ABSTRACT

Aim The human model of pulmonary embolism is currently unavailable. The objective of this study was to evaluate whether venous inert gas lung embolization after diving simulation is a model of pulmonary embolism.

Methods Twelve recreational divers underwent two single air compressions, each in different post-compression posture, in the chamber to 30 m/40 min bottom time with standard decompression and ascent rates. Cardiopulmonary variables and precordial bubble grade were measured in sitting or lying supine before and 40, 70 and 100 min after the respective compression.

Results The volume of airways decreased post-compression in supine (24%, p<0.01), as well as in sitting posture (28%, p<0.05). As a sign of lung embolization, the alveolar dead space increased significantly only in supine posture (from 27 to 65 mL, p<0.05). Transcutaneous arterial oxygen tension decreased post-compression from 11,8 to 9,5 kPa in supine posture (p<0.01) and from 11,3 to 9,72 kPa in sitting posture (p<0.005). Minute ventilation and breathing frequency increased significantly only in sitting posture. Cardiovascular depression was suggested from reductions in systolic blood pressure (both postures), heart rate and pulse pressure (sitting posture) and from apparent, but not significant decreases in cardiac output (both postures). Most of the signs were most pronounced at 40 minutes post-compression and persisted at 100 min post-compression.

Conclusion Small, transient post-compression lung embolization by inert gas bubbles induces some of the cardiopulmonary signs of pulmonary embolism, especially if the diver is lying after the compression.

Key words: diving, pulmonary embolism, decompression, Doppler, ventilation
INTRODUCTION

It is known that, after air diving with standard decompression, the venous nitrogen bubbles can be detected (with Doppler ultrasound) in some divers (1). These bubbles are eliminated in lungs and normally do not appear on the arterial site. It is reasonable to assume that gas bubbles (up to 20 μm in diameter) cause at least some, transient occlusion of the small arteries of the lung. In accord with this, previous human studies on diving detected mild post-dive simulation spirometric abnormalities (2-5). Moreover, our previous study suggested that the degree of such embolization may be substantial, since it was associated with transient, but material decreases in lung diffusing capacity and arterial oxygen tension (6). This in turn suggested that air diving may model some aspects of pulmonary embolism (PE). To evaluate this we have thoroughly investigated the cardiopulmonary effects of air diving. Since the pulmonary distribution of nitrogen bubbles is probably affected by body posture, we have also compared the sitting with supine post-dive simulation postures.

PATIENTS AND METHODS

Experimental procedure

Cardiopulmonary variables and precordial bubble grade were measured four times: 30 minutes before dive simulation (time baseline, tb), and 40, 70 and 100 minutes postdive simulation (t40, t70 and t100). The sequence of measurements during each of four sessions were as follows: Doppler monitoring, mask breathing, heart rate (HR), arterial blood pressure (BP), arterial oxygen saturation (SaO₂) and cardiac output (Q̇). Each test sequence lasted around 20 minutes. Transcutaneous measurements were done continuously 30 minutes before dive simulation and 100 minutes post-dive simulation. The values from mask breathing and values of transcutaneous O₂ and CO₂ are the mean values in the last two minutes of each session (tb, t40, t70, t100).

Dive simulation profiles

Twelve male recreational divers, medically fit to dive based on the annual medical examination revealing no clinical signs of cardiopulmonary disease, were included in the study. Only male subjects were available for the study, since the number of recreational female divers was rather limited. Anthropometric data including spirometric parameters are shown in the Table 1. Four subjects were medium-heavy smokers, while the remaining eight were non-smokers. All divers were recreational divers, experienced only in compressed air diving up to the depth of 50 m and they never used only oxygen or had saturation dives. The subjects were exposed to 4 bar absolute pressure for 40 minutes (bottom time including compression in a three-compartment recompression chamber, Draeger, Germany). The standard decompression table (7) was followed with decompression stop at 3 m for 15 min and ascent rate of 9 m /min so that ascent up to decompression stop lasted 3 min. Descent rate was 15 m/min. Each diver performed two dive simulations with measurements of cardiopulmonary parameters before and after dive simulation in sitting (N=11) and supine (N=12) positions. One diver performed only one dive simulation in supine position but was also included in the study. The time difference between the two dives was at least 24 hours, which is sufficient time for normalization of cardiopulmonary function. In four divers the interval between the two dive simulations was one day, and in the remaining seven

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>FVC (l)</th>
<th>% of predicted value</th>
<th>FEV1 (l)</th>
<th>% of predicted value</th>
<th>FEV1/FVC</th>
<th>% of predicted value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>27.3</td>
<td>184.6</td>
<td>81.2</td>
<td>5.93</td>
<td>105.8</td>
<td>4.96</td>
<td>105.71</td>
<td>85.45</td>
</tr>
<tr>
<td>SD</td>
<td>6.9</td>
<td>7.4</td>
<td>8.9</td>
<td>0.8</td>
<td>12.62</td>
<td>0.68</td>
<td>9.3</td>
<td>7.03</td>
</tr>
</tbody>
</table>

* FVC, forced vital capacity; FEV1, forced expiratory volume in 1 sec.; Mean, average; SD, standard deviation
it was between three and seven days. During the dive simulation subjects performed no exercise, and the order of the two dives (sitting and supine) was randomly assigned. Subjects were in the supine position at least 30 min prior to the test sequence. Smoking was prohibited at least 12 hours before the experiment. The relative humidity was maintained between 20-30% and temperature between 21 °C -22 °C in the laboratory by the automated conditioning system. Informed consent was signed by all subjects and the study protocol was approved by the local Ethical Committee of the University of Split Clinical Hospital.

**Doppler ultrasonic bubbles monitoring**

Venous bubbles were detected using a continuous wave Doppler apparatus TSI model 9008 (Techno Scientific Inc, Canada) equipped with a 2.5 MHz probe. The precordial probe was directed onto the pulmonary artery flow. The Spencer Doppler Scale (8) with grades was used: grade 0, no bubbles; grade I, an occasional bubble with the majority of cardiac cycles free of bubbles; grade II, many but less than half of the cardiac cycles contain bubbles; grade III, bubbles in most of the cardiac cycles but not obscuring the heart sounds; grade IV, numerous bubbles obscuring the heart sounds. The recording was made for 1 min after the heart rate had stabilized to a resting rate and after deep knee bend (squatting down slowly and then rising to upright position, repeated twice). The signals were assessed aurally and recorded on tape (Sony TCM-40DV) and graded in a blind manner by two investigators (DB and IMT).

**Ventilatory measurements**

Ventilatory parameters were collected continuously on a breath-by-breath basis (Cosmed Quark b', Italy) with mask breathing. Pulmonary ventilation \( (V_e) \) was measured by the flow meter composed of a bi-directional digital turbine and optoelectronic transducer. The Quark b' uses ultrafast analyzers for \( CO_2 \) (infrared analyzer with a response time of <120 ms) and \( O_2 \) (zirconia heated analyzer with a response time <150 ms). The analyzers were calibrated with a calibrating gas mixture composed of 5% \( CO_2 \), 16% \( O_2 \) and balance \( N_2 \), while the flow meter was calibrated with a 3 L calibration syringe. Oxygen uptake \( (V_O_2) \) and carbon dioxide output \( (V_CO_2) \) were determined from the continuous measurement of the concentrations of \( CO_2 \) and \( O_2 \) in the inspired and expired air. Inspiratory duration \( (T_i) \), expiratory duration \( (T_e) \), total respiratory cycle duration \( (T_{TOT}) \), respiratory frequency \( (f_b) \), ventilation \( (V_e) \) and tidal volume \( (V_t) \) were all analyzed on a breath-by-breath basis and averaged in 2 min intervals.

The anatomic dead space \( (V_{an}) \), the alveolar dead space \( (V_{dl}) \) and the physiologic dead space \( (V_{db}) \) were determined from the end-tidal, mixed expired and transcutaneous arterial \( CO_2 \) tensions \( (PET_{CO2}, P_{aCO2}, P_{tcCO2}) \) using the Bohr equations:

\[
\frac{v_m - PET_{CO2} \cdot P_{tcCO2}}{PET_{CO2} - P_{tcCO2}} \cdot V_t
\]

\[
\frac{v_m - P_{aCO2} \cdot PET_{CO2}}{P_{aCO2} - PET_{CO2}} \cdot V_t
\]

\[
\frac{v_m - P_{tcCO2} \cdot PET_{CO2}}{P_{tcCO2} - PET_{CO2}} \cdot V_t
\]

In these equations \( PET_{CO2} \) and \( P_{tcCO2} \) approximate the mixed-alveolar and arterial \( CO_2 \) tensions, respectively.

The alveolar-arterial \( O_2 \) difference \( (A-a DO_2) \) was calculated as a difference between end-tidal, mixed expired and transcutaneous oxygen tension \( (PET_{O2}) \) and transcutaneous oxygen tension \( (P_{tcO2}) \).

**Transcutaneous blood gas measurements**

\( P_{tcO2} \) and \( P_{tcCO2} \) were measured with a single \( P_{O2}/P_{CO2} \) electrode (TINA electrode ES280, Radiometer, Denmark) and its monitoring system (TCM3). The monitor was calibrated with following gas mixture: 5% \( CO_2 \), 20.9% \( O_2 \) and balance \( N_2 \). After the start of the sensor’s heating of the skin, equilibration of the electrode occurred within 10-15 min. All gas pressures were expressed in mm Hg and combined electrode was heated to 45 °C and placed on the upper chest 5 cm below the mid-clavicle. All subjects tolerated well this temperature which produced maximum arterialisation of \( P_{O2} \). The site for placement of the electrode was wiped clean with alcohol, rubbed dry...
with gauze in preparation for the electrode fixation rings, which were attached and filled with the manufacturer’s (Radiometer) standard contact solution. The monitor automatically divided the actual Ptc\textsubscript{CO2} value by a 1.47 correction factor, and the corrected values are reported in this study. The 1.47 correction factor is based on the observed difference between transcutaneous and arterial carbon dioxide values at 45 °C obtained from the literature (9). Arterial saturation (Sa\textsubscript{O2}) was measured with pulse oxymeter with finger probe (Dash 2000, GE, USA).

**Cardiovascular measurements**

During the entire test heart rate (HR) was registered continuously with Polar belt (Polar, Finland), while arterial blood pressure was measured non-invasively with oscillometric method (Dash 2000, GE, USA). Mean arterial pressure was calculated as 2/3 diastolic blood pressure (DBP) + 1/3 systolic blood pressure (SBP). Cardiac output (Q\textsubscript{c}) was determined non-invasively (Cosmed Quark b2, Italy) by the indirect Fick method with CO\textsubscript{2} rebreathing technique from the following equation: $Q\textsubscript{c} = \frac{\dot{V}\textsubscript{CO2}}{(C\textsubscript{av CO2} - C\textsubscript{a CO2})}$ where $\dot{V}\textsubscript{CO2}$ is CO\textsubscript{2} output, $C\textsubscript{av CO2}$ is the mixed venous CO\textsubscript{2} content, and $C\textsubscript{a CO2}$ is the arterial CO\textsubscript{2} content. $\dot{V}\textsubscript{CO2}$ was obtained during the last 20 breaths before rebreathing test. Based on the fraction of end-tidal CO\textsubscript{2} (FET\textsubscript{CO2}), the end-tidal CO\textsubscript{2} pressure (PET\textsubscript{CO2}) was calculated and used to estimate Pa\textsubscript{a CO2} according to the formula of Jones et al. (10): $Pa\textsubscript{a CO2} = 5.5 + 0.90 \times PET\textsubscript{CO2} - 0.0021 \times V\textsubscript{T}$. The mixed venous pressure of CO\textsubscript{2} (P\textsubscript{av CO2}) was estimated with the Collier equilibrium method, by rebreathing from a bag containing CO\textsubscript{2} (11). The equilibrium (Feq\textsubscript{CO2}) was estimated by extrapolating the regression line between 8- and 12-s rebreathing intersect, to 20-th s after the start of the rebreathing maneuver. The Peq\textsubscript{CO2} was calculated without “downstream” correction. The content of CO\textsubscript{2} in venous blood (C\textsubscript{av CO2}) was calculated from P\textsubscript{CO2} using the equation: $ln(C\textsubscript{av CO2}) = 0.396 ln(P\textsubscript{av CO2}) + 2.38$. Vanhees et al. (12) have shown that equilibrium method (the one which uses low, instead of high CO\textsubscript{2} concentration in the rebreathing bag at the beginning of rebreathing) is more reproducible than exponential method for measurements at rest. $Q\textsubscript{c}$ was measured in duplicate and the rebreathing bag was thoroughly flushed between two rebreathing periods. The average of two measurements was reported.

**Statistical analysis**

Data are expressed as mean ± standard deviation (SD). Comparisons between pre-dive simulation and post-dive simulation cardiopulmonary parameters were done using the Friedman analysis of variance, followed by paired Wilcoxon signed-rank post-hoc testing. P< 0.05 was considered significant. The software used was STATISTICA 5.0 (Statsoft, USA)

**RESULTS**

Eleven divers completed both dive simulations, while one of them performed dive simulation only once. None of them had any clinical signs indicating decompression sickness. Venous gas embolism (VGM) was detected in 4 divers in sitting posture (Spencer grade I in two divers and II in two divers) and in 2 divers in supine posture (Spencer grade I). The baseline and post-dive simulation values of various cardiopulmonary parameters are presented in Tables 2 and 3. The following post-dive simulation changes reached statistical significance.

Ventilation. $V\textsubscript{T}$ decreased post-dive simulation in both postures for about 12%. $F\textsubscript{b}$ increased only in sitting posture and the same was found for the product of these two variables ($V\textsubscript{T} \times F\textsubscript{b}$). The increase in $F\textsubscript{b}$ was a consequence of similar decreases in $T\textsubscript{E}$ (-25%) and $T\textsubscript{I}$ (-17%). Alveolar ventilation ($\dot{V}\textsubscript{A}$), calculated as ($\dot{V}\textsubscript{T} - \dot{V}\textsubscript{DB}$) x $F\textsubscript{b}$, decreased only in the supine position. Ventilatory equivalents for O\textsubscript{2} ($\dot{V}\textsubscript{E} / \dot{V}\textsubscript{O2}$) and CO\textsubscript{2} ($\dot{V}\textsubscript{E} / \dot{V}\textsubscript{CO2}$) increased similarly for about 12% in sitting posture, while $\dot{V}\textsubscript{E} / \dot{V}\textsubscript{O2}$ decreased in supine position.

Gas exchange and alveolar gas tensions. and were unaltered in either posture. Respiratory quo-
Tient (RQ) decreased for about 7% in the supine posture due to small opposite changes in \( V_{CO2} \) and \( VO_2 \) (increase in \( VO_2 \) and decrease in \( V_{CO2} \)). \( SaO_2 \) decreased in both postures, however more in supine posture (1.4% vs. 1.1%). In accord with this \( PtcO_2 \) decreased, more in supine, than in sitting posture (19%, p<0.01 vs. 14%, p<0.005). \( PtcCO_2 \) increased only in supine posture, indicating alveolar hypoventilation. A-a \( DO_2 \) increased in both postures, however with larger effect in the supine posture (110% vs. 64%).

Anatomic and alveolar dead space. \( V_{DA} \) decreased post-dive simulation more in both postures (24%, p<0.01 vs. 28%, p<0.05). \( V_{DB} \) increased only in supine posture, while \( V_{DB} / V_T \) ratio increased in both postures. The alveolar dead space increased significantly only in supine posture (144%, p<0.05). Ventilation of \( V_{DA} \) and \( V_{DB} \) also increased only in supine posture.

Cardiovascular parameters. Similar reductions in SBP were noted in both postures (-4.5%). A difference between SBP and DBP (pulse pressure, PP) and HR decreased only in supine posture.

Table 2. Acute effects of dry diving on cardiopulmonary function in twelve divers: supine post-dive posture*
DISCUSSION

Experimental, animal studies on pulmonary embolization (PE) used glass or plastic beads or blood clots. Data obtained (13, 14) are more consistent than results of clinical studies (15-18). However, differences in coagulation, thrombotic system, putative mediators, size and composition of embolic material, use of anesthesia and eventually mechanical ventilation impose problems in extrapolating those results to humans. Noninvasive human model of PE is currently not available.

Venous gas microbubbles (VGM) appear in the venous circulation during and after the decompression phase of the dive simulation and may be filtered by the pulmonary circulation causing pulmonary gas exchange abnormalities (19) and inflammatory reactions (20). Gas bubbles are easily deformable and are trapped in the pulmonary arterioles from where they are eliminated with molecular diffusion of gas directly across the arteriolar wall into the alveolar spaces (21). The lungs have important non-respiratory function in filtering VGM and thereby protecting perfusion of the vital organs (brain and heart) (22). The effect of VGM depends on the gas volume. Large amount of venous bubbles cause immediate mechanical damage to the vascular endothelium (23). On the contrary, small quantities of VGM, known as “silent bubbles”, cause impairment in endothelial-dependent vasoactive response, probably by biochemical agents (24).

Table 3. Acute effects of dry diving on cardiopulmonary function in eleven divers: sitting post-dive posture*

<table>
<thead>
<tr>
<th>Sitting position</th>
<th>t6</th>
<th>t40</th>
<th>t70</th>
<th>t100</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ventilation and breathing pattern</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V_{t}$(L MIN$^{-1}$)</td>
<td>9.9</td>
<td>1.2</td>
<td>10.9</td>
<td>1.5‡</td>
</tr>
<tr>
<td>$V_{E}$(L MIN$^{-1}$)</td>
<td>9.7</td>
<td>1.2</td>
<td>11.0</td>
<td>1.3‡</td>
</tr>
<tr>
<td>$V_{t}$(L BREATHS$^{-1}$)</td>
<td>768</td>
<td>105</td>
<td>678</td>
<td>104§</td>
</tr>
<tr>
<td>FB (BREATHS MIN$^{-1}$)</td>
<td>13.1</td>
<td>1.9</td>
<td>16.4</td>
<td>3.2§</td>
</tr>
<tr>
<td>$T_{W}$(S)</td>
<td>1.82</td>
<td>0.32</td>
<td>1.36</td>
<td>0.2§</td>
</tr>
<tr>
<td>$T_{E}$(S)</td>
<td>2.77</td>
<td>0.54</td>
<td>2.3</td>
<td>0.53§</td>
</tr>
<tr>
<td>$V_{t} / V_{A}$</td>
<td>28.2</td>
<td>3.1</td>
<td>31.9</td>
<td>3.55‡</td>
</tr>
<tr>
<td>$V_{t} / V_{CO_{2}}$</td>
<td>34.9</td>
<td>3.8</td>
<td>39.3</td>
<td>5.4‡</td>
</tr>
<tr>
<td><strong>Dead space</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V_{DA}$(ML)</td>
<td>103.7</td>
<td>34.5</td>
<td>99.2</td>
<td>48.0</td>
</tr>
<tr>
<td>$V_{DB}$(ML)</td>
<td>110.3</td>
<td>39.5</td>
<td>135.3</td>
<td>36.4</td>
</tr>
<tr>
<td>$V_{DA}$(ML)</td>
<td>24.3</td>
<td>11.9</td>
<td>44.5</td>
<td>23.1</td>
</tr>
<tr>
<td><strong>Gas exchange</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$VO_{2}$(L MIN$^{-1}$)</td>
<td>349.8</td>
<td>31.5</td>
<td>342.1</td>
<td>44.8</td>
</tr>
<tr>
<td>$VCO_{2}$(L MIN$^{-1}$)</td>
<td>283.1</td>
<td>26.1</td>
<td>277.8</td>
<td>34.1</td>
</tr>
<tr>
<td>RQ</td>
<td>0.81</td>
<td>0.06</td>
<td>0.82</td>
<td>0.08</td>
</tr>
<tr>
<td>PET$<em>{CO</em>{2}}$(kPa)</td>
<td>13.9</td>
<td>0.5</td>
<td>13.9</td>
<td>0.3</td>
</tr>
<tr>
<td>PET$<em>{CO</em>{2}}$(kPa)</td>
<td>5.0</td>
<td>0.2</td>
<td>4.9</td>
<td>0.3</td>
</tr>
<tr>
<td>PTC$<em>{CO</em>{2}}$(kPa)</td>
<td>11.3</td>
<td>1.4</td>
<td>9.72</td>
<td>1.7§</td>
</tr>
<tr>
<td>PTC$<em>{CO</em>{2}}$(kPa)</td>
<td>5.1</td>
<td>0.2</td>
<td>5.3</td>
<td>0.5</td>
</tr>
<tr>
<td>A-A DO$_{2}$(kPa)</td>
<td>2.8</td>
<td>1.4</td>
<td>4.6</td>
<td>1.7‡</td>
</tr>
<tr>
<td>SaO$_{2}$(%)</td>
<td>98.45</td>
<td>1.04</td>
<td>97.64</td>
<td>1.03‡</td>
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<tr>
<td><strong>Cardiovascular parameters</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>SBP (kPa)</td>
<td>17.2</td>
<td>1.2</td>
<td>16.3</td>
<td>1.0‡</td>
</tr>
<tr>
<td>DBP (kPa)</td>
<td>10.4</td>
<td>1.4</td>
<td>10.9</td>
<td>0.9</td>
</tr>
<tr>
<td>HR (BEATS MIN$^{-1}$)</td>
<td>81.0</td>
<td>8.1</td>
<td>72.6</td>
<td>6.7‡</td>
</tr>
<tr>
<td>PP (kPa)</td>
<td>6.8</td>
<td>1.4</td>
<td>5.3</td>
<td>1.3‡</td>
</tr>
<tr>
<td>MAP (kPa)</td>
<td>12.6</td>
<td>1.1</td>
<td>12.7</td>
<td>0.7</td>
</tr>
<tr>
<td>SV (ML)</td>
<td>82.9</td>
<td>17.4</td>
<td>89.5</td>
<td>24.8</td>
</tr>
<tr>
<td>SVR (kPa/ L MIN$^{-1}$)</td>
<td>2.01</td>
<td>0.67</td>
<td>2.23</td>
<td>0.71</td>
</tr>
<tr>
<td>Q$_{t}$(L MIN$^{-1}$)</td>
<td>6.5</td>
<td>1.85</td>
<td>6.14</td>
<td>1.69</td>
</tr>
</tbody>
</table>

Variables and P values see in Table 2
We found many functional signs of lung micro-embolization, despite smaller lung occlusion than expected from our previous study. Some of the differences may be due to more intensive diving simulation protocol and faster ascent rate in the previous study. Dry diving protocol used in this study seems to mimic massive PE rather remotely, in terms of small, non-solid occlusion. However, the post-dive simulation presence of most of the embolic cardio-pulmonary sequelae, such as arterial desaturation, cardio-depression, tachypnea and bronchoconstriction suggests that dry diving may model PE with emboli of smaller size (silent embolism).

However, in our study the acute cardiopulmonary effects of diving simulation signs were mostly confined to subjects in post-dive simulation supine posture. This can be explained as follows. The pulmonary distribution of incoming bubbles is probably affected both by distribution of blood flow and buoyancy, causing more bubbles in the upper regions than would be expected from regional perfusion (25). Bubbles that occlude vessels of the baseline, pre-dive simulation alveolar dead space (which is more confined to apical parts when sitting) clearly do not increase it. Such events are more likely when sitting than lying, which explains a greater post-dive simulation increase in the alveolar dead space in the later case.

Despite buoyancy effect, in sitting posture the greater percentage of bubbles are expected to occlude the well-perfused basal parts of the lung than when laying supine. Consequently, in sitting (or standing) posture the elimination of basal, low V/Q areas from gas exchange is less deleterious than elimination of apical parts with higher V/Q. This explains greater arterial oxygen desaturation in supine posture.

We have observed rather large post-dive simulation decrease in the anatomic dead space, suggesting that VGM causes significant airway constriction. On the other hand, the alveolar dead space increased, suggesting the presence of lung embolization. Therefore, the components of the physiologic dead space changed in opposite directions. Animal studies (19, 26, 27) have shown similar changes in $V_{DA}$, $V_{DB}$ and $V_{DA'}$. These findings were related to arterial hypoxemia and hypercapnia (secondary to PE), which induce centrally mediated reflex, with constriction of the large airways (28).

In this study most of divers produced relatively few detectable bubbles after dive simulation, so that the bubble load was lower than in our previous study (6). Yet, an increase in physiological dead space after dive simulation, corresponding to several percent of lung occluded, was a consistent finding. We have thus shown that relatively safe dive profile is often associated with transient, minor occlusion of the lung blood vessels, mostly in absence of detectable bubbles. Thus, measuring of changes in physiological (alveolar) dead space appeared to be the more sensitive marker of VGM than precordial Doppler monitoring. This may be caused by bubbles to small to be detected by Doppler, which are subsequently trapped in the lung microcirculation.

Tachypnea with a low tidal volume is a frequent clinical feature of PE and it is also found in experimental studies. The tachypneic response to venous air embolism in dogs was significantly attenuated with ibuprofen (a cyclooxygenase inhibitor), dimethylthiourea (a hydroxyl radical scavenger) and bilateral cervical vagotomy (29). We observed a mild tachypnea after dive simulation, but only in the sitting posture, where ventilation increased, on account of increased ventilation of dead space. Tachypnea was demonstrated by similar reductions in active ($T_i$) end passive ($T_e$) portions of the respiratory cycle. In sitting posture the alveolar ventilation even decreased. Thus, unlike gas exchange parameters, ventilation and breathing pattern were more affected in sitting than in supine post-dive simulation posture. This may be associated with higher Doppler bubble grades observed in sitting posture. It appears that in our subjects the lung’s dissipating capacity for gas microemboli was not great enough to prevent acute breathing pattern changes.

In the previous study (6) the arterial blood gases were measured twice (pre-dive simulation and post-dive simulation), whereas in the present...
study we used a non-invasive, continuous transcutaneous monitoring of blood gases with single $P_{O_2}/P_{CO_2}$ electrode. This technique has been evaluated for estimation of gas exchange during rest and exercise (30-32). It has been concluded that combined $P_{O_2}/P_{CO_2}$ electrode can be used for reliable estimate of gas exchange at rest and during exercise for $P_{CO_2}$ whereas for $P_{O_2}$ a single arterial sample before exercise is recommended. Since we used this technique at resting conditions and since every diver was his own control, we believe that the techniques employed are acceptable substitutes for arterial blood measurements.

In our divers mild arterial desaturation was observed that persisted at 100 min post-dive simulation (in supine posture). Proposed mechanisms of hypoxemia in PE have included right to left shunting (33-35), impaired diffusion at the alveolar-capillary interface, due to regional decreases in capillary transit time (36), inequality of ventilation and perfusion (15, 37, 18) and decreased mixed venous oxygen tension secondary to reduced cardiac output (17). The reduction of cardiac output in PE is usually associated with substantial occlusion and consequent increased right ventricular afterload. However, humorally mediated depression cannot be ruled out. Moreover, our results have shown that reductions in arterial oxygen tension and signs of cardiac depression are common to small and massive PE. This suggests that these signs of PE are at least partly mediated neuro-humorally.

Although cardiac output was not significantly affected by VGM in our study, the signs of cardiac depression were observed in reductions in systolic blood pressure, pulse pressure and heart rate (the latter two only in supine posture). It appears that small embolization and small power of the study were behind these findings.

Factors other than VGM could affect cardiopulmonary function after dive simulation. To isolate these effects, one could perform control dives with prolonged or oxygen decompression (as we had used in the previous study). Since we have not performed control dives in this study, the effects of submersion and respiratory mechanical load during the dive might have influenced also. However, in the previous study (6) the acute effects of dry diving were confined to air decompression with documented bubble load, but not to oxygen decompression. This is the circumstantial evidence that the acute effects of dry diving are due to VGM, rather than other effects of diving.

Also, we used noninvasive cardiopulmonary measurements, which might have produced inaccurate estimates of some of the variables. The trancutaneous estimates of arterial $O_2$ and, to a lesser degree, $CO_2$ may deviate from real values, depending on the patient’s hemodynamic status. The methods work best in neonates, due to thin skin (38), and worst in hemodynamically unstable patients, where trancutaneous $O_2$ values are strongly influenced by changes in cutaneous blood flow (39). In healthy individuals, as in this study, the methods are considered reliable in monitoring trends due to respiratory changes (30-32, 40). In case of $O_2$ the absolute readings are systematically below the corresponding arterial values (due to skin oxygen consumption), whereas, after temperature correction, the $CO_2$ readings are close to arterial values (40). Certainly, in trend monitoring, as in this study, one should control for the baseline drift of the measuring device. It is important to wait until the equilibrium is established, which may vary between individuals. After that time, which was never more than 15 min, we have not observed the systematic drift or any instability of the measuring device.

However, in case of $CO_2$ rebreathing measurement of cardiac output, the problem of reproducibility was more exaggerated. Many authors have compared this technique against direct Fick method or termodilution in rest or exercise in healthy individuals and in several patient groups. Although the reports describing the method as accurate and reproducible prevail (41-45, for example), some authors found it less useful (46, 47) or even unacceptable (48). In general the method works better in exercise than at rest (44, 47). In healthy individuals at rest, as in this study, the reproducibility of the method, expressed as the
standard deviation of the percentage difference between duplicate estimates at separate days, was 9.1% in the study of Nugent at al. (44). If this estimate applies to our study with small sample size (N=12), it turns out that the power of the study to detect statistically significant changes in cardiac output, i.e. to extract the physiological changes in the variable from the composite effects of real changes and random measurement errors, was rather low.

It is estimated that from 40-60% of all pulmonary embolisms are asymptomatic and thus untreated, but are often substantial and with potential late sequelaes (49). The availability of a simple, non-invasive test to detect PE could decrease the proportion of undiagnosed PE (by follow-up of patients at high risk of developing PE) and facilitate the prompt diagnosis for patients evaluated for suspected PE. Clinically relevant PE is often initiated by asymptomatic micro-embolizations. Furthermore, our results suggest that such micro-embolizations are associated with detectable cardiopulmonary abnormalities. Thus, it appears that non-invasive cardio-respiratory monitoring could have a role in early diagnosis and follow-up of PE, in combination with other established noninvasive methods, such as planar or SPECT V/Q scanning (50), CT pulmonary angiography (51) and novel approaches, including transthoracic ultrasound (52) and laboratory tests (53).

We conclude that small, transient post-dive simulation lung embolization by inert gas bubbles induces some of the cardiopulmonary signs of PE, especially if the diver is lying after the dive simulation. Thus, dry diving with standard decompression with post-dive simulation supine posture appears to model some aspects of pulmonary embolism.

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