RESEARCH ARTICLE

Risk factors for immersion pulmonary edema in recreational scuba divers: a case-control study

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ABSTRACT

Background: Immersion can cause immersion pulmonary edema (IPE) in previously healthy subjects. We performed a case-control study to better identify IPE risk factors.

Methods: We prospectively included recreational scuba divers who had presented signs of IPE and control divers who were randomly chosen among diving members of the French Underwater Federation. We sent an anonymous questionnaire to each diver, with questions on individual characteristics, as well as the conditions of the most recent dive (controls) or the dive during which IPE occurred. Univariate logistic regressions were performed for each relevant factor. Then, multivariate logistic regression was performed.

Results: Of the 882 questionnaires sent, 480 (54%) were returned from 88 cases (90%) and 392 control divers (50%). Multivariate analysis identified the following independent risk factors associated with IPE:

- being aged over 50 years ((OR) 3.30, (95%CI) 1.76-6.19);
- female sex (OR 2.20, 95%CI 1.19-4.08);
- non-steroidal anti-inflammatory drug (NSAID) intake before diving (OR 24.32, 95%CI 2.86-206.91);
- depth of dive over 20 m (OR 2.00, 95%CI 1.07-3.74);
- physical exertion prior to or during the dive (OR 5.51, 95%CI 2.69-11.28);
- training dive type (OR 5.34, 95%CI 2.62-10.86); and
- daily medication intake (OR 2.79, 95%CI 1.50-5.21); this latter factor appeared to be associated with hypertension in the univariate analysis.

Conclusions: To reduce the risk of experiencing IPE, divers over 50 years of age or with hypertension, especially women, should avoid extensive physical effort, psychological stress, deep dives and NSAID intake before diving.

KEYWORDS: pulmonary edema; scuba diving; immersion

INTRODUCTION

Several studies have reported that immersion can cause stress failure of the blood-gas barrier leading to immersion pulmonary edema (IPE) in previously healthy subjects during endurance swimming, breath-hold diving and scuba diving [1-8].

The pathophysiology of IPE is not completely understood and appears to be multifactorial. In all cases, the main issue is the redistribution of peripheral blood into central circulation due to immersion, which leads to an increase in cardiac preload as well as in pulmonary vascular pressure and a decrease in pulmonary compliance. Emotional stress and physical exertion contribute to this high vascular pressure, which may be further increased by wearing a diving wetsuit [9]. Cold exposure causes arteriolar constriction that may increase cardiac afterload; the wetsuit can also impair ventilatory mechanics [10]. During scuba diving, subjects undergo other respiratory constraints such as increased inspired gas density and resistance due to the breathing apparatus, leading to an increase in the respiratory workload [11].

IPE is thought to involve two populations: relatively young subjects such as triathletes or military divers under intense physical exertion during immersion and older recreational divers with prior cardiovascular abnormalities and probably undiagnosed left ventricular dysfunction [12].

The purpose of the present study was to analyze the risk factors of IPE during recreational scuba diving with a case-control study.

METHODS

Case and control subjects and study design

From March 2011 to November 2015, we prospectively recruited recreational scuba divers who presented signs of IPE as defined in Table 1. The majority of these divers were treated in two French hyperbaric centers: Brest, near the Atlantic Ocean and Toulon, near the Mediterranean Sea.

For each case, we contacted eight control divers randomly chosen from diving members of the French Underwater Federation (FFESSM). We excluded subjects under 18 years old, subjects who had a contraindication for diving exceeding one month at the time of the survey and subjects with a history of respiratory illness while diving.

We sent by post the same questionnaire to all divers, cases and controls, with questions on individual characteristics (age, sex, weight, size, smoking status, cardio-respiratory and metabolic history, daily medication), as well as the conditions of the most recent dive (controls) or of the dive during which IPE occurred (cases) and health status at the moment of the dive (sickness at the moment of the dive, medication taken before diving). When responders answered "yes" to the questions on medication intake, they were asked to name the medication.

The responses to the questionnaires were collected anonymously.

The survey protocol was approved by our institutional Ethics Committee (Comité d'éthique du CHRU de Brest) and the French National Data Protection Authority (CNIL).

Data analysis

Divers' characteristics were expressed as mean and standard deviation for continuous variables and as number and percentage for categorical variables. Student's t-test was used to compare means between the two diver groups (case group and control group). A non-parametric Mann-Whitney test was used when the distribution was not normal. Chi-square test (or an exact Fisher test when appropriate) was used to compare proportions. Univariate logistic regressions were performed for each relevant factor. Then, multivariate logistic regression was performed using a backward selection procedure with a significance level of 0.05. The statistical analysis was performed using SAS software, version 9.4.

Table 1: Inclusion and exclusion criteria for cases

	CASE INCLUSION CRITERIA
	onset of signs during immersion
and	
	respiratory sickness with dyspnea
and/or	*cough*
and/or	*hemoptysis* and/or *frothy or bloody sputum*
and/or	*weakness*
and	*chest X-ray or CT scan confirming the diagnosis*
	CASE EXCLUSION CRITERIA
	water aspiration
or	*rapid ascent with respiratory blockage*
or	*signs of pneumothorax or pneumomediastinum*

RESULTS

In total, 882 questionnaires were sent to 98 cases and 784 control divers. Of these, 480 (54%) were returned, with 88 from IPE cases (90%) and 392 from control divers (50%), thus allowing reliable analysis of data (i.e., 4.4 control cases for every IPE case).

The sex distribution between responders and non-responders was not statistically different: 69.4% (279) men in the non-responder group versus 67.5% (324) in the responder group ($p = 0.514$). The mean age of responders was significantly higher than that of the non-responders (46.6 years ± 11.9 years versus 42.5 ± 12.7, $p < 0.001$).

Individual characteristics are presented in Table 2. Case divers were significantly older. The proportion of women was significantly higher in the case group, as was history of arterial hypertension, daily medication intake and hypotensive drugs intake. No statistical difference was found for the intake of other drugs.

Dive conditions and health status at the time of the dive (dive during which IPE occurred for the case divers or most recent dive for the control divers) are presented in Table 3. The mean depth of the cases' dives was significantly greater than that of the controls and the mean duration of the cases' dives was significantly shorter than that of the controls. The cases' dives were predominantly associated with training dive sessions and exertion prior to or during the dive.

Univariate analysis and the multivariate analysis are presented in Table 4 and show that the independent risk factors associated with IPE were being older than 50 years of age (odds-ratio (OR) 3.30, 95% confidence interval (95%CI) 1.76-6.19), female sex (OR 2.20, 95%CI 1.19-4.08),

Table 2: Individual characteristics of control divers and case divers

Variable		Cases (N=88)	Controls (N=392)	p*
	N	88	392	
Mean age (yr)		50.9 (SD10.62)	45.3 (SD11.87)	<0.001
Age	< 50 yr	33 (37.5%)	246 (62.8%)	<0.001
(two age classes)	≥ 50 yr	55 (62.5%)	146 (37.2%)	
Sex	Male	47 (53.4%)	277 (70.7%)	0.002
	Female	41 (46.6%)	115 (29.3%)	
Body Mass Index: N		88	385	0.033
	mean	25.9 (SD 4.18)	25.0 (SD3.67)	
Obesity: yes		13 (14.8%)	35 (8.9%)	0.119
	missing data	0 (0%)	7 (1.8%)	
Cigarette smoker: yes		9 (10.2%)	66 (16.8%)	0.121
	missing data	0 (0%)	1 (0.3%)	
New dive after long hiatus: yes		18 (20.5%)	82 (20.9%)	1.000
	missing data	1 (1.1%)	4 (1%)	
Total number of dives in lifetime	1-50	20 (22.7%)	100 (25.5%)	0.692
	51-200	32 (36.4%)	127 (32.4%)	
	>200	33 (37.5%)	160 (40.8%)	
Hypertension		19 (21.6%)	26 (6.6%)	<0.001
History of cardiomyopathy		4 (4.5%)	9 (2.3%)	0.270
Hyperlipidemia		16 (18.2%)	44 (11.2%)	0.075
Daily medication intake		43 (48.9%)	84 (21.4%)	<0.001
Daily hypotensive medication intake		17 (19.3%)	26 (6.6%)	<0.001
Daily diabetes medication intake		4 (4.5%)	4 (1%)	0.041
Daily antiplatelet medication intake		2 (2.3%)	4 (1%)	0.304

Data are presented as mean and standard deviation (SD) for continuous variables and as number and percentage for categorical variables.
* p-value from chi-square or Fisher test for proportions or from Student's t-test or Mann-Whitney test for means

non-steroidal anti-inflammatory drugs (NSAID) intake before diving (OR 24.32, 95%CI 2.86 – 206.91), depth of dive greater than 20 m (OR 2.00, 95%CI 1.07 – 3.74), physical exertion prior to or during diving (OR 5.51, 95%CI 2.69 – 11.28), training dive type (OR 5.34, 95%CI 2.62 – 10.86) and daily medication intake (OR 2.79, 95%CI 1.50-5.21).

DISCUSSION

Our study explored the frequently alleged reported risk factors, such as age, physical exertion and daily medication intake (primarily for hypertension). In addition to these factors we also found a risk associated with being female, dive depth, training dives and NSAID intake before diving. To our knowledge, this is the first study on the risk factors of IPE using a case-control study design with a control group randomly chosen from a large population of scuba divers.

Table 3: Dive conditions and health status at the time of dive

Variable		Cases (N=88)	Controls (N=392)	p*
Feeling ill before diving		4 (4.5%)	15 (3.8%)	0.761
	missing data	1 (1.1%)	1 (0.3%)	
Medication intake before diving (other than daily medication)		23 (26.1%)	35 (8.9%)	<0.001
	missing data	0 (0%)	1 (0.3%)	
NSAID intake before diving		12 (13.6%)	1 (0.3%)	<0.001
Seasickness medication intake before diving		3 (3.4%)	7 (1.8%)	0.401
Antibiotic intake before diving		0 (0%)	2 (0.5%)	1.000
Nasal congestion medication intake before diving		0 (0%)	3 (0.8%)	1.000
Mean dive depth (msw)		29.7 (SD 12.18)	26.1 (SD10.91)	0.006
	N :	87	381	
Dive depth				0.034
	<= 20 m	28 (31.8%)	170 (43.4%)	
	> 20 m	59 (67%)	211 (53.8%)	
Mean dive duration (min)		25.9 (SD 11.00)	43.9 (SD13.32)	<0.001
	N	82	373	
Type of breathing gas				0.054
	Air	80 (90.9%)	352 (89.8%)	
	Nitrox	4 (4.5%)	35 (8.9%)	
	Trimix	2 (2.3%)	1 (0.3%)	
Type of dive				<0.001
	Training dive	36 (40.9%)	40 (10.2%)	
	Exploratory dive	49 (55.7%)	340 (86.7%)	
Feeling cold		20 (22.7%)	60 (15.3%)	0.088
	missing data	1 (1.1%)	3 (0.8%)	
Thermal protection suited to the water temperature				0.092
	No	11 (12.5%)	26 (6.6%)	
	Borderline	6 (6.8%)	32 (8.2%)	
	Yes	58 (65.9%)	312 (79.6%)	
Physical exertion before and/or during diving		34 (38.6%)	32 (8.2%)	<0.001
	missing data	1 (1.1%)	7 (1.8%)	

Data are presented as mean and standard deviation (SD) for continuous variables and as number and percentage for categorical variables.

* p-value from chi-square or Fisher test for proportions or from Student's t-test or Mann-Whitney test for means; NSAID : Non-steroidal anti-inflammatory drug

Table 4: Univariate and multivariate analyses

Variable	Univariate analysis	Multivariate analysis		
	OR (95% CI)	p*	OR (95% CI)	p†
Age ≥ 50 yr	2.81 (1.74-4.53)	<0.001	3.30 (1.76-6.19)	<0.001
Female	2.10 (1.31-3.37)	0.002	2.20 (1.19-4.08)	0.012
Daily medication intake	3.50 (2.16-5.68)	<0.001	2.79 (1.50-5.21)	0.001
NSAID intake before diving	61.74 (7.91-481.83)	<0.001	24.32 (2.86-206.91)	0.003
Dive depth > 20 m	1.70 (1.04-2.78)	0.035	2.00 (1.07-3.74)	0.031
Physical exertion before and/or during diving	7.08 (4.03-12.42)	<0.001	5.51 (2.69-11.28)	<0.001
Training dive	6.24 (3.64-10.72)	<0.001	5.34 (2.62-10.86)	<0.001
Hypertension	3.88 (2.03-7.39)	<0.001		
Hyperlipidemia	1.76 (0.94-3.29)	0.077		
Medication intake before diving	3.60 (2.00-6.48)	<0.001		
Feeling cold	1.64 (0.93-2.89)	0.090		
Obesity	1.73 (0.87-3.43)	0.115		
Cigarette smoker	0.56 (0.27-1.17)	0.125		
Thermal protection suited to the water temperature				
Borderline vs No	0.44 (0.14-1.36)	0.102		
Yes vs No	0.44 (0.21-0.94)			

* p-value from Chi-square or Fisher test for proportions or from Student's t-test or Mann-Whitney test for means; † p-value from Wald test; OR odds ratio; 95% CI, 95% confidence interval; NSAID: non-steroidal anti-inflammatory drug

Subclinical pulmonary edema may be quite common after an open-sea scuba dive. One report showed that a scuba dive can lead to increased right-sided cardiac preload and higher pulmonary arterial pressures without increase in left ventricular stroke volume in a young population of professional divers [13]. An imbalance between right and left ventricular stroke volumes causes an accumulation of fluid in the pulmonary vasculature [14]. Fluid clearance by the lymphatic system is increased by hyperventilation during exercise [15]. At maximum work in prone swimming, minute ventilation and breathing rate seem to be lower compared to maximum work on land [16]. Poor coordination between breathing and swimming stroke may hamper the ability to increase minute ventilation and may limit the ability to increase fluid clearance [17]. Acute pulmonary edema occurs when hydrostatic pulmonary capillary pressure is high and when the lymphatic system becomes overloaded. Small modifications that increase this imbalance between the right and left ventricles can lead to symptomatic pulmonary edema.

Age is a commonly suggested risk factor in the majority of IPE cases reported from recreational practice. Peacher, et al. report a mean age of 40-49 years in IPE cases involving recreational divers [12], and several case reports confirm that IPE occurs mostly in divers older than 40 years [18]. Our case-control study demonstrated that IPE divers were significantly older than controls. Cardiorespiratory changes associated with aging tend to increase inspiratory workload, particularly upon exertion [19,20], and cause progressive alteration of myocardial contractility [21]. Mean pulmonary arterial pressure (MPAP) during exercise is also age-related, with values that can exceed 30 mm Hg during mild exercise, particularly in elderly individuals [22]. Daily medication intake appeared to be another independent risk factor in the multivariate analysis: It may be related to hypertension, as there was a significant difference between cases and controls for a history of hypertension and hypotensive medication intake in the comparison of cases and controls and in the univariate analysis. Interestingly, hypertension is another common risk factor suggested in case reports [12,23] and could be a risk factor associated with a recurrence of IPE [24]. Greater systemic vascular resistance combined with reduced myocardial deformation capacity due to left ventricular hypertrophy predisposes to an inability to increase left ventricular stroke volume appropriately, which may in turn accentuate the ventricular stroke volume imbalance [14]. Furthermore, not surprisingly, physical exertion was revealed as another risk factor. IPE cases have been described during the swim leg in triathletes [8] or in military divers [3]. During exercise MPAP increases as does the cardiac output. This increase is proportional to the workload and more pronounced in immersion with high interindividual variability that may explain individual susceptibility [25]. In a case-control study, Moon, et al. found an exaggerated increase in MPAP and pulmonary artery wedge pressure (PAWP) during exercise in individuals who have experienced IPE that could be reduced by the administration of sildenafil prior to the exercise in immersion [26].

Although men can be afflicted with IPE, several case reports have pointed out that the proportion of women with IPE seems to be higher than the proportion of women in the diver community [7]. Our study confirmed this sex difference. Women have smaller lung volumes and airway diameters, leading to the development of higher mechanical ventilatory constraints and of more intensive utilization of their ventilatory reserve compared with men during exercise [27]. Interestingly, women are more prone to developing hypoxemia even at submaximal exercise intensity. This may be due in part to their increased mechanical ventilatory constraints [28]. Greater alveolar pressure variations may weaken the blood-gas barrier and make women more prone to stress failure of this barrier. Reversible cardiomyopathy may be associated with IPE and may result from catecholamine release during psychological stress and from tissue hypoxia related to IPE, but no sex difference has been explicitly demonstrated [29], although there is a strong association between menopausal women and stress cardiomyopathy such as the takotsubo syndrome [30].

The influence of the dive depth can be attributed to several factors. When symptoms occur at great depth, ascension may require more time and thereby lead to a more serious injury likely to be more easily diagnosed than a mild injury. Depth may be associated with psychological stress, cold exposure, hyperoxia, high breathing workload, with an increase in inspired gas pressure and decompression stress. Hyperoxia increases systemic vascular resistance [31]. However, it may have a relatively protective effect on pulmonary vascular pressure at thermoneutrality, or have no effect at all, which is not consistent with hyperoxia as a risk factor for IPE [32].

We attempted to evaluate the role of psychological stress by asking questions about the personal perception of the diving experience, whether the dive had occurred after a long hiatus, or on the number of dives performed during last year, but there were no differences between the groups. However, training dives was revealed as an independent risk factor, possibly associating psychological stress and exertion.

NSAID intake before diving has been suggested as a risk factor in a case of pulmonary edema [33]; in a retrospective survey, Miller found fish oil consumption as an independent risk factor in triathletes [8]. The importance of NSAIDs may be attenuated in our study by the fact that only a few divers in this study admitted taking this type of medication before diving. Nevertheless, these divers were mostly in the case group. NSAID intake may increase the risk of IPE because it slightly increases systemic blood pressure; it may also damage pulmonary capillary integrity [33].

We failed to show any influence of cold exposure. The subjective perception of cold was not different between cases and controls. Furthermore, our assessment of whether the thermal protection (diving suit) was suitable, unsuitable or borderline with respect to temperature and to dive duration showed no difference between the two groups. The lack of a cold effect was unexpected because cold is frequently suspected to be risk factor [1,18]. This discrepancy may be due to the limited range of water temperatures recorded in this study involving divers mostly from metropolitan France.

LIMITATION

The main limitation of this study includes self-reported risk factors. Self-reported health status – in particular, silent diseases such as hypertension, diabetes or mild cardiovascular abnormalities – may be underestimated in the population, especially for the control divers who probably did not undergo medical examination as thoroughly as case divers. Diving conditions may not be reliably reported because divers filled out the questionnaire retrospectively. We tried to ask only for objective data because subjective feelings during a dive, such as psychological stress, are more likely to be distorted when retrospectively reported.

Only 54% of the divers who received our questionnaire answered, with a greater participation rate in case divers than control divers. This difference in participation rate can also contribute to a risk factor selection bias. The lack of response risk was taken in account when elaborating the study design. Miller, et al. obtained responses from about one-third of the people who actually received the newsletter he used to contact the triathletes [8]. Pons, et al. obtained 460 responses from 1,250 divers contacted (36.8%) [34]. We contacted eight control divers for each case to obtain three responses: We obtained 4.4 control responses for each case, which was more than expected.

We analyzed whether there was a sex or age difference between responders and non-responders and found only an age difference, thereby enhancing the significance of the age risk factor.

The incidence of clinical IPE is not well known. In a survey of 460 active scuba divers, 1.1% had a history consistent with the development of IPE [34]. A survey carried out by the French Ministry of Sports estimated the population of scuba divers to be about 340,000 [35]; if 1% of this population were to experience IPE, there should be 3,400 injured divers in France, which is not reflected in the small size of our case group and the small number of case reports published. This injury may be underrecognized and underdiagnosed. Furthermore, there is a risk of recurrence, reportedly reaching up to 30% of cases [36]. IPE is a cause of death that is probably under-reported [37]. A better understanding of the mechanism and risk factors is absolutely necessary to improve prevention.

CONCLUSION

Based on our analysis, we recommend that divers older than 50 or with hypertension, especially women, avoid strenuous effort, psychological stress and deep dives. In particular, diving to great depths – e.g., deeper than 20 meters – appears to increase the risk of IPE occurrence, and further complicates the management of respiratory distress in case of IPE by increasing the time to exit the water and adding a risk of decompression illness. Finally, NSAID intake before diving appears to be associated with an increased risk of IPE. This may require further studies to better analyze its role and the mechanisms involved.

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Conflict of interest

The authors report no conflict of interest with the submission of this paper.

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