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Reliability of right-to-left shunt screening in the prevention of scuba diving related-decompression sickness☆,☆☆

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ABSTRACT

Objectives: The aim of this study was to investigate the relationship between right-to-left shunt (RLS) and the clinical features of decompression sickness (DCS) in scuba divers and to determine the potential benefit for screening this anatomical predisposition in primary prevention.

Methods: 634 injured divers treated in a single referral hyperbaric facility for different types of DCS were retrospectively compared to 259 healthy divers. All subjects had a RLS screening by contrast Transcranial Doppler (TCD) ultrasound according to a standardized method. The number of bubbles detected defined the degree of RLS (small if 5–20 bubbles, large if >20 bubbles).

Results: TCD detected 63% RLS in DCS group versus 32% in the control group ($p < 0.0001$) The overall prevalence of RLS was higher in divers presenting a cerebral DCS (OR, 5.3 [95% CI, 3.2–8.9]; $p < 0.0001$), a spinal cord DCS (OR, 2.1 [95% CI, 1.4–3.1]; $p < 0.0001$), an inner ear DCS (OR, 11.8 [95% CI, 7.4–19]; $p < 0.0001$) and a cutaneous DCS (OR, 17.3 [95% CI, 3.9–77]; $p < 0.0001$) compared to the control group, but not in divers experiencing ambiguous symptoms or musculoskeletal DCS. There was in increased risk of DCS with the size of RLS. The determination of diagnostic accuracy of TCD testing through the estimation of likelihood ratios revealed that predetermination of RLS did not change significantly the prediction of developing or not a DCS event.

Conclusion: The assessment of RLS remains indicated after an initial episode of spinal cord, cerebral, inner ear and cutaneous form of DCS but this approach is definitely not recommended in routine practice.

1. Introduction

Scuba diving can lead to specific injuries such as decompression sickness (DCS), resulting from nitrogen bubble formation in supersaturated tissues during divers' ascent. These bubbles can cause local tissue damage or be released into the venous circulation from peripheral tissues. Paradoxical embolization of venous bubbles through a right-to-left shunt (RLS), either intrapulmonary or cardiac (i.e. persistent foramen ovale or PFO), with subsequent passage in the arterial blood, is commonly recognized as a pathological condition that may promote the development of certain types of DCS including spinal cord, cerebral and inner ear injuries [1–6]. It has been demonstrated that the prevalence of RLS (with a feature of atrial shunt >93% [7]) was greater in DCS divers, ranging from nearly 50% (spinal cord) [2,4] to 80% (inner ear) [3] compared to 22–36% in asymptomatic divers [1,7] and 25–34% in the general population from autopsy studies [8]. The increased relative risk of DCS with this anatomical predisposition was estimated between 2.5 and 6.5 from previous meta-analysis [9,10]. For that reason, the great majority of divers transferred in our facility for DCS are screened for RLS before discharge by contrast enhanced-transcranial Doppler (TCD) ultrasonography, a minimally invasive method which has proven to have a high sensitivity and good accuracy compared with other techniques [11,12]. However, the discrepancy between the low incidence of DCS (between 0.01% and 0.03% per dive according to the diving population) [13] and the high prevalence of RLS in healthy individuals raises the question among military and professional diving authorities to establish a routine RLS screening during the medical examination for dive recruitment. Therefore, the aim of this controlled study was 1) to investigate the relationship between RLS and the clinical features of DCS and 2) to evaluate the reliability of RLS screening as a strategy of primary prevention for reducing the risk of DCS.

2. Methods

2.1. Participants

All the medical forms of divers referred for DCS and treated at Sainte Anne's Military Hospital (Toulon, France) from 1998 to 2013 were

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retrospectively consulted by two hyperbaric physicians (EG, PL). Exclusion criteria were: incomplete clinical data, lack of TCD results and patients with cerebral air embolism resulting from pulmonary barotrauma. After analysing the results of the physical examination and the radiological findings, injured divers were classified in subgroups depending on the topography of the lesions and the final diagnosis, i.e. spinal cord, cerebral, inner ear, musculoskeletal and cutaneous forms of DCS. Ambiguous DCS were separately reported. This latter category corresponded to divers with an uncertain diagnosis of DCS because of the atypical presentation of neurological symptoms and the inconclusive radiological investigations. Patients who had multiple features of DCS were categorized according to the more pronounced symptoms. The spinal cord DCS subgroup was divided into two outcome categories: patients with sequelae and those with complete recovery. Sequelae were defined as a significant residual deficit (urinary disorders, ataxia, motor or sensory symptoms), three months after the initial insult. The control group consisted on asymptomatic divers without history of DCS recruited from local diving clubs and military diving groups that were volunteers to participate in the study during the same period. The study design was approved by the local institutional ethics committee (Sainte Anne's military hospital) and all participants gave their written informed consent.

2.2. TCD ultrasonography examination

The presence and functional size of RLS were assessed with a pulsed TCD ultrasonography (Explorer CVS, Diagnostic Medical Systems, Perols, France) using a standardized protocol routinely performed in our facility by experimented operators since many years. This technique was found to have a good inter-and intra-investigator reproducibility (kappa values >0.8) [14].

A mixture of 19 ml saline and 1 ml air is agitated 6 times between two 10 ml syringes, connected to a 3-way stopcock, to create microbubbles as sonographic contrast. The emulsion is then injected into a 18-gauge catheter placed in the antecubital vein of the patient laid in supine position. Middle cerebral artery flow is monitored through the temporal bone window using a 2-Mhz probe set at 50-60 mm depth for detecting circulating microbubbles on the Doppler spectrogram in real time. For each diver, the test was repeated twice: the first time at rest, during normal breathing and, the second one, followed by a provocative manoeuver consisting on blowing into a manometer and maintaining a pressure of 40 mm Hg during 5 s before the release of the forced expiration. TCD was considered as positive (indicating the presence of an RLS) when we recorded at least five typical high intensity transient signals called “hits”, 15 s after the injection at normal breathing, and 10 s after the end of the provocative manoeuver. RLS was classified into three grades according to the current literature [7,11]: absence of RLS if <5 hits, small RLS if 5–20 hits, large RLS if >20 hits. Doppler signals recorded onto digital tape were analysed later by 2 trained observers (EG, PL).

2.3. Statistical analyses

Data were expressed as mean +/− SD. Comparisons between groups were completed using the Student's *t*-test for a continuous variable and the Chi squared test or Fisher's exact test for categorical variables. A p value of <0.05 was considered to indicate a statistically significant difference. The performance of RLS testing was estimated through the calculation of sensitivity, specificity, and the likelihood ratios. In practice, the positive likelihood ratio (LR+) summarizes how many times more likely divers victims of DCS are to have a RLS than asymptomatic divers. The prediction is considered enough high if LR+ is >10. Conversely, the negative likelihood ratio (LR−) describes how many times less likely injured divers are to have a negative screening of RLS compared to divers without DCS. Thus, a very low LR− (below 0.1) virtually rules out the risk that a diver without RLS will develop DCS. Statistical analyses were done using either Graphpad Prism 6.00 (GraphPad Software, San Diego, CA) or internet program to calculate odd ratios (OR) and likelihood ratios for 2 × 2 tables with 95% CIs around them [15].

3. Results

A total of 722 patients were admitted and 634 (87%) were finally included. 259 healthy divers served as controls. Both groups were matched with respect to gender and diving experience. There was, however, a significant difference in age between DCS divers and controls (43.6 +/− 11.3 vs 34.6 +/− 9.0, respectively, $p < 0.0001$). TCD examination revealed that 398 RLS (63%) were present in the group of divers affected by DCS while 82 cases only (32%) were tested positive for RLS in the control group ($p < 0.0001$) (Table 1). the global odd of suffering a DCS was 3.6 [95% CI, 2.7–4.9] in divers with RLS and the relative risk increased in parallel with RLS size with an odd at 4.1 [95% CI, 2.9–5.7] for only high-grade RLS (Fig. 1). When considering the different clinical features, the prevalence of RLS (including the small ones) was higher in divers presenting with cerebral, spinal cord, inner ear DCS and cutaneous forms of DCS compared to the control group. Conversely, the proportion of RLS in divers suffering from musculoskeletal DCS and in those with ambiguous presentation was comparable to that of control group.

Additional analysis revealed that residual deficit following spinal cord DCS was not associated with the presence of RLS (OR, 0.7 [95% CI, 0.4–1.3]; $p = 0.3$). The accuracy indices of TCD ultrasonography regarding the different features of DCS are displayed in Table 2. The data show that the reliability of RLS screening is not enough to correctly identify the divers at risk of DCS development or not with numerical values of LRs always above 0.1 or below 10.

4. Discussion

The role of RLS in DCS has been largely debated [1–6]. In a recent study, Wilmshurst showed that the risk of a diver suffering shunt-related DCS was closely related to the dimensions of the PFO rather than just the presence of the defect [7]. Other studies have also demonstrated that the functional characteristics of the RLS, i.e. shunting at rest or after Valsalva maneuver and amount of vascular bubbles crossing atrial defects, may be associated with a greater likelihood of DCS development [1,16,17]. In the present work based on the largest cohort of injured divers ever studied before, 63% of TCD-tested DCS patients

Table 1
Association between RLS and each form of DCS (in brackets the value corresponding only to the inclusion of large RLS).

	n	RLS−	RLS+	% RLS	OR	95% CI	p-Value
Control group	259	177	82 (55)	32			
All DCS	634	236	398 (333)	63	3.6 (4.1)	2.7–4.9	<0.0001
Spinal cord DCS	255	128	127 (110)	50	2.1 (2.8)	1.4–3.1	<0.0001
Inner ear DCS	201	31	170 (148)	85	11.8 (15.4)	7.4–19	<0.0001
Cerebral DCS	97	28	69 (50)	71	5.3 (5.7)	3.2–8.9	<0.0001
Ambiguous DCS	47	35	12 (9)	25	0.7 (0.8)	0.4–1.5	0.4
Musculoskeletal DCS	16	12	4 (3)	25	0.7 (0.8)	0.2–2.3	0.6
Cutaneous DCS	18	2	16 (13)	89	17.3 (21)	3.9–77	<0.0001

RLS = right-to-left shunt; DCS = decompression sickness.

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