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Editorial

Pulmonary oxygen toxicity in occupational diving

Occupational—or commercial—diving is a global industry, employing tens of thousands of people worldwide who are engaged in a broad variety of work. With renewable energy sources on the rise and a fast-changing world into the digitally connected age, more and more activities are being deployed on the seabed. Ranging from the installation of offshore wind turbine parks, working on undersea communication cables or maintenance work on offshore drilling wells, there will always be a demand for highly skilled divers to perform these tasks, and probably more than ever in the foreseeable future.

Regardless of whether diving is recreational or occupational, being underwater and breathing compressed air exposes the diver to several health hazards that are unique to diving. Generally, the two most infamous diving-related ailments are decompression sickness and trauma caused by rapid pressure changes, known as barotrauma, which can result in pneumothorax, subcutaneous and mediastinal emphysema, or even blocking of the coronary, cerebral or other end-organ arteries with arterial gas emboli [1]. Although less known as these effects of diving, adverse reactions to breathing gases can pose serious health issues to the diver as well. One of the concerns is oxygen toxicity.

The clinical manifestation of oxygen toxicity is divided into two groups: acute and chronic oxygen toxicity. When exposed to an excessive amount of oxygen, for example, in hyperbaric environments, an acute-onset neurologic reactions can occur, ranging in severity from mild fasciculations to tonic–clonic seizures, which is known as central nervous system oxygen toxicity. When exposed to prolonged and slightly elevated levels of oxygen, symptoms of the lower airways can manifest, known as pulmonary oxygen toxicity (POT). Symptoms range from a retrosternal burning sensation upon breathing, coughing and chest pain, to shortness of breath.

POT does not only affect divers; patients receiving hyperbaric oxygen therapy or intensive care unit patients ventilated for days with elevated levels of oxygen are also at risk of developing POT [2]. An oxygen pressure of 50 kPa, the equivalent of an F_iO_2 of 0.5 or 50% oxygen mix at sea level (101 kPa), has been reported to cause POT, although a higher pressure is commonly required to cause symptoms. For example, when breathing 100% oxygen at sea level, it takes usually 24–48 h to develop the first clinical symptoms of POT. The higher the inspired fraction of oxygen and the longer the exposure, the faster these symptoms develop.

Although the exact mechanism of POT is not fully understood, the most likely pathophysiologic mechanism is alveolar damage by hyperoxia-induced reactive oxygen species (ROS). These ROS are highly unstable and interfere with the lipid bilayer of cell membranes, causing a chain reaction, bilayer destruction, and cellular injuries and apoptosis of the alveolar cells. If this alveolar damage occurs extensively, it can cause an inflammatory reaction similar to acute respiratory distress syndrome. This process, called the exudative phase, is still fully reversible if the hyperoxic exposure ceases. However, if hyperoxic exposure continues, the damage can become irreversible, resulting in interstitial alterations and eventually lung fibrosis with loss of lung function, known as the proliferative phase [3]. These long-term health effects may result in a reduced work capacity or may require the diver to change career path altogether. Furthermore, these end-stage pulmonary alterations are major risk factors for contracting pulmonary barotrauma.

In the past 50 years, various physiological parameters have been studied in the context of long-term health surveillance of occupational divers. Most of these publications focused on data obtained during routine yearly medical assessments of occupational divers, including spirometry endpoints, such as forced vital capacity (FVC), forced expiratory value in 1 s (FEV_1), FVC/FEV_1 ratio, peak expiratory flow and forced expiratory flow 25–75% ($FEF_{25-75\%}$). In addition, diffusion tests, such as diffusion rate of carbon monoxide (DL_{CO}) or nitric oxide (DL_{NO}), and body plethysmography tests are also employed to monitor pulmonary function of occupational divers and have been used in longitudinal studies [4,5]. The results of these studies and reviews were often contradictory, as were the reported influences of confounders such as smoking, type of diving and type of breathing gas. Regardless of whether the results of the studies were statistically reliable or not, the majority concluded that the long-term health of divers does not seem to be affected within the current limits of exposure. Nonetheless, as the demand for industrial activities on the sea floor increases, the need to go deeper and extend dive times is also predicted to increase.

In order to minimize the risk of POT whilst performing deeper and extended dives, various preventive guidelines have been developed during the past few decades. The first guideline to be established was the Unit of Pulmonary Toxicity Dose (UPTD) model, developed in the late 1960s. It is based on the correlation between a decreasing vital capacity (VC) in spirometry tests and severity of the hyperoxic exposure. It allows quantification of hyperoxic exposure and sets the safe limit for regular diving operations as 615 UPTDs per dive, corresponding to a 2% decrease in VC [3].

Unfortunately, the UPTD model is a rather crude estimation when it comes to establishing the adverse effects of POT at the individual level. A decrease in VC of 2% lies well within the 4.8% normal day-to-day pulmonary physiological variation [6]. Furthermore, the hyperbaric exposures used in the original studies to establish the UPTD model were dry/hyperbaric chamber exposures, whereas the model is mostly used to predict POT in individuals engaged in wet/in-water dives. When the human body is immersed or submerged, the intrathoracic vascular volume increases by 500–700 ml, which can result in a temporary state of pulmonary hypertension or decreased pulmonary compliance [7]. The additional effects of these pulmonary-vascular changes on POT are largely unknown. Despite these drawbacks, it is still one of the most widely used instruments in determining safe limits for diving while avoiding POT.

Various other models have been developed since the UPTD model. Starting in 2002, Arieli introduced the POT-index or K-index, which provides a more precise estimation of POT, as well as an estimation of POT incidence and the recovery time needed after hyperoxic exposure [8]. As with the UPTD model, the K-index model is based on the VC derived from pulmonary function tests and has its limitations, especially when it is applied to divers engaged in repetitive dives [9]. Shykoff developed a model for predicting POT based on FVC, FEV_1 and $FEF_{25–75\%}$. In contrast to the previous models, this model incorporates dry and wet dives, and can also take into account if the diver is at rest or performing physical labour. Like Arieli's POT-index, it can also calculate recovery times, and subsequently, the risks of POT for repetitive dives [10].

Although Arieli's and Shykoff's models offer advantages over UPTD, they remain a one-model-fits-all design and are not tailored to individual divers, who often show differences in their responses to hyperoxia that are large enough to restrict the ability of any model to describe about half of the individual variability [11].

Current research is focused on a more individual approach [12]. By measuring volatile organic compounds (VOCs) in exhaled breath after hyperbaric hyperoxic exposure, pre-clinical signs of pulmonary damage can be assessed, allowing for a personal threshold estimation of developing POT. Similar VOC measurements are currently being used for predicting loss of asthma control and differentiating between asthma and other pulmonary diseases [13]. From a preventive perspective, this technique could be used to provide an early warning of POT, without putting the diver at risk of developing irreversible pulmonary pathology. Since susceptibility to POT varies greatly interpersonally and even in the same individual over different days, the risk of over- or underestimation of pulmonary damage is minimized using this method.

With the increase in industrial activities on the seabed, the demand for longer and deeper dives will grow concomitantly. To protect divers from developing POT, one of the health risks associated with prolonged and increasingly deeper dives, various preventive models such as the UPTD model and POT-index model have been developed in the past 50 years. However, these models are not individually tailored; thus, they offer a one-model-fits-all design that might be too restrictive at a collective level or too liberal at an individual level. A new diagnostic method tailored to the individual diver is currently being developed and is based on identifying VOCs associated with pulmonary damage in exhaled breath. With the advent of such a method, dive times could be optimized while considering individual sensitivity and variances in response to hyperoxia and POT, thus lowering the occupational risk for the individual diver.

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