoms over years', 'regular skin bends' and 'bent a number of times'. Of the three divers who had DCS following successful PFOC, only one reported symptoms similar to their original DCS, that being paraesthesia, rash and bruising. This diver described his dives as 'provocative', which was supported by the dive profiles; i.e., air dives to 50 and 60 metres' seawater (msw) with a surface interval of 3.5 h. Repeat transthoracic echocardiography (TTE) with bubble contrast and Valsalva after this event failed to reveal a shunt. This diver is now adhering to more conservative practices. The other two divers had symptoms that were less indicative of a PFO, with one freely claiming that the dive had been provocative and this has resulted in the subsequent adoption of safer practices. Neither of the last two divers had medical contact for these episodes prior to this study. There were three divers who reported symptomatology that was ambiguous and did not require medical attention. These were not included for the calculation of incidence.

Twenty-eight (38%) of the divers decreased their maximum dive depth following their DCS incident whilst 10 of the 73 (13.7%) increased their diving depth. Four ceased diving permanently with one diver planning to resume once lifestyle factors permit. Divers were allocated to one of four groups based on self-reported diving history: 'Recreational' and 'Deeper' for amateur divers with the cut-off being 30 msw, 'Technical' for cave divers and those utilising trimix, and 'Commercial' (Table 1).

Figure 1
Diving modifications post-presentation for divers with and without PFOC



RETURN TO DIVING AND MODIFICATIONS TO DIVING PRACTICE

All of those who returned to diving without PFOC and 38/55 (69%) of those who had PFOC adopted more conservative diving practices (Table 2). Many divers utilised multiple practices to mitigate risk with these modifications generally applied for all dives. The modifications included: the use of nitrox (n = 29), shallower dives (n = 27), initiation or increased use of safety stops (n = 26), decrease in 'no-deco' limits (n = 22), dropping from multiple to single dives in a day (n = 19), decrease in repetitive dives per day (n = 17), increase in surface interval (n = 16), increased hydration (n = 14), reduced exertion during dives (n = 12), slower ascents (n = 5) and cessation of diving (n = 5). Fifteen divers made no modifications whilst the others made between one and nine modifications. Divers who underwent PFOC were less likely to adopt more conservative diving practices than those who did not undergo closure (Figure 1).

INFLUENCE OF DEFECT SIZE ON RETURN TO DIVING AND CHANGES TO DIVING PRACTICES

There were 38 patients with 'large' defects, of which 33 returned to diving after repair (25 adopted more conservative practices and two now dive deeper), two returned without repair and two have neither undergone repair nor returned to diving. One diver reported that PFOC was successful but that additional defects were noted. These were not corrected, and the diver has resumed diving with a conservative approach and at interview has had no further incidents.

Twenty-six 'small' defects were noted and 12 of these patients have returned after repair (six modified practice conservatively and two went deeper), 12 returned without repair (all modified their diving), one underwent repair and plans to return pending lifestyle improvements and one has ceased diving.

Nine were not classified as there was no reference made to size of defect or bubble numbers in the echocardiography report; seven returned after repair, one repaired but has not returned and one has returned without undergoing repair.

MIGRAINE

Thirty-four of the divers suffered migraine with an almost equal gender distribution (16/18 male/female). Eighteen were associated with aura. Of the 23 of who underwent PFOC, 17 showed partial or complete cessation of migraines and six had no resolution. Three reported improvements in their symptoms, despite not having undergone PFOC. In the repair group of 23, the size of the defect was documented in 19: Twelve had a large defect (eight of these with aura), seven were small. Only one patient of the 18 with aura failed to improve following PFOC.

SIDE EFFECTS OF PFOC

Two divers who reported suffering 'palpitations' prior to their episode of DCS had symptomatic improvement in their palpitations following PFOC: one was also associated with resolution of migraine, the other reported that they no longer suffered palpitations at depth. Atrial fibrillation was reported in two patients following PFOC. One of these has, with the passage of time, had complete resolution and continues to dive, and the other has ceased diving. There were four reports of residual defect after closure on follow-up echocardiography. Two of these patients subsequently achieved PFOC whilst undergoing unrelated cardiac procedures, one during angioplasty for angina pectoris and the other during open cardiac surgery. Two patients continue to have PFO. One of these is awaiting a repeat procedure whilst the other has resumed diving despite continuing to report slight chest discomfort. One person ceased diving due to procedural complications of PFOC (he was not forthcoming as to the specifics), but is otherwise well.

Discussion

This retrospective study of 73 divers diagnosed with PFO over the period 2005–2015, revealed presentations that were typical for those suffering from DCS and included divers with a wide range of ages, years of experience and diving practices. We found that many among this cohort of divers adopted strategies that were to later be codified in the Joint Position Statement (JPS) on PFO and Diving of 2015,[12] with only five deciding not to continue with scuba diving. Whilst none of our cohort underwent PFOC purely for the management of migraine, almost all those with migraine associated with aura reported symptom resolution following PFOC.

An example of the local recommendations for the adoption of conservative diving practices (CDPs) can be seen in a recent publication which formed the basis for our questionnaire.[13] These recommendations and others are noted widely[14–16] and, as with many guidelines, there is often a low level of concordance. The Lippmann document[13] has similar recommendations for CDPs to those in statement five of the JPS and other earlier publications. For the management of the diver with a PFO, three options were proffered including cessation of diving, adoption of CDPs and closure of the PFO. Discussion of PFOC came with the overriding caveat that it is no guarantee against further DCS, and that the adoption of CDPs was not mutually exclusive of PFOC. This study group followed four strategies which included cessation of diving, closure without CDP, closure with CDP, and CDP without closure. All those opting for no repair modified their diving practices as did more than half of the divers after undergoing PFOC, and 53 of the 73 divers, independent of PFO closure status.

The questionnaires did not delve deeply into how the various modifications were used or seek quantification of these changes. For example, respondents who indicated that they had adopted the use of nitrox usually did not specify whether or not it was used based on air decompression times, which would reduce DCS risk. On the other hand, if nitrox was used to extend dive times it would not necessarily reduce risk and would not be a CDP.

The observed reduction in the incidence of DCS post-PFO diagnosis is similar that seen in other studies[4,17] and suggests that PFOC and CDP, whether alone or in combination, may lower the risk of DCS, especially for those with a large PFO. The reported incidence also reflects the caveat in the JPS that, although the risk of DCS may reduce to that of the general diving population,[9] it does not decrease to zero. The reported complications post-PFOC (8%) were comparable to those reported by Vanden Eade (7%)[18] and Rayhill (6.8%)[5] suggesting that PFOC is generally well tolerated. Of note, a third study (in divers) reported a much higher incidence of complication (19%) in a similar cohort.[17]

The risk of DCS is not related purely to the presence or size of a PFO but is also a function of other right-to-left defects.[19] These include other atrial septal defects and non-specific pulmonary shunts. Such persistent anomalies must be accounted for when counselling divers on the risks of further DCS following PFOC. One of our cohort volunteered that further shunts had been identified but not occluded. He continues to dive as per the JPS recommendations with a more conservative profile and at follow-up interview had not reported any adverse sequelae.

It is recommended in the JPS[12] that closure be confirmed by echocardiography. One study[18] notes that two of

four divers who suffered DCS 'post-closure' had their assessment performed by a junior trainee which may explain why a residual defect 'post-closure' was not identified. Experienced cardiological opinion must be sought. At the Alfred Hospital, referrals are limited to two cardiologists, both of whom have an interest in diving medicine.

INCIDENCE OF DCS

The calculated incidence of DCS was based upon self-reporting of confirmed cases which may have led to an under-estimation. The unconfirmed self-reported cases were confined to a small number of divers but if correct would have increased the incidence markedly. The incidence post-intervention is likely to be more accurate due to divers being more aware of DCS and there often being less time between interview and incidents. Unlike a recent report in which subjects were enrolled on the basis of PFO with or without DCS,[17] all of our subjects had DCS confirmed by a diving physician, although some were not recompressed as the manifestations were considered relatively minor (e.g., mild cutis marmorata only) or presentations were delayed such that treatment was inappropriate.

Presentations to the Alfred for diving-related DCS requiring hyperbaric oxygen (HBO) have declined by more than 70% over the past 25 years from more than 70 per year in the early 1990s to less than 36 per year by the mid-2000s and down to 20 per year by the late 2010s. Despite there being an approximately 40% reduction in the entry-level certification numbers in Australia from 2007 to 2013,[20] other general diving activity data do not demonstrate such a reduction[21] and do not adequately account for the decreased presentations of DCS. It is possible that the drop in observed DCS cases may be reflective of better education leading to the adoption of more conservative and therefore safer diving practices (as seen in almost three quarters of our cohort) along with slower ascent rates and the incorporation of safety stops.

Transoesophageal echocardiography (TOE) has been suggested by some experts[22] as the gold standard for PFO investigation. Our experience is rather the contrary in that TOE requires the patient to be sedated and therefore unable to perform a Valsalva manoeuvre. While TOE is essential for placement of the closure device, we do not recommend it as a screening tool. On the other hand, transthoracic echocardiography (TTE) can be a very effective tool in detecting a right-to-left shunt when used by an experienced technician and with the aid of bubble contrast and provocative manoeuvres, such as Valsalva and sniffing.

MIGRAINE

Guidelines in the neurology literature are inconsistent regarding PFOC and migraine.[5,23] This study demonstrates that for divers with migraine associated with aura, PFOC may resolve their migraines. This cohort, while small, had an almost complete resolution of migraine with aura which has had significant positive impact on their quality of life. The benefits of PFOC must be balanced against the small risk of complications[5] and these probably preclude recommending PFOC for migraine. The use of PFOC in prevention or recurrence of cryptogenic stroke[11] and other conditions continues to be debated and should be referred to appropriate specialists.

FURTHER RESEARCH

Echocardiography

The echocardiologic nomenclature to describe PFO is inconsistent making comparisons between studies difficult. Variables described include size (large/small, millimeters, length, width etc), bubbles (number, +/- Valsalva, timing, transit time), patency (pencil, probe or not), grade (0–3), intensity of atrial opacification, mobility of septum, and words such as 'significant'.[6,8,10,15,17,24–30]

It is unclear whether these variations are due to individual sonographers, general sonographic practice or cardiological reporting. The present study condenses these reported variables to form two groups referred to as 'large' and 'small'. To strengthen further studies, a consistent vocabulary should be agreed upon and implemented.[31]

Advice to divers

In a retrospective audit of 105 divers undergoing PFOC for DCS in the period 2005–2014,[15] 81 of 95 "*were cleared to resume unrestricted diving*". One episode of cutaneous DCS was noted in a diver who had residual shunt following 'PFOC'. The number of dives post-PFOC was not noted and although 'unrestricted diving' was permitted, it is unclear as to whether there were any recommendations for CDP. Our results were similar with regard to number of divers, side effect profile and migraine resolution but there was a difference in diving practices post-PFOC with 69% of our cohort altering diving behaviour after being counselled to adopt CDP. Both these cohorts pre-date the JPS of 2015 and have vastly different approaches: one permitting unrestricted diving with the other recommending CDP. Further study is required to assess if closure and unrestricted diving is as safe an approach as closure with the adoption of CDP, particularly in light of the JPS of 2015.

LIMITATIONS

DCS presentations

The Alfred Hospital, Melbourne houses the sole public hyperbaric chamber for the state of Victoria. As such, independent of where a diver has suffered their DCS or received their HBO, if resident in Victoria, their follow-up is generally at the Alfred. The DAN AP cohort, on the other hand, included residents from throughout Australia. That there were only two divers common to both data sets,

most likely reflects participation rates in scuba diving and membership of DAN AP not being spread evenly across the country.

DCS incidence

Our quoted incidences for DCS are subject to recall bias as dive experience was self-reported with regards to frequency, experience and dive profile. It is unclear how the 26 divers who were lost to follow-up would have altered our data. While the number of episodes of confirmed DCS were easy to quantify, a number of divers volunteered events before diagnosis that were difficult to clarify: 'multiple/regular skin bends', 'symptoms over years', 'bent a number of times', 'slight feeling of chest discomfort' and 'sometimes itchy in the chest'. Thus the 'true' numerator may be higher and the denominator different. The combination likely results in potential under-reporting of the incidence for DCS pre-diagnosis.

The two melded data sets were collected following slightly different methodologies, questionnaires and follow-up. The main difference between them was the format of reporting diving depths pre and post diagnosis. For simplicity, the non-technical divers were allocated to two groups: 'recreational' and 'deeper' with an arbitrary cut-off at 30 msw.

Conclusions

This study demonstrates that between 2005–2015 there were a number of mitigation strategies being enacted by divers diagnosed with a PFO after suffering an episode of DCS. These strategies included the management of the PFO and modifications to diving practices similar to those subsequently recommended in the JPS of 2015. That these strategies have appeared to lower the risk of DCS in this cohort provides further validation for the recommendations in the JPS. This should encourage the dissemination and use of conservative diving practices and the JPS guidelines to divers and their practitioners. There is significant variation in the terminology for PFO assessment which renders direct comparison between studies difficult. This situation could be remedied by the adoption of a simple and reproducible grading system.

References

1 Wilmshurst PT, Ellis BG, Jenkins BS. Paradoxical gas embolism in a scuba diver with an atrial septal defect. BMJ. 1986;293(6557):1277. doi: 10.1136/bmj.293.6557.1277. PMID: 3096463. PMCID: PMC1342110.

2 Wilmshurst PT, Byrne JC, Webb-Peploe MM. Relation between interatrial shunts and decompression sickness in divers. Lancet. 1989;2(8675):1302–6. doi: 10.1016/s0140-6736(89)91911-9. PMID: 2574256.

3 Moon RE, Camporesi EM, Kisslo JA. Patent foramen ovale and decompression sickness in divers. Lancet. 1989;1(8637):513–4. doi: 10.1016/s0140-6736(89)90064-0. PMID: 2564057.

4 Koopsen R, Stella PR, Thijs KM, Rienks R. Persistent foramen ovale closure in divers with a history of decompression sickness. Neth Heart J. 2018;26:535–9. doi: 10.1007/s12471-018-1153-x. PMID: 30178210. PMCID: PMC6220018.

5 Rayhill M, Burch R. PFO and migraine: Is there a role for closure? Curr Neurol Neurosci Rep. 2017;17(3):20. doi: 10.1007/s11910-017-0730-5. PMID: 28283958.

6 Lairez O, Cournot M, Minville V, Roncalli J, Austruy J, Elbaz M, et al. Risk of neurological decompression sickness in the diver with a right-to-left shunt: Literature review and meta-analysis. Clin J Sport Med. 2009;19:231–5. doi: 10.1097/JSM.0b013e31819b0fa2. PMID: 19423977.

7 Bove AA. Risk of decompression sickness with patent foramen ovale. Undersea Hyperb Med. 1998;25:175–8. PMID: 9789338.

8 Torti S. Risk of decompression illness among 230 divers in relation to the presence and size of patent foramen ovale. Eur Heart J. 2004;25:1014–20. doi: 10.1016/j.ehj.2004.04.028. PMID: 15191771.

9 Billinger M, Zbinden R, Mordasini R, Windecker S, Schwerzmann M, Meier B, et al. Patent foramen ovale closure in recreational divers: effect on decompression illness and ischaemic brain lesions during long-term follow-up. Heart. 2011;97:1932–7. doi: 10.1136/heartjnl-2011-300436. PMID: 21917666.

10 Zier LS, Sievert H, Mahadevan VS. To close or not to close: Contemporary indications for patent foramen ovale closure. Expert Rev Cardiovasc Ther. 2016;14:1235–44. doi: 10.1080/14779072.2016.1224178. PMID: 27616622.

11 Seiler C. Patent foramen ovale (PFO): Is there life before death in the presence of PFO? Eur J Clin Invest. 2015;45:875–82. doi: 10.1111/eci.12469. PMID: 26017145.

12 Smart D, Mitchell S, Wilmshurst P, Turner M, Banham N. Joint position statement on persistent foramen ovale (PFO) and diving. South Pacific Underwater Medicine Society (SPUMS) and the United Kingdom Sports Diving Medical Committee (UKSDMC). Diving Hyperb Med. 2015;45:129–31. PMID: 26165538.

13 Lippmann J. Decompression illness: a simple guide and practical advice on the recognition, management and prevention of DCI. Ashburton, Australia: JL Publications; 2011. p. 50–1.

14 UHMS best practice guidelines - Prevention and treatment of decompression sickness and arterial gas embolism. North Palm Beach (FL): Undersea and Hyperbaric Medical Society; 2011. [cited 2020 August 01]. Available from: https://www.uhms.org/images/DCS-AGE-Committee/dcsandage_prevandmgt_uhms-fi.pdf.

15 Pearman A, Bugeja L, Nelson M, Szantho GV, Turner M. An audit of persistent foramen ovale closure in 105 divers. Diving Hyperb Med. 2015;45:94–7. PMID: 26165531.

16 Balestra C, Germonpré P, Marroni A. Intrathoracic pressure changes after Valsalva strain and other maneuvers: Implications for divers with patent foramen ovale. Undersea Hyperb Med. 1998;25:171–4. PMID: 9789337.

17 Anderson G, Ebersole D, Covington D, Denoble PJ. The effectiveness of risk mitigation interventions in divers with persistent (patent) foramen ovale. Diving Hyperb Med. 2019;49:80–7. doi: 10.28920/dhm49.2.80-87. PMID: 31177513. PMCID: PMC6704009.

18 Vanden Eede M, Van Berendoncks A, De Wolfe D, De Maeyer C, Vanden Eede H, Germonpré P. Percutaneous closure of patent foramen ovale for the secondary prevention of decompression illness in sports divers: mind the gap. Undersea

Hyperb Med. 2019;46:625–32. PMID: 31683360.
19 Wilmshurst PT, Morrison WL, Walsh KP. Comparison of the size of persistent foramen ovale and atrial septal defects in divers with shunt-related decompression illness and in the general population. Diving Hyperb Med. 2015;45:89–93. PMID: 26165530.
20 Lippmann J. Analysis of scuba diving-related fatalities in Australia [Internet]. Deakin University; 2018. [cited 2020 August 01]. Available from: http://dro.deakin.edu.au/view/DU:30114177.
21 Lippmann J, Stevenson C, McD Taylor D, Williams J. Estimating the risk of a scuba diving fatality in Australia. Diving Hyperb Med. 2016;46:241–6. PMID: 27966203.
22 Pinto FJ. When and how to diagnose patent foramen ovale. Heart. 2005;91:438–40. doi: 10.1136/hrt.2004.052233. PMID: 15772190. PMCID: PMC1768819.
23 Tariq N, Tepper SJ, Kriegler JS. Patent foramen ovale and migraine: Closing the debate – a review. Headache. 2016;56:462–78. doi: 10.1111/head.12779. PMID: 26952049.
24 Henzel J, Rudziński PN, Kłopotowski M, Konka M, Dzielińska Z, Demkow M. Transcatheter closure of patent foramen ovale for the secondary prevention of decompression illness in professional divers: a single-centre experience with long-term follow-up. Kardiol Pol. 2017;76:153–7. PMID: 28980295.
25 Honěk J, Šrámek M, Šefc L, Januška J, Fiedler J, Horváth M, et al. Effect of catheter-based patent foramen ovale closure on the occurrence of arterial bubbles in scuba divers. JACC Cardiovasc Interv. 2014;7:403–8. doi: 10.1016/j.jcin.2013.12.199. PMID: 24630875.
26 Liou K, Wolfers D, Turner R, Bennett M, Allan R, Jepson N, et al. Patent foramen ovale influences the presentation of decompression illness in scuba divers. Heart Lung Circ. 2015;24:26–31. doi: 10.1016/j.hlc.2014.07.057. PMID: 25130890.
27 De Castro S, Cartoni D, Fiorelli M, Rasura M, Anzini A, Zanette EM, et al. Morphological and functional characteristics of patent foramen ovale and their embolic implications. Stroke. 2000;31:2407–13. doi: 10.1161/01.str.31.10.2407. PMID: 11022072.
28 Walsh KP, Wilmshurst PT, Morrison WL. Transcatheter closure of patent foramen ovale using the Amplatzer septal occluder to prevent recurrence of neurological decompression illness in divers. Heart. 1999;81:257–61. doi: 10.1136/hrt.81.3.257. PMID: 10026348. PMCID: PMC1728953.
29 Klingmann C, Rathmann N, Hausmann D, Bruckner T, Kern R. Lower risk of decompression sickness after recommendation of conservative decompression practices in divers with and without vascular right-to-left shunt. Diving Hyperb Med. 2012;42:146–50. PMID: 22987461.
30 Wilmshurst P, Nightingale S, Walsh K, Morrison W. Effect on migraine of closure of cardiac right-to-left shunts to prevent recurrence of decompression illness or stroke or for haemodynamic reasons. Lancet. 2000;356(9242):1648–51. doi: 10.1016/s0140-6736(00)03160-3. PMID: 11089825.
31 Turner M. Patent foramen ovale and decompression illness in divers. Lancet. 1996;348(9040):1515. doi: 10.1016/S0140-6736(05)65963-6. PMID: 8942797.

Acknowledgements

The authors wish to thank Assoc. Prof A Walton (Cardiology), Dr D McGaw (Cardiology) and Dr E Paul (Statistics) for their assistance. We would also like to thank the study participants for their time in completing questionnaires and interviews.

Conflicts of interest and funding

No conflicts of interest were disclosed. Part of this study was funded by the Australasian Diving Safety Foundation (previously DAN Asia-Pacific).

Submitted: 14 May 2020
Accepted after revision: 01 August 2020

Decompression illness treated at the Geneva hyperbaric facility 2010–2016: A retrospective analysis of local cases

Julian Thaler[1], Rodrigue Pignel[2], Marie-Anne Magnan[2], Michel Pellegrini[2], Pierre Louge[2]

[1] *Department of Intensive Care Medicine, Valais Hospital, Sion, Switzerland*
[2] *Hyperbaric Medicine, Geneva University Hospitals, Geneva, Switzerland*

Corresponding author: *Dr Julian Thaler, Department of Intensive Care Medicine, Valais Hospital, Avenue du Grand-Champsec 80, 1951 Sion, Switzerland*
julianmatthias.thaler@hopitalvs.ch

Key words
Diving; Decompression illness; Arterial gas embolism; Epidemiology; Scuba; Recompression

Abstract
(Thaler J, Pignel R, Magnan M-A, Pellegrini M, Louge P. Decompression illness treated at the Geneva hyperbaric facility 2010–2016: A retrospective analysis of local cases. Diving and Hyperbaric Medicine. 2020 December 20;50(4):370–376. doi: 10.28920/dhm50.4.370-376. PMID: 33325018.)
Introduction: The Geneva hyperbaric chamber is the main treatment centre for decompression illness (DCI) in Switzerland. The characteristics, symptomatology, treatment and short-term outcome of divers treated at this chamber have not previously been investigated.
Methods: This was a retrospective study of patients treated with hyperbaric oxygen (HBO) for DCI from 2010 to 2016. Data were analysed to provide a description of the cases and statistical analysis for possible factors associated with an unfavourable outcome.
Results: One hundred and thirty-five patients were treated for DCI. Ninety-two were included in the study. Sixty-four presented with neurological and 28 with mild DCI. One hundred and thirty-five patients were treated for DCI. Ninety-two were included in the study. Sixty-four presented with neurological and 28 with mild DCI. Patients with mild DCI mainly had musculoskeletal symptoms (79%). Patients with neurological DCI mainly had spinal (55%), followed by vestibular (36%) symptoms. Arterial gas embolism was diagnosed in 30% of cases. Diving depths ranged between 15 and 142 metres, and dive times between two and 241 min. Median time to treatment was 6 h. Patients with neurological DCI had a high rate (25%) of persisting deficits after treatment. Older age was associated with an unfavourable outcome in univariate but not in multivariate analysis. No adverse effects of HBO were observed. For spinal DCI, a high Boussuges score was associated with persisting deficits after treatment.
Conclusions: Our findings are consistent with other series. Severe DCI was associated with a high rate of persisting deficits. No single factor was associated with a negative outcome. A Boussuges score > 7 had sensitivity of 90% and positive predictive value 53% for predicting an unfavourable outcome in spinal DCI.

Introduction

Despite its landlocked geographical situation, scuba diving is a popular sport in Switzerland with an overall low number of reported injuries. However, cases of decompression illness (DCI) requiring recompression therapy are reported regularly (10–29 cases per year).[1] In Switzerland, there are currently only two hyperbaric facilities: the main chamber (altitude 375 metres above sea level) located at HUG (University Hospitals of Geneva) with another chamber in Basel in private practice. Most of the patients with DCI are treated at the chamber in Geneva, but sometimes divers are treated in Basel (about 0–6 cases/year). The purpose of this study was to describe the cases of DCI treated at the HUG chamber and to investigate the influence of potential risk factors associated with a poor outcome. This study was the first investigation of a case series of patients treated at the HUG chamber and the first one in Switzerland looking at outcomes and potentially associated risk factors.

Methods

The study was approved by the local ethics committee (swissethics). A letter of non-objection to the use of their data for the purposes of this research was sent to each patient.

This was a retrospective, descriptive study of DCI cases treated with hyperbaric oxygen (HBO) at the HUG chamber. Patients that were treated for DCI between 2010 and 2016 and who did not refuse consent were included in the survey.

The year 2010 was chosen as a starting point as it was the first year with full implementation of an electronic medical record system, and 2016 was the end point for internal logistical reasons. Medical records were reviewed and the following data extracted: age, gender, month and place of incident, delay between surfacing and first symptoms, delay between first symptoms and hyperbaric treatment, breathing gas used, maximum depth, dive time, single or repetitive

dive, emergency events during the dive, symptoms and classification of DCI (mild or severe neurological).

The presumed pathophysiological mechanism was evaluated for each case: inadequate elimination of nitrogen (classically regarded as 'decompression sickness' [DCS]) versus the introduction of bubbles to the arterial circulation by pulmonary barotrauma (arterial gas embolism [AGE]). We calculated the Boussuges score of severity for neurological DCI with spinal involvement.[2] We extracted the following data on treatment and outcome: treatment applied before HBO (if any), type and number of hyperbaric treatment sessions applied, response after the first HBO treatment, total treatment days and early outcome (in particular, any persisting neurological deficits after the final HBO treatment).

Cases in the final dataset were divided into two groups: The first group consisted of patients with mild DCI presenting with fatigue, joint/muscle pain ('bends') or skin rash. Divers with isolated patchy tingling in the skin as well as mottled or marbled skin rash without an objective neurologic change were also included in this group given their good prognosis even if possibly of 'neurological' origin.[3] The second group consisted of patients with severe DCI, all of them presenting with neurological deficits. A similar classification was used in a previous case series.[4]

Cases per year, the geographic location of dive sites, seasonal occurrence and dive parameters were considered. Mistakes or procedural errors or events contributory to the 'probability of injury' were reviewed. The ratio of mild and severe DCI, the most frequent main symptoms and whether pharmacologic treatment was performed prior to arrival at the chamber were evaluated. Univariate analyses for associations between dive and diver characteristics and mild or severe DCI were performed.

At the end, we analysed the cases for 'outcome' by type of DCI (mild vs. severe), the 'Boussuges score' in cases of spinal neurological DCI and the percentage of persisting neurological deficits after the last treatment session.

Logistic regression analysis was applied for a negative outcome (persistent symptoms after final treatment session) in the group of neurological DCI cases for the following covariables: sex, age, single or repetitive dive, interval from surfacing to first symptoms as well as interval from first symptoms to treatment. All mild DCI cases had a complete resolution of symptoms and were therefore not analysed further.

STATISTICAL ANALYSIS

The Shapiro-Wilk test was used for assessing the assumption of normality. Data were expressed as mean (normally distributed data) or median with a range for non-normal data. Fisher's exact test and the Mann Whitney U-test were used for group analysis. We performed univariate as well as multivariate analysis of several risk factors for a negative outcome. Statistical significance level was set at $P < 0.05$. Statistical analyses were performed using jamovi for MAC, version 1.08, retrieved at https://www.jamovi.org/ using R: A language and environment for statistical computing by R Core Team (2018).

Results

One hundred and thirty-five patients with suspected or diagnosed DCI were treated in a range from 10 cases (2011) to 30 cases (2015) per year (Figure 1). Forty-three were excluded from the final analysis. In 18 patients treatment was conducted in a rather speculative manner after hazardous hyperbaric exposures without symptoms of DCI. These were excluded from further analysis as no clear diagnosis of DCI was made. Twenty travellers who had suffered from DCI abroad and were referred to our unit on return were also excluded from further analysis as most of the patients had already been treated with HBO. Two professional tunnel workers were excluded. Finally, there were 3 refusals of data disclosure (Figure 2).

Figure 1
Number of divers treated with HBO for DCI per calendar year over the study period

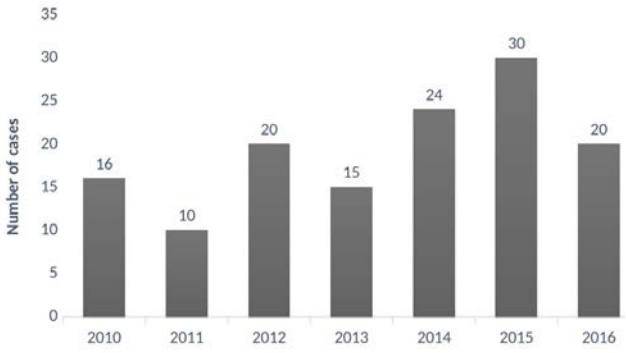


Figure 2
Flowchart explaining selection of patients presented in this study; DCI = decompression illness

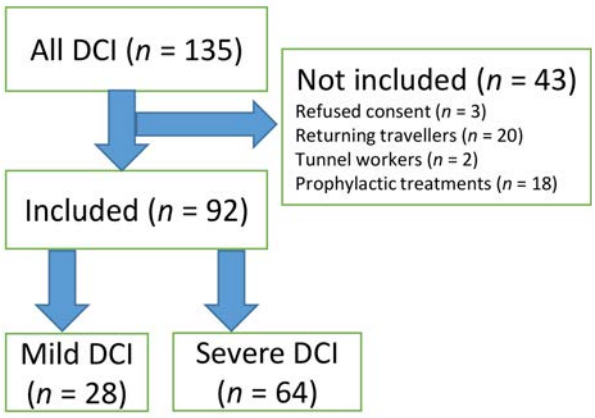


Table 1
Dive parameters for 92 divers presenting with decompression illness

Dive parameters	
Maximum depth (mfw), Median (range)	45.5 (18–142)
Dive time (min), Median (range)	41 (2–241)
Dive modality (scuba/rebreather/apnoea) *n*	89 / 2 / 1
Breathing mixture (air/nitrox/trimix) *n*	80 / 4 / 8
Normal dive/Emergency event *n* (%)	66 (71%) / 26 (29%)
Single dive/Repetitive dive *n* (%)	72 (78%) / 20 (22%)

Table 2
Diver and dive characteristics with divers stratified into mild or severe DCI. Data are median (range) unless otherwise indicated. mfw = metres' freshwater

Parameter	**Mild DCI (*n* = 28)**	**Severe DCI (*n* = 64)**	**All (*n* = 92)**	***P***
Age, mean (range)	41 (16–68)	45 (21–81)	44 (16–81)	0.09
Male sex, *n* (%)	24 (85%)	59 (92%)	83 (90%)	0.44
Maximum depth (mfw)	45 (15–130)	46 (18–142)	46 (15–142)	0.99
Dive time (min)	44 (10–120)	40 (2–241)	41 (2–241)	0.42
Repetitive dive, *n* (%)	7 (25%)	13 (20%)	20 (22%)	0.59
Time surfacing – symptoms (min)	60 (0–600)	15 (0–780)	30 (0–780)	0.39
Time symptoms – HBO (min)	360 (30–7,200)	310 (76–5,760)	360 (30–7,200)	0.64

There were 92 divers retained in the final dataset. The mean age of males (n = 83) was 44 y (range 16–81) and females (n = 9) 41 y (range 21–68). Most injuries occurred during summer months in Switzerland (85%), with a further 8% in France (7% of dive sites unknown). Dive parameters are shown in Table 1.

Self-reported emergency events were noted in 27 (29%) of cases, most commonly omission of decompression obligations in 13 (14%). Unplanned rapid ascents, often due to loss of buoyancy control, malfunctioning or free flowing regulator/dry suit inflator, or while helping distressed dive buddies, were less common (10 divers, 11%). The other four divers reported stress events (lost buddy, cold and equipment problems) without rapid ascents.

Patients presented with mild DCI in 28 cases (30%) and severe neurological DCI in 64 cases (70%). Patients with mild DCI presented mainly with diffuse muscular and/or periarticular pain (76%) and, to a lesser extent, with cutaneous symptoms (16%) and fatigue (8%). Neurological DCI patients presented mainly with spinal symptoms (55%), vestibular symptoms (34%) or cerebral/cerebellar symptoms (11%). AGE as probable pathophysiological mechanism was diagnosed in 19 (30%) of the latter cases presenting with neurological deficits. The diagnosis of AGE was made in patients with a combination of low gas load, rapid ascent and early onset of symptoms. Computed chest tomography scanning for the detection of a pulmonary barotrauma, blebs or bullae was not systematically performed in these cases.

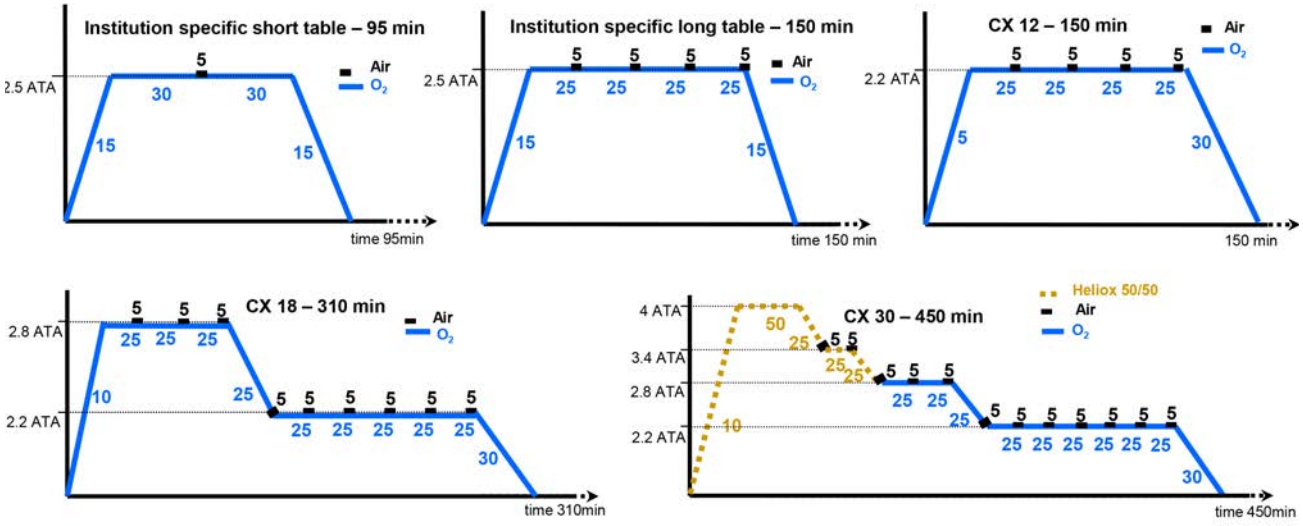
Median time to first symptoms after surfacing was 30 (range 0–780) min. Median time between first symptoms and hyperbaric treatment was 360 (range 0–7,200) min. Delays between surfacing and first symptoms as well as delays between first symptoms and hyperbaric treatment were shorter in the group presenting with severe DCI but this was not statistically significant. Furthermore, there was no association between age, sex, dive time, maximum depth, and type of DCI (mild versus severe) in univariate analysis. Divers and dives characteristics in regard to the type of DCI are shown in Table 2.

Concerning pre-hospital treatment, either oral or intravenous hydration was used in 48 (52%) of cases (mild as well as neurologic DCI). Twenty-nine (32%) of the patients received acetylsalicylic acid.

Treatment protocols utilised at our institution at the discretion of the responsible hyperbaric physician were

Figure 3

Recompression tables used at HUG. ATA = atmospheres absolute pressure (1 ATA = 101.3 kPa)



Comex (CX, Compagnie maritime d`expertises) tables: CX30 Heliox (7 h 30 min overall run time with a maximal pressure of 405 kPa breathing Heliox 50%), CX18 (5 h 10 min overall run time with a maximal pressure of 284 kPa), CX12 (2 h 30 min overall run time with a maximal pressure of 223 kPa). Additionally, institution specific HBO tables (short tables of 95 min at 253 kPa or long tables of 150 min at 253 kPa with air breaks) were used, mainly for consolidation treatment sessions (treatment tables used are shown in Figure 3).

Hyperbaric treatments were run until there was no further benefit over two consecutive treatments (in severe cases two times daily, in less severe cases once a day, weekends included). For patients with mild DCI initial recompression tables used were predominantly CX12 (21, 75%) or the institution specific tables. CX18 and CX30 Heliox were used for more symptomatic patients who had conducted deeper dives (7, 25%). Thirty patients (47%) with severe DCI were treated with CX18, institution specific long tables (9, 14%) or CX30 Heliox tables (25, 39%). Initial worsening despite hyperbaric treatment occurred in seven of the severe DCI patients. All of them had neurologic DCI occurring after deep (mean 70 mfw) bounce dives. Four of these patients were initially treated with a CX18 table. For these four patients with worsening of symptoms, the CX18 table was interrupted after 15–30 minutes and escalated to a CX30 Heliox table with success. The other three patients were already on a CX30 table.

Severe DCI cases had a significantly higher number of treatment sessions (median 5, range 1–55) than patients with mild DCI (median 2, range 1–4) due to severity and longer time to resolution of symptoms. There was no relation between longer dive time or deeper depth and the number of treatment sessions needed for either group.

As expected, there was a strong and significant correlation between the severity of DCI and outcome as all mild DCI cases had a complete recovery (OR for negative outcome:19.8; $P = 0.002$) whereas 16/64 (25%) of patients in the severe DCI group had a negative outcome with persistent deficits after the final treatment session. Persistent deficits included hypaesthesia/dysaesthesia, residual vestibular syndrome, urinary sphincter troubles and severe disabilities such as limb paresis, paraparesis, para- and tetraplegia. Most commonly reported were motor weakness/paresis (7/16) and sphincter troubles (6/16 cases). For severe DCI with spinal medullary injury, a Boussuges score of > 7 was significantly associated with a negative outcome in univariate analysis (Table 3).

In univariate analysis of the severe DCI group, older age was significantly associated with worse outcome (OR 3.86); however, in logistic regression analysis this could not be reproduced. In multivariate analysis no single factor was significantly associated with a negative outcome in severe DCI (Table 4). No adverse effect of recompression therapy occurred during any of the treatment sessions.

Table 3

Boussuges scale analysis in spinal cord DCI. When stratified by scores > 7 or ≤ 7 this system exhibited the following characteristics: sensitivity 90%, specifity 58%, positive predictive value 53%, negative predictive value 92%

Boussuges score	Sequelae	No sequelae	Total
≤ 7	1	11	12
> 7	9	8	17
Total	10	19	29

Table 4
Correlation of risk factors and adverse outcome in severe DCI cases. CI = confidence interval; HBO = hyperbaric oxygen; mfw = metres' freshwater; OR = odds ratio

Comparison	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (≥ 45 vs. < 45 y)	3.86 (1.09–13.70)	0.04	1.03 (0.97–2.82)	0.27
Female vs. male	0.57 (0.06–4.80)	0.60	0.58 (0.5–5.88)	0.65
Repetitive vs. single dive	0.42 (0.08–2.19)	0.48	0.46 (0.08–2.44)	0.36
Surface to first symptoms (> 60 vs. ≤ 60 min)	0.21 (0.04–1.03)	0.06	0.97 (0.95–1.00)	0.08
Symptoms to HBO (> 360 vs. ≤ 360 min)	0.27 (0.06–1.10)	0.07	1.0 (0.99–1.00)	0.49
Depth (> 40 vs. ≤ 40 mfw)	0.83 (0.25–2.70)	0.76		
Dive time (> 60 vs. ≤ 60 min)	1.22 (0.32–4.61)	0.74		
HBO treatments (> 6 vs. ≤ 6)	24.5 (5.6–100.5)	< 0.01		
Mild vs. severe DCI	19.8 (1.2–336)	< 0.01		

Discussion

The number of DCI cases treated in this seven-year period is comparable to other centres situated in Central Europe.[4] In our local catchment area, more patients were treated during the summer months, likely due to the favourable weather conditions in Swiss lakes and the summer holiday season. Most accidents took place in Switzerland. As Geneva is situated at the French border with popular diving sites nearby (Lac Leman, Lac d`Annecy) several French divers were treated as well. Switzerland is a mountainous country: all diving done is done at > 300 m altitude and is formally 'altitude diving'; however, our divers mostly dived at moderate altitude (for example Lac Leman 372 m, Thunersee 558 m, Lac Neuchâtel 429 m). It is unknown if this affects the incidence of DCI compared to other locations.

Emergency events (mostly omitted decompression obligations or rapid ascents) were reported in 27 (29%) of the 92 cases. Other analyses have found a comparable number of human errors associated with diving accidents.[5] In contrast to other dive sites, most dives were performed using a drysuit because of the cold water temperatures year-round, which is a risk factor for rapid ascents as drysuit diving increases task loading. The rapid ascents reported by several divers were mostly due to drysuit issues. However, we could not collect enough data for a specific analysis. In those cases with technical problems, it remains unclear whether redundant equipment was carried, which is of high importance when diving in cold water as there may be an elevated risk of free flowing or freezing regulators.

Arterial gas embolism (AGE) was diagnosed in 28 (30%) of divers, mostly in divers who did not have a high tissue gas load to explain the symptoms such as in most of the cases with sudden rapid ascents. However, making a firm diagnosis of AGE or DCS as causative mechanisms based on symptoms is often difficult, and the two frequently coexist.[6] Additionally, as explained before, systematic chest CT scanning or other investigations to help differentiate between the two were not consistently performed.

Of the cases treated 64/92 (70%) were severe DCI cases, in contrast to other publications where mild DCI was the predominant type.[4] At the moment, we cannot discern the reasons and there are no data available on under reported untreated cases of mild DCI in Switzerland. Univariate analysis of mild versus severe DCI cases revealed no significant differences between the dive or divers' profiles.

The number of treatment sessions differed significantly between mild and severe DCI reflecting our policy of repeated treatment sessions until no significant improvement occurred on two consecutive treatments (in concordance to international practice).[7] This reflects our knowledge that during the treatment of DCI pain typically resolves much faster than neurological symptoms.[8] Treatment schedules for mild and neurologic DCI vary between institutions and individual hyperbaric physicians. Our approach (shorter and shallower tables for mild DCI, deeper and longer tables ± heliox for severe DCI) seems to be in accordance with international practice, even if there is a lack of scientific evidence as to the optimal selection of therapeutic tables.[9] For mild illness or follow-on treatments, tables like our institution specific tables, with frequent variations, are used in other European institutions as intermediate protocols between CX12 and CX18 tables.

No adverse effects of recompression therapy were reported in our series whereas in recent literature, up to 17.4% of patients experienced adverse events.[10] Strict operational protocols and in-chamber monitoring (gas pressures, camera observation, highly qualified attendants) are applied in our centre and may have contributed. One third of the patients received aspirin preclinically, usually given by French emergency providers as this is a part of their treatment algorithm.[11] At HUG no specific pharmacologic treatment was used, as good scientific evidence is lacking.

As expected, there was a strong and significant correlation between the severity of DCI and outcome as all mild DCI cases had a complete recovery (OR for negative outcome if severe:19.8, $P = 0.002$) and 16/64 (25%) of neurologic DCI patients had sequelae after the last hyperbaric session. For different reasons, we did not consistently follow up or interview the patients at a later time, especially those with sequelae, which is a limitation of the study. In the recent literature, a quite similar percentage (33%)[12] of incomplete resolution after spinal cord DCI was reported with other authors finding between 22% and 61%.[13,14] In univariate analysis of risk factors, older age (> 45 years) was associated with a negative outcome (Table 4). Older age is often considered to be a risk factor for decompression sickness itself.[15,16] However, in multivariate analysis applied to reveal variables associated with a poor outcome in severe DCI, none, including age, reached significance.

Delayed (i.e., > 6 hours) commencement of treatment was not associated with a worse outcome in this case series; however, our study was not designed for specifically answering the question of effect of delay to HBO. In other studies, delay to hyperbaric treatment was associated with a less favourable outcome in neurological DCI.[17,18] These findings may make the case for in-water recompression in remote locations.[19]

In this study, median time from first symptoms to HBOT was 6 hours due to a great many of our patients presenting late after the first symptoms and probably also as a result of the geographical position of our hospital at the southwestern edge of Switzerland, prolonging transport times even if helicopter evacuation to a hyperbaric facility can theoretically be achieved in a time frame of less than one hour all over the country.[20] A recent study showed that delayed treatment > 48 hours was nonetheless effective in reducing the symptoms of DCI.[21]

The Boussuges score takes into account objective neurological deficits and the course of illness (stability or deterioration) on admission.[2] For spinal DCI, there was a significant association between a high Boussuges score (> 7) and persistent neurological deficits after the completion of the final treatment session with 90% sensitivity, however specificity (58%) was lower than in other case series.[2,22] Because of the low number of cases of spinal DCI where data allowing a Boussuges classification was available (29 patients) no multivariate analysis was conducted.

Conclusions

Of 135 divers presenting to the Geneva hyperbaric centre over a seven-year period, 92 were analysed for risk factors for mild versus severe DCI and negative outcome defined as persisting neurologic deficits after the last treatment session. No differences in the dive parameters were associated with mild versus severe DCI. Median delay between first symptoms and treatment was 6 h. Comex treatment tables were successfully used alongside HUG tables instead of US Navy tables. No adverse effects of recompression therapy were reported.

All patients presenting with mild symptoms made a full recovery, whereas 16 of 64 (25%) of patients with severe DCI showed a persistent neurological deficit after the last HBOT session. Our results are comparable with those of other reported case series.

In univariate analysis, older age was significantly associated with a worse outcome. However, in multivariate analysis no single risk factor was significantly associated with a negative outcome. Because of the rather large number of variables analysed for a small sample of a selected patient group, conclusions should be drawn with caution. The study is not sufficiently powered to rule out risk factors, which is one of the limitations. Other limitations are the retrospective design with a selected group of subjects and poor control over the exposure factors, covariates and potential confounders. A Boussuges score > 7 was associated with an unfavourable outcome in spinal DCI in this series.

Finally, our survey shows that despite adequate HBOT, neurological DCI is still associated with significant morbidity and a high rate of persistent deficits.

References

1 FTU/DAN EUROPE Suisse. Tauchunfälle - Fallsammlunge 2017. Zürich: FTU/DAN; 2018. Available from: https://ftu.ch/de/downloads/statistiken/ftu-unfallberichte/test3.pdf. [cited 2018 Dec 10]. German.

2 Boussuges A, Thirion X, Blanc P, Molenat F, Sainty JM. Neurologic decompression illness: A gravity score . Undersea Hyperb Med. 1996;23:151–5. PMID: 8931282.

3 Germonpré P, Balestra C, Obeid G, Caers D. Cutis Marmorata skin decompression sickness is a manifestation of brainstem bubble embolization, not of local skin bubbles. Med Hypotheses. 2015;85:863–9. doi: 10.1016/j.mehy.2015.09.022. PMID: 26432631.

4 Kot J, Sićko M, Michałkiewicz M, Lizak E, Góralczyk P. Recompression treatment for decompression illness: 5-year report (2003–2007) from national centre for hyperbaric medicine in Poland. Int Marit Health. 2008;59:69–80. PMID: 19227740.

5 O'Connor P, O'Dea A, Melton J. A methodology for

identifying human error in U.S. Navy diving accidents. Hum Factors. 2007;49:214–26. doi: 10.1518/001872007X312450. PMID: 17447664.
6 Neumann T. Arterial gas embolism and decompression sickness. News Physiol Sci. 2002;17:77–81. doi: 10.1152/nips.01370.2001. PMID: 11909997.
7 UHMS Best Practice Guidelines, 2011 April 04. [cited 2020 Feb 25]. Available from: https://www.uhms.org/images/DCS-AGE-Committee/dcsandage_prevandmgt_uhms-fi.pdf.
8 Moon RE, Gorman DF. Treatment of the decompression disorders. In: Brubakk AO, Neuman TS, editors. Bennett and Elliott's physiology and medicine of diving, 5th ed. Edinburgh: Saunders; 2003. p. 600–50.
9 Antonelli C, Franchi F, Della Marta ME, Carinci A, Sbrana G, Tanasi P, et al. Guiding principles in choosing a therapeutic table for DCI hyperbaric therapy. Minerva Anestesiol. 2009;75:151–61. PMID: 19221544.
10 Hadanny A, Meir O, Bechor Y, Fishlev G, Bergan J, Efrati S. The safety of hyperbaric oxygen treatment retrospective analysis in 2,334 patients. Undersea Hyperb Med. 2016;43:113–22. PMID: 27265988.
11 Bessereau J, Coulange M, Genotelle N, Barthélémy A, Michelet P, Bruguerolle B, et al. Aspirin in decompression sickness. Therapie. 2008;63:419–23. doi: 10.2515/therapie/2008067. PMID: 19236833.
12 Gempp E, Blatteau JE. Risk factors and treatment outcome in scuba divers with spinal cord decompression sickness. J Crit Care. 2010;25:236–42. doi: 10.1016/j.jcrc.2009.05.011. PMID: 19682840.
13 Aharon-Peretz J, Adir Y, Gordon CR, Kol S, Gal N, Melamed Y. Spinal cord decompression sickness in sport diving. Arch Neurol. 1993;50:753–6. doi: 10.1001/archneur.1993.00540070065017. PMID: 8323480.
14 Ball R. Effect of severity, time to recompression with oxygen, and retreatment on outcome of forty-nine cases of spinal cord decompression sickness. Undersea Hyperb Med. 1993;20:133–45. PMID: 8329940.
15 Desola J, Sala J, Bohe J, Garcia A, Abos R, Canela J. Prognostic factors of dysbaric disorders. Evidence-based conclusions after a multivariant analysis of 554 cases. In: Cali-Corleo R, editor. Proceedings of the 26th Annual Meeting of the European Underwater and Baromedical Society. Valetta, Malta: EUBS; 2000. p. 17–23.
16 Vann RD. Mechanisms and risks of decompression. In: Bove AA, editor. Bove and Davis' diving medicine, 4th ed. Saunders. 2004:127–64. doi: 10.1016/B978-0-7216-9424-5.50013-7.
17 Blatteau JE, Gempp E, Simon O, Coulange M, Delafosse B, Souday V, et al. Prognostic factors of spinal cord decompression sickness in recreational diving: retrospective and multicentric analysis of 279 cases. Neurocrit Care. 2011;15:120–7. doi: 10.1007/s12028-010-9370-1. PMID: 20734244.
18 Blatteau JE, Gempp E, Constantin P, Louge P. Risk factors and clinical outcome in military divers with neurological decompression sickness: Influence of time to recompression. Diving Hyperb Med. 2011;41:129–34. PMID: 21948497.
19 Doolette DJ, Mitchell SJ. In-water recompression. Diving Hyperb Med. 2018;48:84–95. doi: 10.28920/dhm48.2.84-95. PMID: 29888380. PMCID: PMC6156824.
20 Steffensmeier D, Albrecht R, Wendling J, Melliger R, Spahn DR, Stein P, Wyss C. Specialist advice may improve patient selection for decompression therapy following diving accidents: a retrospective observational study. Scand J Trauma Resusc Emerg Med. 2017;25:101. doi: 10.1186/s13049-017-0447-0. PMID: 29052534. PMCID: PMC5649053.
21 Hadanny A, Fishlev G, Bechor Y, Bergan J, Friedman M, Maliar A, et al. Delayed recompression for decompression sickness: retrospective analysis. PLoS One. 2015;10(4):e0124919 doi: 10.1371/journal.pone.0124919. PMID: 25906396. PMCID: PMC4408070.
22 Pitkin AD, Benton PJ, Broome JR. Outcome after treatment of neurological decompression illness is predicted by a published clinical scoring system. Aviat Space Environ Med. 1999;70:517–21. PMID: 10332950.

Acknowledgements

We would like to thank the hyperbaric technicians and nurses of the HUG.

Conflicts of interest and funding: nil

Submitted: 11 February 2020
Accepted after revision: 16 August 2020

Investigating critical flicker fusion frequency for monitoring gas narcosis in divers

Xavier CE Vrijdag[1,2], Hanna van Waart[1], Jamie W Sleigh[1,3], Costantino Balestra[4], Simon J Mitchell[1,5]

[1] *Department of Anaesthesiology, University of Auckland, Auckland, New Zealand*
[2] *Deep Dive Dubai, Dubai, United Arab Emirates*
[3] *Department of Anaesthesia, Waikato Hospital, Hamilton, New Zealand*
[4] *Environmental, Occupational and Ageing (Integrative) Physiology Laboratory, Haute Ecole Bruxelles-Brabant (HE2B), Brussels, Belgium*
[5] *Department of Anaesthesia, Auckland City Hospital, Auckland, New Zealand*

Corresponding author: *Xavier Vrijdag, Department of Anaesthesiology, School of Medicine, University of Auckland, Private bag 92019, Auckland 1142, New Zealand*
x.vrijdag@auckland.ac.nz

Key words
CFFF; Diving research; Narcosis; Nitrogen; Oxygen; Physiology

Abstract
(Vrijdag XCE, van Waart H, Sleigh JW, Balestra C, Mitchell SJ. Investigating critical flicker fusion frequency for monitoring gas narcosis in divers. Diving and Hyperbaric Medicine. 2020 December 20;50(4):377–385. doi: 10.28920/dhm50.4.377-385. PMID: 33325019.)
Introduction: Critical flicker fusion frequency (CFFF) has been used in various studies to measure the cognitive effects of gas mixtures at depth, sometimes with conflicting or apparently paradoxical results. This study aimed to evaluate a novel automatic CFFF method and investigate whether CFFF can be used to monitor gas-induced narcosis in divers.
Methods: Three hyperbaric chamber experiments were performed: 1) Automated and manual CFFF measurements during air breathing at 608 kPa (n = 16 subjects); 2) Manual CFFF measurements during air and heliox breathing at sea level (101.3 kPa) and 608 kPa (n = 12); 3) Manual CFFF measurements during oxygen breathing at sea level, 142 and 284 kPa (n = 10). All results were compared to breathing air at sea level.
Results: Only breathing oxygen at sea level, and at 284 kPa, caused a significant decrease in CFFF (2.5% and 2.6% respectively compared to breathing air at sea level. None of the other conditions showed a difference with sea level air breathing.
Conclusions: CFFF did not significantly change in our experiments when breathing air at 608 kPa compared to air breathing at sea level pressure using both devices. Based on our results CFFF does not seem to be a sensitive tool for measuring gas narcosis in divers in our laboratory setting.

Introduction

The critical flicker fusion frequency (CFFF) has been used to quantify cognitive impairment in various environments and during exposures to drugs. CFFF is based on the phenomenon that the participant can perceive a flickering light as non-flickering if the frequency is above the 'fusion frequency'. By increasing or decreasing the frequency of the flickering light the fusion frequency can be determined. A decrease in fusion frequency is supposedly correlated with cognitive impairment,[1] whereas an increase in fusion frequency is interpreted as indicating improvement. For example, various hypnotic drugs decrease the CFFF, while an increase in CFFF can be achieved with stimulating drugs.[2]

In hyperbaric environments (underwater or in a hyperbaric chamber), CFFF has been used in studies exposing participants to various gas mixtures and pressures to investigate the narcotic effects (or lack thereof) of gases such as nitrogen,[3–7] helium[5,8] and oxygen.[9,10]

The CFFF device used in previous research involved the investigator in having to change the flicker frequency, communicate with the participant and write down the fusion frequency. In most research, the test is repeated three times in order to check its consistency. This method is time consuming and it is difficult to achieve simultaneous measurements in multiple participants. An automatic method for the estimation of the CFFF has been proposed.[11] A computerised device which tested stimuli at six constant frequencies multiple times in random order, estimates the peak frequency of the fitted sigmoidal response curve as the flicker fusion frequency. The measurement took six minutes on average, which is similar to the commercially available devices that use a flickering stimulus of steadily increasing or decreasing frequency. The downside of these devices is

the need for a connection to a personal computer to control the flickering light and to store the results, making this impossible to use in the hyperbaric and diving environment.

The initial primary goal of this study was to evaluate a new automated CFFF device by comparing its measurements of gas narcosis to those obtained using a manual system, prior to adopting the former device for pending gas narcosis studies. The results obtained during this comparison were inconsistent with expected CFFF variations; and hence a further two experiments were conducted with a manual device used by others in previous studies to re-evaluate changes in CFFF during exposure to hyperbaric air, heliox and oxygen, and its consequent use as an objective measure of narcosis. This study is part of a larger programme investigating novel approaches to measuring gas narcosis in divers.

Methods

This paper describes three experiments: 1) Automated and manual CFFF measurements during air breathing at sea level pressure and at 608 kPa; 2) Manual CFFF measurements during air and heliox breathing at sea level pressure and at 608 kPa; 3) Manual CFFF measurements during oxygen breathing at sea level pressure, 142 and 284 kPa.

The first experiment with the novel automated CFFF device took place at the hyperbaric facility at Deep Dive Dubai, in March 2018. The study protocol was approved by the Dubai Scientific Research Ethics Committee of the Dubai Health Authority, United Arab Emirates (reference 10/2017_06).

The second and third experiments with the conventional manual CFFF device took place at the Slark Hyperbaric Unit, Waitemata District Health Board, Auckland, New Zealand, in January–August 2019. The protocol of this randomised, cross-over study was approved by the Health and Disability Ethics Committee, Auckland (reference 16/NTA/93), and was registered with the Australian New Zealand Clinical Trial Registry (ANZCTR) with the Universal Trial Number U1111-1181-9722. These CFFF measurements were a sub-study in a larger body of work investigating use of quantitative electroencephalography to measure gas-induced narcosis that will be reported elsewhere.

PARTICIPANTS

Participants were certified, healthy adult divers, aged between 18 and 60 years and had normal visual acuity, either corrected or uncorrected. Exclusions were use of recreational drugs, tobacco, psychoactive medication, excessive alcohol (> 21 standard drinks per week) or over five caffeine-containing beverages a day. Participants abstained from any caffeinated drink on the measurement day, and from alcohol for at least 24 hours before the measurement. They had at least six hours of sleep the night before the measurement. Experiments two and three had as an additional requirement that participants were certified technical divers that were trained to do decompression dives, using oxygen as decompression gas. All participants provided written informed consent.

AUTOMATED CFFF DEVICE

The first experiment utilised a CFFF device suitable for hyperbaric environments built by Probe Embedded Solutions (Enschede, the Netherlands). The device could be controlled from the backside by an operator using three buttons and a small screen. The participants' side only had a cold white LED. This device had two modes: manual and automatic.

In manual mode both the operator and the participant held the CFFF device. The participant was instructed to hold the base of the device with one hand and point the LED towards the eye. Care was taken to minimise movement of the device and head of the participant during the experiment. With the other hand the participant raised a finger when he/she could see the LED flicker and lowered the finger when the LED was perceived not to flicker.

The manual mode started with a flickering frequency of 50 Hz, which was above the normal perceivable flicker frequency. The frequency could be decreased or increased by 0.5 Hz by the operator. The current frequency was not shown on the screen to blind the operator. The operator started the measurement by lowering the frequency until the participant raised their finger. This was repeated three times, the second and third recording started at two Hz above the previous fusion frequency; again with the frequency lowered until the participant raised their finger.

The automatic CFFF mode was programmed on the same device. The participant held the CFFF device with a finger on the reverse-side button and pointed the LED towards the eye. They pushed the button every time they perceived the LED to flicker.

The automatic mode started with a flickering frequency of 40 Hz, which is near the normal perceived flicker fusion frequency. The frequency was either increased (push of button) or decreased (no action for 2 seconds) in 8 iterations by a decreasing frequency step (respectively 20, 10, 5, 2.5, 1.25, 0.67, 0.33, 0.17 Hz). This resulted in a theoretical minimum and maximum CFFF between 0.17 (all decreased) and 79.83 (all increased) Hz. This was automatically repeated three times with a 0.5 second LED off interval.

For both manual and automatic modes, after the three recordings the results were displayed on the device including the mean frequency of the three CFFF recordings. The results were stored on an SD card for offline analysis. At the end of the three recordings the operator checked the results for errors, values outside of the physiological range, and repeated measurements if needed.

MANUAL CFFF DEVICE

The second and third experiments used a device previously used in a hyperbaric study.[7] This device had a blue LED visible to the participant, with two buttons and a screen (which displayed the current flicker frequency), not visible to the participant. The buttons increased and decreased the flicker frequency in 0.25 Hz steps. The participant held the device stable and minimised head movement while looking at the flickering light. The device was set to a starting frequency of 30 Hz, which was below the normal perceived flicker fusion frequency, and the participant confirmed that he/she could see the light flickering. The participant increased the frequency by holding the button, until the light was no longer perceived to flicker. This was considered the fusion frequency, which was recorded by the operator. This measurement was repeated till three recordings were within 1 Hz of each other (Figure 1).

EXPERIMENT ONE – AIR

The hyperbaric chamber was a rectangular 10-person chamber (Oxyheal 5000, National City, CA, USA). All measurements (including baseline measurements) were conducted inside the hyperbaric chamber with comfortable ambient light intensity held constant to minimise any biasing influence of ambient light. Both CFFF modes were recorded in random order while breathing environmental air, at sea level pressure immediately before compression, and at least five minutes after reaching 608 kPa (equivalent to 50 metres' seawater [msw] depth) (Figure 2). Participants were compressed in groups of 2–4 persons. Decompression was according to the US Navy decompression tables, including 100% oxygen breathing from 193 kPa to sea level pressure.

EXPERIMENT TWO – AIR AND HELIOX

The hyperbaric chamber was a cylindrical 5-person chamber (W.E. Smith Engineering PTY LTD, Australia). All measurements were conducted inside the hyperbaric chamber with constant comfortable ambient light intensity. Participants returned for two sessions at least 48 hours apart, breathing either air or heliox (20.8% oxygen, balance helium) in randomised order. CFFF was recorded inside the

Figure 1

Flow diagram of critical fusion frequency manual (left) and automatic (middle) modes during experiment one and manual mode (right) during experiments two and three

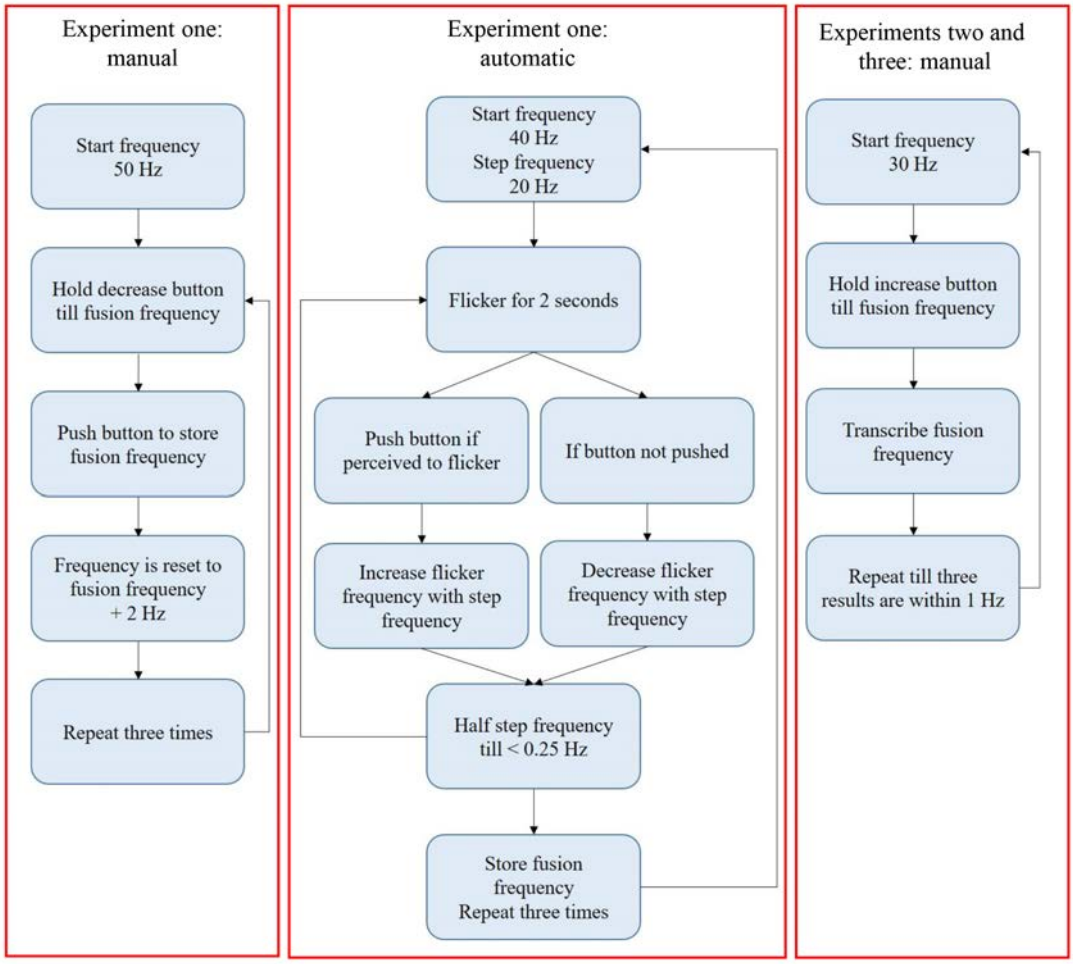
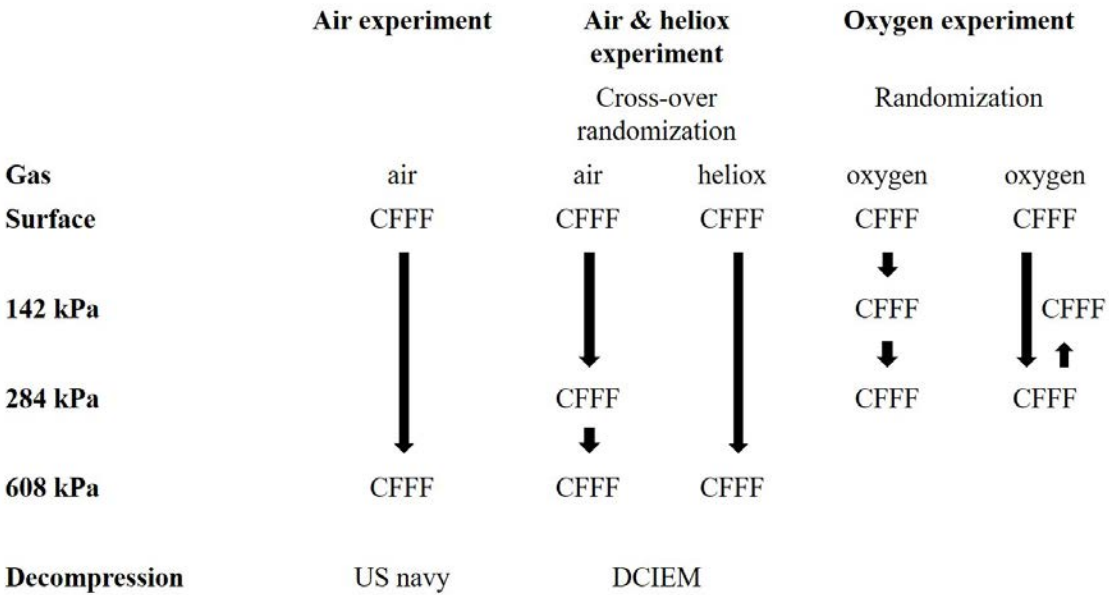


Figure 2
Diagram summarising procedures in all three experiments



hyperbaric chamber at sea level pressure immediately before compression. In the air sessions participants underwent a CFFF measurement at 284 kPa (equivalent to 18 msw depth) and 608 kPa. In the heliox sessions, participants breathed heliox for measurements at sea level pressure and continued breathing heliox during compression for a second measurement at 608 kPa (Figure 2). After each CFFF measurement end-tidal carbon dioxide was measured using a mainstream capnograph (EMMA, Masimo, Irvine, CA, USA). Measurements at 608 kPa were impossible due to device incompatibility, so readings were taken immediately after ascent to the first decompression stop at 284 kPa. The ascent took two minutes. Decompression was according to the DCIEM decompression tables, including 100% oxygen breathing from 193 kPa (equivalent to 9 msw depth) to sea level pressure.

EXPERIMENT THREE – OXYGEN

The same cylindrical 5-person hyperbaric chamber and ambient lighting intensity was used. A baseline CFFF measurement was taken at sea level pressure while breathing environmental air inside the hyperbaric chamber. Participants switched to 100% oxygen for a second sea level pressure measurement. The third and fourth measurement took place in randomised order at 142 (equivalent to 4 msw depth) and 284 kPa breathing oxygen (Figure 2).

In all experiments each measurement was preceded by a five-minute acclimatisation period for the pressure and/or gas mixture.[3] Again, end-tidal carbon dioxide was measured after each CFFF measurement at the measurement depth.

OUTCOMES

The primary outcome was the relative change (percentage) in mean CFFF (mean of the three recordings) of each exposure to a breathing gas and/or pressure compared to baseline air breathing at sea level pressure. Secondary outcome measures for studies two and three were the number of recordings per measurement required to achieve the required level of concordance and the end-tidal carbon dioxide after each measurement.

STATISTICAL ANALYSIS

All data were analysed with SPSS version 25 (IBM, Armonk, NY, USA). Descriptive statistics were generated to characterise the study participants. The relative CFFF value was calculated as percentage from baseline for each individual in each condition. All outcome measures were tested for normality with the Kolmogorov–Smirnov test. All data were normally distributed and were subsequently described by their mean and standard deviation (SD). Differences between relative (percentage) baseline and intervention measures were analysed with paired *t*-tests and reported as mean difference (MD) with 95% confidence intervals (95%CI). Statistical significance was set at $P < 0.05$.

Results

The 40 participants in this study had between 15 and 10,000 dives. Most were technical divers, although there were five non-technical divers in the first experiment. In all three experiments there was a high number of instructors and almost half of the participants had experience breathing

Table 1
Demographic data for subjects in all experiments

Parameter	Air experiment *n* = 16		Air - heliox experiment *n* = 12		Oxygen experiment *n* = 10	
	Mean	Range	Mean	Range	Mean	Range
Age (years)	35.3	20–54	35.8	24–55	36.4	24–49
Body mass index (kg·m^{-2})	23.8	19.1–29.3	26.7	19.5–31.9	26.6	19.5–35.5
Diving experience (years)	11.4	1–29	15.3	3–28	16.6	3–31
Dives	2,679	15–10,000	921	160–2,000	1,203	160–3,500
	n	%	*n*	%	*n*	%
Gender (male)	10	63	7	58	7	70
Certification						
Supervised diver	2	13	0	0	0	0
Autonomous diver	2	13	6	50	6	60
Dive Leader	1	6	1	8	1	10
Dive instructor	11	69	5	42	3	30
Technical diver	11	69	12	100	10	100
Narcotic experience (> 50 msw air)	8	50	7	58	4	40

air at 608 kPa or deeper. Sixteen participated in the air experiment, twelve in the air-heliox experiment and twelve in the oxygen experiment (Table 1). Owing to device failure, two participants were unable to perform the CFFF recordings in the oxygen experiment.

EXPERIMENT ONE – AIR

Neither the manual nor the automatic version of the CFFF measurements were significantly different during air breathing at 608 kPa compared to air breathing at sea level pressure (Table 2).

EXPERIMENT TWO – AIR AND HELIOX

The manual CFFF measurements were not significantly different in any of the air or heliox exposures compared to the air breathing at sea level pressure (Table 2). On average 3.8 (with up to six) CFFF recordings were needed to obtain results that met the requirement of having three recordings within 1 Hz. There was no significant difference in end-tidal carbon dioxide levels between the hyperbaric exposures and baseline air breathing.

EXPERIMENT THREE – OXYGEN

Breathing oxygen at sea level pressure and at 284 kPa caused a significant decrease in CFFF of 2.5 and 2.6%, respectively, compared with air breathing at sea level pressure. The CFFF measured during oxygen breathing at 142 kPa trended in the same direction (Table 2). On average 3.8 (with up to seven) CFFF recordings were needed to obtain results that met the requirement of having three recordings within 1 Hz. There was a significant decrease in end-tidal carbon dioxide level from baseline air breathing to oxygen breathing at 142 kPa (5.3 (SD 1.1) kPa at baseline to 4.6 (0.9) kPa, MD = 0.65 [95% CI 0.25–1.05], P = 0.005). End-tidal carbon dioxide levels in the other oxygen exposures were not significantly different from baseline air breathing.

Discussion

In both experiments one and two, CFFF measured by either method appeared insensitive to the known narcotic effects of nitrogen in air breathed at 608 kPa. Given that helium is a non-narcotic gas it is not surprising that there was no significant change in CFFF during heliox breathing at 608 kPa in experiment two, but the key point here is that CFFF also did not distinguish between the effects of air (79% nitrogen) and heliox (79% helium) when breathed at a pressure widely acknowledged to induce narcosis when air is breathed. In experiment three a reduction in CFFF was found when breathing oxygen at sea level and 284 kPa, with a similar trend at 142 kPa. As will be discussed below, the effects of oxygen were measured in an attempt to help interpret the results of experiments one and two. Summaries of the design and findings of other relevant studies are shown in Tables 3 and 4 respectively. Review of this literature reveals a complicated and often contradictory picture.

Several studies during air breathing conducted at 406 kPa (equivalent to 30 msw depth), have invoked nitrogen narcosis to explain a reduction in CFFF at this depth.[4,7,12] However, this result does not extrapolate to greater depth/pressures even though it is known that cognitive performance is further reduced with increased depth.[13] Several studies,

Table 2

Critical flicker fusion frequency (CFFF) measurements presented as mean absolute frequency (Hz) and percentage relative change compared to the baseline measurement (breathing air at sea level). * indicates significant difference compared with baseline; $P < 0.05$; MD = mean % difference between baseline and exposure; 95% CI = 95% confidence interval

Exposure	Sea level air CFFF (Hz (%))	Exposure CFFF (Hz (%))	Relative change	
			MD (%)	95% CI
Air experiment – automatic and manual CFFF				
608 kPa manual	43.9 (100)	44.0 (100.1)	0.1	-3.3 to 3.5
608 kPa automatic	44.8 (100)	43.9 (102.2)	2.2	-1.3 to 5.8
Air and heliox experiment – manual CFFF				
284 kPa air	37.9 (100)	38.1 (100.6)	0.6	-0.1 to 1.4
608 kPa air		38.4 (101.3)	1.3	-0.5 to 3.1
Sea level heliox		38.6 (101.9)	1.9	-1.0 to 4.8
608 kPa heliox		38.5 (101.6)	1.6	-0.9 to 4.0
Oxygen experiment – manual CFFF				
Sea level oxygen	37.9 (100)	36.9 (97.5)	-2.5	-4.1 to -0.8 *
142 kPa oxygen		37.3 (98.6)	-1.4	-3.7 to 0.9
284 kPa oxygen		36.9 (97.4)	-2.6	-4.3 to -0.9 *

including the present experiments, performed at 608 kPa while breathing air, did not show impairment, but instead showed either no change (the present study) or an increase in CFFF in two others.[5,6] The increase in CFFF seen in both latter studies was attributed to 'oxygen hyper-alertness', due to the increased partial pressure of inspired oxygen of 127 kPa during air breathing at 608 kPa. Oxygen hyper-alertness [14,15] is hypothesised to be caused by an increased availability of oxygen in the neuronal tissue,[16] which is postulated to cause accelerated nerve conduction.[17] This was also proposed as a mechanism to explain an increase in CFFF during normobaric 100% oxygen breathing.[10]

However, in contrast to Hemelryck et al.[10] the present results for 100% oxygen breathing at sea level pressure showed a small reduction in CFFF; while in another study by Kot et al.[9] 70% oxygen breathing at sea level did not produce any change.[9] Similarly, both the Kot study[9] and the present study showed a decrease in CFFF during oxygen breathing at higher pressures:142 kPa and 284 kPa in the present study; and 142 kPa in the study by Kot. This was explained by Kot as a manifestation of oxygen narcosis,[9] based on the concept that oxygen is twice as soluble in oil as nitrogen and hence should have a narcotic effect;[18] although probably not to the extent predicted by inspired partial pressure alone because it is metabolised in tissues.[19] To confuse matters further, Kot[9] reported an increase in CFFF when breathing oxygen at 284 kPa which was attributed to a hyperexcitability effect associated with cerebral oxygen toxicity.[20] After a latent period, oxygen can cause tonic-clonic seizures, but non-convulsive signs and symptoms appear to have a neuronal origin as well.[21] The present study demonstrated the opposite, consistent with all our results during oxygen breathing. Other than the uncertain oxygen narcosis hypothesis (which would not explain the similar result at sea level pressure) there is no obvious explanation for this.

Besides nitrogen and oxygen, carbon dioxide can influence cognitive impairment.[22,23] The relevant physiological pathway has been debated. Carbon dioxide may either have a direct narcotic effect or it might facilitate nitrogen and/or oxygen narcosis or hyper-alertness through cerebral vasodilation.[24] The present study recorded a decreasing trend in end-tidal carbon dioxide during oxygen breathing, essentially excluding any interference by hypercapnia in the relevant CFFF results. It was not possible to measure end-tidal carbon dioxide at 608 kPa in experiment two, and the possibility of a change in end-tidal carbon dioxide between leaving 608 kPa and arrival at 284 kPa where the measurement was made cannot be completely excluded, though there was no evidence of hypercapnia in the subjects.

In addition to the effects of the respired gas and the exposure pressure described above, other factors proposed to influence CFFF include: the prior diving or gas-exposure experience of the subjects;[5,9] subject fatigue;[12,25] the colour and intensity of the flickering light and intensity of the ambient light;[26] the latency of the measurement after beginning of the exposure;[3] the nature of the hyperbaric exposure (immersed or dry);[6,12] the definition of consistency in determining the result;[4] and others (Tables 3 and 4). All of these factors have been invoked to explain results that are inconsistent with an expected (or unexpected) narcotic effect, or the many inconsistencies between studies. This will mean that there may be debate about how the results of the present study were obtained or interpreted, but this would miss the wider point: namely, there is a substantial question-mark over the

Table 3
Details of studies reporting CFFF results in pressure exposures. HBT = Human Breathing Technology; NS = not specified; PES = Probe Embedded Solutions; ROAD = Robotics for Assisted Diving

Study	Environment	Device manufacturer	Light colour	Flicker / fusion	# recordings
Seki et al.[8]	Chamber	Shibata	NS	Flicker	Average of 5
Balestra et al.[4]	Pool	HBT	Blue	NS	Average of 3
Hemelryck et al.[10]	Surface	HBT	Blue	NS	Average of 3
Kot et al.[9]	Chamber	HBT	Blue	NS	NS
Tikkinen et al.[6]	Chamber	Schuhfried	White	Both	Average of 8
Lafere et al.[12]	Outdoor	HBT	Blue	Flicker	Average of 3
Lafere et al.[7]	Chamber	HBT	Blue	Flicker	Average of 3
Rocco et al.[5]	Outdoor	ROAD	Blue	Fusion	Average of 3
Present study (Experiment one)	Chamber	PES	White	Fusion	Average of 3
Present study (Experiments two and three)	Chamber	HBT	Blue	Flicker	Average of 3

Table 4
Results of studies reporting CFFF in pressure exposures. Results are percentage change in CFFF compared to baseline

Study	*n*	Exposure	Result (%)	Hypothesis
Seki et al.[8]	2	6.2 MPa, Heliox PO_2 38-52 kPa, 2 days	80	Extreme pressure
Balestra et al.[4]	20	430 kPa, air, 15 min	93.5	Nitrogen narcosis
Hemelryck et al.[10]	20	101 kPa, oxygen, 10 min	117	Hyper-alertness
Kot et al.[9]	16	101 kPa, 70% oxygen, 25 min	99	Oxygen narcosis
	16	140 kPa, oxygen, 25 min	94	Oxygen narcosis
	65	280 kPa, oxygen, 25 min	103	Oxygen toxicity
Tikkinen et al.[6]	30	608 kPa, air, 5 min	103	Hyper-alertness
Lafere et al.[12]	20	405 kPa, air, 15 min	94.5	Nitrogen narcosis
Lafere et al.[7]	8	405 kPa, air, 15 min	95	Nitrogen narcosis
	8	405 kPa, EAN40, 15 min	99	Hyper-alertness
Rocco et al.[5]	22	608 kPa, air, 15 min	105	Nitrogen narcosis Hyper-alertness
	18	608 kPa, Trimix 21/35, 15 min	107	
	11	608 kPa, Heliox 21/79, 15 min	111	

usefulness of an assessment modality that has produced so many conflicting findings across multiple studies, and which seems subject to influence by many variables and to difficulty in interpretation.

At a simplistic level the primary finding of this study is clear: in our hands CFFF failed to detect or quantify a narcotic effect known to be present (in the 608 kPa air exposures). Therefore, CFFF does not appear to be a candidate outcome measure for our programme of investigating gas narcosis in hyperbaric environments. Consistent with the 'wider point' articulated above, there is little merit in debating the fine detail of the methods, but several aspects are worth emphasising. First, the air exposures where a narcotic effect was expected were conducted with two different devices and (in experiment two) in collaboration with an author very experienced in using CFFF in diving research, who gave guidance on data collection and analysis methods, and provided the second manual CFFF device. Second, under-powering of these studies could explain the lack of statistically significant differences. These experiments had 10 to 16 participants per condition, similar to the number of participants in other studies, which varied between 8 and 30 per study condition with one outlier having 65 participants (Table 4). However statistical significance is largely irrelevant given that the measurement method seems unable to monitor gas narcosis on an individual level. Moreover, the fundamental direction of change was not consistent with the expected narcotic effects of air at high pressure. Thirdly, CFFF measurements were not recorded

until after an equilibration period with the respired gas of at least five minutes in every condition. In respect of nitrogen in the brain, based on a cerebral compartmental half-life of 1.2 minutes,[27] this should allow for ≥ 94% equilibration with the arterial PN_2. Finally, given the potential influence of many factors (discussed above) in affecting CFFF results, it is impossible to use absolute values to define normal or abnormal, and the use of subjects as their own controls in assessment of change between different conditions seems the most legitimate approach to utilising CFFF in this type of study; hence this approach was adopted here.

Conclusions

CFFF measured automatically or manually with different devices was insensitive to the narcotic effect of nitrogen in air at 608 kPa. The present programme requires a measurement method that provides robust and consistent quantification of the cognitive changes caused by gas narcosis in individual subjects. In this study CFFF does not appear to achieve this aim. Review of the relevant literature reveals inconsistent and sometimes paradoxical results with various groups attempting to sometimes explain their data using often contradictory hypotheses. It is concluded that CFFF may not be, in our laboratory setting, the optimal measurement method to monitor the effects of gas narcosis in divers.

References

1 Rota-Bartelink A. The diagnostic value of automated flicker threshold perimetry. Curr Opin Ophthalmol. 1999;10:135–9. PMID: 10537764.

2 Smith JM, Misiak H. Critical flicker frequency (CFF) and psychotropic drugs in normal human subjects – a review. Psychopharmacologia. 1976;47:175–82. doi: 10.1007/BF00735818. PMID: 1273214.

3 Bennett PB, Cross AVC. Alterations in the fusion frequency of flicker correlated with electro-encephalogram changes at increased partial pressures of nitrogen. J Physiol. 1960;151:28–9. doi: 10.1113/jphysiol.1960.sp006464.

4 Balestra C, Lafère P, Germonpré P. Persistence of critical flicker fusion frequency impairment after a 33 mfw SCUBA dive: Evidence of prolonged nitrogen narcosis? Eur J Appl Physiol. 2012;112:4063–8. doi: 10.1007/s00421-012-2391-z. PMID: 22476770.

5 Rocco M, Pelaia P, Di Benedetto P, Conte G, Maggi L, Fiorelli S, et al. Inert gas narcosis in scuba diving, different gases different reactions. Eur J Appl Physiol. 2019;119:247–55. doi: 10.1007/s00421-018-4020-y. PMID: 30350155.

6 Tikkinen J, Wuorimaa T, Siimes MA. A comparison of simple reaction time, visual discrimination and critical flicker fusion frequency in professional divers at elevated pressure. Diving Hyperb Med. 2016;46:82–6. PMID: 27334995.

7 Lafère P, Hemelryck W, Germonpré P, Matity L, Guerrero F, Balestra C. Early detection of diving-related cognitive impairment of different nitrogen-oxygen gas mixtures using critical flicker fusion frequency. Diving Hyperb Med. 2019;49:119–26. doi: 10.28920/dhm49.2.119-126. PMID: 31177518. PMCID: PMC6704008.

8 Seki K, Hugon M. Critical flicker frequency (CFF) and subjective fatigue during an oxyhelium saturation dive at 62 ATA. Undersea Biomed Res. 1976;3:235–47. PMID: 969026.

9 Kot J, Winklewski PJ, Sicko Z, Tkachenko Y. Effect of oxygen on neuronal excitability measured by critical flicker fusion frequency is dose dependent. J Clin Exp Neuropsychol. 2015;37:276–84. doi:10.1080/13803395.2015.1007118. PMID: 25715640.

10 Hemelryck W, Rozloznik M, Germonpré P, Balestra C, Lafère P. Functional comparison between critical flicker fusion frequency and simple cognitive tests in subjects breathing air or oxygen in normobaria. Diving Hyperb Med. 2013;43:138–42. PMID: 24122188.

11 Feshchenko VA, Reinsel RA, Veselis RA. Optimized method of estimation of critical flicker frequency (CFF). In: Proceedings of the symposium on computer applications in medical care. American Medical Informatics Association; 1994. p. 1006. PMID: 7949848. PMCID: PMC2247846.

12 Lafère P, Balestra C, Hemelryck W, Guerrero F, Germonpré P. Do environmental conditions contribute to narcosis onset and symptom severity? Int J Sports Med. 2016;37:1124–8. doi: 10.1055/s-0042-110573. PMID: 27737486.

13 Bennett PB, Rostain JC. Inert gas narcosis. In: Brubakk AO, Neuman TS, editors. Physiology and medicine of diving. 5th ed. Philadelphia (PA): Saunders; 2003. p. 300–22.

14 Scholey AB, Moss MC, Neave N, Wesnes K. Cognitive performance, hyperoxia, and heart rate following oxygen administration in healthy young adults. Physiol Behav. 1999;67:783–9. doi: 10.1016/S0031-9384(99)00183-3. PMID: 10604851.

15 Chung SC, Sohn JH, Lee B, Tack GR, Yi JH, You JH, et al. The effect of transient increase in oxygen level on brain activation and verbal performance. Int J Psychophysiol. 2006;62:103–8. doi: 10.1016/j.ijpsycho.2006.02.006. PMID: 16678926.

16 Weenink RP, Hollmann MW, Vrijdag XCE, Van Lienden KP, De Boo DW, Stevens MF, et al. Hyperbaric oxygen does not improve cerebral function when started 2 or 4 hours after cerebral arterial gas embolism in swine. Crit Care Med. 2013;41:1719–27. doi: 10.1097/CCM.0b013e31828a3e00. PMID: 23632435.

17 Brerro-Saby C, Delliaux S, Steinberg JG, Jammes Y. The changes in neuromuscular excitability with normobaric hyperoxia in humans. Exp Physiol. 2010;95:153–9. doi: 10.1113/expphysiol.2009.049460. PMID: 19684094.

18 Smith RA, Paton WD. The anesthetic effect of oxygen. Anesth Analg. 1976;55:734–6. doi: 10.1213/00000539-197609000-00027. PMID: 987735.

19 Mitchell SJ, Doolette DJ. Recreational technical diving part 1: An introduction to technical diving methods and activities. Diving Hyperb Med. 2013;43:86–93. PMID: 23813462.

20 Dean JB, Mulkey DK, Garcia AJ, Putnam RW, Henderson RA. Neuronal sensitivity to hyperoxia, hypercapnia, and inert gases at hyperbaric pressures. J Appl Physiol (1985). 2003;95:883–909. doi: 10.1152/japplphysiol.00920.2002. PMID: 12909594.

21 Ciarlone GE, Hinojo CM, Stavitzski NM, Dean JB. CNS function and dysfunction during exposure to hyperbaric oxygen in operational and clinical settings. Redox Biol. 2019;27:101159. doi: 10.1016/j.redox.2019.101159. PMID: 30902504. PMCID: PMC6859559.

22 Gill M, Natoli MJ, Vacchiano C, MacLeod DB, Ikeda K, Qin M, et al. Effects of elevated oxygen and carbon dioxide partial pressures on respiratory function and cognitive performance. J Appl Physiol (1985). 2014;117:406–12. doi: 10.1152/japplphysiol.00995.2013. PMID: 24947022.

23 Freiberger JJ, Derrick BJ, Natoli MJ, Akushevich I, Schinazi

EA, Parker C, et al. Assessment of the interaction of hyperbaric N_2, CO_2 and O_2 on psychomotor performance in divers. J Appl Physiol (1985). 2016;121:953–64. doi: 10.1152/japplphysiol.00534.2016. PMID: 27633739.

24 Dunworth SA, Natoli MJ, Cooter M, Cherry AD, Peacher DF, Potter JF, et al. Hypercapnia in diving: A review of CO_2 retention in submersed exercise at depth. Undersea Hyperb Med. 2017;44:191–209. PMID: 28779577.

25 Lafère P, Balestra C, Hemelryck W, Donda N, Sakr A, Taher A, et al. Evaluation of critical flicker fusion frequency and perceived fatigue in divers after air and enriched air nitrox diving. Diving Hyperb Med. 2010;40:114–8. PMID: 23111908.

26 Karkar R, Kocielnik R, Zhang X, Allen P, Zia J, Ioannou G, et al. Beacon: Designing a portable device for self-administering a measure of critical flicker frequency. Proc ACM Interactive, Mobile, Wearable Ubiquitous Technol. 2018;2:1–27. doi: 10.1145/3264927.

27 Mitchell SJ, Doolette DJ. Selective vulnerability of the inner ear to decompression sickness in divers with right-to-left shunt: The role of tissue gas supersaturation. J Appl Physiol (1985). 2009;106:298–301. doi: 10.1152/japplphysiol.90915.2008. PMID: 18801958.

Acknowledgements

We are grateful to all divers who participated in this study. Furthermore, we would like to acknowledge the staff of Deep Dive Dubai and the Slark Hyperbaric Unit for their support during the data collection. We would like to thank Rob Reilink and Saskia Ton for their assistance in the conceptualisation of the new CFFF device.

Conflicts of interest and funding

Professor Simon Mitchell is the Editor of *Diving and Hyperbaric Medicine*. He took no part in the peer-review and decision-making processes for this paper, which were managed entirely by the Deputy Editor, Dr Lesley Blogg. There were no other conflicts of interest.

The second and third experiments of this study were supported by funding from the Office for Naval Research Global (ONRG), United States Navy (N62909-18-1-2007).

Submitted: 12 April 2020
Accepted after revision: 28 July 2020

Hyperbaric oxygen but not hyperbaric air increases insulin sensitivity in men with type 2 diabetes mellitus

David C Wilkinson[1,2], Ian M Chapman[2], Leonie K Heilbronn[2]

[1] *Hyperbaric Medicine Unit, Royal Adelaide Hospital, Adelaide, Australia*
[2] *Adelaide Medical School, The University of Adelaide, Adelaide, Australia*

Corresponding author: *Dr David Wilkinson, Hyperbaric Medicine Unit, Royal Adelaide Hospital, Port Road, Adelaide SA 5000, Australia*
david.wilkinson@sa.gov.au

Key words
Blood sugar level; Diabetes; Endocrinology; Hyperbaric research; Metabolism

Abstract
(Wilkinson DC, Chapman IM, Heilbronn LK. Hyperbaric oxygen but not hyperbaric air increases insulin sensitivity in men with type 2 diabetes mellitus. Diving and Hyperbaric Medicine. 2020 December 20;50(4):386–390. doi: 10.28920/dhm50.4.386-390. PMID: 33325020.)
Introduction: We have previously shown that hyperbaric oxygen treatment (HBOT) increased insulin sensitivity in men who were obese or overweight, both with and without type 2 diabetes. The aim of this study was to test whether this insulin-sensitising effect is seen in hyperbaric air (HA).
Methods: Men with type 2 diabetes who were obese or overweight were randomised to two groups: HBOT (n = 13) or HA (n = 11). A hyperinsulinaemic euglycaemic glucose clamp (80 mU·m^{-2}·min^{-1}) was performed at baseline and during hyperbaric intervention. Both groups were compressed to 203 kPa (two atmospheres absolute) for 90 minutes followed by a linear 30-minute decompression. The HBOT group breathed oxygen via a hood while the HA group breathed chamber air. Insulin sensitivity was assessed from the glucose infusion rate (GIR) during the last 30 minutes in the hyperbaric chamber (SS1) and the first 30 minutes after exit (SS2). Data were analysed for within-group effect by paired student t-test and between-group effect by one-way ANOVA.
Results: HBOT increased GIR by a mean 26% at SS1 (P = 0.04) and 23% at SS2 (P = 0.018). There was no significant change in GIR during or after HA. A between-group effect was evident for the change in GIR at SS1 in HBOT vs HA (P = 0.036).
Conclusions: The pathway by which insulin sensitivity is increased in men with type 2 diabetes requires the high oxygen partial pressures of HBOT and should be further investigated. Insulin sensitivity was not changed in hyperbaric air.

Introduction

Hyperbaric oxygen treatment (HBOT) is defined as breathing near 100% oxygen while in a hyperbaric chamber pressurised to more than 101 kPa or 1 atmosphere absolute (atm abs).[1] HBOT administered by clinical facilities typically uses pressure between 203-284 kPa (2–2.8 atm abs), with a duration of treatment 90–120 minutes. HBOT is an evidence-based treatment for conditions including decompression illness, cerebral arterial gas embolism, necrotising fasciitis, non-healing ulcers and wounds and delayed radiation injuries.[1]

Although HBOT is not used to treat diabetes mellitus *per se*, the increasing prevalence of this disease means that diabetes, particularly type 2 diabetes, is a frequent co-morbidity in patients treated with HBOT. For some years, it has been apparent that people with diabetes who undergo HBOT may experience a decrease in their plasma glucose level (PGL) during their treatment. Using a hand-held glucometer to measure PGL before and after 237 HBOT sessions in 27 patients with a mixture of type 1 and type 2 diabetes,[2] a mean fall in PGL of 2.04 mmol·L^{-1} was found. Another study measured laboratory glucose in a group of five patients with type 2 diabetes over the 2-hour duration of their HBOT session and found a mean fall of 3.5 mmol·L^{-1} at the end of HBOT.[3] There was no change in serum insulin levels.

In the present study, the effect of HBOT on insulin resistance and its reciprocal term, insulin sensitivity was investigated. Insulin resistance is defined as a relative impairment in the ability of insulin to exert its effect on glucose in target tissues (particularly muscle and liver). The development of insulin resistance is the best predictor for those likely to develop type 2 diabetes in the future.[4] Of the many investigative techniques used to assess insulin sensitivity, the hyperinsulinaemic euglycaemic glucose clamp is considered the gold standard.[5,6] In recent studies we have described an acute effect of HBOT to increase insulin sensitivity, as measured with the glucose clamp technique. A pilot study initially revealed that insulin sensitivity was increased in a cohort of men with and without diabetes receiving a clinical course of HBOT.[7] Progressively it was demonstrated that insulin sensitivity was increased during the third HBOT

session in a cohort of men with and without diabetes,[8] and most recently that the increase can be measured during the first HBOT session.[9]

The aim of this study was to determine whether the insulin-sensitising effect seen during HBOT (while breathing oxygen at a very high partial pressure) is also present during an equivalent pressure excursion but using air as the breathing gas rather than oxygen.

Methods

The study was approved by the Human Research Ethics Committee of the Royal Adelaide Hospital (R20160801) and the University of Adelaide and entered on a trial registry site (NCT03138746, clinicaltrials.gov). The study was carried out in accordance with the Declaration of Helsinki. All participants provided written, informed consent. The study was performed in the Hyperbaric Medicine Unit at the Royal Adelaide Hospital. Participant recruitment commenced in August 2018 and was closed due to reasons external to the study in December 2019.

PARTICIPANTS

Twenty-five participants were enrolled via a web-based recruitment company. Inclusion criteria were men aged 40 years or older who were obese or overweight (Body Mass Index (BMI) > 25 $kg \cdot m^{-2}$) with type 2 diabetes. Exclusion criteria included the presence of significant other medical issues, other non-prescribed medication that could affect glucose homeostasis, smoking, individuals who regularly perform high intensity exercise (> twice per week) and current intake of > 140 g alcohol per week. All participants were assessed for fitness to enter the hyperbaric chamber by a hyperbaric physician (DCW). Participants were randomised into two groups, HBOT and hyperbaric air (HA), stratified for BMI (BMI < 33 or BMI ≥ 33) by computer-generated, randomised block design in groups of four.

STUDY DESIGN

Participants attended the Hyperbaric Medicine Unit on two occasions after overnight fasting (10 hours) and modification of their diabetic medication. On the first visit, participants sat in comfortable reclining chairs, breathing room air while the baseline glucose clamp was performed over 3.5 hours. Intravenous cannulae were inserted, one in each forearm with one for the insulin and glucose infusions and the other for blood sampling. A primed insulin (Actrapid, Novo Nordisk, Baulkham Hills, Australia) solution was infused (80 $mU \cdot m^{-2} \cdot min^{-1}$) with blood samples taken at 5–10 minute intervals and PGL measured by a hand-held glucometer (Accu-Chek Performa, Roche Diagnostics, Sydney, Australia). PGL was clamped at 5.5 $mmol \cdot L^{-1}$ with a variable infusion of 25% dextrose (Baxter Healthcare, Old Toongabbie, Australia). Insulin sensitivity can be assessed at a pre-determined point in the glucose clamp during a steady state (SS) period when glucose infusion rate (GIR) and PGL readings are stable. Insulin sensitivity was assessed using the GIR during two separate but consecutive 30-minute steady state (SS) periods in the last hour of the infusion: SS1 corresponded with 2.5–3 hours; and SS2 with 3–3.5 hours. The raw GIR data for each participant were adjusted for body surface area.

Table 1
Participant characteristics for HBOT (n = 13) and hyperbaric air (n = 11) groups. (BMI, body mass index; BSA, body surface area)

Parameter	HBOT mean (SD)	HA mean (SD)
Age	62.3 (8.7)	56.3 (7.1)
Weight (kg)	108.2 (21.5)	102.4 (13.1)
Height (cm)	176.4 (6.7)	179.8 (10.3)
BMI ($kg \cdot m^{-2}$)	34.7 (6.8)	31.8 (4.7)
BSA (m^2)	2.23 (0.21)	2.21 (0.17)

Table 2
Diabetes medication used by participants. DPP = dipeptidyl peptidase; GLP = glucose-like peptide; SGLT = sodium-glucose co-transporter

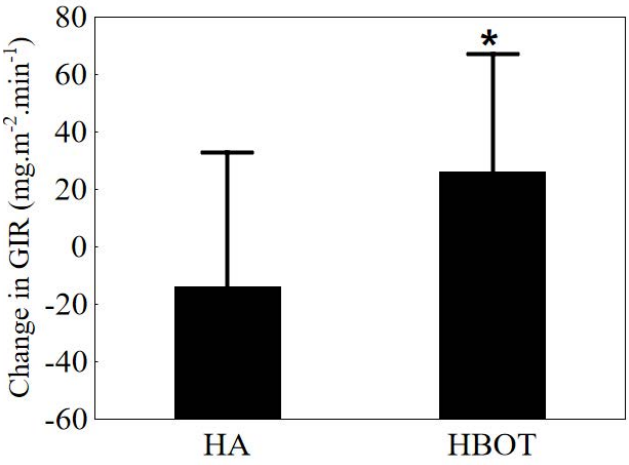
Medication	Number (n = 24)
Metformin	21
Insulin	5
SGLT-2 inhibitors	8
DPP-4 inhibitors	7
GLP-1 receptor agonists	4
Sulphonylureas	2

Two days later, participants returned after overnight fasting for a second glucose clamp using the same protocol, this time overlaid with a 2-hour session in the hyperbaric chamber. The insulin infusion was established one hour prior to entering the chamber. The large, triple-lock, multiplace hyperbaric chamber (Fink Engineering Pty Ltd, Warana, Australia) was compressed using air to 203 kPa (2 atm abs) and held at this pressure for 90 minutes followed by a 30-minute linear decompression back to ambient pressure. In the hyperbaric chamber, oxygen was delivered to the HBOT group via a hood system the same as used in clinical HBOT treatments (Amron International Inc, Vista, CA) which was connected on reaching 203 kPa pressure and continued for the 2-hour session (apart from a routine 5-minute 'air break' taken half-way through by temporarily detaching the hood). The HA group, who underwent exposure to the same pressure profile, breathed chamber air throughout the hyperbaric session. The participants remained in their reclining chairs once the clamp procedure had commenced and were wheeled into and out of the hyperbaric chamber. Blood samples were sent out of the chamber via the medical lock for PGL estimation. Insulin sensitivity was determined

Table 3
Glucose infusion rates ($mg \cdot m^{-2} \cdot min^{-1}$) for HBOT and HA groups at baseline and during the hyperbaric intervention

Period	HBOT		HA	
	Baseline mean (SD)	Hyperbaric mean (SD)	Baseline mean (SD)	Hyperbaric mean (SD)
Steady state 1	151 (71)	177 (86)	180 (73)	166 (83)
Steady state 2	173 (87)	198 (85)	189 (91)	189 (81)

Figure 1
Change in glucose infusion rate ($mg \cdot m^{-2} \cdot min^{-1}$), expressed as mean change and SD, for hyperbaric air (HA) and hyperbaric oxygen treatment (HBOT) groups at steady state 1. *P = 0.036



by the GIR during the same two SS periods, so SS1 coincided with the last 30 minutes of the 2-hour hyperbaric session and SS2 with the first 30 minutes after exit from the chamber. At each visit, blood was taken for serum insulin concentration before commencing the clamp infusions for fasting levels and during SS1 and SS2 to demonstrate hyperinsulinemia. Steady-state insulin concentrations were not different between groups or between SS1 and SS2.

STATISTICAL CONSIDERATIONS

Statistical analyses were performed using Statistica (version 12, Statsoft, Tulsa, OK). Power analysis of earlier data suggested sample size of 20 in each group for power of 80% and α of 0.05 would be sufficient to detect a 25% difference in GIR between groups. GIR data were normally distributed by Shapiro-Wilk and Kolmogorov-Smirnov tests. HBOT and HA groups were analysed by paired student *t*-test for within-group effects and ANOVA for between-group effect. Significance was considered at $P < 0.05$.

Results

Of the 25 men enrolled, one participant experienced technical issues during his hyperbaric session and loss of data required exclusion. The other 24 participants completed the study without complication and their characteristics are shown in Table 1. There were no significant differences between the two groups. The participants were prescribed between one and four medications in the management of their diabetes (median two), summarised in Table 2.

The GIR data for both the HBOT and HA groups at baseline and during the hyperbaric exposure, for SS1 and SS2 can be seen in Table 3. Within the HBOT group, there was a mean 26% increase in GIR (median 17%) when compared to baseline, during SS1 (P = 0.04). There was a mean 23% increase in GIR (median 19%) during SS2 (P = 0.018). The HA group revealed no significant changes in GIR at SS1 or SS2.

One-way ANOVA for the change in GIR revealed a difference between groups at SS1 for HBOT vs. HA (Figure 1, P = 0.036). A trend towards a between-group difference was evident at SS2 (P = 0.088).

Discussion

This study has demonstrated that one session of HBOT significantly increased peripheral insulin sensitivity in men with type 2 diabetes, but exposure to an equivalent pressure profile without breathing supplemental oxygen (the hyperbaric air group) had no effect. The effect of HBOT persisted for at least the first 30 minutes after exit from the hyperbaric chamber.

The insulin-sensitising effect of HBOT observed in this study is consistent with that observed in earlier studies. In a group of patients referred for clinical HBOT (five men who were not obese and without diabetes and five men who were obese with type 2 diabetes), the glucose clamp revealed a significant increase in insulin sensitivity in the whole group during the third HBOT (37% increase) and the thirtieth HBOT (41% increase) although subgroup analysis revealed the change was statistically significant only in the group with diabetes.[7] A subsequent study recruited a cohort of men who were obese or overweight, both with (n = 8) and without (n = 11) type 2 diabetes.[8] A hyperinsulinemic euglycemic glucose clamp performed during the third HBOT demonstrated an increase in insulin sensitivity of 57% in those with type 2 diabetes and 29% in those without. This increase was still apparent during the first 30 minutes after exit from the hyperbaric chamber. A further study performed the glucose clamp technique during the first HBOT session on men who were obese or overweight but

without diabetes (n = 9).[9] This demonstrated a significant 23% increase in insulin sensitivity during the first HBOT session. Encouragingly, the magnitude of the insulin-sensitising effect in the current study is comparable with the effect sizes previously published and is large enough to be clinically significant. The effect has an onset of action within one HBOT session but its duration is not known. However, this study again found that the insulin-sensitising effect of HBOT was still active for at least the first 30 minutes after exit from the hyperbaric chamber.

The mechanism of action for the insulin-sensitising effect of HBOT is also unknown. However, an important new contribution from this study is the finding that the hyperbaric air group showed no change in insulin sensitivity. One can say for the first time that the hyperbaric environment itself – where the increase in absolute pressure is transmitted throughout the human body and generates a number of recognised physiological responses – has no independent effect on insulin sensitivity, in men with diabetes at least; it also requires the very high oxygen partial pressures that are only delivered during clinical HBOT to increase insulin sensitivity. There have been no reports or studies that the authors are aware of to suggest that breathing high concentrations of oxygen in the absence of hyperbaric conditions affects insulin sensitivity, and it seems likely that both high oxygen concentrations and high pressures are needed to produce this effect.

Previous findings that this effect can be detected in men with and without diabetes suggest that HBOT initiates a common metabolic response which is not confined to people with diabetes mellitus.[8] If the underlying mechanism for this insulin-sensitising effect can be identified, it may offer a new therapeutic target. In earlier work we found that the insulin-sensitising effect of HBOT was associated with some reductions in serum inflammatory cytokines;[8] however, this may only be part of the story. A number of the therapeutic benefits of clinical HBOT have now been shown to require the deliberate generation of oxidative stress as a consequence of breathing hyperbaric oxygen.[10] Reactive oxygen species can be damaging to biological tissue; however, they have other vital roles where they act as signalling molecules in a number of cellular pathways for a range of growth factors, cytokines and hormones.[11] Independently, other research has pointed out that reactive oxygen species can have both an inhibitory as well as a stimulatory effect on the intracellular glucose transport pathway.[12]

The finding that there was no change to insulin sensitivity in hyperbaric air is an important outcome in its own right. Whilst this study was not specifically designed to answer scuba diving questions, it is interesting to consider that the hyperbaric air group undertook a simulated (dry) scuba dive, albeit perhaps not a typical dive profile. Their intervention was the equivalent of diving, on air, to 10 metres' seawater (msw) for a 90-minute bottom time followed by a very slow ascent to the surface over 30 minutes (so results for any 'deeper' intervention cannot be assumed). This is relevant because people with diabetes do present to dive physicians with a desire to undertake scuba diving as recreation, with medical approval. For the dive physician, the medical assessment is complex and must consider the potentially disastrous consequences that could result from hypoglycaemia occurring underwater. Prospective observational studies have followed recreational divers with diabetes using detailed protocols for PGL management, suggesting that they can safely monitor and manage their PGL to allow diving.[13–15] However, it has never been determined if the potentially hazardous event encountered in hyperbaric medicine – the precipitous fall in PGL in a person with diabetes during HBOT – could also occur in response to the hyperbaric stimulus of the underwater environment. While other medical concerns will certainly exist for the potential diver with diabetes, this study provides the first evidence that exposure to a hyperbaric profile breathing air similar to that encountered in the recreational diving environment has no effect on insulin sensitivity. This encouraging finding may also be relevant to people in other hyperbaric environments.

One limitation to these studies is that we have only investigated men. Insulin sensitivity can change physiologically in adolescence and during pregnancy and different parts of the menstrual cycle in women. However, the studies have demonstrated an insulin-sensitising effect of HBOT that is not limited to those with diabetes and is likely to be a metabolic response to HBOT. As such, one would expect to see the same effect in women, although this has never been tested. Other limitations include the relatively small sample size. Despite this, the magnitude of the effect is large enough to achieve statistical significance and is comparable to previous studies. The already labour-intensive glucose clamp was made more complicated by performing it within a hyperbaric chamber. Previous studies have allowed the development of experience in the use of this technique in the hyperbaric environment. Strategies include keeping participants sedentary in reclining chairs and wheeling them, plus the infusions, into and out of the hyperbaric chamber to minimise exertion. The regular blood samples were passed out of the hyperbaric chamber through the medical lock for PGL analysis while the glucometer itself utilised a glucose dehydrogenase reagent which is less affected by high oxygen environments.[16]

Conclusions

This study has further strengthened the evidence that acute exposure to hyperbaric oxygen leads to a clinically significant increase in insulin sensitivity in men with type 2 diabetes. This effect is still evident during the first 30 minutes after exit from the hyperbaric chamber although its duration beyond that time is not known. Importantly, it has been shown for the first time that this insulin-sensitising

effect does not occur when breathing hyperbaric air at 203 kPa (2 atm abs, 10 msw equivalent). This may be relevant to other hyperbaric environments such as recreational diving but further work would be required to definitively establish the absence of an effect when breathing air at greater depths. The insulin-sensitising effect requires the very high partial pressures of oxygen only encountered during clinical HBOT. Further research should be encouraged to discover the mechanism for this novel effect on metabolism, as it could translate to new clinical therapies to improve glucose regulation.

References

1 Weaver LK, editor. Hyperbaric Oxygen therapy indications, 13th ed. North Palm Beach (FL): Best Publishing Company; 2014.

2 Trytko B, Bennett MH. Blood sugar changes in diabetic patients undergoing hyperbaric oxygen therapy. SPUMS Journal. 2003;33:62–9.

3 Ekanayake L, Doolette DJ. Effects of hyperbaric oxygen treatment on blood sugar levels and insulin levels in diabetics. SPUMS Journal. 2001;31:16–20.

4 Warram JH, Martin BC, Krolewski AS, Soeldner JS, Kahn CR. Slow glucose removal rate and hyperinsulinemia precede the development of type II diabetes in the offspring of diabetic parents. Ann Intern Med. 1990;113:909–15. doi: 10.7326/0003-4819-113-12-909. PMID: 2240915.

5 Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin sensitivity and resistance in vivo: Advantages, limitations, and appropriate usage. Am J Physiol Endocrinol Metab. 2008;294(1):E15–E26. doi: 10.1152/ajpendo.00645.2007. PMID: 17957034.

6 Wallace TM, Matthews DR. The assessment of insulin resistance in man. Diabet Med. 2002;19:527–34. doi: 10.1046/j.1464-5491.2002.00745.x. PMID: 12099954.

7 Wilkinson D, Chapman IM, Heilbronn LK. Hyperbaric oxygen therapy improves peripheral insulin sensitivity in humans. Diabet Med. 2012;29:986–9. doi: 10.1111/j.1464-5491.2012.03587.x. PMID: 22269009.

8 Wilkinson D, Nolting M, Mahadi MK, Chapman I, Heilbronn L. Hyperbaric oxygen therapy increases insulin sensitivity in overweight men with and without type 2 diabetes. Diving Hyperb Med. 2015;45:30–6. PMID: 25964036.

9 Wilkinson D, Szekely S, Gue B, Tam CS, Chapman I, Heilbronn LK. Assessment of insulin sensitivity during hyperbaric oxygen therapy. Diving Hyperb Med. 2020;50:238–43. doi: 10.28920/dhm50.3.238-243. PMID: 32957125. PMCID: PMC7819732.

10 Fosen KM, Thom SR. Hyperbaric oxygen, vasculogenic stem cells, and wound healing. Antioxid Redox Signal. 2014;21:1634–47. doi: 10.1089/ars.2014.5940. PMID: 24730726. PMCID: PMC4175035.

11 Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. Plast Reconstr Surg. 2011;127(Suppl 1):131S–141S. doi: 10.1097/PRS.0b013e3181fbe2bf. PMID: 21200283. PMCID: PMC3058327.

12 Tiganis T. Reactive oxygen species and insulin resistance: the good, the bad and the ugly. Trends Pharmacol Sci. 2011;32(2):82–9. doi: 10.1016/j.tips.2010.11.006. PMID: 21159388.

13 Dear G deL, Pollock NW, Uguccioni DM, Dovenbarger J, Feinglos MN, Moon RE. Plasma glucose responses in recreational divers with insulin-requiring diabetes. Undersea Hyperb Med. 2004;31:291–301. PMID: 15568417.

14 Edge CJ, St Leger Dowse M, Bryson P. Scuba diving with diabetes mellitus – the UK experience 1991–2001. Undersea Hyperb Med. 2005;32:27–37. PMID: 15796312.

15 Pollock NW, Uguccioni DM, Dear G deL, Bates S, Albushies TM, Prosterman SA. Plasma glucose response to recreational diving in novice teenage divers with insulin-requiring diabetes mellitus. Undersea Hyperb Med. 2006;33:125–33. PMID: 16716063.

16 Tang Z, Louie RF, Lee JH, Lee DM, Miller EE, Kost GJ. Oxygen effects on glucose meter measurements with glucose dehydrogenase- and oxidase-based test strips for point-of-care testing. Crit Care Med. 2001;29:1062–70. doi: 10.1097/00003246-200105000-00038. PMID: 11378622.

Acknowledgements

The authors thank Dr. Bo Liu and the staff of the Hyperbaric Medicine Unit, Royal Adelaide Hospital for their help in performing this study. DCW acknowledges the support received for research through the provision of an Australian Government Research Training Program Scholarship.

Conflicts of interest and funding

This study was funded by the Royal Adelaide Hospital Research Committee. No conflicts of interest were declared.

Submitted: 11 June 2020
Accepted after revision: 22 August 2020

Dysbaric osteonecrosis (DON) among the artisanal diving fishermen of Yucatán, Mexico

Daniel Popa[1,2], Anthony Medak[2], Walter Chin[3], Oswaldo Huchim-Lara[4], Evelyne Fliszar[5], Tudor Hughes[5], Ian Grover[2]

[1] *Rush University Department of Emergency Medicine, Chicago IL, USA*
[2] *UCSD Department of Emergency Medicine, Division of Hyperbaric and Undersea Medicine, San Diego, USA*
[3] *Winship Cancer Institute of Emory University, Atlanta GA, USA*
[4] *La Universidad Marista de Mérida School of Medicine, Mérida, Yucátan, Mexico*
[5] *UCSD Department of Radiology, San Diego CA, USA*

Corresponding author: *Dr Daniel Popa, Rush University Department of Emergency Medicine, 1750 W. Harrison St., Kellogg Suite 108, Chicago, IL 60612, USA*
dan_popa@rush.edu

Key words
Bone necrosis; Decompression sickness; Diving at work; Indigenous divers; Surface supplied diving

Abstract
(Popa D, Medak A, Chin W, Huchim-Lara O, Fliszar E, Hughes T, Grover I. Dysbaric osteonecrosis (DON) among the artisanal diving fishermen of Yucatán, Mexico. Diving and Hyperbaric Medicine. 2020 December 20;50(4):391–398. doi: 10.28920/dhm50.4.391-398. PMID: 33325021.)
Introduction: Artisanal diving fishermen in Yucatán, Mexico have high rates of decompression sickness as a result of frequently unsafe diving practices with surface supplied compressed air. In this study, we investigated the prevalence of dysbaric osteonecrosis (DON), a type of avascular necrosis, in the most susceptible joints in a cohort of these fishermen.
Methods: We performed radiographs of bilateral shoulders, hips, and knees of 39 fishermen in Mexico and surveyed them about their medical and diving histories. We performed pairwise correlations to examine if the fishermen's diving behaviours affected the numbers of joints with DON.
Results: The radiographs revealed Grade II or higher DON in 30/39 (76.9%) of the fishermen. Twenty-two of 39 fishermen (56.4%) had at least two affected joints. The number of joints with DON positively correlates with the lifetime maximum diving depth and average bottom time.
Conclusions: These findings represent among the highest prevalence rates of DON in divers and reflect the wide-spread scale of decompression sickness among these fishermen. Through this work, we hope to further educate the fishermen on the sequelae of their diving with the aim of improving their diving safety.

Introduction

Decompression sickness (DCS) among compressed gas divers occurs when dissolved gas absorbed into tissues while at depth (in a hyperbaric environment) comes out of solution and forms bubbles following ascent. While DCS can involve many tissues, bony tissue is frequently affected and can lead to dysbaric osteonecrosis (DON). DON is atraumatic bony infarction, often symptomatic when involving the articular surfaces of long bones, and first described in 1941.[1] However, it was known to affect bridge caisson and tunnel workers, both exposed to hyperbaric environments, in the early 1900s. Severe cases of DON can lead to debilitating bony collapse and impaired function limiting not only employment but also activities of daily living. Osteonecrosis occurs in the bones adjacent to the joints including the head, neck, and shafts of long bones, which from hereon are simply referred to as the joints.

Artisanal diving fishermen of Yucatán state in Mexico typically use surface supplied compressed air, via a 'hookah' system, aboard small open cockpit boats to fish for a variety of marine species including grouper, lobster, and sea cucumber. Hookah systems involve the use of a shipboard air compressor supplying the air to the diver below via a long hose (Figure 1). This technology allows the diving fisherman a virtually unlimited gas supply which permits unsafe diving practices, far exceeding normal recommended safety limits for time while at depth. As a result, an epidemic of DCS plagues this population.[2–4]

Despite frequent DCS, the diving fishermen continue to exceed established safety limits likely due to economic pressures or the drive to earn additional income. In this study, we sought to characterise the prevalence of DON among artisanal diving fishermen with the ultimate goal of informing these divers of the sequelae of DCS and educating them in strategies to reduce their risk of DCS while maintaining their livelihoods as fishermen.

Figure 1
A fisherman from Río Lagartos preparing bait in his fishing boat. A typical Yucatán hookah compressor lies in the bow of the boat with its engine covered by a plastic tarp

Figure 2
A map of the Yucatán Peninsula showing the major fishing communities of the northeast coast. The nearest X-ray facility and hyperbaric chamber to treat DCS are located in the larger community of Tizimín

Methods

The protocol was approved by the institutional review board at the Universidad Marista de Mérida in Yucatán (project # CE_009_2017). Informed consent was obtained from all individual participants included in the study.

Thirty-nine artisanal diving fishermen from Yucatán, Mexico agreed to participate. All subjects work and dive within the fishing communities of Río Lagartos and San Felipe in Yucatán, Mexico (Figure 2). We utilised a non-probabilistic convenience technique to invite subjects to participate in the study and recruited fishermen among the fishing cooperatives of the respective villages. Cooperative officers assisted in recruitment efforts by calling some of the fishermen. Inclusion criteria included membership in a fishing cooperative and a history of fishing the local waters using surface supplied compressed air. Exclusion criteria were age less than 18 years old and no prior diving. Fishermen may become involved in diving fishing as young as 15 years in a supportive role but do not start diving until reaching 18 years.[2] After obtaining consent, we surveyed the fishermen regarding medical and social histories, diving behaviour and experience, and episodes of DCS.

Table 1
The Steinberg modification of the Ficat scoring system for AVN used for DON. Originally, the classification system was developed to grade AVN of the hip but can be used to grade other joints. MRI = magnetic resonance imaging

Grade	Findings
0	Normal X-ray, MRI, or bone scan. Diagnosed histologically
I	Normal X-ray, abnormal MRI or bone scan (but minimal joint pain)
II	Sclerosis and/or cyst formation in the femoral head (or equivalent)
III	Subchondral collapse (crescent sign) without flattening
IV	Flattening of the femoral head (or equivalent) without joint narrowing or acetabular involvement
V	Flattening of the femoral head (or equivalent) with joint narrowing and/or acetabular involvement
VI	Advanced degenerative changes

Nine radiographs were performed per subject: anterior-posterior (AP) and abducted AP views of each shoulder (four total), AP and frog-leg views of each hip (four total), and one AP view of bilateral knees over the course of one week. The radiology technician used a Compagnie Générale de Radiologie (CGR, 1976) analog X-ray machine to obtain the radiographs.

The X-ray films were transported to our facility where two musculoskeletal fellowship-trained, board-certified radiologists independently interpreted the radiographs using the Steinberg modification of the Arlet and Ficat avascular necrosis (AVN) grading system (Table 1).[5–7] The radiologists were blinded to the subjects' demographic information as well as their medical and diving history. The radiologists subsequently resolved conflicting interpretations of the radiographs through consensus.

Furthermore, self-reported diving behaviours were correlated with the number of joints affected by DON. A Shapiro-Wilk test was used to assess normality and distribution of the data set. A parametric and non-parametric Levene's test was used to assess equality of variance. Univariate tabulation across all variables was conducted. A pairwise correlation matrix was conducted across outcome variables: number of affected joints; number of DCS events; lifetime maximum depth;

Table 2
Demographic information and diving behaviour of the artisanal diving fishermen in the study cohort. Of note, the fishermen do not use dive computers or depth gauges. Rather, they estimate depth based on the number of arm's lengths or strokes needed to swim to the bottom. One arm's length approximates to 1.5 msw. BMI = body mass index; DCS = decompression sickness; Max = maximum; msw = metres' seawater; SD = standard deviation

Parameter	Mean (SD)	Range	Median
Age (years)	44.7 (8.5)	26–62	45
BMI ($kg \cdot m^{-2}$)	32.7 (4.7)	23.6–43.2	32.8
Years diving	26.8 (8.5)	10–47	27
Prior DCS episodes	9.0 (7.7)	0–35	8
Dive depth (Arm lengths)	7.8 (5.3)	1–20	8
Dive depth (msw)	11.8 (7.9)	1.5–30	12
Max. depth (Arm lengths)	17.6 (5.6)	7–36	17
Max. depth (msw)	26.4 (8.4)	10.5–54	25.5
Bottom time (minutes)	107.2 (72)	20–360	90

Table 3
Past medical history of the artisanal diving fishermen in the study cohort (n = 39)

Medical history	*n* (%)
Regular alcohol	29 (74.4)
Joint pain over last year	27 (69.2)
Hypercholesterolaemia	17 (43.6)
Skeletal / joint trauma	9 (23.1)
Hypertension	5 (12.8)
Diabetes mellitus	3 (7.7)
Arthritis	2 (5.1)
Lung disease	2 (5.1)

average diving depth; average bottom time; and fishing years. A Chi-square test of independence was conducted among outcome variables, number of affected joints, and number of DCS events and amount of treatment. A user-written algorithm was utilised to create tables and plots. We utilised STATA version 16 for data analysis.

Results

Thirty-nine diving fishermen from the two fishing villages of Río Lagartos and San Felipe completed the study, each undergoing nine radiographs as well as the survey of demographic data, diving behaviour, and health data (Tables 2 and 3). All but one of the fishermen (97.4%) reported a history of DCS. Thirty of the 39 fishermen (76.9%) displayed Grade II or higher DON. Of those 30, all subjects had Grade II severity with one exception. Representative images of the radiographic findings of the fishermen can be seen in Figure 3. One fisherman displayed Grade IV DON of the right shoulder seen on both AP and abducted AP

Figure 3
Representative radiographs showing Grade II DON in the joints studied. Areas of sclerosis are indicated with red arrows. Top row-AP and abducted AP views of the right shoulder; Middle row-AP and frog leg views of the left hip; Bottom row-AP view of bilateral knees

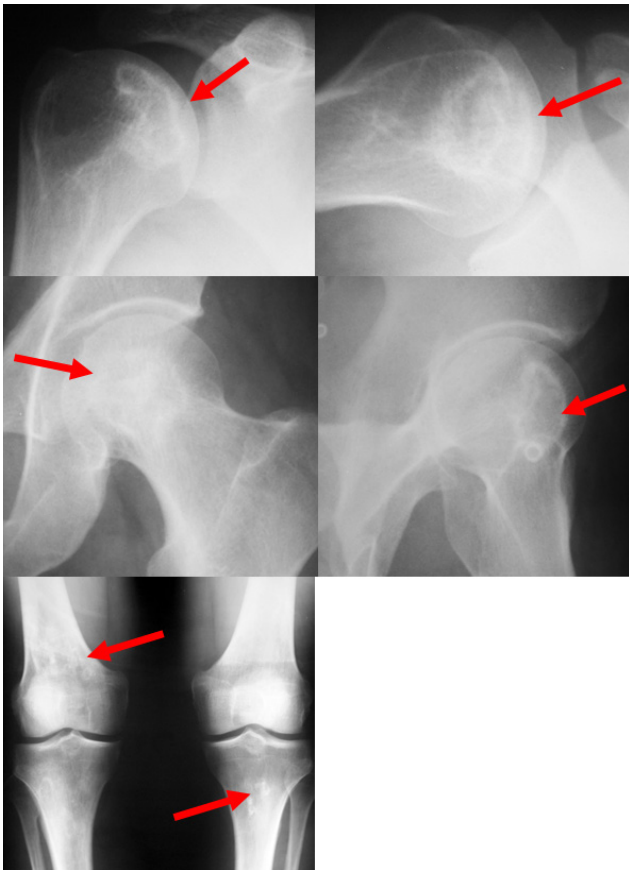


Figure 4
A 51 year-old male fisherman displayed Grade IV DON in both AP and abducted AP views of the right shoulder. Areas of collapse indicated with red arrows

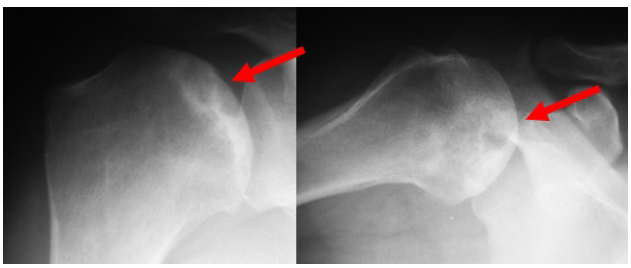
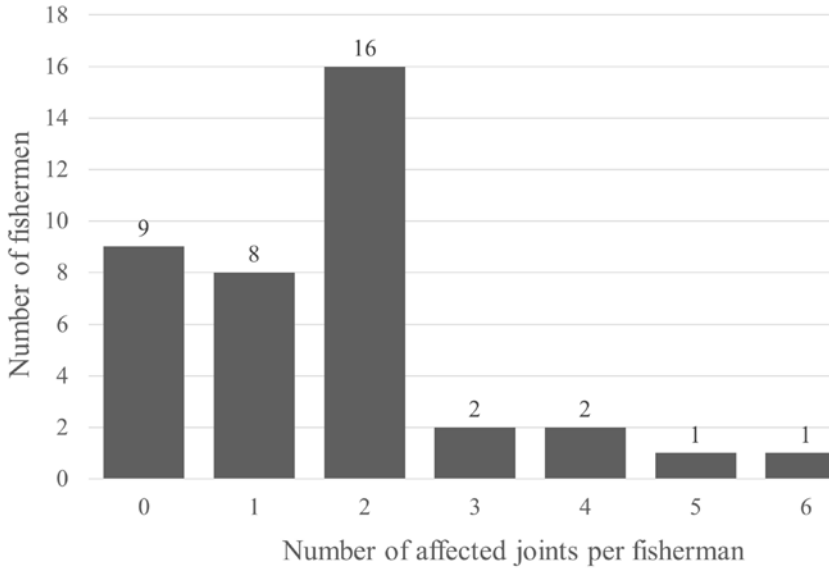


Table 4
Prevalence of DON among the artisanal diving fishermen according to joint type and laterality. As an example, right shoulder entries denote fishermen with DON in the right shoulder but not the left and may have other joints affected as well

Joint(s)	Number of fishermen	% of DON (n = 30)	% of all fishermen (n = 39)
Right shoulder	2	6.7	5.1
Left shoulder	3	10	7.7
Bilateral shoulders	22	73.3	56.4
Right hip	4	13.3	10.3
Left hip	0	0	0
Bilateral hips	3	10	7.7
Right knee	1	3.3	2.6
Left knee	1	3.3	2.6
Bilateral knees	2	6.7	5.1

Figure 5
Histogram of the number of joints with AVN per diving fisherman



radiographs and no other joints affected by DON (Figure 4). The percent agreement between the two radiologists was 94% agreement (220/234 joints). One of the debated joints was a disagreement in the grade of DON, while 6 of the debated joints had one radiologist diagnosing possible or probable DON rather than definite DON. So without these, there was only 3% (7/234 joints) disagreement between the radiologists with all joint findings ultimately achieving a consensus diagnosis.

Within this cohort, DON affected the shoulders to a much greater degree than the hips or knees (Table 4). Both shoulders were typically involved. Of the subjects with DON, 27 of 30 (90%) displayed shoulder involvement with 22 (73.3%) having bilateral involvement. The hips and knees also reflected this trend where bilateral DON prevailed. One subject demonstrated Grade II DON of all six joints and 22 of the 39 fishermen (56.4%) in the entire cohort had two or more joints with DON (Figure 5).

In addition, we attempted to correlate the self-reported diving behaviour of the fishermen with the number of affected joints (Table 5). The number of joints with DON positively correlated with the lifetime maximum depth (correlation coefficient = 0.53) and average bottom time (correlation coefficient = 0.36) but not the number of DCS episodes requiring hyperbaric oxygen treatment (HBOT), average diving depth, or years fishing. Furthermore, the number of

Table 5

Pairwise correlation matrix table of surveyed diving behaviour variables with the number of DON affected joints. Each cell displays the correlation coefficient (r) (top), *P*-value (middle), and number of fishermen included (bottom). * indicates significance at the $P < 0.05$ level. # DON joints = number of joints affected by DON. # DCS = episodes of DCS that required HBOT. Max. depth = lifetime maximum diving depth. Avg. depth = typical depths fished. Bottom time = typical bottom times during fishing. Fishing years = years spent doing surface supplied diving in order to fish

Variable	# DON joints	# DCS	Max. depth	Avg. depth	Bottom time
# DCS	r = 0.280 *P* = 0.08 *n* = 39				
Max. depth	r = 0.527* *P* = 0.006 *n* = 26	r = 0.180 *P* = 0.379 *n* = 26			
Avg. depth	r = -0.054 *P* = 0.747 *n* = 38	r = -0.235 *P* = 0.156 *n* = 38	r = 0.156 *P* = 0.458 *n* = 25		
Bottom time	r = 0.364* *P* = 0.027 *n* = 37	r = 0.270 *P* = 0.106 *n* = 37	r = 0.351 *P* = 0.079 *n* = 26	r = -0.410* *P* = 0.013 *n* = 36	
Fishing years	r = 0.087 *P* = 0.601 *n* = 39	r = 0.320* *P* = 0.047 *n* = 39	r = 0.016 *P* = 0.938 *n* = 26	r = 0.218 *P* = 0.189 *n* = 38	r = 0.070 *P* = 0.681 *n* = 37

years fishing positively correlated with the number of DCS episodes (correlation coefficient = 0.32), while average bottom time negatively correlated with average diving depth (correlation coefficient = -0.41).

Discussion

This cohort of fishermen displays a high prevalence (76.9%) of DON compared to most groups of diving fishermen described in the literature. Indeed, 56.4% of them had multiple joints affected by DON. For a population of diving fishermen, the long-term implications of such radiographic findings on their ability to work in physically demanding jobs and their ability to perform simple activities of daily living is quite concerning.

Previously, DON has been described among caisson (bridge support) workers as well as working divers (fishermen, military divers, etc.). Rates of DON among these populations vary widely, likely a function of the variable risk associated with each diving community's dive profiles, as well as other risk factors. Previous work has established that groups of artisanal fishermen with high rates of DON have dive profiles that allow for significant inert gas loading.

A study of Hawaiian coral divers demonstrated DON in 13 of 20 (65%) subjects.[8] In Honduran lobster divers studied in 1994–1995, 69% had evidence of DON.[9] Interestingly, this cohort displayed a higher percentage of lesions in the distal femur and proximal tibia than in the humeral head. This is contrary to the trend most often seen in divers where the humeral head is predominantly affected. Several groups of Japanese shellfish divers have been studied and the rate of DON ranged from 28% to 100%.[10–13] The study that detected DON in 100% of its divers used MRI imaging to make the diagnosis. Korean shellfish divers had a 67% prevalence of DON while Turkish sponge divers had a rate of 70–85% DON.[14,15] In contrast to these artisanal diving fishermen, the rates of DON in recreational SCUBA divers is considerably lower.[16,17] Also, commercial divers not engaged in fishing have been shown to have a low prevalence of DON (4.2% in British North Sea commercial divers) although a more recent study among Turkish diving instructors showed a 25% prevalence of DON.[18,19] A comprehensive review of DON among professional divers describes rates of DON among these different populations.[7]

The mechanism by which DON develops remains unclear. DON occurs in bones with yellow (fatty) marrow and not in bones with red (hematopoietic) marrow. Nitrogen absorption and release occurs slowly in fatty marrow as a result of relatively low blood flow. Current evidence shows that DON can develop after a significant hyperbaric exposure causes gas loading of the fatty tissue. Subsequently, inadequate decompression can lead to bubble formation that could disrupt the tissue. These bubbles also could cause an ischaemia-reperfusion injury, platelet aggregation, fibrinogen deposition, disseminated intravascular coagulation (DIC), lipid emboli and the release of vasoactive substances.[20] The ultimate result of this cascade of events caused by the bubbles could be the ischaemic bone infarction of DON. Analyses have shown a very high correlation between divers that have suffered DCS (the 'bends') and the development of DON. A prevalence of 4/21 (19%) DON was reported among French recreational divers who presented to hyperbaric facilities with musculoskeletal DCS and underwent MRIs

immediately after their injury and 3–4 months later.[17] According to others, "*more than 60% of divers with DON have experienced one or more symptomatic episodes of limb bends in spite of a certain degree of under-reporting and self-treatment of mild DCS symptoms*."[20]

The patient with early DON is usually asymptomatic and has no physical findings (Grade 0-II). Once bony collapse occurs (Grade III and IV), the patient typically becomes symptomatic. Symptoms include joint pain, reduced range of motion, and muscle spasms. Late findings include joint deformity, crepitus, and contractures. Rarely, DON in its early stages is reversible. Once DON has developed, it is usually progressive and carries a poor prognosis. Most patients will eventually develop Grade IV DON equivalent to secondary degenerative arthritis.

Examining the correlation between fishing behaviours and the number of joints affected, we found that the diving fishermen who reported deeper lifetime maximum depths and longer average bottom times tended to have more joints affected, although this correlation was not terribly strong and was based on self-reported data. Among this population, the deeper diving fishermen are likely subjected to more bubble stress which in turn leads to more DON. Similarly, longer bottom times also likely lead to more bubble stress and in turn more DON in the same way. However, deeper lifetime maximum depths or longer average bottom times may simply be markers for other causative factors such as riskier diving, increased overall workload (such as more effort obtaining the catch, increased lifting power required to offload the catch, or both), or some other unknown factors.

We found no correlation between episodes of DCS or years fishing with the number of joints affected. The fishermen identify episodes of DCS as times they have required treatment in the nearest hyperbaric chamber in Tizimín, not necessarily episodes of joint pain. Retrospectively quantifying pain-only DCS episodes is essentially impossible among this working population due to the frequency of joint pain, self-treating with medication (predominantly non-steroidal anti-inflammatory medication such as diclofenac) and alcohol, and confounders such as muscle strain or soreness from heavy fishing activity. Hence, the number of DCS episodes the fishermen reported is surely an underestimate and fails to capture episodes of Type I (i.e., pain only) DCS. Previous work by members of our group has shown that among a group of 105 diving fishermen, 97 (92.4%) had at least one episode of DCS that required HBOT over a 25-year span during which medical records were available.[21] Unsurprisingly, more years fishing correlated with more episodes of DCS requiring HBOT, while deeper average depths correlated with shorter average bottom times. Of note, the fishermen undergo HBOT when they cannot tolerate or manage their joint pain with self-treatment or have significant symptoms they or the community recognise as DCS. The fishermen do not generally use in-water recompression techniques in part due to the shallow depths near shore because of the gentle sloping Yucatán Shelf. HBOT is provided at the nearest chamber in Tizimín and most often consists of U S Navy Treatment Table 5 as the first line treatment with U S Navy Treatment Table 9 used for subsequent treatments if needed.[2]

Currently, no specific treatment for DON exists. Once a patient has progressed to Grade IV DON and symptoms are no longer responding to conservative measures, then total joint replacement is often the treatment of choice. Early treatment for decompression sickness with HBOT has been shown to reduce the risk of DON in sheep.[22] At the present time, no formal HBOT protocol for DON has been developed in the United States. Italian hyperbaric physicians have created a protocol, however, with promising early data for the treatment of femoral head necrosis.[23] This protocol consists of daily treatments, 5–6 days per week, with at least 60 minutes of 100% O_2 between 223–253 kPa, for a total of 60–90 treatments. Nevertheless, this protocol has not been examined in treating DON or other affected joints beyond the hip. Given the lack of clearly effective therapies for DON, the high prevalence of DON among the artisanal diving fishermen in Yucatán will likely lead to significant morbidity in the future, especially if diving behaviour and safety practices do not improve.

With our current understanding of the pathophysiology of DON, including ischaemia-reperfusion injury and the release of vasoactive substances, HBOT could plausibly prove an effective treatment modality for these diving injuries. A prospective human study is warranted to test this hypothesis, however.

LIMITATIONS

This study's primary limitations centre around its observational design without age-matched controls. AVN, regardless of etiology, is a known, relatively uncommon disease with 20,000–30,000 new cases per year in the United States (approximately 0.01% among the total population).[24] Alcohol use, a risk factor for AVN, was high among the fishermen (Table 3). However a study examining 1,157 patients undergoing treatment for excessive alcohol consumption showed 5.3% of their cohort had AVN, higher than the regular population but far lower than the prevalence we found among the fishermen.[25] Compared to the present cohort with such a well-known risk factor as DCS and the staggering amount of DCS in this population, it is considered likely that the radiographic findings within this cohort are secondary to DON and not some other AVN aetiology.

The subject recruitment methodology may have also added some selection bias as it was a convenience sample of volunteers. However, previous work has shown a rate of DCS requiring HBO_2 therapy of over 92% in these fishermen, so the current rate of 38/39 divers (97.4%) with a history DCS is sufficiently similar to suggest that selection bias was unlikely to play a significant role in the high rates of

DON described here.[21] In addition, the analog radiographs were not of the highest quality in comparison to the latest technology; however, they represent the most feasible option available in that region of Mexico. Furthermore, the subjects were surveyed about their diving behaviour and history of DCS which is subject to recall bias in addition to the fact that true depth gauges are not used during their diving. Rather, they estimate depth based on the number of arm's lengths or strokes needed to swim to the bottom. Not all fishermen answered all the survey questions. Our analysis sought to correlate the surveyed diving behaviour results with the radiographic findings but should not be taken to imply causation.

Conclusions

The artisanal diving fishermen in Yucatán, Mexico exhibit some of the highest rates of DON described in the literature. Likely, their extremely high rates of decompression sickness have contributed to these findings. In the future we hope to repeat this study with a larger cohort, incorporating MRI exams, and ultimately providing these radiographic findings to the fishermen. Through this feedback, we hope that they will modify their diving behaviour and institute a diving 'safety stop', as is common among recreational divers. This routine practice allows the diver to more safely unload nitrogen from tissues and reduce the likelihood of bubble formation, in turn reducing the risk of DCS, and therefore of DON.

References

1 Grutzmacher KT. Veranderungen an schultergerenk als folge von drucklufterkrankung. Rontgenpraxis (Leipzig). 1941;13:216–218. German.

2 Huchim-Lara O, Chin W, Salas S, Rivera-Canul N, Cordero-Romero S, Tec J, et al. Decompression sickness among diving fishermen in Mexico: observational retrospective analysis of DCS in three sea cucumber fishing seasons. Undersea Hyperb Med. 2017;44:149–56. doi: 10.22462/3.4.2017.8. PMID: 28777905.

3 Huchim-Lara O, Salas S, Chin W, Montero J, Fraga J. Diving behavior and fishing performance: The case of lobster artisanal fishermen of the Yucatan coast, Mexico. Undersea Hyperb Med. 2015;42:285–96. PMID: 26403014.

4 Chin W, Huchim O, Wegrzyn GH, Sprau SE, Salas S, Markovitz GH. CO and CO_2 analysis in the diving gas of the fishermen of the Yucatan Peninsula. Undersea Hyperb Med. 2015;42:297–305. PMID: 26403015.

5 Ficat R, Arlet J. Forage-biopsie de la tete femorale dans I'osteonecrose primative. Observations histo-pathologiques portant sur huit forages. Rev Rhum. 1964;31:257–64. French.

6 Steinberg ME, Hayken GD, Steinberg DS. A quantitative system for staging avascular necrosis. J Bone Joint Surg Br. 1995;77:34–41. doi: 10.1302/0301-620x.77b1.7822393. PMID: 7822393.

7 Uguen M, Pougnet R, Uguen A, Loddé B, Dewitte JD. Dysbaric osteonecrosis among professional divers: A literature review. Undersea Hyperb Med. 2014;41:579–87. PMID: 25562949.

8 Wade CE, Hayashi EM, Cashman TM Jr., Beckman EL. Incidence of dysbaric osteonecrosis in Hawaii's diving fishermen. Undersea Biomed Res. 1978;5:137–47. PMID: 675879.

9 Jones JP, Salbador G, Lopez F, Ramirez S, Doty SB. High-risk diving and dysbaric osteonecrosis. In: Smith N, editor. Proceedings of the 14th meeting of the US-Japan cooperative program in natural resources (UNJR), Panel on diving physiology. Silver Spring (MD): National Oceanographic and Atmospheric Administration; 1998. p. 77–88.

10 Shinoda S, Hasegawa Y, Kawasaki S, Tagawa N, Iwata H. Magnetic resonance imaging of osteonecrosis in divers: Comparison with plain radiographs. Skeletal Radiol. 1997;26:354–9. doi: 10.1007/s002560050247. PMID: 9229418.

11 Kawashima M, Tamura H, Noro Y, Takao K, Kitano M, Lehner CE, et al. Decompression sickness in divers: pathogenesis and prevention of dysbaric osteonecrosis. Kagoshima Univ. Res. Center S. Pac, Occasional Papers. 1995. [cited 2020 April 23]. Available from: https://ir.kagoshima-u.ac.jp/?action=pages_view_main&active_action=repository_view_main_item_detail&item_id=2586&item_no=1&page_id=13&block_id=21.

12 Kawashima M, Tamura H, Noro Y, Takao K, Yoshida K, Tsunoe T, et al. Diving profile and dysbaric osteonecrosis. In: Smith N, editor. Proceedings of the 14th meeting of the US-Japan cooperative program in natural resources (UNJR), Panel on diving physiology. Silver Spring (MD): National Oceanographic and Atmospheric Administration; 1998. p. 89–116.

13 Ota Y, Matsunaga H. Bone lesions in divers. J Bone Joint Surg Br. 1974;56:3–16. PMID: 4818853.

14 Yoo MC, Cho YJ, Lee SG. Bony lesions of professional Divers in Korea. J Korean Orthop Assoc. 1992;27:331–40. doi: 10.4055/jkoa.1992.27.1.331.

15 Toklu AS, Çimşit M. Dysbaric osteonecrosis in Turkish sponge divers. Undersea Hyperb Med. 2001;28:83–88. PMID: 11908699.

16 Kenney IJ, Sonksen C. Dysbaric osteonecrosis in recreational divers: A study using magnetic resonance imaging. Undersea Hyperb Med. 2010;37:281–8. PMID: 20929185.

17 Gempp E, Blatteau J-E, Simon O, Stephant E. Musculoskeletal decompression sickness and risk of dysbaric osteonecrosis in recreational divers. Diving Hyperb Med. 2009;39:200–4. PMID: 22752739.

18 Evans A, King JD, McCallum RI, Walder DN, Golding FC, Trowbridge WP, et al. Aseptic bone necrosis in commercial divers. A report from the decompression sickness central registry and radiological panel. Lancet. 1981;2(8243):384–8. PMID: 6115158.

19 Cimsit M, Ilgezdi S, Cimsit C, Uzun G. Dysbaric osteonecrosis in experienced dive masters and instructors. Aviat Space Environ Med. 2007;78:1150–4. doi: 10.3357/ASEM.2109.2007. PMID: 18064920.

20 Jones JP, Neuman TS. Dysbaric osteonecrosis. In: Brubakk AO, Neuman TS, editors. Bennett and Elliott's physiology and medicine of diving, 5th ed. London: Saunders; 2003. p. 659–717.

21 Mendez-Dominguez N, Huchim-Lara O, Chin W, Carrillo-Arceo L, Camara-Koyoc I, Cárdenas-Dajdaj R, et al. Body mass index in association with decompression sickness events: cross-sectional study among small-scale fishermen-divers in southeast Mexico. Undersea Hyperb Med. 2018;45:445–51. doi: 10.22462/07.08.2018.9. PMID: 30241124.

22 Lehner CE, Wilson MA, Dueland RT. Early recompression treatment of limb bends can prevent dysbaric osteonecrosis. Proceedings of the 14th meeting of the US-Japan cooperative program in natural resources (UNJR), Panel on diving physiology. Silver Spring (MD): National Oceanographic and Atmospheric Administration; 1998. p. 117–137.
23 Camporesi E, Vezzani G, Zanon V, Manelli D, Enten G, Quartesan S, et al. Review on hyperbaric oxygen treatment in femoral head necrosis. Undersea Hyperb Med. 2017;44:497–508. doi: 10.22462/11.12.2017.1. PMID: 29281187.
24 Moya-Angeler J, Gianakos AL, Villa JC, Ni A, Lane JM. Current concepts on osteonecrosis of the femoral head. World J Orthop. 2015;6:590–601. doi: 10.5312/wjo.v6.i8.590. PMID: 26396935.
25 Orlić D, Jovanović S, Antičević D, Zečević J. Frequency of idiopathic aseptic necrosis in medically treated alcoholics. Int Orthop. 1990;14:383–6. doi: 10.1007/BF00182650. PMID: 2076924.

Acknowledgements

The authors would like to thank the fishermen and cooperatives of Río Lagartos and San Felipe for their generous time and willingness to participate in this study.

Conflicts of interest and funding

No conflicts of interest were declared. The authors would like to thank the San Diego Center for Excellence in Diving that generously provided funding for this project.

Submitted: 23 April 2020
Accepted after revision: 28 August 2020

Guideline

Children and diving, a guideline

Mattijn Buwalda[1], Abraham L Querido[2], Robert A van Hulst[3]

[1] *Medical and Educational Services, De Meent 51A, Odijk, The Netherlands*
[2] *Praktijk Querido, Larenseweg 14, Hilversum, The Netherlands*
[3] *Department of Anaesthesiology and Hyperbaric Medicine, Academic Medical Center, Amsterdam, The Netherlands*

Corresponding author: *Dr Mattijn Buwalda, Medical and Educational Services, De Meent 51A, Odijk, The Netherlands*
mattijnb@gmail.com

Key words
Recreational diving; Children; Physiology; Psychology; Diving incidents; Review article

Abstract

(Buwalda M, Querido AL, van Hulst RA. Children and diving, a guideline. Diving and Hyperbaric Medicine. 2020 December 20;50(4):399–404. doi: 10.28920/dhm50.4.399-404. PMID: 33325022.)
Scuba diving is an increasingly popular recreational activity in children and adolescents. During the dive medical examination aspects of human physiology, anatomy, and psychology, that differ between adults and children, deserve our special attention. For example, lack of mental maturity, diminished Eustachian tube function and heat loss can pose problems during diving. It is important that children who wish to take up scuba diving are seen by a dive physician, with extra attention to Eustachian tube function. In children, asthma, bronchial hyperreactivity, pulmonary hypertension, and right-to-left shunts are contra-indications for scuba diving. Attention deficit hyperactivity disorder is a relative contra-indication. This article provides a review of the current literature and presents recommendations for recreational diving in children and adolescents. These recommendations are based solely on 'expert' opinion and were accepted by the Dutch Society of Diving and Hyperbaric Medicine in 2020.

Introduction

The issue of children and diving is still an emotional one, with little scientific evidence.[1] The South Pacific Underwater Medicine Society (SPUMS) Committee on Medical Standards for Recreational Diving recommended in 1990 a minimum age of 16 years for scuba diving training and this advice was purely based on safety factors.[2] The 2010 (current) SPUMS guideline does not recommend diving for children under the age of 14 years[3] and is solely founded on the belief that younger children do not have the emotional maturity and confidence to safely manage underwater emergencies.[4]

However, along the years, the age at which children (were allowed to) start scuba diving decreased steadily. Facilitated by the dive industry who developed courses especially aimed at children, more and more children took up scuba diving. The Professional Association of Diving Instructors (PADI) changed its minimum age requirement from 12 to 10 years after evaluating their own data from 30 years training children younger than 12 in combination with data obtained from other organisations, like the Confédération Mondiale des Activités Subaquatiques (CMAS), during the same time period.[5] The CMAS has a junior programme with a minimum age of 8 years, while currently American scuba training agencies have agreed on age limits of 8–12 years.[1]

In 2003 The Dutch Society of Diving and Hyperbaric Medicine (DSDHM) issued a national guideline in which the minimum age for scuba diving was set at 14 years.[6] However, younger children do dive and need to be assessed by sports dive physicians for medical examination and advice. The DSDHM felt it necessary to evaluate the minimum age for diving and they tasked us with undertaking this review on their behalf. These new guidelines are officially accepted by the board and members of the DSDHM. In order to update the guideline for children and diving we performed a PubMed search to see if there are new insights on scuba diving in children.

Methods

Author ALQ performed a PubMed search with the search terms: ("*Diving*"[Mesh] OR "*diving*"[tiab] OR "*scuba*"[tiab]) AND ("Child"[Mesh] OR "*Adolescen*t"[Mesh] OR Child*[tiab]). It resulted in 750 titles from which 11 were judged to be relevant. We did not include non-English publications. In addition, existing guidelines and handbooks on diving medicine and diving medical books which discussed medical examinations were screened to identify additional information.

Results

From the 11 titles judged to be relevant there were three observational studies, three opinions, two reviews, one original article, one case report, and only one prospective study with children. The last review dated from eight years ago. Chapters devoted to diving and children in the various dive medical textbooks were brief and provided little background information. Recreational scuba diving incidents, injuries and fatalities of children were reported in several retrospective case series, case reports and in several annual dive medical statistics reports. Unfortunately, those reports usually only mentioned the ratio of accidents in young and adult divers. For a better understanding of the child's physiology and psychology we have chosen to review the literature on the basis of the organ systems.

COGNITIVE AND PSYCHOLOGICAL ASPECTS

Brain development begins in utero and continues into adolescence,[7] however, lateral regions of the prefrontal cortex are the latest developing areas involved in executive functions.[8] Because of incompletely developed prefrontal cortex, executive functioning is only fully established late in the second decade. The executive functions are the cognitive processes that help to regulate, control and manage thoughts and actions.

The cognitive, social and emotional development of an adolescent (12 to about 16 years of age) is stormy. Their ability to suppress and regulate impulses is not yet well developed, there is an increase in risk behaviour, they often have intense mood swings and, partly as a result, a reduced concentration. Considering these processes, one may assume that diving requires good executive functioning, in particular good response inhibition (ability to inhibit one's own response to distractions), sustained attention and cognitive flexibility (human ability to adapt the cognitive processing strategies to face new and unexpected conditions in the environment).[9]

There are five types of situations where normal routine behavioural activation is not sufficient, and executive functions are required to achieve optimum performance.[10] These are: 1) Situations involving planning or decision-making; 2) Situations involving error-correction; 3) Situations where the response is novel and not well-learned; 4) Situations judged to be difficult or dangerous; and 5) Situations that require overcoming habitual responses.

Diving is a safe sport, but it does require good executive functions to be able to anticipate unexpected situations, for example a buddy who gets into trouble because of equipment failure. As the ability to pay attention is the key executive function, testing the child's attention must be an essential part of the diving medical examination. In case of doubt, the dive medical examiner could obtain information from the teachers, diving instructor and parents, or ask for further psychological testing.

Finally, executive dysfunction mainly occurs in children with a diagnosis of attention deficit hyperactivity disorder (ADHD), attention deficit disorder (ADD), autism or dyslexia. For example, in a child with ADHD, executive functions such as: response inhibition, sustained attention, working memory, time management, task initiation and goal-oriented behaviour are insufficiently developed. Therefore, ADHD is a relative contraindication for diving.[11]

ENT ASPECTS

The Eustachian tubes are relatively narrow and run a more horizontal path in young children.[12] This may affect the ability to equalise up to eight years, the age after which we allow children to dive in swimming pools. Middle ear diseases in childhood play an important role in daily ENT practice due to their high incidence.[13] The most important factor is dysfunction of the Eustachian tubes.[14] Children have shorter, more horizontal tubes, immature floppy elastic cartilage and larger adenoids compared with adults. Although most children 'grow out' of this, previous ENT surgery, an atopic constitution, frequent ear infections and problems during air flights should alert the diving physician to a possible persisting tube dysfunction. Also, in young divers, middle ear squeeze is the most common dive medical problem.[15] In a five-year prospective study of 205 children aged 8–13 years, there were four tympanic membrane ruptures after pool and open water dives.[16]

The dive medical examiner should pay extra attention to the historical indicators of Eustachian tube function mentioned above. The ability to equalise should be checked by asking for 'clicking' sounds and by otoscopic examination of the ears. The dive medical exam in the presence of the parents is a good opportunity to explain and practise equalising techniques. If possible, the ability to equalise should be checked in an introductory dive in the swimming pool before embarking on the full course.

PULMONARY ASPECTS

At eight years of age the number of alveoli reaches its maximum.[17] However, a relatively low lung elasticity and airway diameter lead to a higher breathing effort and increased airway collapse at the end of expiration compared to adults.[18] This makes young children in theory more vulnerable to air trapping and pulmonary barotrauma. During subsequent adolescence, the alveoli and airways grow until they reach adult size at approximately 16 years of age.[17]

Adults with mild, well-controlled asthma can, with some precautions, dive safely.[19] However, children seem to be more susceptible to bronchoconstrictive stimuli such as

exertion and cold dry air. In a study of 16 healthy children (age 10–13 years) pulmonary function tests were done pre- and post-breathing cold dry air during a cycle ergometer test and before and after two dives at 1 m and 8 m depth, with a total dive time of 25 min. Water temperatures ranged between 21.5 (SD 1.1)°C at the surface and 15.9 (0.4)°C at 8 m depth. The forced vital capacity (FVC), forced-expiratory volume in 1 s (FEV1), FEV1 / FVC and mid expiratory flow at 50 and 25% of FVC (MEF 50, MEF 25) were all significantly decreased after the cold-air exercise test and after the dives. There were no clinical signs of airway obstruction. The three children with the largest bronchoconstrictive responses had the lowest BMI. The response to the cold air challenge was not predictive for the post-dive pulmonary function.[20] In case of a history of asthma, complaints or symptoms, pulmonary function tests should be performed.

CARDIOVASCULAR ASPECTS

The foramen ovale usually closes in the third month of life. The incidence of a patent foramen ovale (PFO) decreases with age from 36% at 10–19 years to 25% at 30–79 years.[21] The slightly increased incidence of a PFO in children is probably not relevant because of the depth restrictions advocated by the international diving agencies.

Children with congenital heart disease such as atrial septal defect (ASD), ventricular septal defect (VSD), pulmonary stenosis (PS), coarctation of the aorta (CoA), tetralogy of Fallot (ToF), transposition of the great arteries (TGA) and the like are usually operated upon at young age.[22,23] As surgical techniques for congenital heart disease have improved considerably these last decades, children have a better prognosis and life expectancy and most will reach adulthood. Consequently, it is possible that children who have been operated in the past, may want to start scuba diving. After extensive surgery they are usually asymptomatic, but the possibility exists that they still have a reduced exercise capacity.[24] Also, there is an increased risk of atrial and ventricular arrhythmias, heart failure, and other complications, and in some cases, reoperation is indicated.[25] Children with congenital heart disease with pulmonary hypertension and/or existing right-to-left shunts are considered ineligible for scuba diving.

MUSCULOSKELETAL ASPECTS

The weight of full diving gear depends on thickness of the wetsuit, tank and buoyancy compensating device (BCD) size, and weight belt requirements; on average a child will carry about 15 kg. There is an obvious limit of weight that a child can carry on his/ her back. The American Occupational Therapy Association (AOTA) recommends that backpacks weigh no more than 10% of the student's body weight.[26] There are no international guidelines on the maximum weight of dive equipment used by children who venture scuba diving. Some diving medicine experts have suggested body size limits (145 cm and 40 kg approximately) but this would also preclude some small frame adults.[1]

A long and persisting myth was that growth plates in long bones would be extra susceptible to bubbles in children. This purely theoretical concept kept on being copied in articles and textbooks. The effects of scuba diving on growth plates in both children and adolescents have neither been studied nor reported in the medical literature.[12]

Children usually have a thin subcutaneous fat layer and a rather straight body profile around the waist. This makes them more vulnerable to hypothermia. The weight belt can easily slip off resulting in an uncontrolled ascent with the risk of pulmonary barotrauma. Therefore, the DSDHM advises, for safety reasons, to use a BCD with an integrated lead system.

HYPOTHERMIA

The risk of hypothermia usually begins in water colder than 25°C (77°F).[12] Children generally have a higher surface area to body weight ratio, a lower body mass index and weight and relatively less subcutaneous fat tissue. This results in a faster heat loss than adults, who also have greater heat reserves.[27] Until the mid-teens, children are far more vulnerable to hypothermia than adults. Hypothermia in children (as well as in adults) not only affects bronchomotor tone but locomotor and cognitive abilities as well. During mild hypothermia (central temperature of 35–33°C) symptoms may include confusion, disorientation and amnesia.[28] The cooling of peripheral muscles and nerves can have detrimental effects on function of the hands and function of the legs in swimming.[29]

Increased heat loss in children compared to adults necessitates exposure protection that needs to fit correctly to avoid hypothermia during diving. Children have a natural tendency to grow and, as wetsuit sizes are limited, the young diver may very well end up with loose wrist, ankle and collar seals. Adequate hydration with hot drinks and changing out of the diving suit in a warm environment immediately after diving minimises the likelihood of hypothermia.

Hypothermia prevention in young divers is especially important in regions with a moderate climate such as the Netherlands and the North European countries. The average seasonal water temperature of Dutch rivers, lakes and coastal waters range between four and 20°C. The minimum water temperature at which wetsuits are optional is 14°C,[30] which is therefore advised as safe boundary. This limits the annual period in which young divers are allowed to dive.

DIVE ACCIDENTS IN YOUNG DIVERS

Lethal and non-lethal dive accidents in children are reported in several retrospective case series, case reports and in the

annual dive medical statistics published by the Divers Alert Network (DAN).[27,31,32] One study retrospectively described 22 dive accidents in children below the age of 18 who were treated for arterial gas embolism (AGE) (six cases) and decompression sickness (DCS) (16 cases) at the University of Hawaii between 1983 and 2003.[32] Half of the AGE cases had a history of asthma or had to make an emergency ascent because they panicked underwater. Nine out of the 16 DCS cases (41%) were caused by being out of air.

The incidence rate of diving accidents in children is unknown. Dive statistics usually only mention the ratio of accidents in young and adult divers. For example: In data from DAN 2012–2015, there were 12/636 (1.9%) paediatric scuba diving fatalities in the US or Canada, all between the ages of 12–17.[31]

Drowning and AGE seem to be the cause of death in most cases. Running out of air and uncontrolled ascents are common accident mechanisms. Most accidents are caused by insufficient or total lack of training or high-risk diving (too deep, wreck, cave).[27]

ARE CHILDREN MORE PRONE TO DCS?

Age, body mass index and poor exercise tolerance are correlated to circulating venous bubbles.[33] The question arises whether children have less venous bubbles after diving and/or are less susceptible for DCS compared to adults. This question is difficult to answer as our literature search revealed only three studies looking at DCS and venous gas embolism. In a prospective study from 2003, 205 divers aged 8–13 years were diving to 5–10 m depth. As may be expected, due to limited diving depth, there were no clinical signs of DCS.[16] A limitation of this study was a high dropout rate (25%/year).

In a study that evaluated the occurrence of venous bubbles in 10 young divers (13.1 (SD 2.3) years) after a shallow dive (12 (3) m) for a short time (26 (7) min) no circulating venous bubbles were detected after the children surfaced.[34] A more recent study used standardised dives to look at bubble formation in children.[35] Bubbles were seen on echocardiography in six out of 28 (21%) young divers (13.5 (1.1) years) who made two standardised dives of 25 minutes to 10 metres' seawater. There were no symptoms. This small study demonstrated that bubbles also form during relatively short and superficial dives in children and adolescents.

Unfortunately, both the recent British Sub-Aqua Club and DAN annual reports about the incidence rate of DCS do not differentiate age.[36,37] There are some case reports in the literature, but we have to conclude that the incidence of DCS in young divers is unknown but presumably very low.[12,38,39,32] Also, the question, whether young divers are more vulnerable to decompression stress compared to adult divers, cannot be answered. This will not change in the foreseeable future, as age-related restrictions in depth and duration of diving issued by international diving organisations and ethical considerations do not allow for prospective studies using 'adult' nitrogen loads.

UNRESOLVED ISSUES

There are still many gaps in our knowledge and a lack of evidence about young divers and several such 'loose ends' may warrant future research efforts.

First, a buddy pair consisting of a parent and a 12 year-old child is not rare. Young children are probably not able to help their parent-diver in distress, not only because of a not fully developed executive functioning, but also because of a lack of physical strength. It is suggested that the dive medical examiner will also advise parents in this matter. This advice could be, for instance, to dive under guidance with a diving professional.

Second, children with a mental or physical disability might not be accepted in mainstream dive clubs or courses. The International Association for Handicapped Divers (IAHD) offers courses for children and adults with a disability as well as for instructors.[40] The judgment whether a child with a disability is eligible for an IAHD course requires special expertise and experience from the dive physician.

Finally, adult diabetics can dive with necessary precautions and restrictions. Dive medical organisations do not allow diabetic patients < 18 years to dive[41] although there is support for allow diabetics > 16 years to dive if in a special training programme.[42] A small study in seven 16–17 year-old novice divers with insulin dependent diabetes did not show symptoms or complications of hypoglycemia.[43] This study showed that in closely monitored situations some diabetic adolescents can dive safely. Whether this also holds true for younger diabetic divers is unknown.

Summary

The DSDHM felt it necessary to update their guideline on children and diving. A literature search did not reveal much new knowledge to have emerged over the last 20 years. Most, if not all guidelines, are still expert or consensus based. We believe that, with the necessary precautions, it is safe to lower the minimum age for scuba diving from 14 years to 12 years (or 10 years depending on the circumstances). We have tried to present an overview of the current knowledge and have formulated some recommendations.

Recommendations

These recommendations are based on expert opinions from the diving medical physicians of DSDHM and the best knowledge from existing literature.

1. The DSDHM strongly advises a diving medical examination for all children who would like to take up scuba diving. The self-declaration form, which is used by some diving organisations, is designed for adults. If used for children, it will most probably be completed by the parents. It is not uncommon for children to be put under pressure by the parents to take up scuba diving. It is important confirm there is no parental pressure on the child to start diving.

2. Good executive functioning is important in scuba diving, in particular good response inhibition, sustained attention and cognitive flexibility. Because (some) symptoms of ADHD and ADD may be due to underlying executive functioning, those conditions can be a relative contraindication for scuba diving. If in doubt about executive functioning, it is advisable to obtain information from the teachers, the diving instructor and parents or a psychiatrist/sports diving physician may be asked to carry out a specialist examination.

3. The dive medical examiner should pay extra attention to Eustachian tube function. One should ask about previous glue ears, tympanic membrane surgery, frequent ear infections and an atopic constitution. If possible, the ability to equalise should be checked in a swimming pool try dive before embarking on the full course.

4. The DSDHM advises to preclude children from diving who have asthma or signs of bronchial hyperreactivity (with or without medication). Above the age of 14, adult guidelines apply.

5. Children with operated congenital heart disease should be carefully screened by a cardiologist with expertise in scuba diving. Children with residual pulmonary hypertension and/or residual atrial or ventricular septum defects are unfit for scuba diving.

6. Children should use integrated weight pockets.

7. This guideline for diving and children differentiates between diving in the relatively cold Dutch (and Northern European) waters and diving abroad in tropical waters. While diving for children aged 10–12 years in the Dutch (and Northern European) waters is discouraged, the risk of hypothermia may be much lower in the Red Sea or Thailand. Children from ages 12–14 years can dive in the Dutch lakes provided the water temperature is > 14°C and they wear an adequately fitting wetsuit.

8. Certified sports diving physicians should also be trained to examine children and form an opinion on whether a young candidate should be regarded fit or unfit for diving. In case of doubt or a complicated underlying condition a specialist may be asked for consultation or to carry out an additional examination.

References

1 Bennett PB, Cronje FJ, Campbell E. Children and Diving. In: Assessment of diving medical fitness for scuba divers and instructors. Flagstaff (AZ): Best Publishing Company; 2006. p. 207–8.

2 Edmonds C, Bennett M, Lippmann J, Mitchell SJ. Children. In: Diving and subaquatic medicine, 5th ed. Boca Raton (FL): CRC Press; 2015. p. 675–9.

3 The South Pacific Underwater Medicine Society guidelines on medical risk assessment for recreational diving, fourth edition, December 2010. [cited 2020 May 06]. Available from: https://www.spums.org.au/content/spums-full-medical-0.

4 Walker RM. Assessing children's fitness for scuba diving. Med J Aust. 2002;176:450. doi: 10.5694/j.1326-5377.2002.tb04474.x. PMID: 12057003.

5 Richardson D. Children and diving. SPUMS Journal. 2003;33:83–9.

6 DSDHM. The Dutch Society of Diving and Hyperbaric Medicine. [cited 2020 May 06]. Available from: https://www.duikgeneeskunde.nl/dsdhm/.

7 Rosenberg K, Trevathan W. Bipedalism and human birth: The obstetrical dilemma revisited. Evolutionary Anthropology: Issues, News, and Reviews. 1995;4:161–8 doi: 10.1002/evan.1360040506.

8 Fuster JM. Frontal lobe and cognitive development. J Neurocytol. 2002;31:373–85. doi: 10.1023/a:1024190429920. PMID: 12815254.

9 Cañas JJ, Quesada JF, Antolí A, Fajardo I. Cognitive flexibility and adaptability to environmental changes in dynamic complex problem-solving tasks. Ergonomics. 2003:46:482–501. doi: 10.1080/0014013031000061640. PMID: 12745698.

10 Shallice T. Multiple levels of control processes. In: Umilta C, Moscovitch M, editors. Attention and performance XV: Conscious and nonconscious information processing. Cambridge (MA): MIT Press; 1994. p. 395–420.

11 Querido AL, van Hulst RA. Diving and attention deficit hyperactivity disorder. Diving Hyperb Med. 2019;49:41–7. doi: 10.28920/dhm49.1.41-47. PMID: 30856666. PMCID: PMC6526049.

12 Tsung JW, Chou KJ, Martinez C, Tyrrell J, Touger M. An adolescent scuba diver with 2 episodes of diving-related injuries requiring hyperbaric oxygen recompression therapy: A case report with medical considerations for child and adolescent scuba divers. Pediatr Emerg Care. 2005;21:681–6. doi: 10.1097/01.pec.0000181415.26235.0e. PMID: 16215475.

13 Minovi A, Dazert S. Diseases of the middle ear in childhood. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2014;13:Doc11. doi: 10.3205/cto000114. PMID: 25587371. PMCID: PMC4273172.

14 Dhooge IJ. Acute otitis media in children. In: Graham JM, Scadding GK, Bull PD, editors. Pediatric ENT. Heidelberg: Springer; 2007. p. 399–420. doi: 10.1007/978-3-540-33039-4_41.

15 Klingmann C, Praetorius M, Baumann I, Plinkert PK. Otorhinolaryngologic disorders and diving accidents: An analysis of 306 divers. Eur Arch Otorhinolaryngol. 2007;264:1243–51. doi: 10.1007/s00405-007-0353-6. PMID: 17639445.

16 Vandenhoven G, Collard F, Schamp E. Children and diving: medical aspects. Eight years' sports medical follow-up of the first scuba diving club for children in Belgium. SPUMS Journal. 2003;33:70–3.

17 Davies GM, Reid L. Growth of the alveoli and pulmonary arteries in childhood. Thorax. 1979;25:669–81. doi: 10.1136/thx.25.6.669. PMID: 5533319. PMCID: PMC472209.

18 Mansell AL, Bryan AC, Levison H. Relationship of lung recoil to lung volume and maximum expiratory flow in normal children. J Appl Physiol Respir Environ Exerc Physiol. 1977;42:817–23. doi: 10.1152/jappl.1977.42.6.817. PMID: 881381.

19 British Thoracic Society Fitness to Dive Group, Subgroup of the British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines on respiratory aspects of fitness for diving. Thorax. 2003;58:3–13. doi: 10.1136/thorax.58.1.3. PMID: 12511710. PMCID: PMC1746450.

20 Winkler BE, Tetzlaff K, Muth CM, Hebestreit H. Pulmonary function in children after open water SCUBA dives. Int J Sports Med. 2010;31:724–30. doi: 10.1055/s-0030-1262803. PMID: 20677123.

21 Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: An autopsy study of 965 normal hearts. Mayo Clin Proc. 1984;59:17–20. doi: 10.1016/s0025-6196(12)60336-x. PMID: 6694427.

22 Silva LM, Kuipers IM, van den Heuvel F, Mendes R, Berger RMF, van Beynum IM, et al. KinCor, a national registry for paediatric patients with congenital and other types of heart disease in the Netherlands: Aims, design and interim results. Neth Heart J. 2016;24:628–39. doi: 10.1007/s12471-016-0892-9. PMID: 27632192. PMCID: PMC5065536.

23 The Netherlands Heart Institute, CONCOR registry. [cited 2020 April 20]. Available from: https://www.heart-institute.nl/index.php?pagina=CONCOR.

24 Diller GP, Dimopoulos K, Okonko D, Li W, Babu-Narayan SV, Broberg CS, et al. Exercise intolerance in adult congenital heart disease: Comparative severity, correlates, and prognostic implication. Circulation. 2005;112:828–35. doi: 10.1161/CIRCULATIONAHA.104.529800. PMID: 16061735.

25 Verheugt CL, Uiterwaal CSPM, Grobbee DE, Mulder BJM. Long-term prognosis of congenital heart defects: A systematic review. Int J Cardiol. 2008;131:25–32. doi: 10.1016/j.ijcard.2008.06.023. PMID: 18687485.

26 American Occupational Therapy Association (AOTA). [cited 2020 May 06]. Available from: https://www.aota.org/Publications-News/ForTheMedia/PressReleases/2019/091719-Backpack-Safety-Tips.aspx.

27 Winkler BE, Muth CM, Tetzlaff K. Should children dive with self-contained underwater breathing apparatus (SCUBA)? Acta Paediatr. 2012;101:472–8. doi: 10.1111/j.1651-2227.2011.02589.x. PMID: 22212048.

28 Golden FStC. Proceedings: Recognition and treatment of immersion hypothermia. Proc R Soc Med. 1973;66:1058–61. PMID: 4759741.

29 Golden FS, Tipton MJ. Human thermal responses during leg-only exercise in cold water. J Physiol. 1987;391:399–405. doi: 10.1113/jphysiol.1987.sp016744. PMID: 3443951.

30 Tipton M, Bradford C. Moving in extreme environments: Open water swimming in cold and warm water. Extrem Physiol Med. 2014;3:12. doi: 10.1186/2046-7648-3-12. PMID: 24921042. PMCID: PMC4052348.

31 Buzzacott P, Trout B, Caruso J, Nelson C, Denoble PJ, Nord D, et al. DAN annual diving report 2012–2015 edition. Durham (NC): Divers Alert Network; 2015. [cited 2020 May 06]. Available from: https://www.diversalertnetwork.org/medical/report/AnnualDivingReport-2015Edition.pdf.

32 Smerz R. Epidemiology and treatment of decompression illness in children and adolescents in Hawaii, 1983–2003. SPUMS Journal. 2005;35:5–10.

33 Carturan D, Boussuges A, Burnet H, Fondarai J, Vanuxem P, Gardette B. Circulating venous bubbles in recreational diving: Relationships with age, weight, maximal oxygen uptake and body fat percentage. Int J Sports Med. 1999;20:410–4. doi: 10.1055/s-2007-971154. PMID: 10496123.

34 Lemaitre F, Carturan D, Tourny-Chollet C, Gardette B. Circulating venous bubbles in children after diving. Pediatr Exerc Sci. 2009;21:77–85. doi: 10.1123/pes.21.1.77. PMID: 19411713.

35 Geyer L, Brockmeier K, Graf C, Kretzschmar B, Schmitz KH, Webering F, et al. Bubble formation in children and adolescents after two standardised shallow dives. Int J Sports Med. 2019;40:31–7. doi: 10.1055/a-0777-2279. PMID: 30458551.

36 Buzzacott P, Denoble PJ, editors. DAN annual diving report 2018 edition: A report on 2016 diving fatalities, injuries, and incidents. Durham (NC): Divers Alert Network; 2018. [cited 2020 May 06]. p. 112. Available from: https://www.diversalertnetwork.org/medical/report/AnnualDivingReport-2017Edition.pdf.

37 Cumming B, Watson J. National diving incidents report 2017. British Sub Aqua Club. [cited 2020 May 06]. Available from: https://www.bsac.com/document/diving-incident-report-2017/.

38 Edmonds C. Children and diving: A review of SPUMS articles. SPUMS Journal. 2003;33:206–211.

39 Davis M. Decompression sickness in a 14-year-old diver. SPUMS Journal. 2003;33:2,75–6

40 IAHD website: courses. [cited 2020 April 19]. Available from: https://www.iahd.org/en/courses-en/overview-courses-en.

41 UK Diving Medical Committee: Medical conditions. [cited 2020 May 06]. Available from: http://www.ukdmc.org/medical-conditions/diabetes-mellitus/.

42 Divers Alert Network: Guidelines for diabetes and recreational diving. [cited 2020 May 06]. Available from: https://www.diversalertnetwork.org/research/scientific-summaries/diabetes-diving.html.

43 Pollock NW, Uguccioni DM, Dear G, Bates S, Albushies TM, Prosterman SA. Plasma glucose response to recreational diving in novice teenage divers with insulin-requiring diabetes mellitus. Undersea Hyperb Med. 2006;33:125–33. PMID: 16716063.

Conflicts of interest and funding: nil

Submitted: 30 May 2020
Accepted after revision: 28 August 2020

Technical report

First impressions: Use of the Azoth Systems O'Dive subclavian bubble monitor on a liveaboard dive vessel

Peter Germonpré[1,2,3], Paul Van der Eecken[4], Elke Van Renterghem[2,5], Faye-Lisa Germonpré[6], Costantino Balestra[3,7]

[1] *Centre for Hyperbaric Oxygen Therapy, Military Hospital Brussels, Belgium*
[2] *Medyssea EVR, Expedition and Diving Medicine, Ghent, Belgium*
[3] *Environmental, Occupational, Ageing (Integrative) Physiology Laboratory, Haute Ecole Bruxelles-Brabant (HE2B), Brussels, Belgium*
[4] *ENT Department, St Lucas Hospital, Ghent, Belgium*
[5] *Emergency Department, St Lucas Hospital, Ghent, Belgium*
[6] *Medical Student, Ghent University, Ghent, Belgium*
[7] *DAN Europe Research Department, Brussels, Belgium and Roseto, Italy*

Corresponding author: *Dr Peter Germonpré, Centre for Hyperbaric Oxygen Therapy, Military Hospital Brussels, Belgium* *peter.germonpre@mil.be*

Key words
Bubble detection; Bubbles; Decompression; Recreational diving; Risk assessment; Surveillance

Abstract
(Germonpré P, Van der Eecken P, Van Renterghem E, Germonpré F-L, Balestra C. First impressions: Use of the Azoth Systems O'Dive subclavian bubble monitor on a liveaboard dive vessel. Diving and Hyperbaric Medicine. 2020 December 20;50(4):405–412. doi: 10.28920/dhm50.4.405-412. PMID: 33325023.)
Introduction: The Azoth Systems O'Dive bubble monitor is marketed at recreational and professional divers as a tool to improve personal diving decompression safety. We report the use of this tool during a 12-day dive trip aboard a liveaboard vessel.
Methods: Six divers were consistently monitored according to the user manual of the O'Dive system. Data were synchronised with the Azoth server whenever possible (depending on cell phone data signal). Information regarding ease of use, diver acceptance and influence on dive behaviour were recorded.
Results: In total, 157 dives were completely monitored over 11 diving days. Formal evaluations were only available after six days because of internet connection problems. Sixty-one dives resulted in the detection of bubbles, mostly in one diver, none of which produced any symptoms of decompression illness.
Conclusions: The O'Dive system may contribute to increasing dive safety by making divers immediately aware of the potential consequences of certain types of diving behaviour. It was noted that bubble monitoring either reinforced divers in their safe diving habits or incited them to modify their dive planning. Whether this is a lasting effect is not known.

Introduction

Scuba diving exposes the diver to a certain risk of decompression pathology (decompression illness – DCI). Some forms of DCI are classified as 'barotrauma', related to compression or overexpansion of existing gas spaces in the body; 'decompression sickness' (DCS) on the other hand is (at least in part) caused by the formation of inert gas bubbles in tissue or blood vessels during and/or after decompression.[1,2] Regardless of the decompression algorithm used, detectable vascular gas emboli (VGE) may be detected after recreational, technical and professional diving;[3] the quantity of VGE is considered to be related to the risk of DCS after a dive.[4,5] Low VGE grades or absence of VGE after a dive are statistically associated with a safe decompression (low risk of DCS).[6] Even though in diving medicine research, VGE grades are sometimes considered an imperfect 'research endpoint' (as the ideal endpoint would be DCS)[7] it is at present accepted that VGE are an important tool for decompression physiology and safety research.[6,8]

Different methods of detection of VGE are possible: during field studies, bubbles are usually detected in the right atrium and pulmonary artery (acoustically, using Doppler or visually, using 2D cardiac ultrasound).[9] Various grading systems have been proposed, either categorical[10–12] or semi-quantitative.[13] Recently, detection of VGE in the subclavian veins has been re-evaluated and confirmed to correlate with DCS risk better than precordial monitoring. In (existing) dive databases with known outcome, subclavian monitoring was associated with high bubble grades (HBG) more than precordial monitoring when (and only when)

dive exposure severity was also accounted for (and for rest recordings only).[14] Based on this premise and building on novel biophysical modelling of decompression,[15–17] a simple 'self-measurement' tool has been developed and is currently marketed to recreational and professional divers. This tool, the Azoth Systems O'Dive sensor and app, guides the diver through a series of self-measurements, and after uploading the audio signals and related dive data to the Azoth Systems server, uses a proprietary algorithm to estimate the 'quality of decompression' (QI, which is inversely proportional to an estimated 'risk for DCS') for that dive. The algorithm is based on existing dive data (amongst others French Navy and Defence Research and Development Canada databases), but reportedly also builds on contributed O'Dive app data to continuously adjust and optimise the evaluation (Azoth Systems, personal communication). According to the O'Dive website, "*this allows scuba divers to personalise their diving practice by taking into consideration the gas microbubbles detected in their venous system after diving*". This 'retrospective view' of dive safety would then "*allow them dive after dive to improve their self-knowledge and to better anticipate their own body's reactions*".

The O'Dive app works with a connected ultrasonic sensor for bubble detection, which is linked to any iOS or Android phone or tablet by wireless connection. The sensor is simple and robust although not waterproof (IP54) (Azoth Systems, personal communication), and the sensor, ultrasound gel, mirror (for self-observation by the diver during the measurements) and wireless USB-C charger are contained in a small waterproof case.

This report will relate hands-on experience with the system during an actual dive trip in remote areas, in particular with regard to: the practical of use of the O'Dive system in real 'liveaboard' conditions, on multiple divers; some results obtained with the O'Dive system and how these were perceived by the divers; and adaptations made to the diving practice in response to the O'Dive results and their apparent effect.

Methods

This was a feasibility study, performed by DAN Europe research staff and volunteer divers during a dive cruise aboard a 'liveaboard' dive vessel, in the southern atolls area of The Maldives.

This study conforms to the Declaration of Helsinki and was part of a series of non-invasive bubble detection studies carried out by the Environmental, Occupational, Ageing (Integrative) Physiology Laboratory, Haute Ecole Bruxelles-Brabant (HE2B), Brussels, Belgium, approved by the Academic Bioethical Committee of Brussels (B200-2020-088). All divers received an oral explanation of the procedure, and the consequences of possibly detected bubbles were discussed beforehand. All participants were aware that, according to current scientific knowledge, the presence of bubbles does not indicate DCS to be present or imminent and does not need treatment if no symptoms of DCS are present. All divers were to dive according to their own dive plan, and no specific dive profiles were imposed. There was to be no interference with the group dive planning. All participants, experienced divers, gave written informed consent.

Diving was performed according to Maldivian law, which means: 'no deco diving' (no mandatory decompression stops), all dives less than 30 metres' seawater (msw) depth, less than 60 min, and surfacing with a minimum of 50 bars in the dive tank.

One person dived 'nitrox on air profiles' for increased security; nitrox tanks were limited, as due to a broken nitrox compressor they were filled when encountering other dive boats; all other divers used compressed air.

Several types of dive computers were used: Suunto D4i, Suunto D6, Suunto Zoop (RGBM algorithm), Mares Puck, Oceanic Geo (Buhlmann ZHL-16 algorithm). Average dive depths were around 25 msw, with an initial deep phase, then gradually ascending over 30 min to 10 msw, ending with a safety stop at 5 msw. Total dive times were mostly 60 min.

The O'Dive set consisted of an O'Dive One ultrasonic sensor with 2MHz wavelength (firmware version V6.08) and an iPad with the O'Dive One 'Vision' app (V. 1.8.42) (Azoth Systems, Ollioulles, France). The O'Dive set (a small waterproof case with the sensor and ultrasound gel, and an iPad in splashproof casing) were taken on board the 'dhoni' (small boat) dive vessel, and the first measurements were taken 10–20 minutes after exiting the water and taking off the dive gear. The second measurement was performed once back on the liveaboard vessel, respecting as much as possible the 30 min interval between two measurements.

The system requires measuring venous Doppler signals over the left and right subclavian vein, which then are counted as 'one measurement'. In short, the diver is instructed to, while seated and not moving, apply ultrasound gel on the sensor and place it in the subclavicular region, first on the left side. Visual instructions are displayed by the app. The mirror can be used to check the positioning (the primary intention is for the diver to perform the measurements on himself). Then, after confirmation that the sensor has been placed, the app displays an undulating line indicating the breathing-in and out rhythm to be followed, and a waveform pattern to check the signal quality. Once satisfied with the positioning, the diver can start the recording and this runs for 20 seconds. After this, the app indicates whether the recording was of sufficient quality to allow analysis, and if not, instructs the diver to repeat the measurement. Then, the right side is measured in a similar way, and once this is done, the app notifies that after 30 min a second set of measurements is

Table 1
Relevant data for participating divers. * = Nitrox used but computer set on air

Parameter	Diver 1	Diver 2	Diver 3	Diver 4	Diver 5	Diver 6
Age (years)	56	54	61	45	63	66
Sex	M	F	F	F	F	M
Body Mass Index (kg·m^2)	22.9	20.4	22.7	19.9	26	22.9
Dive experience (years)	35	35	40	29	35	40
Dive experience (dives)	1,500	800	2,190	2,000	1,100	3,800
Dive computer used	Suunto D4i	Oceanic Geo	Suunto Zoop	Suunto D6	Mares Puck	Suunto Zoop
Gas used	Air	Nitrox*	Air	Air	Air	Air

due. The diver then needs to input the depth, immersion time, dive duration, and stops performed in order to allow analysis. This permits the system to calculate the 'dive severity' as well as the timings of the two sets of recordings.

Whereas the app is conceived so that each diver can perform the measurements easily on him- or herself, for practical reasons all measurements were performed by one person (PG) on all divers, including himself. This allowed for a rapid succession of measurements and the 'investigator' to serve as time keeper for the second measurements.

Synchronisation of recordings must be performed with the Azoth server through Wi-Fi or cellular data. Analysis of the Doppler data is performed at the Azoth server side, and returned to the app upon the next synchronisation. Results are then presented in bar graphs, with the main indicator the 'quality of decompression' (Quality Index, QI) from 0 to 100, with colour codes (green: from 100 to 75; yellow: from 75 to 50; orange: below 50). The QI is lowered by two factors: a dive severity component (Cs) taking into the account the conservatism level of actual dive profile and a vascular bubbles component (Cb) computed from bubble counts, according to the formula QI = 100 – Cs – Cb.

Furthermore, the O'Dive app offers suggestions on how the QI of this dive could have been better, by simulating, for example, the effect of an extra or prolonged safety stop, the use of nitrox during that dive profile, etc. Because the app does not require the actual dive profile to be uploaded in order to allow evaluation, it is not entirely clear how these parameters are integrated in the O'Dive decompression model, only that the simulations "*are personalised by taking into account the vascular bubbles dynamics observed on your past dives which can evolve with the time*" (quoted from the app's help file and on the O'Dive website http://www.o-dive.com).

A 'tek' version of the O'Dive app is available', which includes the possibility to enter various gas mixes (bottom gas, decompression gas) into the data, select open or closed circuit diving, provide gradient factors, as well as allowing a link with some brands of dive computer to upload the actual dive profile. For the present evaluation, the 'O'Dive One' recreational version was used. The O'Dive 'Vision' software used was a special 'research' version that provided some form of a real-time monitoring system, in the sense that not only a Doppler waveform is displayed on the tablet, but also an acoustic signal of the heartbeat (from the neighbouring subclavian artery), breathing sounds and bubble sounds (heard as 'bubbly sounds' or clicks interspersed between the other audio). The 'public' version of the O'Dive app has the audio muted, and the displayed waveform is specifically treated as to not visualise the heartbeat and bubble signals, but only indicates by the waveform amplitude whether the sensor positioning is 'good' or 'suboptimal' (Azoth Systems, personal communication).

Evaluation of the O'Dive system's user-friendliness and diver acceptance was primarily subjective and impressions were collected throughout the dive trip from participant divers. A short questionnaire (using a modified Likert scale) was presented to the divers at the end of the trip, enquiring about their impressions.

Results

VGE DETECTION

Six divers were monitored over a period of 11 days. Demographic data are summarised in Table 1.

In total, 157 dives were monitored. For four divers, all dives were fully monitored, in two divers some data were missing (the second measurement of a dive was not performed for reasons unrelated to the device, such as the diver not being available due to lunch or other personal reasons). Monitoring several divers implied the creation of a separate account for each diver in the app, however switching between the various accounts was easy and fast, as the option to 'remain logged on' obviated the need to each time enter a password.

Positioning the sensor and recording the signals was straightforward, as the O'Dive app provides step-by-step instructions, and evaluates the quality of the recorded data immediately. If the signal is not sufficiently clear

Table 2
O'Dive data. Cb = vascular bubbles component of the QI; QI = dive quality index; VGE = vascular gas emboli

Parameter	Diver 1	Diver 2	Diver 3	Diver 4	Diver 5	Diver 6
Dives monitored	28	23	29	23	27	27
Mean QI	85	88	88	85	74	86
Dives with VGE *n* (%)	10 (36%)	7 (30%)	3 (10%)	11 (48%)	26 (96%)	4 (15%)
Mean Cb for dives with VGE	10.8	10.6	9.3	10.2	16.5	9.3
Mean Cb for all dives	3.9	3.2	1.0	4.9	15.9	1.4

to allow evaluation by the O'Dive servers (for instance because of incorrect positioning), the app indicates that the measurement must be repeated because of 'low signal quality' or 'interpretation difficulties'.

During the first five days, no synchronisation with Azoth's server was possible because of low speed cellular data signal. After this, daily synchronisation was done, and each day, the analysis results of the previous day's dives was available, and was briefly reviewed by most of the participant divers (without detailed discussion).

Bubble signals were detected after 61 of the 157 dives (39%). In all divers, bubble signals were detected after some of the deeper or more strenuous dives, however, the O'Dive evaluation mostly remained 'green' (QI > 75) for all divers except one. In this diver (diver five), VGE were detected after virtually every dive (26 of 27 dives). In accordance with the intended use of the O'Dive system, adaptations were performed by that diver for subsequent dives such as more 'classical multi-level' dive profiles (deepest part first, followed by longer time at the 10 msw zone, followed by a safety stop). Further suggestions for improving the 'quality of decompression' offered by the O'Dive app (and visualised by simulating the modification alongside the actual analysis) were either to increase the safety stop duration (which would have necessitated a > 10min extension), to use hyperoxic mixes during decompression, or to dive nitrox for that profile (nitrox 32 would have increased the safety to almost maximal). This 'nitrox on air profile' suggestion was tested on one of the last dives (first dive of the day), and seemed indeed to result in an improvement of the QI (see Discussion). O'Dive data are summarised in Table 2.

Because of the small size of the test population and the lack of homogeneity, no clear correlation can be established between the number and frequency of detected VGE ('VGE dives' and/or Cb component) and biometric data. However, (female) diver four with the lowest body mass index (BMI 19.9 $kg \cdot m^{-2}$) had the second most frequent 'VGE dives' (11/23, 48%), though each time with a Cb of 10 or less and an average Cb of 4.9. Female diver five had the highest BMI (26.0 $kg \cdot m^{-2}$) and also the most frequent 'VGE dives' (26/27, 96%), with a Cb of 10 to 40, and a much higher average Cb of 15.9. Female diver two (with the second lowest BMI: 20.4 $kg \cdot m^{-2}$) used nitrox 32% as breathing gas while keeping the computer on 'air' setting ('nitrox on air profiles') for increased security because of a known persistent ('patent') foramen ovale (PFO), and had only seven 'VGE dives' (7/23, 30%). Using the simulation of the O'Dive app, if she would have been using air, not nitrox for these same dives, she would have had (according

Figure 1
Field measurements using the O'Dive system

to the Azoth model) VGE in 17/23 dives (74%) with an average Cb of 15.

EASE OF USE OF THE O'DIVE SYSTEM

The O'Dive system was found by the investigator (PG) easy to set up and use, even on the limited space of a 'dhoni' dive deck (see Figure 1). Switching between the various accounts to test different divers was straight forward and fast. Time to scan was typically less than 2 minutes per diver (20 seconds to prepare the sensor, 20 seconds per side). The tablet used was a regular iPad in a rugged splashproof housing. Over the test period, almost two flasks of ultrasound gel were used (400 ml) as well as six boxes of paper tissue.

DIVER ACCEPTANCE

Diver acceptance was very good, and none of the divers found the testing cumbersome or too time consuming. The results of the short questionnaire (modified Likert scale), while not formally validated, indicate that:

- The scanning after each dive was not considered bothersome;
- The procedure was considered simple and easy;
- The information obtained from the app was 'easy to understand';
- Most divers would not to adapt their next dive depending on the previous dive scanning (note that a formal O'Dive evaluation was only available the next day, with already two or three further dives performed);
- Diver five indicated that she adapted her general diving behaviour since being scanned (motivated by the O'Dive evaluation of her previous dives), and also indicated that she was feeling 'somewhat more stressed during the dives'. Indeed, some mental stress was noted immediately prior and during the scanning. This may have been due to the visual and acoustic indication that VGE were present, and it is for this reason that the public version of the O'Dive app does not disclose these indicators in real time (Azoth Systems, personal communication). The goal is to obtain a maximum acceptability of the method to all divers, not inducing extra stress (Azoth Systems, personal communication);
- Some divers considered a systematic scanning useful (but the questionnaire did not probe whether they would buy the system for personal use);
- One diver indicated that as a diving professional the system might be useful to monitor their personal exposure and take a day 'off' in case this exposure seemed to become too 'hazardous' (not further specified).

From an observer point of view, it was noted that using the O'Dive system generated multiple instances of discussing safe diving behaviour, the uncertainties of decompression theory and practice, and how to mitigate those. Divers with already 'safe' diving habits (e.g., performing systematic long safety stops, diving 'nitrox on air profiles') felt reinforced in this behaviour, and issues such as staying well within the no-decompression limit of the dive computer, the usefulness or uselessness of 'deep stops', how to prolong the safety stop and the advantages and risks of nitrox were all discussed in depth.

Discussion

VGE DETECTION

VGE incidence

The results confirm that after a significant proportion (61/157 dives, 39%) of recreational dives, VGE are detected,[3] even though all dives were performed well within the no-decompression limits of the dive computers used, all included a 3–6 min safety stop at 5 msw, and not more than three dives per day were made, with surface intervals never shorter than 90 min. Even though diving was performed in a group and all divers had, for each dive, (roughly) a similar dive profile as the other divers, there was a large inter-personal variability in numbers of VGE detected. Two of the divers almost never produced VGE (divers three and six), one diver had VGE after virtually every dive (diver five), and two divers had moderate amounts of VGE every 4–5 dives only (divers one and four) (data not shown). No external factors which could have led to a form of 'preconditioning'[18] were any different between the divers. While this is not a formal confirmation of previously reported inter- and intra-personal differences in VGE production[19] (as personal characteristics were not matched between divers), it is an interesting observation that in a single dive group, similar dives would lead to different VGE in different divers, and that the dive profile in itself might not always be correct in predicting 'the risk' of a dive.

Bubble grades

O'Dive bubble grades, as provided by Azoth after the end of the trip, were generally low (grade 0 to grade 1, except for diver five with regular grade 2's, two dives with grade 3 and one dive with grade 4 bubbles). No separate VGE detection method was simultaneously performed so a correlation between the O'Dive grading and other validated VGE grading methods, as recommended by Møllerløkken et al.[7] could not be established.

Although preliminary data from another dive trip, where O'Dive bubble grades were compared with 2D ultrasound recordings, show a good match between O'Dive grades and Eftedal-Brubakk (EB) grades (Costantino Balestra, personal communication), this lack of formal validation makes the O'Dive system as yet unsuited as a research tool. Until such formal validation takes place, access to the sound recordings (to perform actual bubble counts according to the Kisman-Masurel or EB scale) would be necessary for research. These recordings can be made available by Azoth (and actually were for the dives of this trip) but due to the

nature of the trip and the fact that the actual profiles of the dives were not recorded, a formal comparison is not intended at this point.

Dive behaviour modification in response to O'Dive data

Diver five had a consistently lower QI after each dive, and on many occasions bubbles were heard during scanning (Cb in the range of 20 to 40, consistently). Simulations from the O'Dive app suggested that using nitrox for each dive profile (i.e., 'nitrox on air') would have increased the QI ('safety') much more than performing longer safety stops. Because nitrox was not readily available, this diver modified her diving behaviour by optimising the dive profiles to be more straightforward 'multi-level' and increasing her safety stop duration. Near the end of the trip, as this did not seem to have much effect, it was decided to do a first dive of the day (dive 24/27 for this diver, with surface interval > 14 hours) with 'nitrox on air'. The O'Dive app was 'tricked' by indicating that this dive was still made on air only. Evaluation by the Azoth analysis later on indeed indicated an improved QI of 76 ('green') and a Cb of only 10, suggesting an effect of the reduced nitrogen load. The next three dives were again on air but still yielded 'green' QIs and Cb of 10 or less; this may have been the effect of a reduced inert gas accumulation (from that one nitrox dive) or just a coincidence (different dives), however, the sudden drop from Cb in the 20–30 range during the nine previous dives, was obvious (data not shown).

Diver two, using 'nitrox on air' for every dive, had VGE after some dives (7/23, 30%) and low Cb (average 3.2). The O'Dive app simulation indicated that, would she have been doing these dives on air, 74% of these dives would have generated VGE and the average Cb would have been 14.9, not 3.2. The QI would have decreased from average 89 to 64 (data not shown). Even though this simulation remains speculative (these air dives were not performed) it seems logical that a higher nitrogen load would lead to higher VGE counts in this diver and thus possibly a higher risk of DCS. In this regard, the O'Dive app simulation clearly stimulated this diver to continue using 'nitrox on air', even though subjectively she felt the dives were 'not very strenuous' and 'safe'.

The other divers indicated that they felt reinforced in their diving behaviour by the O'Dive evaluations. Diver six, a diving professional, stated that she might consider 'taking a day off' in case the O'Dive results would indicate an increasingly high VGE presence.

VGE and decompression sickness

Diver three had a long history of repeated DCS symptoms after diving (presenting as cutis marmorata and general fatigue), which was attributed to the presence of a PFO). Because of the impact on her diving pleasure (it occurred even after dives much less strenuous than the ones performed during this trip) and the ever-present risk of more serious DCS to occur, she had her PFO closed percutaneously four years ago. After this procedure, she had a complete absence of any symptoms following similar or even more strenuous dives. In this diver, because the closure of a PFO has no known impact on the propensity to generate decompression-related VGE, it was expected that VGE would have been detected after most dives (which did not arterialise through the PFO anymore, hence did not cause symptoms of DCS). However, no or very few bubbles were detected, and only after three dives (see Table 2). The O'Dive sensor's detection limit for bubbles has not been officially specified by the developers (Azoth Systems, personal communication), therefore it is possible that smaller-than-detectable bubbles were responsible in this diver for the regular symptoms of DCS prior to the PFO closure.[8,20] Alternatively, as the O'Dive sensor scans only the subclavian veins, it is possible that VGE were present but originated from the splanchnic or femoral vein territories[21] and thus were not detected in the subclavian veins.[14,22] As no simultaneous subclavian scanning and echocardiographic imaging was performed, this remains speculative.

DIVER ACCEPTANCE

Divers were able to recognise breath sounds, arterial sounds and bubble sounds (when obvious) on their own scan, and bubble sounds seemed to make a bigger impression than the colour graphs. None of the divers found the testing cumbersome or too time consuming. This may have been because they did not have to perform the measurements themselves and were only called to the scanning position when required by the investigator. A self-scanning procedure would undoubtedly have impacted more on their post-dive time management and thus on their overall experience.

The primary intended use of the O'Dive system is indeed to be a self-evaluation by each diver; however, the option of a scanning procedure to be offered by dive clubs or instructors to their clients is specifically mentioned by the manufacturers as a possibility.

STUDY STRENGTHS AND WEAKNESSES

This small field study was primarily intended to report on the real-world use of the O'Dive system, not to report on the safety of certain diving practices, or the accuracy or effect of using the O'Dive sensor and app. The participants were all experienced divers. It was felt that these divers would not be unduly impressed by the O'Dive app and hence modify their diving behaviour significantly at the slightest bubble detection, as this would possibly have placed an unacceptable stress on the diving group as a whole. It is possible the O'Dive system would appeal somewhat less to novice divers (it is not cheap, and some decompression physiology background knowledge is assumed).

Diver acceptance was probably slightly over-estimated as no burden was placed on the divers to do the measurements. The main investigator (PG) was experienced in the use of the system. Using a single investigator instead of individual divers measuring themselves was justified by the fact that only one O'Dive system was available, and that it was impossible to estimate the time needed to achieve all measurements on six divers after every dive. On the other hand, taking into their own hands the responsibility for the measurements could in some cases increase the motivation of divers to adopt a 'safer' behaviour.

The proprietary method of quality assessment and evaluation (mainly based on a number of doctoral theses only available in French) and the lack of validation between O'Dive bubble grades and other methods for quantifying VGE, make this tool (for now) unsuitable for proper dive research, even though the scanning procedure is very simple and quick.

The 'suggestions to increase dive safety' offered by the app's simulation function (prolonged safety stop, use of less nitrogen in the breathing gas for a similar profile) yield a 'factor of increased safety', which is visually attractive and easy to understand. However, it is based on a proprietary and non-transparent algorithm. Following these suggestions has not been demonstrated to result in lower rate of DCS (and relies on the statistical assumption that 'less VGE would result in less DCS'). This may possibly lead to a false sense of security.

Conclusions

The O'Dive system may contribute to increasing dive safety by making divers immediately aware of the potential consequences of certain types of diving behaviour. It was noted that this type of monitoring either reinforced divers in their safe diving habits or incited them to modify their dive planning. Whether this is a lasting effect is not known.

References

1 Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. Lancet. 2011;377:153–64. doi: 10.1016/S0140-6736(10)61085-9. PMID: 21215883.

2 Mitchell SJ. DCS or DCI? The difference and why it matters. Diving Hyperb Med. 2019;49:152–3. doi: 10.28920/dhm49.3.152-153. PMID: 31523788. PMCID: PMC6881199.

3 Dunford RG, Vann RD, Gerth WA, Pieper CF, Huggins K, Wacholtz C, et al. The incidence of venous gas emboli in recreational diving. Undersea Hyperb Med. 2002;29:247–59. PMID: 12797666.

4 Eftedal OS, Lydersen S, Brubakk AO. The relationship between venous gas bubbles and adverse effects of decompression after air dives. Undersea Hyperb Med. 2007;34:99–105. PMID: 17520861.

5 Nishi RY, Kisman KE, Eatock BC, Buckingham IP, Masurel G. Assessment of decompression profiles and divers by Doppler ultrasonic monitoring. In: Bachrach AJ, Matzen MM, editors. Underwater physiology VII: Proceedings of the seventh symposium on underwater physiology. Bethesda (MD): Undersea Medical Society; 1981. p. 717–27.

6 Møllerløkken A, Gaustad SE, Havnes MB, Gutvik CR, Hjelde A, Wisløff U, et al. Venous gas embolism as a predictive tool for improving CNS decompression safety. Eur J Appl Physiol. 2012;112:401–9. doi: 10.1007/s00421-011-1998-9. PMID: 21594696. PMCID: PMC3258401.

7 Doolette DJ. Venous gas emboli detected by two-dimensional echocardiography are an imperfect surrogate endpoint for decompression sickness. Diving Hyperb Med. 2016;46:4-10. PMID: 27044455.

8 Blogg SL, Gennser M, Møllerløkken A, Brubakk AO. Ultrasound detection of vascular decompression bubbles: the influence of new technology and considerations on bubble load. Diving Hyperb Med. 2014;44:35–44. PMID: 24687484.

9 Møllerløkken A, Blogg SL, Doolette DJ, Nishi RY, Pollock NW. Consensus guidelines for the use of ultrasound for diving research. Diving Hyperb Med. 2016;46:26–32. PMID: 27044459.

10 Eftedal O, Brubakk AO. Agreement between trained and untrained observers in grading intravascular bubble signals in ultrasonic images. Undersea Hyperb Med. 1997;24:293–9. PMID: 9444060.

11 Spencer MP, Johanson A. Investigation of new principles for human decompression schedules using Doppler ultrasound blood bubble detection. Technical Report to ONR on Contract N00014-73-C-0094. Seattle (WA): Institute for Environmental Medicine and Physiology; 1974.

12 Kisman KE, Masurel G. Method for evaluating circulating bubbles detected by means of the Doppler ultrasonic method using the "K.M. code" (English translation of 283 CERTSM 1983). Toulon: Centre d'Etudes et de Recherches Techniques Sous-Marines; 1983.

13 Germonpré P, Papadopoulou V, Hemelryck W, Obeid G, Lafère P, Eckersley RJ, et al. The use of portable 2D echocardiography and 'frame-based' bubble counting as a tool to evaluate diving decompression stress. Diving Hyperb Med. 2014;44:5–13. PMID: 24687479.

14 Hugon J, Metelkina A, Barbaud A, Nishi R, Bouak F, Blatteau JE, et al. Reliability of venous gas embolism detection in the subclavian area for decompression stress assessment following scuba diving. Diving Hyperb Med. 2018;48:132–40. doi: 10.28920/dhm48.3.132-140. PMID: 30199887. PMCID: PMC6205931.

15 Hugon J. Decompression models: review, relevance and validation capabilities. Undersea Hyperb Med. 2014;41:531–56. PMID: 25562945.

16 Hugon J, Nishi R, Bouak F, Blatteau JE, Gempp E. A stress index to enhance DCS risk assessment for both air and mixed gas exposures. Undersea Hyperb Med. 2015;42:442.

17 Bennani Y. Caractérisation de la diversité d'une population à partir de mesures quantifiées d'un modèle non-linéaire. Application à la plongée hyperbare. 2015. Available from: https://tel.archives-ouvertes.fr/tel-01306349. [cited 2020 March 15]. French.

18 Germonpré P, Balestra C. Preconditioning to reduce decompression stress in scuba divers. Aerosp Med Hum Perform. 2017;88:114–20. doi: 10.3357/AMHP.4642.2017. PMID: 28095955.

19 Papadopoulou V, Germonpré P, Cosgrove D, Eckersley RJ, Dayton PA, Obeid G, et al. Variability in circulating gas emboli after a same scuba diving exposure. Eur J Appl Physiol. 2018;118:1255–64. doi: 10.1007/s00421-018-3854-7. PMID: 29616324.

20 Papadopoulou V, Tang MX, Balestra C, Eckersley RJ, Karapantsios TD. Circulatory bubble dynamics: From physical to biological aspects. Adv Colloid Interface Sci. 2014;206:239–49. doi: 10.1016/j.cis.2014.01.017. PMID: 24534474.
21 Brebeck AK, Deussen A, Range U, Balestra C, Cleveland S, Schipke JD. Beneficial effect of enriched air nitrox on bubble formation during scuba diving. An open-water study. J Sports Sci. 2018;36:605–12. doi: 10.1080/02640414.2017.1326617. PMID: 28531363.
22 Sawatzky KD. The relationship between intravascular Doppler-detected gas bubbles and decompression sickness after bounce diving in humans (Thesis). Toronto (ON): York University; 1991.

Acknowledgements

We acknowledge all the divers, boat crew and cruise directors of the M/V Blue Spirit for their kind collaboration and taking a genuine interest in the research, and dedicating extra time to help us perform the measurements. During the dive trip, expert telephone and (occasional) email support was available from Azoth Systems, and in particular Mr Julien Adler, who also assisted after the field trip with improved access to data. The very latest version of the O'Dive App, specifically dedicated for research and offering access to the raw data (although not used for this report) were made available by Azoth Systems.

Conflicts of interest and funding

Nil conflicts of interest. The O'Dive sensor and app were provided by DAN Europe Research. Azoth Systems funded the immediate release of this paper.

Submitted: 09 April 2020
Accepted after revision: 07 July 2020

Short communication

Considerations for scuba and breath-hold divers during the COVID-19 pandemic: A call for awareness

Antonis Elia[1], Mikael Gennser[1]

[1] *Division of Environmental Physiology, School of Chemistry, Bioengineering and Health, KTH Royal Institute of Technology, Stockholm, Sweden*

Corresponding author: *Dr Antonis Elia, Division of Environmental Physiology, School of Chemistry, Bioengineering and Health, KTH Royal Institute of Technology, Stockholm, Sweden*
antonise@kth.se

Key words
Apnoea; Breath-hold diving; COVID-19; Hypoxaemia; Scuba diving; SARS-CoV-2; Lungs

Abstract

(Elia A, Gennser M. Considerations for scuba and breath-hold divers during the COVID-19 pandemic: A call for awareness. Diving and Hyperbaric Medicine. 2020 December 20;50(4):413–416. doi: 10.28920/dhm50.4.413-416. PMID: 33325024.)
In late 2019, a highly pathogenic novel coronavirus (CoV), severe acute respiratory syndrome (SARS)-CoV-2 emerged from Wuhan, China and led to a global pandemic. SARS-CoV-2 has a predilection for the pulmonary system and can result in serious pneumonia necessitating hospitalisation. Computed tomography (CT) chest scans of patients with severe symptoms, show signs of multifocal bilateral ground or ground-glass opacities (GGO) associated with consolidation areas with patchy distribution. However, it is less well known that both asymptomatic and mild symptomatic patients may exhibit similar lung changes. Presumably, the various pathological changes in the lungs may increase the risk of adverse events during diving (e.g., lung barotrauma, pulmonary oedema, etc.), thus these lung manifestations need to be considered prior to allowing resumption of diving. Presently, it is not known how the structural changes in the lungs develop and to what extent they resolve, in particular in asymptomatic carriers and patients with mild disease. However, current evidence indicates that a month of recovery may be too short an interval to guarantee complete pulmonary restitution even after COVID-19 infections not demanding hospital care.

Introduction

Coronaviruses (CoVs) are large enveloped non-segmented positive sense RNA viruses associated with respiratory disease in humans.[1] Although COVID-19 is caused by a new virus, severe acute respiratory syndrome-(SARS)-CoV-2, genomic analysis shows that it, (*i*) belongs in the same beta-coronavirus clade as Middle Eastern Respiratory Syndrome (MERS) and SARS-CoV-1, (*ii*) shares a homological sequence with SARS-CoV, (*iii*) and like SARS-CoV-1, enters human host cells via the angiotensin-converting enzyme 2 receptor.[1] Moreover, similarly to MERS-CoV and SARS-CoV, SARS-CoV-2 has a predilection for the pulmonary system and can result in severe pneumonia, induce serous fluid, fibrin exudates and hyaline membrane formation in the alveoli.[2,3] Although the magnitude of these pathological manifestations are largely dictated by the severity of the disease, low-dose computed tomography (CT) chest scans indicate that both mild symptomatic patients and asymptomatic carriers commonly exhibit similar lung lesions and airway abnormalities (ground glass opacities [GGO], fibrotic streaks, diffuse consolidation, etc.).[4,5] The pathological manifestations exhibited by severe but also mild symptomatic patients and asymptomatic carriers raise serious safety concerns regarding people involved in diving-related activities and accordingly warrant further consideration. Thus, the purpose of this communication is to raise awareness of the effects of COVID-19 on the pulmonary system and the possible risks associated with exposure to diving-related activities during and/or following COVID-19 infection.

COVID-19 and the pulmonary system

SEVERE SYMPTOMATIC CASES

The most common pulmonary CT-imaging feature in severe COVID-19 patients is the presence of multifocal bilateral GGO associated with consolidation areas with patchy distribution, mainly in peripheral/subpleural lung regions and with greater involvement of the posterior regions and lower lobes.[3,6,7] These areas of GGO may be admixed with focal consolidation and/or associated with superimposed intralobular and/or interlobular reticulations of septal thickening, resulting in a ‘crazy paving pattern’. Additionally, vacuolar and microvascular dilation signs, fibrotic streaks, air bronchograms and bronchus distortion have also been documented.[7] Linear consolidations and

other signs suggesting organising pneumonia such as the reverse halo sign are frequently observed.[3,8] The number of lung segments involved was found to relate to the severity of the disease and with the opacities tending to thicken with its progression.[3,6]

MILD SYMPTOMATIC CASES AND ASYMPTOMATIC CARRIERS

The literature is currently overwhelmed by a plethora of studies delineating the clinical manifestations of severe symptomatic COVID-19 patients. In contrast, limited data are available for asymptomatic carriers and patients with only mild clinical symptoms. Mainly owing to these discrepancies, there is presently limited awareness regarding the alarming lung alterations commonly observed in individuals who have undergone less severe versions of the infection. Newly published data highlighted that out of 932 patients with mild clinical symptoms, 581 (62%) exhibited lung lesions in a low-dose-CT-scan.[5] Similarly, lung GGO, fibrotic streaks and/or diffuse consolidation were also reported in asymptomatic carriers.[4,9,10] Although the CT-scan scores are higher in severe and mild symptomatic than asymptomatic cases, these observations should be considered prior to allowing resumption of diving.

PULMONARY SEQUELAE IN DISCHARGED COVID-19 PATIENTS

To the best of our knowledge, to date, only one study exists that investigated the pulmonary sequelae in discharged COVID-19 patients.[11] In this study, 149 patients (mean age: 43 years) underwent CT-scans at discharge and thereafter at one-week intervals up to three-weeks post. At discharge, CT-scans showed signs of GGO (84%), fibrous stripes (54%), and thickening of the adjacent pleura (22%). Although these residual abnormalities gradually decreased, with pulmonary lesions being completely absorbed by week three in 53% of these patients, in more than 40% GGO and fibrous stripes manifestations persisted throughout the three-week radiological follow-up, implying that a three-week recovery is insufficient to guarantee complete pulmonary restitution.

Notably, such pulmonary CT-changes are not necessarily associated with subjective or verified signs of degraded physical performance. In *Pneumocystis carinii* pneumonia, a disease with similar CT-findings, and which also presents with dry cough and silent hypoxaemia, symptoms have been shown to disappear earlier than the radiological findings.[12] An example of a similar finding with COVID-19 was a fire-fighter who had recovered from a mild case of the disease and was able to complete a 17 km run, but still showed areas of GGO on a subsequent pulmonary CT during a fitness-to-dive examination. Based on the CT-scan findings the diver was not permitted to resume diving (P Ullström MD, personal communication). Similarly, inability to maintain peripheral oxygen saturation during light exercise has been reported in two out of six asymptomatic male divers 5–6 weeks after their initial diagnosis, and four of the six divers' CT-scans still showed "*impressive structural lung changes*".[13] Collectively, these findings may suggest that longer recovery periods could be necessary prior to resuming any diving-related activities. However, at present, no firm conclusions can be drawn either regarding the pulmonary sequelae in COVID-19 patients, or how long after having contracted COVID-19 one should wait before starting to dive. The diverse structural lung manifestations observed across severe, mild and asymptomatic patients suggest that recovery periods amongst patients may vary markedly. Follow-up studies including pulmonary function testing and chest CT-scans will help to clarify the extent of the sequelae on the pulmonary system but also shed some light on the timeframe(s) of recovery.

Drawing from past experiences: SARS-CoV-1

Chest CT findings in confirmed cases of COVID-19 generally resemble those associated with SARS-CoV-1, with viral pneumonia and acute lung injury that may progress to the typical imaging features of acute respiratory distress syndrome in critically ill patients.[2] Studies that investigated the pulmonary sequelae and physical performance characteristics of severe SARS-CoV-1 survivors highlighted abnormal CT findings (e.g., lung fibrotic changes) as well as persisting reductions in exercise capacity (6-min walk test) up to one-year post-discharge.[14,15] Surprisingly, although an initial rapid reduction in the percentage of pulmonary lesions was recorded one-year post discharge (from 9.40% (SD 7.83) to 3.20% (4.78)), no further improvements were documented with the percentage of lesions remaining stable 14 years later (4.60% (6.37)).[16] In contrast, limited and conflicting evidence exists regarding the long-term effects of asymptomatic and less severe SARS-CoV-1 survivors. In 14 asymptomatic young survivors (mean age 14.7 years) residual high-resolution-CT demonstrated thoracic abnormalities even 15 months after initial diagnosis.[17] On the other hand, in less severe adult SARS-CoV-1 survivors (mean age 42 years), spirometry, lung volume measures, and diffusion capacity were within normal limits at three months post-discharge.[18] Conjointly, the aforementioned studies provide further evidence to support that a month of recovery may be too short an interval to guarantee complete pulmonary restitution from a CoV infection.

Possible risks associated with diving during/after COVID-19 pulmonary infection

The various pathological changes in the lungs may increase the risk of adverse events during diving. The initial effect of the viral infection appears to be formation of a local subpleural interstitial oedema which manifests on CT as GGO. It has been pointed out that this fluid accumulation occurs mainly in lung structures where stress and strain are concentrated.[19] As the disease progresses areas of consolidation and fibrotic strands appear more frequently. These changes are considered to be associated with increased

risk of pulmonary barotrauma during scuba diving due to air trapping and stress concentration.[20] It should also be noted that in more severe cases, pneumoceles and pulmonary blebs have been observed. Also, a number of case reports of COVID-19 patients with spontaneous pneumothoraces have been published.[21] Although far from confirmed, it is conceivable that the disease leads to a reduced strength of supportive structures in the lungs.

A major fixture of the COVID-19 infection is arterial hypoxaemia. This appears to be more related to circulatory dysfunction (e.g., inflammation and/or pulmonary thromboembolism) than an inability to ventilate the lungs properly.[19] It is, of course, of major importance that normal physical exercise capacity has been restored prior to restarting breath-hold or compressed gas diving. The fact that the viral infection produces an interstitial oedema indicates that the vasculature in at least some pulmonary areas is more susceptible to fluid leakage than normal. Given that diving activities (especially breath-hold diving) often produce larger transvascular pressures in the pulmonary circulation (e.g., head-out immersion, pulmonary squeeze during deep breath-hold dives, negative hydrostatic imbalance) than normal, it is important that the integrity of the vessels has been restored before resuming diving-related activities to avoid an increased risk of immersion pulmonary oedema. Even though functional tests (e.g., exercise test with pulse oximetry and/or echocardiography[22]) can be utilised to evaluate whether recovery has restored (*i*) normal oxygenation and (*ii*) vascular integrity, complete healing of pulmonary structural defects can only be ascertained by CT-scan of the lungs.

Conclusions

It is clear from the quoted research articles and case reports that pulmonary changes visible on CT-scans are frequent in subjects with only mild symptoms of COVID-19 infection. It is not known how the structural changes in the lungs develop and to what extent they resolve in patients with mild disease. In the one published follow-up study in hospitalised patients only slightly more than half of the patients showed complete radiological resolution three weeks after discharge.[11] Present evidence suggests that a month of recovery may be too short an interval to guarantee complete pulmonary restitution even after COVID-19 infections not demanding hospital care. However, follow-up studies will help to clarify the extent of the sequelae on the pulmonary system and shed light on the timeframe(s) of recovery. In the meantime, a precautionary principle must rule when allowing return to diving.

References

1 Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020;395(10224):565–74. doi: 10.1016/S0140-6736(20)30251-8. PMID: 32007145. PMCID: PMC7159086.

2 Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses. 2019;11(1):59. doi: 10.3390/v11010059. PMID: 30646565. PMCID: PMC6357155.

3 Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): A systematic review of imaging findings in 919 patients. Am J Roentgenol. 2020;215:87–93. doi: 10.2214/AJR.20.23034. PMID: 32174129.

4 Inui S, Fujikawa A, Jitsu M, Kunishima N, Watanabe S, Suzuki Y, et al. Chest CT findings in cases from the cruise ship "Diamond Princess" with Coronavirus disease 2019 (COVID-19). Radiology: Cardiothoracic Imaging. 2020;2(2):e200110. doi: 10.1148/ryct.2020200110.

5 Lagier J-C, Million M, Gautret P, Colson P, Cortaredona S, Giraud-Gatineau A, et al. Outcomes of 3,737 COVID-19 patients treated with hydroxychloroquine/azithromycin and other regimens in Marseille, France: A retrospective analysis. Travel Med Infect Dis. 2020:36:101791. doi: 10.1016/j.tmaid.2020.101791. PMID: 32593867. PMCID: PMC7315163.

6 Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes at chest CT during recovery from Coronavirus disease 2019 (COVID-19). Radiology. 2020;295(3):715–21. doi: 10.1148/radiol.2020200370. PMID: 32053470. PMCID: PMC7233367.

7 Zhou S, Wang Y, Zhu T, Xia L. CT features of Coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. Am J Roentgenol. 2020;214:1287–94. doi: 10.2214/AJR.20.22975. PMID: 32134681.

8 Wang Y, Dong C, Hu Y, Li C, Ren Q, Zhang X, et al. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: A longitudinal study. Radiology. 2020;296(2):E55–E64. doi: 10.1148/radiol.2020200843. PMID: 32191587. PMCID: PMC7233482.

9 Meng H, Xiong R, He R, Lin W, Hao B, Zhang L, et al. CT imaging and clinical course of asymptomatic cases with COVID-19 pneumonia at admission in Wuhan, China. J Infect. 2020;81(1):e33–e39. doi: 10.1016/j.jinf.2020.04.004. PMID: 32294504. PMCID: PMC7152865.

10 Kong W, Wang Y, Hu J, Chughtai A, Pu H. Comparison of clinical and epidemiological characteristics of asymptomatic and symptomatic SARS-CoV-2 infection: A multi-center study in Sichuan Province, China. Travel Med Infect Dis. 2020:37:101754. doi: 10.1016/j.tmaid.2020.101754. PMID: 32492485.

11 Liu D, Zhang W, Pan F, Li L, Yang L, Zheng D, et al. The pulmonary sequalae in discharged patients with COVID-19: A short-term observational study. Respir Res. 2020;21(1):125. doi: 10.1186/s12931-020-01385-1. PMID: 32448391. PMCID: PMC7245637.

12 Datta D, Ali SA, Henken EM, Kellet H, Brown S, Metersky ML. Pneumocystis carinii pneumonia: The time course of clinical and radiographic improvement. Chest. 2003;124:1820–3. PMID: 14605054.

13 Hartig F. Tauchen nach Covid-19-Erkrankung 2020. [cited 2020 June 20]. Available from: https://www.wetnotes.eu/tauchen-nach-covid-19-erkrankung/. [German].

14 Xie L, Liu Y, Fan B, Xiao Y, Tian Q, Chen L, et al. Dynamic changes of serum SARS-Coronavirus IgG, pulmonary function and radiography in patients recovering from SARS after hospital discharge. Respir Res. 2005;6(1):5. doi: 10.1186/1465-9921-6-5. PMID: 15638943. PMCID: PMC545044.

15 Wong K-t, Antonio GE, Hui DSC, Ho C, Chan P-n, Ng W-h, et al. Severe acute respiratory syndrome: Thin-section computed tomography features, temporal changes, and clinicoradiologic correlation during the convalescent period. J Comput Assist Tomogr. 2004;28:790–5. doi: 10.1097/00004728-200411000-00010. PMID: 15538152.
16 Zhang P, Li J, Liu H, Han N, Ju J, Kou Y, et al. Long-term bone and lung consequences associated with hospital-acquired severe acute respiratory syndrome: A 15-year follow-up from a prospective cohort study. Bone Res. 2020;8:8. doi: 10.1038/s41413-020-0084-5. PMID: 32128276. PMCID: PMC7018717.
17 Yu CCW, Li AM, So RCH, McManus A, Ng PC, Chu W, et al. Longer term follow up of aerobic capacity in children affected by severe acute respiratory syndrome (SARS). Thorax. 2006;61(3):240–6. doi: 10.1136/thx.2005.046854. PMID: 16449271. PMCID: PMC2080724.
18 Tansey CM, Louie M, Loeb M, Gold WL, Muller MP, de Jager J, et al. One-year outcomes and health care utilization in survivors of severe acute respiratory syndrome. Arch Intern Med. 2007;167:1312–20. doi: 10.1001/archinte.167.12.1312. PMID: 17592106.
19 Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, Brazzi L, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med. 2020;46:1099–102. doi: 10.1007/s00134-020-06033-2. PMID: 32291463. PMCID: PMC7154064.
20 Francis J. Pulmonary barotrauma: A new look at mechanisms. SPUMS Journal. 1997;27:205–18.
21 Spiro JE, Sisovic S, Ockert B, Böcker W, Siebenbürger G. Secondary tension pneumothorax in a COVID-19 pneumonia patient: A case report. Infection. 2020;18:1–4. doi: 10.1007/s15010-020-01457-w. PMID: 32557347. PMCID: PMC7301769.
22 Sadler C, Alvarez Villela M, Van Hoesen K, Grover I, Lang M, Neuman T, Lindholm P. Diving after SARS-CoV-2 (COVID-19) infection: Fitness to dive assessment and medical guidance. Diving Hyperb Med. 2020;50:281–90. doi: 10.28920/dhm50.3.281-290.

Conflicts of interest and funding: nil

Submitted: 27 June 2020
Accepted after revision: 28 August 2020

Common mental health conditions among navy divers: A brief report

Charles H Van Wijk[1], Jarred H Martin[2], Nazneen Firfirey[1]

[1] *Institute for Maritime Medicine, Simon's Town, South Africa*
[2] *Department of Psychology, University of Pretoria, South Africa*

Corresponding author: *Dr Charles H Van Wijk, Institute for Maritime Medicine, PO Box 494, Simon's Town 7995, South Africa*
chvanwijk@gmail.com

Key words
Anxiety; Depression; Health surveillance; Psychology

Abstract
(Van Wijk CH, Martin JH, Firfirey N. Common mental health conditions among navy divers: A brief report. Diving and Hyperbaric Medicine. 2020 December 20;50(4):417–420. doi: 10.28920/dhm50.4.417-420. PMID: 33325025.)
Introduction: A recent article reported on common mental health conditions among recreational scuba divers, and observed that the prevalence mirrored national population figures. This raised the question of the extent to which this might also be the case among professional divers. No data on commercial divers could be located; this paper presents the situation among navy divers.
Methods: Mental health survey data from 132 South African Navy divers were reviewed to describe the 12-month prevalence of common mood, anxiety, and alcohol misuse disorders.
Results: Prevalence of common mood and anxiety conditions appeared to reflect local general population estimates, and the occurrence of alcohol misuse was higher than local population figures, although the usefulness of the population data could be challenged.
Conclusions: It appeared that common mental health conditions in both sport and navy divers may generally conform to their respective local general population estimates. If this were to be the case in the broader professional diving environment as well, the inclusion of some form of formal mental health screening during commercial diving medical examinations may be beneficial.

Introduction

A recent article in this journal described mental health (MH) issues among recreational scuba divers in the UK.[1] Although the authors indicated some limitations to their data, it did provide a fascinating 'first picture' of this very relevant field. One particularly interesting observation was that the reported prevalence of various common MH conditions (CMHC) among sport divers were similar to the prevalence of those conditions among the general UK population.[1] This raises the question of the extent to which this might also be the case among professional divers. It is a topical question, for such answers may have implications for MH screening during formal diving medical examinations (for both sport and professional diving).

Few data are available on the prevalence of CMHC among sport (i.e., amateur) scuba divers, apart from the abovementioned survey of UK recreational scuba divers that found prevalence rates comparable to the general UK population.[1] Earlier reports did suggest that history of panic attacks were not uncommon among sport divers.[2–3] No prevalence data for CMHC among commercial divers could be located. In the case of military divers, no recent prevalence data could be found either. Historically, generally low levels of psychopathology were reported, suggesting good MH within this population.[4–7] Further, military divers are characterised by lower levels of generalised anxiety, which is considered contextually important in the military diving environment.[8]

For this study we were able to access recent data on South African Navy (SAN) divers, with the aim to explore whether the prevalence of reported CMHC in this specialised group would also reflect published local population prevalence estimates.[9] SAN divers undergo an annual statutory diving medical examination, which includes a mental health screen, and data for one calendar year (namely 2019) were examined. This short communication will describe the occurrence of mood disorder (depression), anxiety disorders (generalised anxiety, post-traumatic stress disorder, panic disorder), and problematic alcohol use.

Methods

Ethics clearance was obtained for this analysis (University of Pretoria Research Ethics Committee, #HUM020/0320).

SAMPLE

The analysis took the form of a retrospective review of an anonymised electronic database kept at the Institute

for Maritime Medicine. Due to the military nature of the sample, only limited biographical data are reported. A total of 132 active duty military divers (16 women, 116 men), with an average age of 30.6 years (SD 6.2, range 22–52) were included in the sample.

MEASURES

Participating divers completed a MH survey consisting of the Patient Health Questionnaire for Depression (PHQ-9),[10] the Generalised Anxiety Disorder questionnaire (GAD-7),[11] the primary care screen for post-traumatic stress disorder (PTSD-5),[12] and the CAGE questionnaire for alcohol use,[13] as well as a two-item scale for panic-like anxiety.[14] All the divers were also formally assessed through an interview with a clinical psychologist.

DATA ANALYSIS

Diagnostic prevalence was calculated based on the interpretation of psychometric scales (i.e., 'self-report' PHQ-9 and GAD-7) using established norms, as well as on psychological interview outcomes across five CMHC, all reported separately in Table 1. Interview outcomes constituted 'formal diagnosis', using DSM-5 criteria.

Results

Table 1 presents the prevalence for common mood, anxiety, and alcohol misuse disorders among SAN divers, as well as a summary of CMHC prevalence of UK scuba divers, and local South African 12-month population estimates, for comparison.

The prevalence of self-reported depression was less than half of the UK sport diver sample, while prevalence based on formal diagnoses mirrored the reported general SA population figures. Within the SAN diver sample, self-reported depression (using the PHQ-9) is slightly underreported, compared to formally diagnosed cases, which in turn was similar to population estimates. The prevalence of self-reported generalised anxiety was substantially less than the UK sport diver sample, although the indicators were still in range of general SA population estimates. The reported prevalence of PTSD and panic disorder were close to reported local population estimates, with alcohol misuse disorders considerably higher than known SA general population figures.

Discussion

The table allows for a number of interesting observations. Firstly, both mood and generalised anxiety were reported less by SAN divers than by UK sport divers. Navy divers are a healthy group, with regular access to healthcare and the associated opportunity for early intervention. Further, in the diving context, close supervisory monitoring may facilitate early referral and thus intervention. The lower proportion of GAD-7 cases (compared to the sport diver sample) could also be attributed in part to the practice of screening out high anxiety in military diving (including through self-selection, previous exclusion, and regular annual screening during diving medical examinations).

Secondly, diagnoses of mood and anxiety disorders in the SAN diver sample at first glance appeared to reflect local 12-month population estimates, similar to the description of UK sport divers. This could to some degree be expected, as the SAN targets recruitment to reflect broader South African demographic composition,[15] which may result in a similar health profile as the general population. However, given organisational recruitment practices, younger mean age, and access to healthcare, it could be argued that a lower prevalence of CMHC compared to the general population would have been expected. In this regard the national comparator data are dated, with actual prevalence estimated

Table 1

Prevalence of common mental health conditions among South African Navy divers and comparable reference groups. *Patient Health Questionnaire-9, moderate to severe depression. ^Generalised Anxiety Disorder-7, moderate to severe generalised anxiety. #Formal diagnoses (FD) were made based on clinical interviews using DSM-5 criteria. PTSD = post-traumatic stress disorder

Source	Sample	Mood disorders		Anxiety disorders				Alcohol abuse disorders
		Depression		Generalised anxiety		PTSD	Panic	
		PHQ-9*	FD#	GAD-7^	FD	FD	FD	Confirmed abuse
St Leger Dowse et al. (2019)[1]	729 UK recreational scuba divers	8%	7%	5%				
Herman et al. (2009)[9]	SA population estimates		4.5%		1.4%	0.6%	0.8%	4.5%
South African Navy divers	132 active duty divers	3.8%	4.5%	0.8%	1.6%	0.8%	0.8%	9.1%

to be somewhat higher.[16] While it could be inferred that the SAN divers might present with lower CMHC figures than the general population, their data highlight the need to consider those CMHC which carry implications for safe diving. The prevalence of panic (similar to local population estimates) was unexpected, as panic-like anxiety is often considered contra-indicative to safe diving. The limited available interview data suggested that panic first presented later in divers' careers, and was not present during training, but this tentative observation requires further exploration.

The third observation is more practical: the severity of mood and generalised anxiety symptoms were slightly under-reported on PHQ-9 and GAD-7. This might be common for self-reporting during occupational medical examinations, given the known concerns around anxiety in professional military diving, and may speak to the need for clinical screening by diving medical practitioners.

Lastly, the higher rate of alcohol misuse disorders, compared to population data, might still be under-reported. This is suggested by even higher rates of alcohol use disorders in a general military population from the same province, and also widely reported in other military contexts.[17,18] Such under-reporting are of concern, as problematic alcohol use could have implications for diving safety. In this regard, while the intake of alcohol before diving is recognised as a risk to safety, it is not uncommon, and although standard texts and manuals indicate alcohol dependence as contra-indicated to diving medical certification, the role of a general history of problematic alcohol use in the framework of occupational diving medical examination is not clear.[19,20] Additional objective screening tools (e.g., blood work) could be considered to examine medical risk that could affect diving safety.

There are limits to the findings. As noted, the comparator data are dated and may not fully reflect current population estimates. Further, given the small sample size, results cannot easily be generalised to all professional diving contexts. The sample profile was also limited to a relatively healthy subset of divers, with more severe cases already excluded through regular diving medical examinations.

Conclusions

This study demonstrated that CMHC in both UK sport divers and SAN divers conform to their respective local population estimates. While the comparator data for South African divers could be challenged, it is plausible that a similar picture may exist in the commercial diving environment, and research is needed to describe MH profiles in the broader professional diving context.

The findings also have practical implication. If divers present with CMHC similar to the general population, it is recommended that formal MH screening during commercial diving medical examinations be considered. Further, given the likelihood that commercial divers may under-report MH issues, some form of confirmatory screening by clinicians may also be beneficial.

References

1 St Leger Dowse M, Whalley B, Waterman MK, Conway RM, Smerdon GR. Diving and mental health: The potential benefits and risks from a survey of recreational scuba divers. Diving Hyperb Med. 2019;49:291–7. doi: 10.28920/dhm49.4.291-297. PMID: 31828748. PMCID: PMC7039781.

2 Colvard D. Anxiety, panic and psychiatric problems in divers. SAUHMA refresher course in Underwater Medicine; 2007 September 28; Johannesburg, South Africa. Available from: https://docs.google.com/viewer?a=v&pid=sites&srcid. [cited 2020 June 06].

3 Colvard DF, Colvard LY. A study of panic in recreational scuba divers. The Undersea Journal. 2003;Q1:40–4.

4 Dembert ML, Mooney LW, Ostfeld AM, Lacorix PG. Multiphasic health profiles of Navy divers. Undersea Biomed Res. 1983;10:45–61. PMID: 6603041.

5 El Sheshai A, Rashed S, Sadek M. Psychiatric and psychometric study among divers. Egypt J Psychiatry. 1994;17:87–93.

6 Tansy WA. The longitudinal health study: a multiphasic medical surveillance program for US Navy submarines and diving personnel. Groton (CT): Naval Submarine Medical Research Laboratory; 1974. Report No. 786. Available from: http://archive.rubicon-foundation.org/8814. [cited 2020 April 14].

7 Van Wijk CH, Meintjes WAJ. Mental health and personality functioning of naval specialists working in extreme environments. Mil Psychol. 2018;29:601–14. doi: 10.1037/mil0000185.

8 Van Wijk CH. Personality profiles of divers: Integrating results across studies. Int Marit Health. 2018;69:297–303. doi: 10.5603/IMH.2018.0046. PMID: 30589070.

9 Herman AA, Stein DJ, Seedat S, Heeringa SG, Moomal H, Williams DR. The South African stress and health (SASH) study: 12-month and lifetime prevalence of common mental disorders. S Afr Med J. 2009;99(5 Pt 2):339–44. PMID: 19588796. PMCID: PMC3191537.

10 Gilbody S, Richards D, Barkham M. Diagnosing depression in primary care using self-completed instruments: UK validation of PHQ-9 and CORE-OM. Br J Gen Pract. 2007;57:650–2. PMID: 17688760. PMCID: PMC2099671.

11 Löwe B, Decker O, Müller S, Brähler E, Schellberg D, Herzog W, et al. Validation and standardization of the generalized anxiety disorder screener (GAD-7) in the general population. Med Care. 2008;46:266–74. doi: 10.1097/MLR.0b013e318160d093. PMID: 18388841.

12 Prins A, Bovin MJ, Smolenski DJ, Mark BP, Kimerling R, Jenkins-Guarnieri MA, et al. The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5): development and evaluation within a veteran primary care sample. J Gen Intern Med. 2016;31:1206–11. doi: 10.1007/s11606-016-3703-5. PMID: 27170304. PMCID: PMC5023594.

13 Dhalla S, Kopec JA. The CAGE questionnaire for alcohol misuse: a review of reliability and validity studies. Clin Invest Med. 2007;30:33–41. doi: 10.25011/cim.v30i1.447. PMID: 17716538.

14 South African Civil Aviation Authority. Guide for aviation medical examiners (revision 21 July 2017). [cited 2020 June 06]. Available from: http://www.caa.co.za/Documents/Aviation%20Medicine/Dames%20Guide.pdf.

15 Marimuthu M. An analysis of the implications of current recruitment and selection practices on the dropout and failure rate of members in the SA Navy [unpublished Master's Thesis]. Stellenbosch: Stellenbosch University; 2017. Available from http://scholar.sun.ac.za/bitstream/handle/10019.1/100995/marimuthu_analysis_2017.pdf?sequence=1. [cited 2020 June 06].
16 Jacob N, Coetzee D. Mental illness in the Western Cape Province, South Africa: A review of the burden of disease and healthcare interventions. S Afr Med J. 2018;108:176–80. doi: 10.7196/SAMJ.2018.v108i3.12904. PMID: 30004359.
17 Ames GM, Cunradi CB, Moore RS, Stern P. Military culture and drinking behavior among U.S. Navy careerists. J Stud Alcohol Drugs. 2007;68:336–44. doi: 10.15288/jsad.2007.68.336. PMID: 17446972.
18 Bekker D, Van Velden DP. Alcohol misuse in patients attending a defence force general medical clinic. SA Fam Pract. 2003;45(2):10–5.
19 Sheldrake S, Pollock NW. Alcohol and diving. Proceedings of the American Academy of Underwater Sciences 31st Symposium. Dauphin Island (AL): AAUS; 2012. Available from https://archive.epa.gov/region10/diving/web/pdf/alcohol_and_diving_2012-2.pdf. [cited 2020 June 06].
20 St Leger Dowse M, Cridge C, Shaw S, Smerdon G. Alcohol and UK recreational divers: Consumption and attitudes. Diving Hyperb Med. 2012;42:201–7. PMID: 23258456. Available from: https://www.ddrc.org/wp-content/uploads/Diving-Research-paper-Alcohol-and-UK-recreation-divers.pdf. [cited 2020 June 06].

Conflicts of interest and funding: nil

Submitted: 14 April 2020
Accepted after revision: 21 July 2020

Impaired consciousness when scuba diving associated with vasovagal syncope

Peter Wilmshurst[1], Margaret Clamp[2]

[1] *Royal Stoke University Hospital, Stoke-on-Trent, United Kingdom*
[2] *MC Occupational Health, Colwick, Nottingham, United Kingdom*

Corresponding author: *Dr Peter Wilmshurst, Consultant Cardiologist, Royal Stoke University Hospital, Stoke-on-Trent, ST4 6QG, United Kingdom*
peter.wilmshurst@doctors.org.uk

Key words
Vasovagal syncope; Neurocardiogenic syncope; Faints; Micturition syncope; Scuba diving

Abstract
(Wilmshurst P, Clamp M. Impaired consciousness when scuba diving associated with vasovagal syncope. Diving and Hyperbaric Medicine. 2020 December 20;50(4):421–423. doi: 10.28920/dhm50.4.421-423. PMID: 33325026.)
Introduction: Drowning is likely to result from impairment of consciousness when scuba diving. Causes include toxic effects of breathing gas, including nitrogen narcosis and oxygen toxicity, and arterial gas embolism.
Methods: Review of the medical records of scuba divers who had impaired consciousness underwater that could not be attributed to toxic effects of breathing gas or arterial gas embolism.
Results: Four scuba divers had episodes of impaired consciousness when at shallow depths (8–18 m) underwater. The descriptions of the episodes were very similar. Three had histories of recurrent episodes of vasovagal syncope on land.
Conclusions: Absence of other causes for their impaired consciousness underwater leads to the conclusion that the probable cause was vasovagal syncope.

Introduction

A history of blackouts, unless long ago and unlikely to recur, is considered a contraindication to scuba diving because of the risk of drowning if unconsciousness occurs underwater.

Vasovagal syncope (neurocardiogenic syncope) is one of the most frequent causes of loss of consciousness. It is usually benign. It is caused by a combination of a neurally mediated increase of parasympathetic tone to cause bradycardia and a reduction of sympathetic tone to cause peripheral vasodilatation.[1,2] The latter causes blood to pool in the legs and causes a sudden reduction of cardiac filling pressures and hence stroke volume. Vasovagal syncope most commonly occurs when people are standing when the effects of blood pooling on cardiac filling and hence cardiac output are greatest. It rarely occurs when people are lying down, because when recumbent the cardiovascular effects of peripheral blood pooling due to vasodilatation are smaller. However, even when lying down, bradycardia occurs and may be sufficient to cause unconsciousness in susceptible people.

The hydrostatic effects of head-out immersion increase venous return so that cardiac filling pressures are elevated.[3] As a result, theoretically there may be some protection against occurrence of vasovagal syncope when surface swimming and scuba diving.

This article describes four individuals who, whilst scuba diving, had impaired consciousness which was almost certainly the result of vasovagal syncope. No other plausible explanation was found. The description of the episode in each case was very similar. Some of the divers described were seen many years ago. As a result, it was possible to contact only the patient seen most recently to obtain permission to publish the histories. So, only essential patient information is presented to avoid identification of the cases. The patient who was contacted gave written consent for data to be published.

Observations

In the last 20 years, four scuba divers (two male and two female, aged 22 to 55 years) presented to the authors with a history of an episode of impaired consciousness whilst scuba diving that could not be attributed to well known causes of unconsciousness in divers such as hypoxia, toxic gas effects and arterial gas embolism. Both women had more than ten episodes of vasovagal syncope over many years. One man had four episodes of micturition syncope, when he got up at night to pass urine, usually after drinking more alcohol than usual for him the evening before. The other man had no history of blackouts out of the water, but the description of his episode underwater was so similar to that in the other three divers that it is believed likely to have a similar mechanism. None of the divers had other significant medical history and none were taking medication.

One diver had performed about 150 uneventful dives previously and her unresponsive event occurred on a dive to 18 metres (m) depth. The other three divers were trainees, who were diving with an instructor on their fifth, ninth and twelfth dives to depths of 8–12 m. All were breathing air on open-circuit scuba. The episodes of impaired consciousness occurred 8 to 17 minutes into the dives and were not during either descent or ascent.

In each case, the diver's buddy or instructor reported that the diver ceased swimming and had a blank staring expression. Some described the diver as 'not with it'. They did not have convulsions and they retained their regulators in their mouths, but they did not respond to signals from their buddy and did not react to a hand waved in front of their facemask. Their buddies took hold of the divers and performed a controlled lift to the surface. Two divers appeared to come round during the ascent and one came round immediately on surfacing. These three were oriented immediately after surfacing. The fourth, a man of 48, was recovered into a boat and, according to his instructor, he 'was not with it' for about 10 minutes.

One male diver recalled feeling cold on his dive. Both the male divers recalled feeling tired and feeling as if they were falling asleep immediately before their impaired consciousness. The experienced female diver recalled a mild headache before she became unresponsive. The fourth diver had no recollection of anything unusual. None of the divers had neurological findings immediately after the events.

When examined subsequently, one had significant postural hypotension (a 26 mmHg drop in systolic blood when standing from lying). Cardiovascular findings were otherwise normal in all. Their electrocardiograms and 24 hours Holter records were normal. Specifically there was no evidence of Long QT syndrome or other cardiac ion-channelopathies. One had an echocardiogram, which was normal. The three novice divers were advised not to dive again. After much discussion, the experienced diver was advised to dive only with an experienced buddy and that the dives should not require compulsory decompression stops.

Discussion

Scuba divers breathing air can lose consciousness at depth as a result of nitrogen narcosis, oxygen toxicity, carbon monoxide toxicity and other toxic gas effects. The shallow depths of the dives in these cases means that gas toxicity is implausible. In addition, three of the divers regained consciousness within minutes without changing their breathing gas source, which would be difficult to explain if the gas source had toxic impurities.

Arterial gas embolism secondary to pulmonary barotrauma can cause unconsciousness during ascent and usually there are neurological findings after surfacing, if only transiently. The impaired consciousness in these cases was unrelated to ascent and there was no neurological abnormality.

None of the divers had convulsive movements and were rapidly orientated, which makes it unlikely that they had an epileptic fit. Absence attacks due to petit mal epilepsy have some similarities to the events underwater but have much shorter durations. In addition, the attacks out of the water in three of the four divers were not consistent with petit mal epilepsy, but rather were recurrent episodes of vasovagal syncope.

It seems likely that these four divers had vasovagal syncope underwater. Three had some premonition or symptoms before impaired consciousness occurred. Their episodes of impaired consciousness underwater did not result in them losing their regulators. The reason that they did not become more deeply unconscious may have been that the hydrostatic effects of immersion mitigated the effects of vasodilatation.

Vasovagal syncope has been reported in a competitive swimmer during a swimming race.[4] Breath-hold divers can experience impaired consciousness and even syncope as a result of hypoxia, particularly during ascent when the partial pressure of oxygen in the lungs and hence in the arterial blood is decreasing rapidly.[5] In a scuba diver breathing air, the partial pressure of oxygen in inspired air (P_iO_2) decreases during ascent in line with absolute pressure, but the P_iO_2 cannot fall below 0.21 bar. So hypoxia is not an issue in scuba divers breathing air if their equipment is functioning properly and they have no acute cardiorespiratory disease (such as immersion pulmonary oedema).

The diving reflex can cause bradycardia in breath-hold divers, but only a small effect from cold stimulation is observed in scuba divers because they are not breath-holding. Elevated P_iO_2 produces a statistically significant but small dose-dependant reduction in heart rate as a result of parasympathetic stimulation and that might be expected to have a small effect on heart rate at depth.[6] The episodes of impaired consciousness occurred at shallow depths, where the degree of elevation of P_iO_2 would be expected to have only a very small effect on heart rate in most divers.[6] The effect might be larger in individuals who had greater susceptibility to changes in autonomic tone as suggested by the history of vasovagal syncope in three of the four. Immersion in test conditions in a swimming pool was found to be a powerful stimulus for both the sympathetic and parasympathetic nervous system in scuba divers.[7] Head-out immersion and submersion in scuba divers caused changes in all measures of heart rate variability consistent with an increase in parasympathetic activity.[7]

In the divers reported here, three of whom were highly susceptible to vasovagal syncope, the parasympathetic activation caused by immersion and by the elevated partial pressure of oxygen might have been great enough to cause a

clinically important bradycardia such that cerebral perfusion was reduced even though cardiac filling pressures were relatively well maintained by hydrostatic compression of peripheral vessels.

This small series of clinical observations suggests that individuals prone to vasovagal syncope are at risk of impaired consciousness when scuba diving. These observations require confirmation by other diving doctors.

References

1 Lewis T. A lecture on vasovagal syncope and the carotid sinus mechanism. Br Med J. 1932;1:873–6. doi: 10.1136/bmj.1.3723.873. PMID: 20776843. PMCID: PMC2520889.

2 Morillo CA, Eckberg DL, Ellenbogen KA, Beightol LA, Hoag JB, Tahvanainen KU, et al. Vagal and sympathetic mechanisms in patients with orthostatic vasovagal syncope. Circulation. 1997;96:2509–13. doi: 10.1161/01.CIR.96.8.2509. PMID: 9355886.

3 Arborelius M Jr, Balldin UI, Lilja B, Lundgren CE. Hemodynamic changes in man during immersion with the head above water. Aerosp Med. 1972;43:592–8. PMID: 5035546.

4 Edenfield KM, Stern AN, Dillon MC, Burkart TA, Clugston JR. A case of vasovagal syncope in a collegiate swimmer during competition. Current Sports Med Rep. 2015;14:86–90. doi: 10.1249/JSR.0000000000000128. PMID: 25757001.

5 Fitz-Clarke JR. Adverse events in competitive breath-hold diving. Undersea Hyperb Med. 2006:33:55–62. PMID: 16602257.

6 Shibata S, Iwasaki K, Ogawa Y, Kato J, Ogawa S. Cardiovascular neuroregulation during acute exposure to 40, 70 and 100% oxygen at sea level. Aviat Space Environ Med. 2005;76:1105–10. PMID: 16370259.

7 Schipke JD, Pelzer M. Effect of immersion, submersion and scuba diving on heart rate variability. Br J Sports Med. 2001;35:174–80. doi: 10.1136/bjsm.35.3.174. PMID: 11375876. PMCID: PMC1724326.

Conflicts of interest and funding: nil

Submitted: 03 April 2020
Accepted after revision: 29 August 2020

Case reports

Persistent extravascular bubbles on radiologic imaging after recompression treatment for decompression sickness: A case report

Juan C Dapena[1], Corine A Lansdorp[2], Simon J Mitchell[3,4]

[1] *Navy Medicine Operational Training Center, Hyperbaric Medicine Department, Pensacola (FL), USA*
[2] *Amsterdam University Medical Centre, location AMC, Department of Anaesthesiology/Hyperbaric Medicine, Amsterdam, The Netherlands*
[3] *Department of Anaesthesiology, School of Medicine, University of Auckland, New Zealand*
[4] *Department of Anaesthesia, Auckland City Hospital, Auckland, New Zealand*

Corresponding author: *Dr Juan C Dapena, Navy Medicine Operational Training Center, Hyperbaric Medicine Department, 220 Hovey Rd, Pensacola, Florida, 32508, USA*
juan.c.dapena.mil@mail.mil

Key words
Decompression illness; Computed tomography; Hyperbaric oxygen; Residual symptoms; Bubbles; Nitrogen

Abstract

(Dapena JC, Lansdorp CA, Mitchell SJ. Persistent extravascular bubbles on radiologic imaging after recompression treatment for decompression sickness: A case report. Diving and Hyperbaric Medicine. 2020 December 20;50(4):424–430. doi: 10.28920/dhm50.4.424-430. PMID: 33325027.)
Decompression sickness (DCS) is a condition arising when dissolved inert gas in tissue forms extravascular and/or intravascular bubbles during or after depressurisation. Patients are primarily treated with 100% oxygen and recompression, which is often assumed to lead to resolution of bubbles. After this, repeated hyperbaric exposures can be provided in case of persistent symptoms, with oxygen delivery to ischaemic tissues, anti-inflammatory properties and reduction of oedema considered the main mechanisms of action. In this case report we present the history and imaging of a diver diagnosed with DCS that was treated with two US Navy Treatment Table 6 recompressions, but who still had multiple extravascular bubbles apparent on CT-imaging after these hyperbaric treatments. Based on these findings we hypothesise that, contrary to general belief, it is possible that large extravascular bubbles can persist after definitive treatment for DCS.

Introduction

Decompression sickness (DCS) is a condition arising when dissolved inert gas in tissue forms extravascular and/or intravascular bubbles during depressurisation.[1] It is well known for its appearance in divers, although it can appear in any person breathing an inert gas (most commonly nitrogen), who is subject to an ambient pressure reduction at a rate that exceeds the rate of washout of the gas. It can also be seen, for example, in tunnel and caisson workers and aviators flying an unpressurised aircraft at high altitude.

The diagnosis of DCS is based on clinical manifestations, with a wide range of possible signs and symptoms, depending on the location of the bubbles.[1] Symptoms frequently reported are pain, numbness/paraesthesia and constitutional symptoms such as headache, light-headedness and fatigue. More severe symptoms such as alteration of mental status, loss of consciousness, spinal cord syndromes and cardiovascular complications are also seen.

The primary treatment for DCS is breathing 100% oxygen during recompression (hyperbaric oxygen treatment [HBOT]). The resulting increase in the gradient between the pressure of nitrogen in bubbles and alveoli washes out the inert gas, leading to resolution of bubbles.[1] In case of persistent symptoms after the initial treatment, repeated HBOT can be provided. Anecdotally, it is often assumed that bubbles are unlikely to persist after an initial definitive HBOT session and consequently that the benefit of additional treatments comes from oxygenation of ischaemic tissues, anti-inflammatory effects and reduction of oedema, rather than actual bubble resolution. There is certainly a marked lack of evidence to the contrary. One report describes the recurrence of low grade venous gas emboli in three subjects following a US Navy Treatment Table 5 administered for mild DCS symptoms arising after a 48 hour shallow saturation dive.[2,3] The implications of this for bubble resolution by longer recompression protocols (such as the US Navy Treatment Table 6, USN TT6) administered after more typical non-saturation bounce dives are unknown.[3] Moreover, to our knowledge, there is no direct evidence at all for persistence of extravascular bubbles after a definitive HBOT recompression.

Here we present the case of DCS treated with two USN TT6 recompressions,[3] but who still had multiple large extravascular bubbles on CT-imaging after these treatments.

Case report

The patient gave permission for his case and radiology to be reported. A 37 year-old male presented after diving off coastal USA. He had performed six repetitive and strenuous dives to a maximum depth of 44 metres' sea water (msw) while spear fishing the day before, breathing nitrox (29% oxygen, 71% nitrogen). The patient reported to have been out diving for about 3.5 hours with an average bottom time of 11 minutes per dive. He reported performing safety stops during ascent at 5 msw for his first three dives, but did not recall safety stops for his last three dives or the rate of ascent of his dives. Unfortunately, the actual data of the diving computer including information on the surface intervals was not available during the consultation.

At the end of the third dive the patient started experiencing pain in his right shoulder, which improved during his fourth and fifth dive but persisted after the sixth. He described it as a burning pain extending up to the base of the neck and as far distally as both elbows, with the pain being extreme during the ride back to shore. The patient also reported chest pain while surfacing from the fifth dive, resolving upon completion of the sixth dive. The next morning the pain in the shoulders and neck was still present and there was soft tissue swelling over both shoulders and upper arms. His girlfriend also noticed swelling of the left hand side of the face. The patient then self-referred to a local hospital for evaluation.

There were no previous diving injuries within his two years of diving experience. There was no other relevant medical history and no allergies or intoxications, other than tobacco use equivalent to five pack years. A neurological examination was normal.

The patient was diagnosed with musculoskeletal and lymphatic DCS, and was treated with a USN TT6 beginning 25 hours after completion of diving.[3] Upon completion of his first treatment his pain had reduced from 10/10 to 6/10 and there was incomplete resolution of his upper limb and facial swelling. Due to minimal improvement of his symptoms a computed tomography (CT) scan was performed, showing a small amount of gas in the manubriosternal joint (Figure 1A) and along the posterior to superior-medial aspect of the right glenohumeral joint (Figure 2A), with no signs of pulmonary barotrauma.

Because of the ongoing complaints, the attending physician contacted the staff of the Undersea and Hyperbaric Medicine fellowship programme in New Orleans. The recommendation was made to give the patient a 2 h break and then provide another USN TT6. After completion he reported persistent pains in the shoulders at a lower intensity, and persistent proximal swelling of both arms. The patient signed himself out of the hospital and drove over nine hours to New Orleans to be evaluated by the fellowship programme staff.

After arrival in New Orleans the patient still had residual pain. A repeated physical examination, as well as a detailed neurological evaluation, was normal except for obvious swelling of both upper arms. Another CT scan of the chest was performed and compared to the previous scan by a radiologist. A small amount of gas in the manubriosternal joint similar to the earlier CT was found (Figure 1B), as well as a small focus of gas anterior to the left sternoclavicular joint (Figure 3B) that was not demonstrated earlier (Figure 3A). The focus of gas that was previously seen along the posterior to superior-medial aspect of the right glenohumeral joint (Figure 2B) was no longer present.

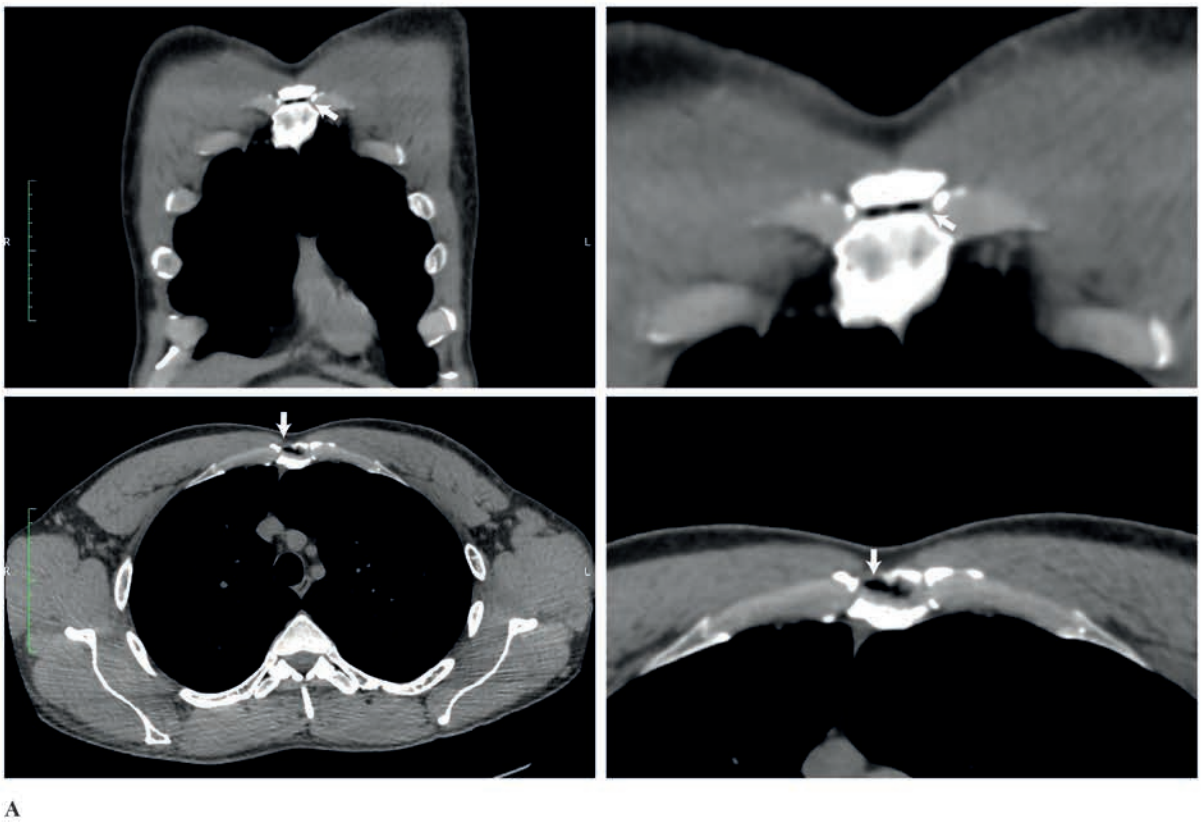
Because two USN TT6 were provided within a short interval and symptoms were relatively mild at this point, the patient was discharged and re-evaluated the next day. He then still had residual aches of the neck and persistent swelling and discomfort of both upper extremities. A single US Navy Treatment Table 9 was provided with partial resolution of his aches.[3] Due to non-medical and unrelated issues, the patient departed the institution after this treatment. A prescription order for a transthoracic echo (to rule out a patent foramen ovale) and magnetic resonance imaging of the neck, thorax and the spinal cord was provided but never carried out by the patient. He returned to spear fishing seven weeks after the incident.

Discussion

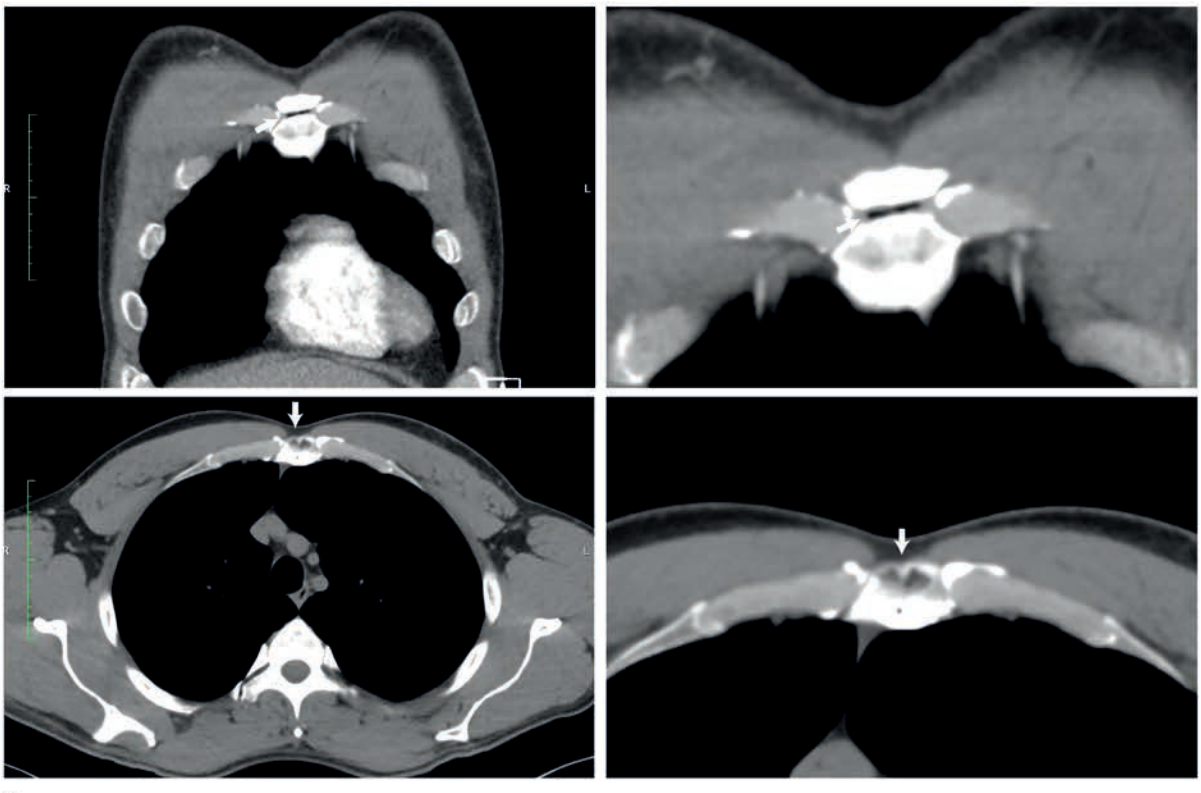
To our knowledge this is the first documented case of persistent extravascular bubbles identified by radiologic imaging after initial and subsequent recompression for DCS that would arguably be perceived as 'adequate'. Indeed, gas persisted in a common location after two USN TT6 recompressions. This is interesting because it challenges a common assumption that bubbles formed during decompression are very unlikely to persist after treatment with definitive HBOT protocols.

This assumption is largely based on the physical mechanisms of bubble resolution in response to HBOT. Apart from the direct effect of recompression on bubble size due to Boyle's law, by increasing the nitrogen pressure in compressed bubbles while at the same time reducing the nitrogen pressure in the alveoli toward zero, HBOT establishes a substantial gradient for diffusion of nitrogen out of bubbles into the blood, and thence to alveoli for elimination. This should be a potent driver for bubble elimination.[1] The likely efficacy of HBOT in this regard is supported by animal experiments, in which air bubbles injected into the spinal cord of decompressed rats all disappeared after breathing 100% oxygen at ambient pressure, even without recompression.[4]

Figure 1
Coronal and axial CT-images of the chest showing a gas focus (arrow) in the sternomanubrial joint, after recompression one (A) and recompression two (B)



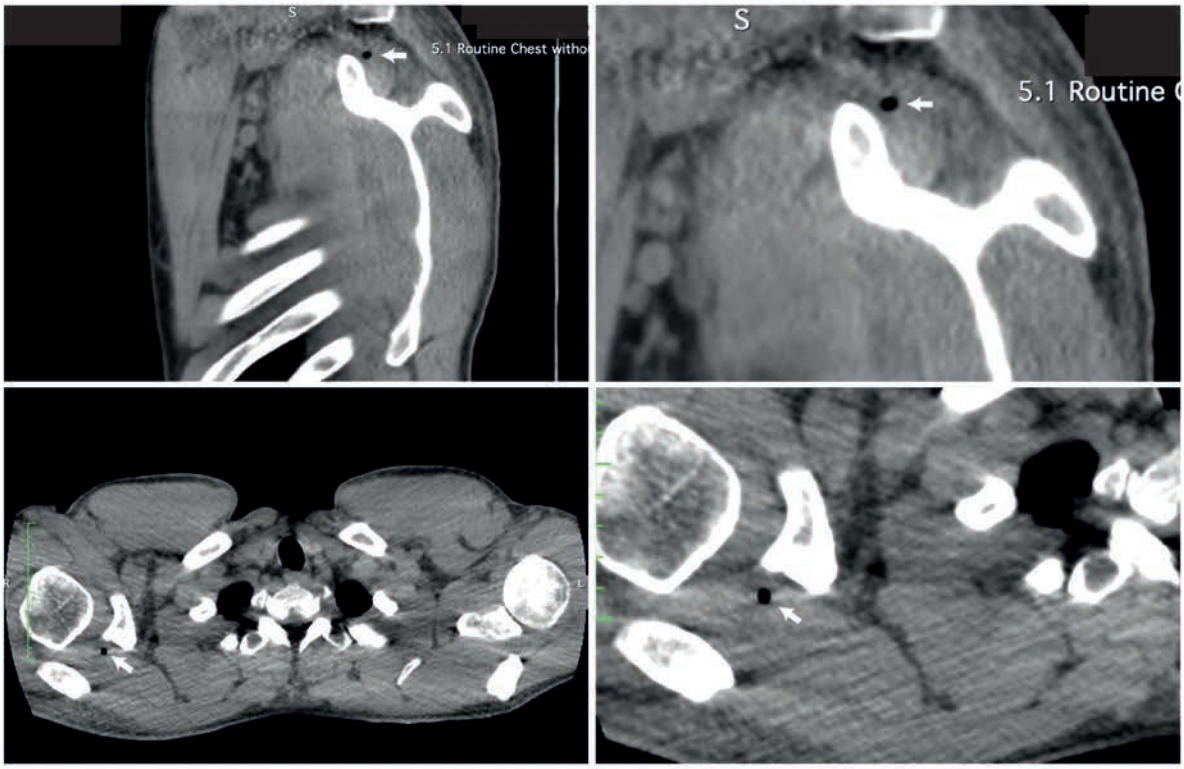
A



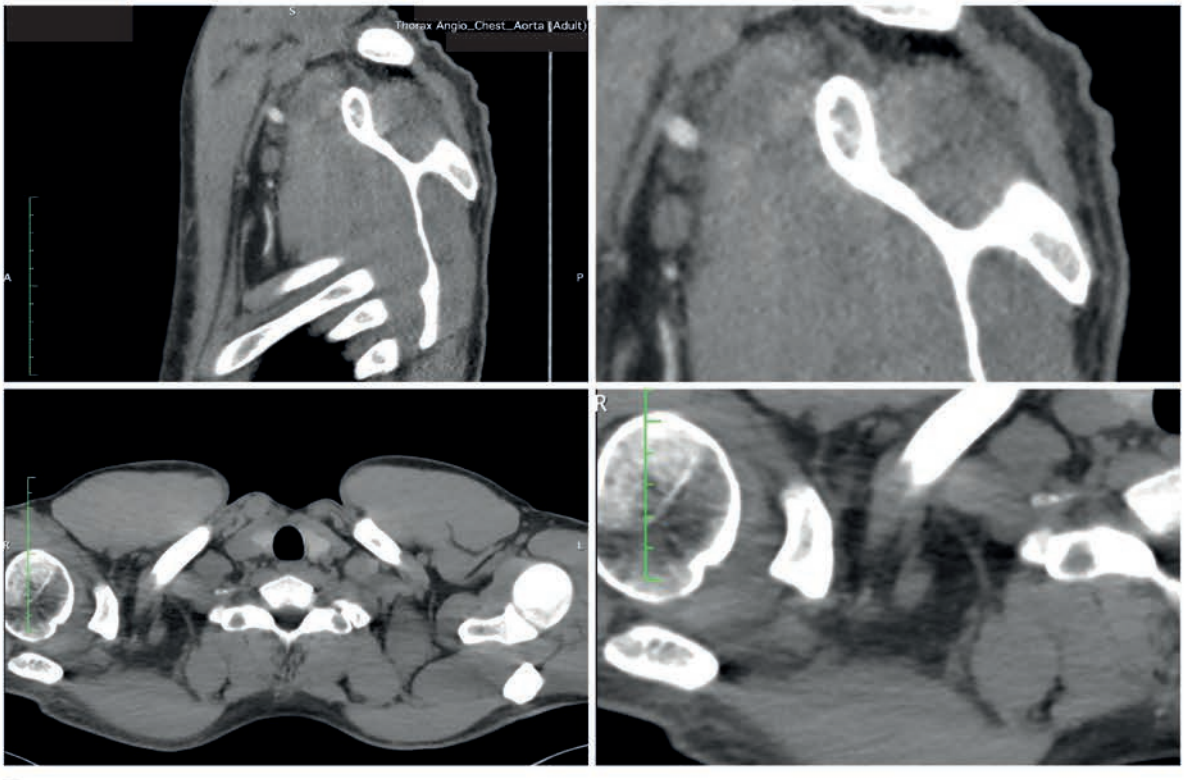
B

Figure 2

Sagittal and axial CT-images of the chest showing a gas focus (arrow) near the right glenohumeral joint and tip of the supraspinatus muscle after recompression one (A), with resolution after recompression two (B)



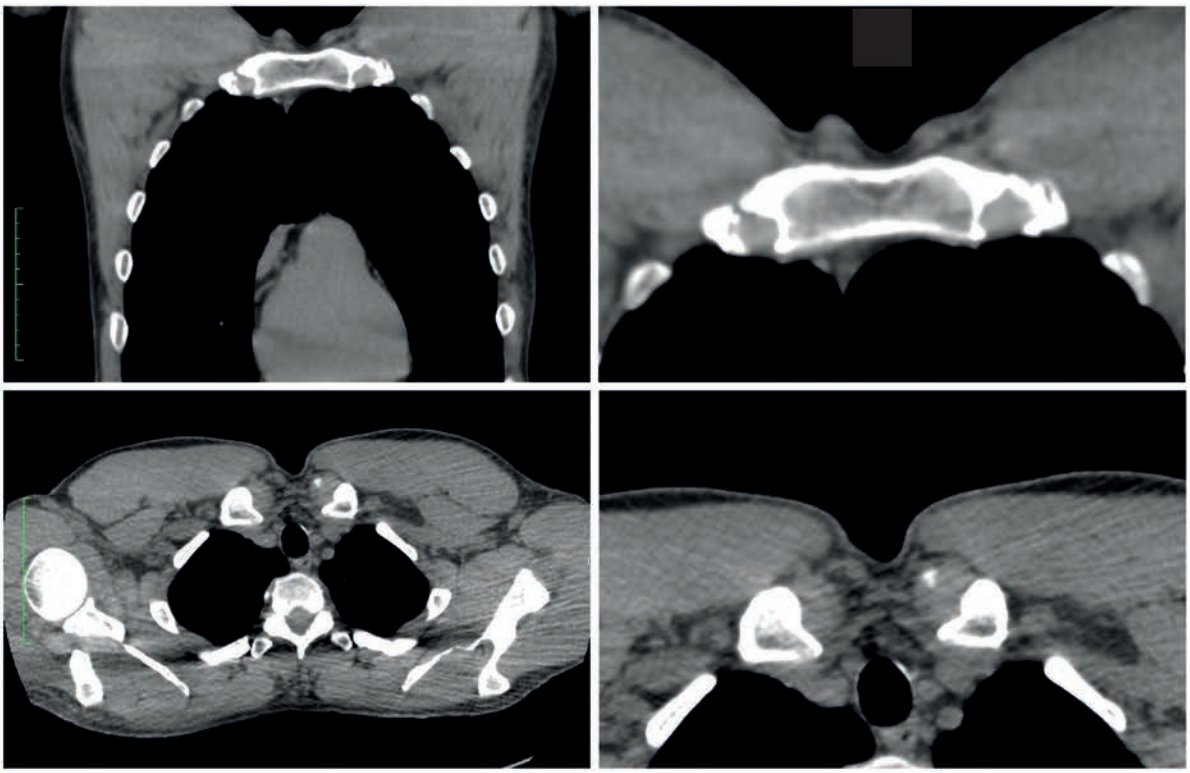
A



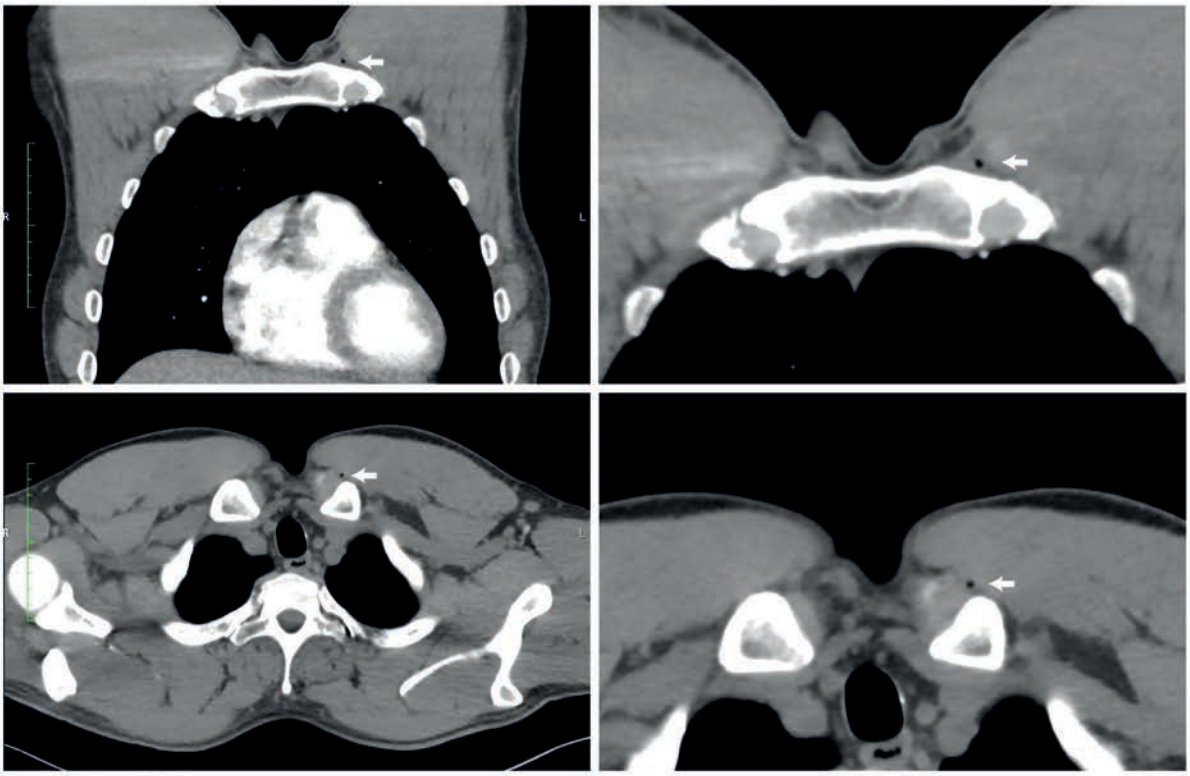
B

Figure 3

Coronal and axial CT-images of the chest showing gas foci (arrows) located anterior to the left sternoclavicular joint and posteromedial to the left pectoralis major muscle after recompression treatment two (B), that were not seen after recompression one (A)



A



B

The potential for venous bubbles (venous gas emboli – VGE) to recur after recompression for DCS has previously been reported.[2] Three of four subjects who completed a US Navy Table 5 treatment for mild DCS arising after a shallow saturation dive exhibited recurrent VGE formation after VGE initially disappeared during the recompression. The authors hypothesised that hyperoxic vasoconstriction during HBOT resulted in decreased tissue perfusion and nitrogen washout, and thus subsequently allowed further VGE formation after reperfusion. In the present case it seems possible that hyperoxic vasoconstriction in 'slow' musculoskeletal tissue (typically exhibiting low perfusion) may have contributed to the lack of efficacy of HBOT in clearing some bubbles from that tissue. Whatever the mechanism responsible, the present case appears to demonstrate persistence of extravascular bubbles (as opposed to VGE) following two USN TT6 recompressions with considerable latency before and between treatments; this represents a previously unrecorded degree of resistance to resolution of diving-related tissue bubbles despite multiple definitive HBOT recompressions.

The finding of a new bubble anterior to the left sternoclavicular joint (that was not present on the first CT scan) was unexpected, although this might be explained based on the technical limitations of CT imaging. It is possible that the gas focus was already present at the time of the first CT, but it was missed because the thickness of the CT slices exceeded the size of the bubble itself.

We acknowledge the possibility of an artefactual source of the gas seen in these CT scans. For example, another possible explanation for persistent bubbles is the so-called 'vacuum phenomenon', which refers to the radiological finding of gas (suspected to be nitrogen) in a joint.[5] It can be a consequence of trauma, inflammation, or cavitation. Radiologically it can be confused for DCS, being differentiated only through clinical correlation. In this case, a diver exhibited signs and symptoms of DCS in the broad anatomic locations in which the bubbles were seen, and did not report previous trauma or rheumatological conditions, decreasing the likelihood of vacuum phenomenon as an explanation for the radiologic findings. Furthermore, two out of three bubbles were not located within a joint.

We also acknowledge that pulmonary barotrauma (PBT) with mediastinal emphysema and extension of gas into the neck cannot be absolutely ruled out as a contributor to, or even the cause of, this diver's symptoms. However, we consider this a less likely explanation than DCS based on the dive and clinical history, symptom pattern, and the distribution of residual gas in sites other than those most affected in a typical case of PBT with mediastinal emphysema.[6] In any event, any debate about bubble origin is largely irrelevant to the key point of this report: that definitive HBOT did not completely resolve the resulting tissue bubbles that seem highly likely to be diving-related.

It is acknowledged that the performance of multiple radiologic investigations in this case was unusual. DCS is a clinical diagnosis and it is not common practice to perform advanced radiologic studies before or between treatments, although CT scans have been contributory to diagnosis of post-dive abdominal pain in several instances by demonstrating intravascular gas in the splanchnic circulation,[7,8] and to informing the differential diagnosis in diver presenting with cerebral and pulmonary symptoms.[9] In contemplating such investigations the balance between clinical value versus radiation exposure and cost must be carefully considered. Typically, however, patients with residual symptoms receive tailing treatments until complete resolution or lack of further improvement occurs, without radiological guidance.[10]

Conclusions

Persistent bubbles most likely arising from DCS were found on CT imaging after repeated definitive hyperbaric treatments. Based on these findings and the lack of an adequate alternative explanation, it is plausible that large extravascular bubbles can persist after definitive HBOT treatment for diving-related illness. If confirmed, this finding has important implications for topics of debate that recur in diving medicine, such as the reasons why flying after definitive recompression for DCS could be associated with recurrence or worsening of symptoms. Although routine decisions about initial and repeat treatment for DCS should remain clinically guided, it would be interesting if selected cases with residual symptoms are similarly investigated in the future, allowing for further insight into this phenomenon.

References

1 Vann RD, Butler FK, Mitchell SJ, Moon RE. Decompression illness. Lancet. 2011;377(9760):153–64. doi: 10.1016/S0140-6736(10)61085-9. PMID: 21215883.

2 Eckenhoff RG, Osborne SF, Parker JW, Bondi KR. Direct ascent from shallow air saturation exposures. Undersea Biomed Res. 1986;13:305–16. PMID: 3535200.

3 Naval Sea Systems Command. US Navy Diving Manual, Revision 7, SS521-AG-PRO-010. Washington (DC): Naval Sea Systems Command; 2016. [cited 2020 February 07]. Available from: http://www.navsea.navy.mil/Portals/103/Documents/SUPSALV/Diving/US%20DIVING%20MANUAL_REV7.pdf?ver=2017-01-11-102354-393.

4 Hyldegaard O, Moller M, Madsen J. Effect of He–O_2, O_2, and N_2O–O_2 breathing on injected bubbles in spinal white matter. Undersea Biomed Res. 1991;18:361–71. PMID: 1746064.

5 Yanagawa Y, Ohsaka H, Jitsuiki K, Yoshizawa T, Takeuchi I, Omori K, et al. Vacuum phenomenon. Emerg Radiol. 2016;23:377–82. doi: 10.1007/s10140-016-1401-6. PMID: 27147527.

6 Bigeni S, Saliba M. Pulmonary barotrauma: A case report with illustrative radiology. Diving Hyperb Med. 2020;50:66–9. doi: 10.28920/dhm50.1.66-69. PMID: 32187620. PMCID: PMC7276275.

7 Schwartz T, Gough-Fibkins S, Santini R, Kopylov D.

Abdominal CT Scan findings of decompression sickness: A case report. J Radiol Case Rep. 2018;12:17–23. doi: 10.3941/jrcr.v12i10.3425. PMID: 30651907. PMCID: PMC6312119.

8 Siaffa R, Liciani M, Grandjean B, Coulange M. Massive portal venous gas embolism after scuba diving. Diving Hyperb Med. 2019;49:61–3. doi: 10.28920/dhm49.1.61-63. PMID: 30856669. PMCID: PMC6526053.

9 Blatteau J-E, Morin J, Roffi R, Druelle A, Sbardella F, Castagna O. Clinical problem solving: Mental confusion and hypoxaemia after scuba diving. Diving Hyperb Med. 2020;50:181–4. doi: 10.28920/dhm50.2.181-184. PMID: 32557408. PMCID: PMC7481120.

10 Moon RE, Gorman DF. Treatment of the decompression disorders. In: Brubakk AO, Neuman TS, editors. Bennett and Elliott's physiology and medicine of diving. 5th ed. Edinburgh: Saunders; 2003. p. 600–50.

Conflicts of interest and funding

Professor Mitchell is the Editor of *Diving and Hyperbaric Medicine* Journal and so had no role in managing the review process or the decision to accept this manuscript. These matters were managed by the European (deputy) editor Dr Lesley Blogg. There were no other conflicts of interest.

Submitted: 24 March 2020
Accepted after revision: 25 June 2020

Hyperbaric oxygen treatment of central retinal vein occlusion with cilioretinal artery occlusion secondary to hormonal treatment: Case report and review

Asma Khallouli[1], Khaled Khelifi[1], Rahma Saidane[1], Racem Choura[1], Afef Maalej[1], Raja Ben Sassi[2]

[1] *Department of Ophthalmology, Military Hospital of Tunis, Tunisia*
[2] *Department of Hyperbaric Oxygen Therapy, Military Hospital of Tunis, Tunisia*

Corresponding author: *Dr Racem Choura, Department of Ophthalmology, Military Hospital of Tunis, Mont Fleury- 1008, Tunisia*
choura.racem@gmail.com

Key words
Cilioretinal artery occlusion; Retinal vein occlusion; Fertility agents; Female

Abstract
(Khallouli A, Khelifi K, Saidane R, Choura R, Maalej A, Ben Sassi R. Hyperbaric oxygen treatment of central retinal vein occlusion with cilioretinal artery occlusion secondary to hormonal treatment: Case report and review. Diving and Hyperbaric Medicine. 2020 December 20;50(4):431–436. doi: 10.28920/dhm50.4.431-436. PMID: 33325028.)
Introduction: This report describes a case of central retinal vein occlusion (CRVO) and cilioretinal artery occlusion (CLRAO) after hormonal treatment for induction of ovulation that was successfully treated with hyperbaric oxygen.
Case report: A 48 year-old woman was admitted to our department for sudden blurred vision in her left eye. The patient had a history of 3-months hormonal treatment for induction of ovulation. The best corrected visual acuity was 7/10 (20/32) in the left eye and 10/10 (20/20) in the right eye. Fundus examination of the left eye revealed flame-shaped haemorrhages, whitening of the retina along the distribution of cilioretinal artery and tortuous retinal veins. Fluorescein angiography confirmed the combination of a non-ischaemic CRVO with CLRAO. The patient was treated with a 2 h session of hyperbaric oxygen at 253 kPa (2.5 atmospheres absolute) once daily for a total of 30 sessions. Best corrected visual acuity improved to 10/10 (20/20) in the left eye.
Conclusions: CRVO and CLRAO are both occlusive disorders. HBOT is a safe low-cost treatment modality that can be beneficial in some ocular pathologies. It can maintain oxygenation of the retina through the choroidal blood supply, decrease oedema and preserve compromised tissue adjacent to the ischaemic area.

Introduction

Veno-occlusive retinal disorders are the most common vascular visual impairing condition after diabetic retinopathy. Central retinal vein occlusion (CRVO) is the most common primary veno-occlusive disorders of the retina. Older age, male gender, arterial hypertension, glaucoma and hyperviscosity syndromes are the major risk factors. However, CRVO may occur in young adults with no systemic or ocular disorders. Characteristic fundus findings consist of retinal vascular tortuosity, retinal hemorrhages in the four quadrants, cotton wool spots, optic disc swelling and macular oedema.[1] Thrombosis within a retinal vein leads to a partial obstruction of blood flow. The subsequent increased intraluminal pressure causes transudation of blood products into the retina according to Starling's law which increases the amount of interstitial fluid and protein. This results in an increase in interstitial oncotic pressure, and thus perpetuates tissue oedema.[2] Macular oedema in retinal vein occlusion is responsible for the visual loss. Unlike ischaemic CRVO with neovascular glaucoma, the non-ischaemic form has typically a more benign course and a better visual outcome. Yet, the conversion to ischaemic CRVO is not rare.

The retina is supplied by the ophthalmic artery, the first intracranial branch of the internal carotid artery, via the central retinal and the ciliary arteries. The central retinal artery supplies the retina as it branches into smaller segments upon leaving the optic disc. The ciliary arteries supply the choroid and the anterior portion of the globe via the rectus muscles. The cilioretinal artery (CLRA), an anatomic variant seen in about 32% of eyes, arises from the short posterior ciliary arteries. In approximately 19% of eyes it contributes to the macular blood supply.[3] The coexistence of CRVO and cilioretinal artery occlusion (CLRAO) is a rare disorder that can be easily overlooked. It was first described in 1968.[4] Several hypotheses have been advanced to explain the simultaneous development of CLRAO and CRVO. It has been postulated that partial obstruction of the posterior ciliary arteries may be the cause of CLRAO.[5] The authors hypothesised a spectrum of ocular vascular lesions intermediate between acute CRVO and acute ischaemic optic neuropathy.[5] The pathogenesis of this condition remains unclear and the possibility of primary occlusion of

the cilioretinal artery must be considered in these eyes.[6] It has also been supposed that optic disk oedema caused by CRVO may result in CLRAO.[7] The pathogenesis of CLRAO in patients with CRVO is not precisely known. However, it is most likely the result of elevated intraluminal pressure in the retinal capillaries due to CRVO that exceeds the pressure in the CLRA.[8]

Therapeutic interventions for ischaemic CRVO can be classified into two major categories. The first is aimed at the obstruction to venous outflow, the causal condition. This category includes antithrombotic agents, thrombolytics, optic nerve sheath decompression, and radial optic neurotomy. These treatments do not appear to offer any benefit. The second category is aimed at the consequences of venous occlusion and includes panretinal laser photocoagulation (PRP) and intravitreal anti-vascular endothelial growth factor/corticosteroid agents. These latter are the most commonly used and appear to be effective.[9]

There is no therapy proven to be effective for CLRAO associated with CRVO.[1] Both CRVO and CLRAO are ultimately hypoxic phenomena. Few authors have reported their experience with HBOT in the treatment for this rare combination.[8] We report a case of apparent success with HBOT in a 48 year-old woman who presented with CRVO and CLRAO after a 3-month history of hormonal treatment for ovulation induction.

Case report

A healthy 48 year-old Caucasian woman was referred to our department for sudden blurred vision in her left eye with onset two days prior. The patient had a history of a 3-month hormonal treatment for induction of ovulation. She reported no previous visual disturbances. Furthermore, she had no cardiovascular risk factors.

At baseline, the best corrected visual acuity was 7/10 (20/32) in the left eye and 10/10 (20/20) in the right eye (Snellen chart). Anterior segment examination and intra ocular pressure were normal. Fundus examination of the left eye revealed whitening of the retina along the distribution of the cilioretinal artery, sparing the fovea, flame-shaped haemorrhages and minimally dilated and tortuous retinal veins (Figure 1).

Fluorescein angiography showed hypofluorescence in the territory of the cilioretinal artery, prolonged arteriovenous filling time and delayed central vein filling, confirming the combination of a non-ischaemic CRVO with CLRAO (Figure 2).

Visual fields were not evaluated. Macular spectral domain optical coherence tomography showed inner layer oedema in the occluded CLRA territory with hyper-reflectivity of the macular retinal inner layer, demonstrating ischaemic damage (Figure 3).

Figure 1
Color and red free fundus photographs demonstrating haemorrhages and venous dilatation consistent with central retinal vein occlusion, and white oedema located in the territory of the cilioretinal artery corresponding to its occlusion

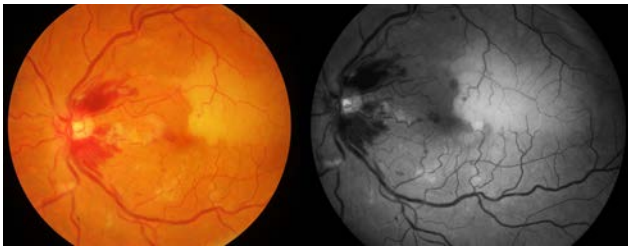


Figure 2
Fluorescein angiography showing marked delay in arteriovenous transit time (longer than 20 seconds), parapapillary retinal haemorrhages and late vessel wall staining associated with non-perfusion of the cilioretinal artery: Combination of a non-ischaemic CRVO and CLRAO

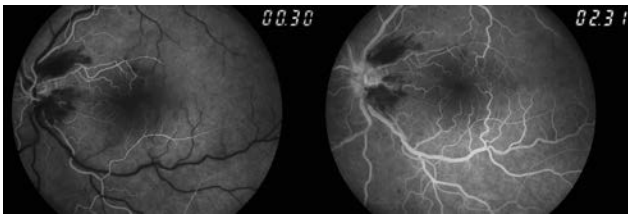
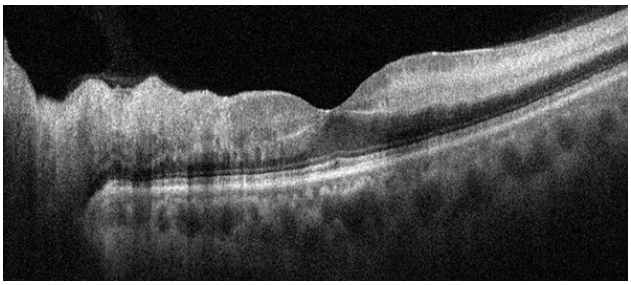


Figure 3
Macular spectral domain optical coherence tomography (SD-OCT) showing inner layer oedema in the territory of the occluded cilioretinal artery with high hyper-reflectivity of the macular retinal inner layer demonstrating ischaemic damages



Optical coherence tomography angiography 6 mm x 6 mm demonstrated an attenuation of both the superficial and deep capillary plexuses, thus defining ischaemic damage in the macular retinal inner layer (Figure 4).

Systemic physical examination revealed no abnormality. Laboratory work up (haematocrit, haemoglobin, white blood cell counts, platelets and erythrocyte sedimentation rate, C-reactive protein, fasting blood lipids and glucose) was unremarkable. Cryoglobulin, lupus anticoagulant, and anti-cardiolipin antibodies were all negative. Antithrombin III, protein C, and protein S activities were normal. Carotid ultrasonography and echocardiography demonstrated no abnormality.

Figure 4
Optical coherence tomography-angiography 6 mm x 6 mm demonstrated an attenuation of both superficial and deep capillary plexus, which correlated precisely with ischaemic damages in the macular retinal inner layer

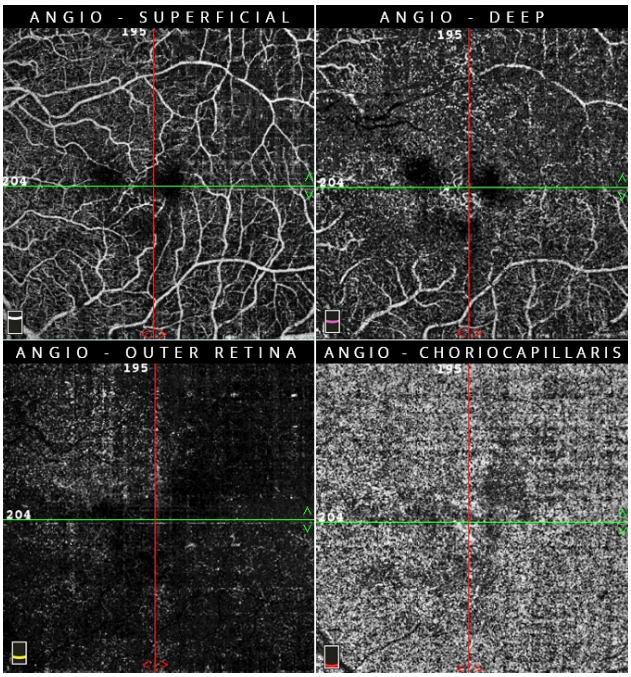


Figure 5
Color and red free fundus photographs at the end of treatment: The haemorrhages were absorbed. The dilation-tortuosity of retinal vessels and the whitening along the course of the cilioretinal artery were completely resolved

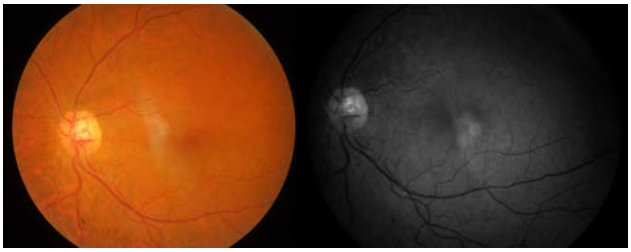
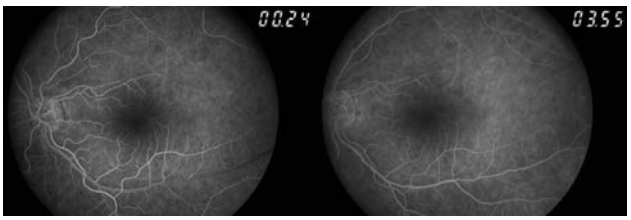


Figure 6
Follow-up fluorescein angiography showing a normal dye arteriovenous transit time and no abnormal fluorescence



The patient was treated with 2-hour daily session of HBOT at 253 kPa (2.5 atmospheres absolute [atm abs]) for a total of 30 sessions. Upon follow-up, best corrected visual acuity had increased to 10/10 (20/20) in the left eye. The haemorrhages were absorbed. The retinal vessel dilation and tortuosity as well as the whitening along the course of the cilioretinal artery had completely resolved (Figure 5). Fluorescein angiography showed a normal arteriovenous dye transit time (Figure 6). Spectral domain optical coherence tomography demonstrated diffuse thinning of the inner nuclear layer, corresponding to the zone of the CLRAO (Figure 7).

Optical coherence tomography angiography of the affected eye showed a wedge-shaped area of capillary non-perfusion in both superficial and deep retinal capillary plexuses in the area supplied by the CLRA. The choriocapillaris was not affected and the central avascular zone was preserved (Figures 8 and 9).

The scheduled treatment was completed successfully without any complication or coincident medical event.

Discussion

CLRAO has been reported in association with embolism, CRVO and a variety of medical conditions as well as with pregnancy.[3] Combined CRVO and CLRAO subsequently reported to account for 40% of all CLRA obstructions.[5,10] There are three forms of CLRAO: isolated non-arteritic; associated with giant cell arteritis; and associated with CRVO.[11]

CLRAO associated with CRVO is a clinical entity thought to be due to transient haemodynamic obstruction of the CLRA. It may be caused by sudden increase in retinal capillary pressure to a level higher than normally present in the CLRA. Thus, retinal capillary pressure due to CRVO may exceed CLRA perfusion pressure, causing CLARO.[12–14] Alternatively, a primary reduction in the perfusion pressure in the cilioretinal and retinal arteries may cause a decrease in retinal circulation and venous stasis and thrombosis.[6,15] In eyes with a cilioretinal supply, the probability that cilioretinal infarction will complicate retinal vein occlusion is thought to increase with the severity of venous obstruction and as the origin of CLRA increases distally from the posterior ciliary artery tree.[16]

Experimental studies have also shown that arterial constriction following venous obstruction is attributable to a decrease in local levels of nitric oxide, which might contribute to a reduction in CLRA perfusion.[17] The central retinal artery has sufficient autoregulatory capacity to maintain perfusion, in contrast to the CLRA arising from the choroidal vascular bed.[16] Furthermore, perfusion pressure in the choroidal vascular bed is lower than that in the central retinal artery.[18]

Figure 7
Macular SD-OCT at the end of treatment demonstrating diffuse thinning of the inner nuclear layer, corresponding to the territory of the cilioretinal artery occlusion

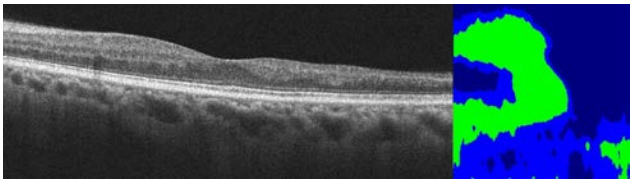


Figure 8
Optical coherence tomography-angiography 6 mm x 6 mm at the end of treatment revealing a wedge-shaped area of capillary non-perfusion in both the superficial and deep retinal capillary plexus in areas supplied by the cilioretinal artery. The choriocapillaris was not affected

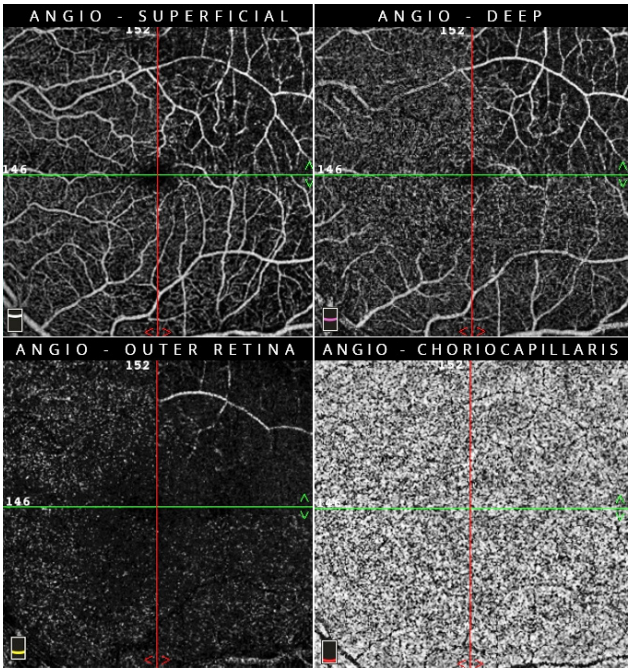
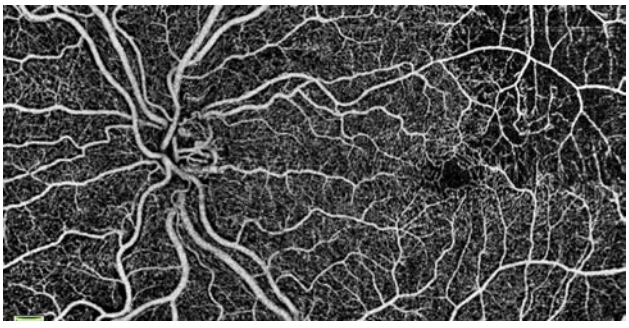


Figure 9
Optical coherence tomography-angiography montage of two 8-mm scans passing through the center part of the macula: It allowed clear visualisation of the ischaemic areas and anomalies related to the disappearance of capillary networks in the territory of the occluded cilioretinal artery. Note that the central avascular zone is preserved



The assessment of cilioretinal infarction through the indicators of the degree of venous obstruction includes: a dye transit time > 30 seconds in the central circulation; venous tortuosity; perivenous cotton wool sentinels; and macular perivenular whitening.[16]

There is no treatment proven to be effective for CLRAO associated with CRVO.[3] Non-ischaemic CRVO often has a favourable course without specific medication. However, ischaemic CRVO usually has a poor visual outcome no matter what treatment is used, and the goals of treatment may be to prevent the development and sequelae of ocular neovascular disease.[19] In regards to the natural history of visual outcome in CLARO, one study reported that visual acuity was ≥ 20/40 in 73% of cases on initial examination and 100% of cases on final follow-up.[11] Therefore, the effectiveness of treatment modalities for visual outcome needs to be evaluated against this background. With respect to arterial occlusions, the American Academy of Ophthalmology Preferred Practice Guidelines states: "*In general, there are no proven therapies or treatments for symptomatic artery occlusions. There are case reports, small case series, and uncontrolled studies that suggest that several potential interventions may be helpful. However, there are no level I data to support any single specific therapy. Initial treatment of an acute central retinal artery obstruction may include digital massage, anterior chamber paracentesis, vasodilation, breathing into a paper bag, carbogen therapy, topical pressure-lowering therapies, or hyperbaric chambers*".[20]

In fact, HBOT is very effective in the large majority of cases if administered early after the onset of vision loss. It is no longer effective in the stage of irreversible ischaemic retinal damage.[1,21,22] The challenge is to administer supplemental oxygen soon enough to prevent irreversible retinal damage. Most oxygen in blood is bound to haemoglobin, which is 97% saturated at atmospheric pressure. Some oxygen is however carried in solution, and this portion is increased at pressure due to Henry's law, which may improve tissue oxygenation.[23] When breathing normobaric air, arterial oxygen tension is approximately 13 kPa (100 mmHg) and tissue oxygen tension is about 7 kPa (55 mmHg). However, 100% oxygen at 304 kPa (3 atm abs) can increase arterial oxygen tensions to ~266 kPa (2000 mmHg), allowing the delivery of 60 ml oxygen per litre of blood (compared to 3 ml·L^{-1} when breathing air at atmospheric pressure). In theory, this would be sufficient to meet the needs of most tissues without any requirement for delivery of oxygen from haemoglobin. The high driving partial pressures allows this dissolved oxygen to diffuse further through poorly perfused tissue and can also enable tissue oxygenation even with impaired haemoglobin oxygen carriage.[24–26]

Both CRVO and CLRAO are ultimately hypoxic phenomena. During HBOT at 203 kPa the inspired partial pressure of oxygen, which determines the arterial oxygen pressure, is almost ten times greater than when breathing air at normal atmosphere pressure. Oxygen at higher pressure

diffuses from the choroidal circulation or other patent retinal vessels to reach the ischaemic retina. This restores cellular metabolism and keeps the retina alive, giving time for emboli to break-up or redistribute. This may explain the phenomenon of visual improvement reported during the first HBOT session with reduction of retinal oedema resulting in better acuity.[27]

HBOT has long been used in treating specific ocular conditions such as rhinoorbital mucormycosis and scleral necrosis.[28] Recent publications reported that HBOT can likewise be a promising treatment modality for certain ophthalmic vascular diseases. HBOT can be used in selected cases of ischaemic optic neuropathy, central retinal artery occlusion, branch retinal artery occlusion with central vision loss, ischaemic central retinal vein occlusion, ischaemic branch retinal vein occlusion, cystoid macular oedema associated with retinal venous occlusion, diabetic retinopathy, Purtscher's retinopathy, radiation retinopathy and sickle cell retinopathy though the level of supportive evidence is not high for some of these indications.[1,28–31] Emergency HBOT was first indicated as treatment for acute central retinal artery obstruction (CRAO) in the 2009 committee report of the Undersea and Hyperbaric Medical Society (UHMS) in the USA, and has subsequently been supported by the European Committee for Hyperbaric Medicine.[27] Recent studies have suggested that HBOT is a safe, easily administered, low-cost and effective treatment in patients with non-arteritic retinal artery occlusion.[32]

A positive response to HBOT should prompt a customised follow-up treatment with supplemental oxygen, in order to maintain retinal viability until the obstructed retinal artery is re-canalized, which typically occurs within 72 hours.[21] HBOT was also reported as a safe and effective treatment for a case of cystoid macular oedema secondary to retinal vein occlusion.[33] HBOT may not only increase oxygenation and perfusion pressure, but also reduces intraocular and episcleral venous pressure which promotes thrombus migration to a more distal site.[3,34] In addition, change in luminal sizes of the retinal veins with distending pressure has been described as an effect of HBOT.[34] These changes lead to blood flow acceleration in the eye. Favourable response to the first HBOT session should prompt a follow-up HBOT regimen. Admission to a stroke centre and hourly monitored visual status following a successful first HBOT session for CRAO has been recommended.[21] Vision loss during follow-up requires aggressive use of intermittent 100% normobaric and hyperbaric oxygen, in order to preserve retinal function until central retinal artery recanalisation occurs.[21] Nonetheless, an evidence-based management plan has not yet been established.

There is no clear recommendation regarding the number or frequency of HBOT sessions in this clinical situation, though guidelines are available for acute CRAO.[35] One group used a daily 2-h HBOT at 253 kPa (2.5 atm abs) for 14 consecutive days to treat a 43 year-old patient with a combination of CRVO and CLRAO.[8] Another reported the use of a daily 90 min HBOT at 243 kPa (2.4 atm abs) in a patient with ischaemic CRVO. The treatment was continued for 30 days, then decreased to two to three sessions per week for a total of 60 sessions. Visual acuity improved from 20/200 to 20/20.[34] In our case, the patient was treated with 2-hour daily session of HBOT at 253 kPa (2.5 atm abs) for a total of 30 sessions. The major parameters for visual prognosis are the time between the onset of symptoms and the starting of HBOT, and the time till retinal reperfusion.[36]

Conclusions

The combination of CRVO and CLRAO is a discreet clinical entity. Although there are several hypotheses to explain this condition, it is most likely that the elevated intraluminal pressure in the retinal capillaries due to CRVO exceeds the pressure in the CLRA. Both disorders are hypoxic phenomena. Although there is no treatment proven to be effective for this entity, HBOT was suggested to be a potential treatment modality. A multicentre, randomised controlled trial to study the results of using HBOT to treat CRVO (with and without CLRAO) would be ideal, but such a study has not yet been done and would be challenging to accomplish. In the interim, evidence from case series and retrospective cohort studies should be published and carefully reviewed in order to make evidence-based, best practice decisions.

References

1 Butler FK Jr, Hagan C, Murphy-Lavoie H. Hyperbaric oxygen therapy and the eye. Undersea Hyperb Med. 2008;35:333–87. PMID: 19024664.

2 Karia N. Retinal vein occlusion: Pathophysiology and treatment options. Clin Ophthalmol. 2010;4:809–16. doi: 10.2147/opth.s7631. PMID: 20689798. PMCID: PMC2915868.

3 Hayreh SS. Acute retinal arterial occlusive disorders. Prog Retin Eye Res. 2011;30:359–94. doi: 10.1016/j.preteyeres.2011.05.001. PMID: 21620994. PMCID: PMC3137709.

4 Oosterhuis JA. Fluorescein fundus photography in retinal vein occlusion. In: Henkes HE, editor. Perspectives in ophthalmology. Amsterdam: Excerpta Medica; 1968.

5 McLeod D, Ring CP. Cilio-retinal infarction after retinal vein occlusion. Br J Ophthalmol. 1976;60:419–27. doi: 10.1136/bjo.60.6.419. PMID: 25233547. PMCID: PMC1017521.

6 Glacet-Bernard A, Gaudric A, Touboul C, Coscas G. Occlusion de la veine centrale de la rétine avec occlusion d'une artère cilio-rétinienne: à propos de 7 cas [Occlusion of the central retinal vein with occlusion of a cilioretinal artery: a propos of 7 cases]. J Fr Ophtalmol. 1987;10:269–77. PMID: 3624794. French.

7 Schatz H, Fong AC, McDonald HR, Johnson RN, Joffe L, Wilkinson CP, et al. Cilioretinal artery occlusion in young adults with central retinal vein occlusion. Ophthalmology. 1991;98:594–601. doi: 10.1016/s0161-6420(91)32245-0. PMID: 2062490.

8 Celebi AR, Kilavuzoglu AE, Altiparmak UE, Cosar CB, Ozkiris A. Hyperbaric oxygen for the treatment of the rare

combination of central retinal vein occlusion and cilioretinal artery occlusion. Diving Hyperb Med. 2016;46:50–3. PMID: 27044464.
9 McAllister IL. Central retinal vein occlusion: A review. Clin Exp Ophthalmol. 2012;40:48–58. doi: 10.1111/j.1442-9071.2011.02713.x. PMID: 22003973.
10 Brown GC, Moffat K, Cruess A, Magargal LE, Goldberg RE. Cilioretinal artery obstruction. Retina. 1983;3:182–7. doi: 10.1097/00006982-198300330-00007. PMID: 6635353.
11 Hayreh SS, Podhajsky PA, Zimmerman MB. Branch retinal artery occlusion. Ophthalmology. 2009;116:1188–94. e1–4. doi: 10.1016/j.ophtha.2009.01.015. PMID: 19376586. PMCID: PMC2759688.
12 Keyser BJ, Duker JS, Brown GC, Sergott RC, Bosley TM. Combined central retinal vein occlusion and cilioretinal artery occlusion associated with prolonged retinal arterial filling. Am J Ophthalmol. 1994;117:308–13. doi: 10.1016/s0002-9394(14)73137-x. PMID: 8129002.
13 Bottós JM, Aggio FB, Dib E, Farah ME. Impending central retinal vein occlusion associated with cilioretinal artery obstruction. Clin Ophthalmol. 2008;2:665–8. doi: 10.2147/opth.s2694. PMID: 19668772. PMCID: PMC2694011.
14 Theoulakis PE, Livieratou A, Petropoulos IK, Lepidas J, Brinkmann CK, Katsimpris JM. Cilioretinal artery occlusion combined with central retinal vein occlusion - a report of two cases and review of the literature. Klin Monbl Augenheilkd. 2010;227:302–5. doi: 10.1055/s-0029-1245291. PMID: 20408080.
15 Hayreh SS, Fraterrigo L, Jonas J. Central retinal vein occlusion associated with cilioretinal artery occlusion. Retina. 2008;28:581–94. doi: 10.1097/IAE.0b013e31815ec29b. PMID: 18398361.
16 McLeod D. Central retinal vein occlusion with cilioretinal infarction from branch flow exclusion and choroidal arterial steal. Retina. 2009;29:1381–95. doi: 10.1097/IAE.0b013e3181b85f41. PMID: 19898176.
17 Donati G, Pournaras CJ, Pizzolato GP, Tsacopoulos M. Decreased nitric oxide production accounts for secondary arteriolar constriction after retinal branch vein occlusion. Invest Ophthalmol Vis Sci. 1997;38:1450–7. PMID: 9191609.
18 Hayreh SS. Pathogenesis of visual field defects. Role of the ciliary circulation. Br J Ophthalmol. 1970;54:289–311. doi: 10.1136/bjo.54.5.289. PMID: 4987892. PMCID: PMC1207817.
19 Flaxel CJ, Adelman RA, Bailey ST, Fawzi A, Lim JI, Vemulakonda GA, et al. Retinal vein occlusions preferred practice pattern®. Ophthalmology. 2020;127:P288–P320. doi: 10.1016/j.ophtha.2019.09.029. PMID: 31757503.
20 Flaxel CJ, Adelman RA, Bailey ST, Fawzi A, Lim JI, Vemulakonda GA, et al. Retinal and Ophthalmic Artery Occlusions Preferred Practice Pattern®. Ophthalmology. 2020;127:259–87. doi: 10.1016/j.ophtha.2019.09.028. PMID: 31757501.
21 Butler FK, Hagan C, Van Hoesen K, Murphy-Lavoie H. Management of central retinal artery occlusion following successful hyperbaric oxygen therapy: Case report. Undersea Hyperb Med. 2018;45:101–7. PMID: 29571239.
22 Murphy-Lavoie H, Butler F, Hagan C. Central retinal artery occlusion treated with oxygen: A literature review and treatment algorithm. Undersea Hyperb Med. 2012;39:943–53. PMID: 23045923.
23 Pittman RN. Regulation of tissue oxygenation. San Rafael (CA): Morgan & Claypool Life Sciences; 2011. Chapter 4, Oxygen Transport. Available from: https://www.ncbi.nlm.nih.gov/books/NBK54103/.
24 Gill AL, Bell CNA. Hyperbaric oxygen: Its uses, mechanisms of action and outcomes. QJM. 2004;97:385–95. doi: 10.1093/qjmed/hch074. PMID: 15208426.
25 Gabb G, Robin ED. Hyperbaric oxygen. A therapy in search of diseases. Chest. 1987;92:1074–82. doi: 10.1378/chest.92.6.1074. PMID: 3315479.
26 Leach RM, Rees PJ, Wilmshurst P. Hyperbaric oxygen therapy. BMJ. 1998;317(7166):1140–3. doi: 10.1136/bmj.317.7166.1140. PMID: 9784458. PMCID: PMC1114115.
27 Elder MJ, Rawstron JA, Davis M. Hyperbaric oxygen in the treatment of acute retinal artery occlusion. Diving Hyperb Med. 2017;47:233–8. doi: 10.28920/dhm47.4.233-238. PMID: 29241233. PMCID: PMC6706338.
28 Lin LJ, Chen TX, Wald KJ, Tooley AA, Lisman RD, Chiu ES. Hyperbaric oxygen therapy in ophthalmic practice: an expert opinion. Expert Rev Ophthalmol. 2020;15:119–26. doi: 10.1080/17469899.2020.1739523.
29 Maalej A, Khallouli A, Choura R, Ben Sassi R, Rannen R, Gharsallah H. The effects of hyperbaric oxygen therapy on diabetic retinopathy: A preliminary study. J Fr Ophtalmol. 2020;43:133–8. doi: 10.1016/j.jfo.2019.07.005. PMID: 31831276.
30 Abdalla Elsayed MEA, Mura M, Al Dhibi H, Schellini S, Malik R, Kozak I, et al. Sickle cell retinopathy. A focused review. Graefes Arch Clin Exp Ophthalmol. 2019;257:1353–64. doi: 10.1007/s00417-019-04294-2. PMID: 30895451.
31 Lin YC, Yang CM, Lin CL. Hyperbaric oxygen treatment in Purtscher's retinopathy induced by chest injury. J Chin Med Assoc. 2006;69:444–8. doi: 10.1016/S1726-4901(09)70289-8. PMID: 17051757.
32 Weiss JN. Hyperbaric oxygen treatment of nonacute central retinal artery occlusion. Undersea Hyperb Med. 2009;36:401–5. PMID: 20112531.
33 Gokce G, Metin S, Erdem U, Sobaci G, Durukan AH, Cagatay HH, et al. Late hyperbaric oxygen treatment of cilioretinal artery occlusion with nonischemic central retinal vein occlusion secondary to high altitude. High Alt Med Biol. 2014;15:84–8. doi: 10.1089/ham.2013.1086. PMID: 24673536.
34 Wright JK, Franklin B, Zant E. Clinical case report: treatment of a central retinal vein occlusion with hyperbaric oxygen. Undersea Hyperb Med. 2007;34:315–9. PMID: 18019081.
35 Menzel-Severing J, Siekmann U, Weinberger A, Roessler G, Walter P, Mazinani B. Early hyperbaric oxygen treatment for nonarteritic central retinal artery obstruction. Am J Ophthalmol. 2012;153:454–9.e2. doi: 10.1016/j.ajo.2011.08.009. PMID: 21996308.
36 Celebi ARC, Kadayifcilar S, Eldem B. Hyperbaric oxygen therapy in branch retinal artery occlusion in a 15-year-old boy with methylenetetrahydrofolate reductase mutation. Case Rep Ophthalmol Med. 2015;2015:640247. doi: 10.1155/2015/640247. PMID: 25722905. PMCID: PMC4334424.

Conflicts of interest and funding: nil

Submitted: 25 March 2020
Accepted after revision: 16 June 2020

Obituary

Douglas Walker 1924–2020

Douglas Walker was born in 1924 in Wallasey on the north west coast of England. He attended a local grammar school and then Liverpool University where he completed his medical degree in 1949. He was conscripted into the army and served as a medical officer stationed in Egypt for two years, rising to the rank of Captain. He then returned to England and worked in his father's medical practice before establishing his own. He married his wife Yvonne in 1956. Around this time, he attended a meeting on diving-related problems, which sparked his interest. Doug learned to dive in the UK in the 1950s at the time when most of the other divers were Royal Navy, civilians and doctors were viewed as 'lessers to be tolerated'. Doug, Yvonne and their three children (Andrew, Lindsay and Geoff) moved to Australia in 1968, where he later became a partner in a medical practice in Narrabeen and remained until his retirement at the age of 79. His fourth child, a son (Iain) was born in 1975.

Doug's involvement with South Pacific Underwater Medicine Society (SPUMS) was extensive and enduring and he was one of only a maximum of eight Life Members. He was the Editor of the SPUMS Journal from 1975 to 1990 and a prolific contributor to the journal. His aim was to transform this from a newsletter to a more formal journal, and rather than asking for permission from a wider group, he simply decided this fell within his prerogative as Editor.

His interest in underwater medicine focused largely on diving accidents and fatalities and he launched his 'Project Stickybeak' in 1972. This project occupied much of the next 48 years of his life. He collected an estimated over 15,000 diving-related academic articles and news stories and, reportedly, there were always sheets and sheets of unintelligible numbers scattered throughout his study as he tracked over 30 variables from each diving fatality.

From 1972 to 2013 he authored or co-authored more than 80 related papers, including very detailed annual fatality reports for Australia from 1972 to 2010, inclusive. He also published three annual fatality reports for New Zealand and one for the USA. Three series compilations of his Australian fatality reports were published by Divers Alert Network Asia-Pacific (DAN AP) in 1998 (1972–1993 series, edited by John Knight), 2002 (1994–1998 series), and 2009 (1999–2002). Doug also collaborated with the late Carl Edmonds, who he considered a 'kindred spirit' in this pursuit, to produce a series of three reports based on scuba deaths in Australia and New Zealand in the 1980s, as well as a report on Australian snorkelling deaths from 1987–1996.

Doug's annual fatality reports set an international benchmark for such analyses. He was like a bloodhound, pursuing the police and individual coroners investigating these deaths and obtaining all available relevant documents for his analysis. Each case was carefully dissected and reported in great detail, and often strong, albeit sometimes arguable, opinions offered on how such incidents might be avoided. In 1995, Doug was awarded a Masters Degree in Public Health, based on his work on diving fatalities.

From 2008, Douglas began working with John Lippmann (the writer) from DAN AP, to produce the report on 2003 Australian diving deaths, and continued as part of the DAN AP fatality investigation team until 2015 when the 2010 accident report was published. Doug often lamented the 'good old days' when information could be readily accessed without the current privacy obstacles and numerous ethics applications. However, his interest never waned, and he continued lobbying for diving safety until his passing at the age of 96.

Doug was an intelligent, passionate and gentle man, a dedicated GP and diving doctor, who was deeply-loved by family and highly-respected by colleagues. He laid a truly remarkable foundation for diving fatality investigation and reporting and set a high benchmark for his successors. The diving medical and general diving community owe him a great debt.

John Lippmann
Australasian Diving Safety Foundation (ADSF)
David Smart
Honorary Past President SPUMS

Notices and news

SPUMS society information and news is to be found mainly on the society website: https://spums.org.au/

SPUMS President's report

Neil Banham

COVID-19 has made 2020 an *annus horribilus* for SPUMS members, their colleagues, family and friends. The changes to our lives as we live them now would have seemed fanciful and inconceivable if suggested to us just a year ago.

COVID-19 has led to drastic changes in the way we practice medicine, and the persisting after effects of COVID are likely to be felt for many years after its passing. For those of us who see patients who dive, consideration of this will be important in assessing their ongoing fitness for this past-time or occupation. Guidelines for this are as yet early and primitive and likely to change as further information becomes available; however our Immediate Past President Professor David Smart discussed this in his final President's message in the June issue of *Diving and Hyperbaric Medicine* (DHM), and further guidelines are being developed.[1]

We have also lost the opportunity for SPUMS members to be able to meet with others of shared interest in diving and diving medicine as has occurred every year since the first SPUMS Conference in 1972 at Heron Island. Sadly, our 49th Annual Scientific Meeting due to be held in Tutukaka in April 2020 had to be postponed to 2021 and as yet, the COVID situation has not allowed this to be confirmed at the time of writing. I was optimistic, but not confident that we would be able to meet in New Zealand as planned next year, but sadly, this will not be the case. At our recent ExCom meeting it was decided that travel to New Zealand was likely to remain uncertain for the foreseeable future, and as such, Tutukaka was deferred until 2022. A proposed conference in Sydney in May 2021 is in its early planning stages, with the fallback option of a virtual conference if travel within Australia again becomes restricted, and most probably as the only option for overseas delegates.

Next year, 2021 marks the 50th anniversary of the founding of SPUMS on 03 May 1971 by Carl Edmonds, Bob Thomas, Douglas Walker, Ian Unsworth and Cedric Deal.[2] Carl Edmonds sadly passed away in late 2019, as did Douglas Walker more recently, both of whom were Editors of our journal. Douglas Walker's obituary is published in this issue. The history of the first 25 years of SPUMS makes for interesting reading,[3] and hopefully there will be a *50 Years of SPUMS 1971–2021* published soon!

However, 2020 has not all been bad. Our journal continues to go from strength to strength, thanks to the tireless work of our Editor Professor Simon Mitchell and his Editorial Assistant Nicky Telles, and to the many contributors and reviewers that make this possible. There has been a record number of submissions this year, substantially increasing the workload of all involved, but with an obvious benefit to SPUMS members for the next few issues at least.

Thanks to a grant from the Australasian Diving Safety Foundation, individual articles from issues prior to 2018 back to 2004 will soon be freely available and readily accessible as PDFs on the DHM website. This is a great leap forward for our society, and hopefully will be further enhanced in the near future when all issues will be available electronically via DHM.

I would like to take this opportunity to wish you all a safe and happy festive season and hope that 2021 is an *annus mirabilis*!

References

1 Smart D. SPUMS President's message. Diving Hyperb Med. 2020;50:190–2.
2 Inaugural meeting. SPUMS Newsletter. 1971;1:2–3.
3 Knight J. Twenty five years of SPUMS 1971-1996. SPUMS Journal. 1996;26:95–105.

Dr Neil Banham
President SPUMS

The SPUMS website is at https://spums.org.au/

Members are encouraged to log in and keep their personal details up to date.

The latest issues of *Diving and Hyperbaric Medicine* are via your society website login.

SPUMS Life Membership Award

Conjoint Professor Michael H Bennett, MBBS(UNSW) DipDHM, DA(Lond), MM(Clin Epi)(Syd), FFARCSI(Dublin), FANZCA, MD(UNSW), DipDHM ANZCA DipAdvDHM

Conjoint Professor Mike Bennett was elected to life membership of SPUMS on 18 August 2020. Due to COVID-19, the SPUMS AGM was held as a virtual meeting this year which prevented the very formal ceremonial presentation that would usually occur for such an important award. Mike is the Academic Head of the Department of Anaesthesia and a Senior Staff Specialist in diving and hyperbaric medicine at the Prince of Wales Hospital (POWH) and Conjoint Professor in the Faculty of Medicine, University of New South Wales in Sydney (UNSW), Australia. He graduated from the University of UNSW in 1979 and spent his early post-graduate training at the Prince Henry/Prince of Wales hospitals before undertaking training in anaesthesia in the UK (and no doubt drank a pint or two of Guinness whilst sitting his Irish anaesthesia fellowship). He returned to Sydney in 1990 as a retrieval specialist on the lifesaving helicopter and here developed an interest in both diving and hyperbaric medicine (DHM). He also has a strong interest in clinical epidemiology and is an experienced clinician. Mike has mentored numerous registrars in diving and hyperbaric medicine, supervising many SPUMS Diploma projects in the POWH hyperbaric unit.

Since 2004 he has been highly involved in the teaching of evidence-based medicine within the Medical Faculty at UNSW. In 2005 he was appointed co-director of the Quality Medical Practice Program there. Mike was the convenor of the Australia and New Zealand Hyperbaric Medicine Group (ANZHMG) Introductory Course in DHM from its inception in 1999 to 2014. He has contributed to most DHM short courses conducted in Australia. Mike is Chair of the Australian and New Zealand College of Anaesthetists (ANZCA) DHM subcommittee, a senior examiner for the ANZCA Diploma of Advanced DHM and Chair of the ANZCA Scholar Role subcommittee. In 2002 he was the recipient of the Behnke Award for outstanding scientific achievement from the Undersea and Hyperbaric Medical Society (USA) and is a past Vice President of the UHMS.

With respect to research, Mike has contributed to a number of textbooks, most importantly co-writing the chapter on DHM in *Harrison's Principles of Internal Medicine*. He has about 200 published papers, the majority in the peer-reviewed literature. His MD thesis, "*The evidence basis of diving and hyperbaric medicine – a synthesis of the high-level clinical evidence with meta-analysis*", was accepted by the UNSW in 2006. Perhaps his most important contribution to DHM has been his involvement as co-author of a series of *Cochrane Reviews* on the role of hyperbaric oxygen treatment in 14 conditions, both acute and chronic. Mike summarises his broad research areas as clinical research, epidemiology, evidence-based medicine and biostatistics.

Where SPUMS is concerned, he has been a member of the Executive Committee since 2001, as President from 2008 to 2014 and Past President, retiring from this post at the 2020 AGM. He facilitated SPUMS and EUBS coming together as joint publishers of *Diving and Hyperbaric Medicine (DHM)*. Mike chaired the ANZHMG, a sub-committee of SPUMS, for a number of years and the SPUMS/EUBS Journal Governance Committee, set up in 2015 to help guide the policies and management of the societies' journal. Mike's academic support of our journal, spanning a quarter century, has been outstanding, with over 50 published articles on a wide range of topics. The editors of DHM regularly sought his advice and support which was provided always willingly and constructively. Mike's first SPUMS ASM was in Rabaul in 1994; he has attended most since. He has also acted as the Scientific Convenor of six SPUMS ASMs, including as Chair of the Tricon Scientific Committee in 2015 and 2018.

Mike is an international giant in diving and hyperbaric medicine. We know of no member of SPUMS more deserving than Michael H Bennett to receive Life Membership, and the SPUMS executive committee congratulates him on his achievements and contribution.

Mike Davis
Editor of DHM 2002 to 2018
David Smart
Honorary Past President, SPUMS

Photo: Cdr Douglas Falconer (SPUMS Secretary), presenting Conjoint Professor Mike Bennett with his life membership certificate.

ADSF Grant for individual articles available on *Diving and Hyperbaric Medicine* journal website

SPUMS would like to convey our sincere appreciation for the funding provided to SPUMS by ADSF to allow individual article conversion of previous issues of our journal *Diving and Hyperbaric Medicine* (DHM).

This work is currently well underway, and when complete, will allow previously published articles being readily and freely accessible via the DHM website. The website already has a large amount of resources and we are expanding this as time and finances allow.

SPUMS Facebook page

Like us at:
http://www.facebook.com/pages/SPUMS-South-Pacific-Underwater-Medicine-Society/221855494509119

Australian and New Zealand College of Anaesthetists Diving and Hyperbaric Medicine Special Interest Group

The new Diploma of Advanced Diving and Hyperbaric Medicine was launched on 31 July 2017. Those interested in training are directed to the ANZCA website http://www.anzca.edu.au/training/diving-and-hyperbaric-medicine.

Training
Documents to be found at this site are:

- Regulation 36, which provides for the conduct of training leading to the ANZCA Dip Adv DHM, and the continuing professional development requirements for diplomats and holders of the ANZCA Certificate of DHM;
- ANZCA Advanced DHM Curriculum which defines the required learning, teaching and assessment of the diploma training programme; and
- ANZCA Handbook for Advanced DHM Training which sets out in detail the requirements expected of trainees and accredited units for training.

Examination dates for 2021
Dates for the 2021 exam will be published late 2020.

Accreditation
The ANZCA Handbook for Advanced DHM accreditation, which provides information for units seeking accreditation, is awaiting approval by Standards Australia and cannot yet be accessed online. Currently six units are accredited for DHM training and these can be found on the College website.

Transition to new qualification
Transitional arrangements for holders of the ANZCA Certificate in Diving and Hyperbaric Medicine and highly experienced practitioners of DHM seeking recognition of prior experience lapsed on 31 January 2019.

All enquiries should be submitted to dhm@anzca.edu.au.

Royal Australian Navy Medical Officers' Underwater Medicine Course 2021

Venue: HMAS Penguin, Sydney

Date: 15–26 March 2021

The MOUM course seeks to provide the medical practitioner with an understanding of the range of potential medical problems faced by divers.

Cost: The course cost is AUD$1,355 (ex GST) TBC.

For information and application forms contact:
Rajeev Karekar, for Officer in Charge
rajeev.karekar@defence.gov.au

SPUMS Diploma in Diving and Hyperbaric Medicine

Requirements for candidates (May 2014)

In order for the Diploma of Diving and Hyperbaric Medicine to be awarded by the Society, the candidate must comply with the following conditions: They must

1 be medically qualified, and remain a current financial member of the Society at least until they have completed all requirements of the Diploma;
2 supply evidence of satisfactory completion of an examined two-week full-time course in diving and hyperbaric medicine at an approved facility. The list of such approved facilities may be found on the SPUMS website;
3 have completed the equivalent (as determined by the Education Officer) of at least six months' full-time clinical training in an approved Hyperbaric Medicine Unit;
4 submit a written proposal for research in a relevant area of underwater or hyperbaric medicine, in a standard format, for approval before commencing the research project;
5 produce, to the satisfaction of the Academic Board, a written report on the approved research project, in the form of a scientific paper suitable for publication. Accompanying this report should be a request to be considered for the SPUMS Diploma and supporting documentation for 1–4 above.

In the absence of other documentation, it will be assumed that the paper is to be submitted for publication in *Diving and Hyperbaric Medicine*. As such, the structure of the paper needs to broadly comply with the 'Instructions for authors' available on the SPUMS website https://spums.org.au/ or at https://www.dhmjournal.com/.

The paper may be submitted to journals other than *Diving and Hyperbaric Medicine*; however, even if published in another journal, the completed paper must be submitted to the Education Officer (EO) for assessment as a diploma paper. If the paper has been accepted for publication or published in another journal, then evidence of this should be provided.

The diploma paper will be assessed, and changes may be requested, before it is regarded to be of the standard required for award of the Diploma. Once completed to the reviewers' satisfaction, papers not already submitted to, or accepted by, other journals should be forwarded to the Editor of *Diving and Hyperbaric Medicine* for consideration. At this point the Diploma will be awarded, provided all other requirements are satisfied. Diploma projects submitted to *Diving and Hyperbaric Medicine* for consideration of publication will be subject to the Journal's own peer review process.

Additional information – prospective approval of projects is required

The candidate must contact the EO in writing (or email) to advise of their intended candidacy and to discuss the proposed topic of their research. A written research proposal must be submitted before commencement of the research project.

All research reports must clearly test a hypothesis. Original basic and clinical research are acceptable. Case series reports may be acceptable if thoroughly documented, subject to quantitative analysis and if the subject is extensively researched in detail. Reports of a single case are insufficient. Review articles may be acceptable if the world literature is thoroughly analysed and discussed and the subject has not recently been similarly reviewed. Previously published material will not be considered. It is expected that the research project and the written report will be primarily the work of the candidate, and that the candidate is the first author where there are more than one.

It is expected that all research will be conducted in accordance with the joint NHMRC/AVCC statement and guidelines on research practice, available at: www.nhmrc.gov.au/_files_nhmrc/publications/attachments/r39.pdf, or the equivalent requirement of the country in which the research is conducted. All research involving humans, including case series, or animals must be accompanied by documentary evidence of approval by an appropriate research ethics committee. Human studies must comply with the Declaration of Helsinki (1975, revised 2013). Clinical trials commenced after 2011 must have been registered at a recognised trial registry site such as the Australia and New Zealand Clinical Trials Registry http://www.anzctr.org.au/ and details of the registration provided in the accompanying letter. Studies using animals must comply with National Health and Medical Research Council Guidelines or their equivalent in the country in which the work was conducted.

The SPUMS Diploma will not be awarded until all requirements are completed. The individual components do not necessarily need to be completed in the order outlined above. However, it is mandatory that the research proposal is approved prior to commencing research.

Projects will be deemed to have lapsed if:

- the project is inactive for a period of three years, or
- the candidate fails to renew SPUMS Membership in any year after their Diploma project is registered (but not completed).

For unforeseen delays where the project will exceed three years, candidates must explain to the EO by email why they wish their diploma project to remain active, and a three-year extension may be approved. If there are extenuating circumstances why a candidate is unable to maintain financial membership, then these must be advised by email to the EO for consideration by the SPUMS Executive. If a project has lapsed, and the candidate wishes to continue with their DipDHM, then they must submit a new application as per these guidelines.

The Academic Board reserves the right to modify any of these requirements from time to time. As of October 2020, the SPUMS Academic Board consists of:

Associate Professor David Cooper, Education Officer, Hobart
Professor Simon Mitchell, Auckland

All enquiries and applications should be addressed to:
Associate Professor David Cooper
education@spums.org.au

Key words
Qualifications; Underwater medicine; Hyperbaric oxygen; Research; Medical society

Notices and news

EUBS notices and news and all other society information is now to be found mainly on the society's website: https://www.eubs.org/

EUBS President's report

Ole Hyldegaard

The EUBS general assembly and 2020

While writing my report, our annual General Assembly (GA) meeting has for the first time ever, commenced as a virtual online voting event. The deadline for this was 15 November and therefore, later than the deadline for my report for this journal and members of EUBS. I would like to congratulate the ExCom of EUBS for handling the situation efficiently and also I would like to thank our Honorary Secretary Peter Germonpré for setting up this process on our website, distributing information to all EUBS members and executing the online voting for members. Hopefully the EUBS ExCom our members will accept and appreciate this procedure for the General Assembly this year and that all members will participate by casting their votes.

Thank you also to our Membership Secretary and Treasurer Kathleen Pye for preparing the accounting and fiscal reports and to Richard Wade (DDRC) for the auditing and external approval of the EUBS financial reporting. This year we have three key questions that require the specific attention of all EUBS members and casting of votes; 1) the approval of the minutes of the GA in 2019 and as published on the EUBS website; 2) the approval of the financial report and 3) the proposed changes in membership fees.

I trust all active EUBS members will cast their votes and hope that you will find the ExCom's preparations and arguments to the point and relevant given the circumstances and the conditions for this year's GA.

With the hope of a large turnout of voting I wish all members a good GA virtual experience and we shall report the results of the voting asap after deadline!

The COVID-19 disease, hyperbaric oxygen treatment and diving related health and safety issues

As the second wave of the COVID-19 pandemic rages on our continent, the EUBS acknowledges the need for continuously updating the situation of both the handling of COVID-19 patients in relation to HBOT and diving health issues as well. Our good colleagues and members of the EUBS ExCom are currently preparing a virtual seminar/workshop on the issues of HBOT for COVID-19 patients and diving related health issues. Stay tuned on the EUBS website and email alerts for further information and registration for this event which, we hope will commence early 2021, if not before.

Ole Hyldegaard
EUBS President

EUBS Notices and news

EUBS 2020 Meeting

The 46th EUBS Annual Scientific Meeting – postponed due to the COVID-19 pandemic, has now been announced for 08–11 September 2021, in Prague, Czech Republic. While at the time of this publication the pandemic is still very much a reality, EUBS hopes to welcome its members and many friends and scientists from around the globe for our '2020–2021 meeting', to gather in person and renew/strengthen our professional and personal relationships.
Keep monitoring the website https://www.eubs2020.com for all news and updates.

EUBS Annual General Assembly

Also due to the COVID-19 pandemic, our annual EUBS General Assembly has been held in a 'virtual meeting' format. All EUBS full members had a chance to express their opinion and vote online regarding the 'current affairs' decisions for our society.

The GA presentation and financial information have been placed on the EUBS website, in the members area section.

EUBS Executive Committee

Following a three-year term by Rodrigue Pignel from Geneva (Switzerland), Oscar Camacho from Porto (Portugal), has been elected as the new Member-at-Large 2020. The Executive Committee wish to express their gratitude for Rodrigue's contributions to the ExCom activities. However, Rod will remain active as member of the Liaison Committee and will continue to develop the OXYNET database. He can be reached by email at rodrigue.pignel@eubs.org.

EUBS social media

All EUBS members are reminded to bookmark and follow our Social Media channels:

Facebook: https://www.facebook.com/European-Underwater-and-Baromedical-Society-283981285037017/
Twitter: @eubsofficial
Instagram: @eubsofficial
While the 'EUBS website news' email messages will continue to be a way to communicate important information directly to our EUBS members, Facebook, Twitter and Instagram will be used to keep also non-members updated and interested in our Society. Our social media is managed by Bengusu Mirasoglu, bengusu.mirasoglu@eubs.org.

EUBS Membership

Do not forget to renew your EUBS membership. If your membership has expired, you will see a message when trying to log in on the EUBS website. You can then immediately renew it online.

EUBS membership gives you significant advantages, such as immediate access to the most recent issues of the DHM Journal, (if selected) a print copy of the e-journal for your convenience, reduced registration fee at our Annual Scientific Meeting (this alone already pays back your membership fee!), reduced membership fees at selected Affiliate Societies, access to the GTUEM database of non-indexed scientific literature, searchable membership database, etc.

In case you have difficulties renewing or accessing your Membership Area, please contact us at secretary@eubs.org.

Membership news

On 15 December 2020, EUBS Member-at-Large Gerardo (Dino) Bosco will take over Presidency of the Italian Underwater and Hyperbaric Society (SIMSI), for a period of two years. He will be taking over from Dr Pasquale Longobardi. This will strengthen the good relationship between our two societies even further. Congratulations!

EUBS website

Visit our EUBS website to be informed of news, conferences and meetings, endorsed documents and courses. You can also find information on travel and research grants, employment opportunities, research projects looking for multicentric collaboration, and much more.

Specifically, have a look at the 'EUBS history' section which has been added under the menu item 'The Society'. There is still some information missing in the list of EUBS meetings, Presidents and Members-at-Large – please dig into your memories and help us complete this list.

By popular demand, EUBS members can now also download the complete abstract book of previous EUBS meetings since 2008 from the member's area.

In case you have any suggestions for adding or correcting the info posted, please contact us at webmaster@eubs.org.

Publications database of the German Diving and Hyperbaric Medical Society (GTÜM)

German Diving and Hyperbaric Medical Society's (GTÜM) website is currently unavailable owing to a new website being built. They have advised that a notification will sent when their database will be available again, They apologise for any inconvenience this may cause.

The Science of Diving

Support EUBS by buying the PHYPODE book 'The science of diving'. Written for anyone with an interest in the latest research in diving physiology and pathology. The royalties from this book are being donated to the EUBS.
Available from: Morebooks
https://www.morebooks.de/store/gb/book/the-science-of-diving/isbn/978-3-659-66233-1

The EUBS website is at **https://www.eubs.org/**

Members are encouraged to log in and keep their personal details up to date.

The latest issues of *Diving and Hyperbaric Medicine* are via your society website login.

Courses and meetings

Scott Haldane Foundation

As an institute dedicated to education in diving medicine, the Scott Haldane Foundation has organised more than 295 courses all over the world, over the past 27 years. SHF is targeting more and more on an international audience with courses world wide. Due to the COVID-19 Pandemic some courses are re-scheduled. Fortunately, we were able to find new dates for all postponed courses. Below the upcoming SHF-courses in early 2021.

The courses Medical Examiner of Diver (part 1 and 2) and SHF in-depth courses, as modules of the level 2d Diving Medicine Physician course, fully comply with the ECHM/EDTC curriculum for Level 1 and 2d respectively and are accredited by the European College of Baromedicine (ECB).

2021

12–13 March	In-depth course Decompression, Recompression and HBOt (Level 2d) Hoeven, NL
19–20 March	Medical Examiner of Divers Part 1 (Level 1) Zeist, NL
25–27 March	Medical Examiner of Divers Part 2 (Level 1) Amsterdam Univ. Med. Centre, NL
10–17 April	Medical Examiner of Divers part 2 (Level 1) Bonaire, Dutch Caribbean
May	28st In-depth course diving and mental health (2d) Venue: tbd
Spring 2021	Internship different types of diving (2d) Royal Dutch Navy-Den Helder NL
On request	Internship HBOt (level 2d certification) NL/Belgium

The course calendar will be supplemented regularly.

For the latest information visit:
https://www.scotthaldane.org

Please also check the COVID-19 News update on the website for the latest schedule changes.

Capita Selecta Diving Medicine

The symposia of the Capita Selecta Diving Medicine of the University of Amsterdam will resume when the COVID-19-regulations of Academic Medical Centre of the University of Amsterdam allow this.

The symposium to celebrate the 50 year anniversary of the Dutch Stichting Duik Research (SDR, Foundation of Diving Research) originally scheduled in October is postponed until the autumn of 2021. Dates are to be confirmed.

Visit: http://www.duikresearch.org/

For more information: n.a.schellart@amsterdamumc.nl

Hyperbaric Oxygen, Karolinska

Welcome to: http://www.hyperbaricoxygen.se/

This site, supported by the Karolinska University Hospital, Stockholm, Sweden, offers publications and high-quality lectures from leading investigators in hyperbaric medicine. Please register to obtain a password via email. Once registered, watch on line, or download to your iPhone, iPad or computer for later viewing.

For further information contact via email:
folke.lind@karolinska.se

DIVING HISTORICAL SOCIETY AUSTRALIA, SE ASIA

P O Box 347, Dingley Village
Victoria, 3172, Australia
Email: hdsaustraliapacific@hotmail.com.au
Website: www.classicdiver.org

Diving and Hyperbaric Medicine: Instructions for authors (summary)

Diving and Hyperbaric Medicine (DHM) is the combined journal of the South Pacific Underwater Medicine Society (SPUMS) and the European Underwater and Baromedical Society (EUBS). It seeks to publish papers of high quality on all aspects of diving and hyperbaric medicine of interest to diving medical professionals, physicians of all specialties, scientists, members of the diving and hyperbaric industries, and divers. Manuscripts must be offered exclusively to *Diving and Hyperbaric Medicine*, unless clearly authenticated copyright exemption accompaniesthe manuscript. All manuscripts will be subject to peer review. Accepted contributions will also be subject to editing.

Address: The Editor, Diving and Hyperbaric Medicine, Department of Anaesthesiology, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand
Email: editor@dhmjournal.com
Phone: (mobile) +64 (0)27 4141 212
European Editor: euroeditor@dhmjournal.com
Editorial Assistant: editorialassist@dhmjournal.com
Journal information: info@dhmjournal.com

Contributions should be submitted electronically by following the link:
http://www.manuscriptmanager.net/dhm
There is on-screen help on the platform to assist authors as they assemble their submission. In order to submit, the corresponding author needs to create an 'account' with a user name and password (keep a record of these for subsequent use). The process of uploading the files related to the submission is simple and well described in the on-screen help provided the instructions are followed carefully. The submitting author must remain the same throughout the peer review process.

Types of articles

DHM welcomes contributions of the following types:

Original articles, Technical reports and Case series: up to 3,000 words is preferred, and no more than 30 references (excluded from word count). Longer articles will be considered. These articles should be subdivided into the following sections: an **Abstract** (subdivided into Introduction, Methods, Results and Conclusions) of no more than 250 words (excluded from word count), **Introduction, Methods, Results, Discussion, Conclusions, References, Acknowledgements**, **Funding** sources and any **Conflicts of interest**. **Legends/captions** for illustrations, figures and tables should be placed at the end of the text file.

Review articles: up to 5,000 words is preferred and a maximum of 50 references (excluded from word count); include an informative **Abstract** of no more than 300 words (excluded from total word count); structure of the article and abstract is at the author(s)' discretion.

Case reports, Short communications and **Work in progress** reports: maximum 1,500 words, and 20 references (excluded from word count); include an informative **Abstract** (structure at author's discretion) of no more than 200 words (excluded from word count).

Educational articles, Commentaries and **Consensus reports** for occasional sections may vary in format and length, but should generally be a maximum of 2,000 words and 15 references (excluded from word count); include an informative **Abstract** of no more than 200 words (excluded from word count).

Letters to the Editor: maximum 600 words, plus one figure or table and five references.

Formatting of manuscripts

All submissions must comply with the following requirements. Manuscripts not complying with these instructions will be suspended and returned to the author for correction before consideration. Guidance on structure for the different types of articles is given above.

The following pdf files are available on the DHM website to assist authors in preparing their submission:

- Instructions for authors (full version)
- DHM Key words
- DHM Mandatory Submission Form 2020
- Trial design analysis and presentation
- EASE participation and conflict of interest statement
- English as a second language
- Guideline to authorship in DHM 2015
- Helsinki Declaration revised 2013
- Is ethics approval needed?

DIVER EMERGENCY SERVICES PHONE NUMBERS

AUSTRALIA – DAN
1800-088200 (in Australia toll free)
+61-3-7018 3076 (International)

NEW ZEALAND – NZUA
0800-4DES-111 (in New Zealand toll free)
+64-9-445-8454 (International)

JAPAN – DAN
+81-3-3812-4999 (Japan)

EUROPE – DAN
+39-6-4211-8685 (24-hour hotline)

UNITED KINGDOM
+44-7740-251-635

AFRICA – DAN
0800-020111 (in South Africa toll free)
+27-828-106010 (International call collect)

USA – DAN
+1-919-684-9111

ADSF
AUSTRALASIAN DIVING SAFETY FOUNDATION

Scholarships for Diving Medical Training for Doctors

The Australasian Diving Safety Foundation is proud to offer a series of annual Diving Medical Training scholarships. We are offering these scholarships to qualified medical doctors to increase their knowledge of diving medicine by participating in an approved diving medicine training programme. These scholarships are mainly available to doctors who reside in Australia. However, exceptions may be considered for regional overseas residents, especially in places frequented by Australian divers. The awarding of such a scholarship will be at the sole discretion of the ADSF. It will be based on a variety of criteria such as the location of the applicant, their working environment, financial need and the perception of where and how the training would likely be utilised to reduce diving morbidity and mortality. Each scholarship is to the value of AUD5,000.00.

There are two categories of scholarships:

1. ADSF scholarships for any approved diving medical training program such as the annual ANZHMG course at Fiona Stanley Hospital in Perth, Western Australia.
2. The Carl Edmonds Memorial Diving Medicine Scholarship specifically for training at the Royal Australian Navy Medical Officers' Underwater Medicine Course, HMAS Penguin, Sydney, Australia.

Interested persons should first enrol in the chosen course, then complete the relevant ADSF Scholarship application form available at: https://www.adsf.org.au/r/diving-medical-training-scholarships and send it by email to John Lippmann at johnl@adsf.org.au.
