Article

Lung Diffusing Capacity in Dutch Special Operations Forces Divers Exposed to Oxygen Rebreathers over 18 Years

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Abstract: Exposure to hyperoxic conditions can induce pulmonary oxygen toxicity (POT). Divers of the Special Operations Forces (SOF) use oxygen rebreather systems during dives, and therefore are frequently exposed to hyperoxic conditions. Few studies have reported on POT in this population. This study reports on long-term pulmonary function tests (PFTs) and diffusing capacity in SOF divers to test the hypothesis that these measures of pulmonary function do not change clinically significantly during their career. The Royal Netherlands Navy performs yearly medical assessments of its military divers. All PFT and diffusing capacity data of SOF divers between the years 2000 and 2020 were analyzed using generalized estimating equations. The study included 257 SOF divers (median age, 27; interquartile range, 24–32), with 1612 dive medical assessments and a maximum follow-up time of 18.8 years. Alveolar volume (V_A) and the diffusing capacity of carbon monoxide (TL_CO) were significantly lower at baseline in smokers. Although these parameters were within the normal range, they declined over time and were significantly associated with age and years of diving. Smoking additionally affected TL_CO and the transfer coefficient for carbon monoxide (K_CO). TL_CO and K_CO were reduced by years of diving with oxygen rebreathers, albeit over clinically insignificant ranges, but smoking increased these changes by factors of 10 and 15, respectively.

Keywords: long-term health effects; pulmonary function testing; TL_CO; DL_CO; hyperoxia

1. Introduction

Immersion in water, as occurs while diving, requires physiological adaptations. Most notably, as the ambient pressure increases with increasing depth, the density of the breathing gas increases [1]. As a result of Boyle’s and Dalton’s laws, breathing pressurized air (which consists of approximately 21% oxygen and 79% nitrogen) under hyperbaric conditions can lead to exposure to high partial pressures of oxygen. For instance, a diver at 20 m depth breathing pressurized air is exposed to a partial pressure of oxygen of 64 kPa, equal to that of 63% oxygen at sea level. Therefore, exposure to hyperoxic conditions is very common in divers, but most pronounced in military divers of the Special Operations Forces (SOF), who frequently engage in oxygen diving using “oxygen rebreathers”, specialized diving equipment for breathing 100% oxygen that produces no bubbles on exhalation [2].

Exposure to hyperoxia, usually defined as a partial pressure of more than 50 kPa, can induce a pathological condition known as pulmonary oxygen toxicity (POT) [3]. POT is reversible in the acute phase, but may cause irreversible damage in later stages [4]. Research that established the “safe limits” of oxygen exposure based on pulmonary function tests (PFTs) was published in the 1970s, and developed an equation for a quantity expressed in “units of pulmonary toxic dose” [5]. While the methodology was sound, these studies had limitations, primarily due to the available research techniques at the time [6]. For
the purposes of the present study, it is worth noting that analysis of hyperbaric hyperoxic exposure in diving and hyperbaric oxygen therapy is based on an equation that includes terms for the oxygen fraction of the breathing gas and ambient pressure (equivalent to depth in diving). Recent studies have shown that the results of PFTs are not affected by lifelong diving [7,8]. However, it is widely accepted that PFTs might not indicate damage from POT at the alveolar level.

The diffusing capacity, or transfer factor of the lung, for carbon monoxide (TL\textsubscript{CO}) is used clinically to evaluate the function of the alveolocapillary membrane, which is affected in the late stages of POT [4,9]. While TL\textsubscript{CO} has limitations for detecting POT after a single dive, and newer techniques such as analysis of exhaled breath are being developed, it remains a viable diagnostic instrument for evaluating the function of the alveolocapillary membrane, and might shed light on the long-term health effects of oxygen diving [6,10]. To our knowledge, no oxygen divers have suffered severe POT in recent history, but this could reflect publication bias or an absence of publications due to the covert nature of military oxygen diving. In addition, subtle changes in diffusing capacity may go unnoticed because of the exceptional physical fitness of military personnel. The “healthy worker” effect may apply here as well, contributing to selection bias.

Military divers in the Netherlands are medically assessed according to international standards by the Diving Medical Center of the Royal Netherlands Navy on an annual basis. This data set provides a unique opportunity to assess the long-term health effects of oxygen diving. The aim of this paper was to evaluate the diffusing capacity of SOF divers, and to detect any long-term health effects that might be related to oxygen diving. Our hypothesis is that the diffusing capacity of SOF divers is not clinically significantly affected by oxygen diving over an entire career.

2. Materials and Methods

The Royal Netherlands Navy Diving Medical Center performs yearly medical assessments of military divers. All fitness-to-dive assessments were performed according to European Diving Technology Committee guidelines, except that the PFT results have been interpreted relative to the GLI-2012 reference that came into effect on 1 January 2015 [11,12]. All data were stored in an electronic medical database.

All medical assessments of Netherlands SOF divers between 1 January 2000 and 1 January 2020 that included PFT (vital capacity (VC) and forced exhaled volume in 1 s (FEV\textsubscript{1})) and diffusing data (for carbon monoxide (TL\textsubscript{CO}) and alveolar volume (V\textsubscript{A}), and consequently the transfer coefficient of the lung for carbon monoxide (K\textsubscript{CO})) were included. Age, sex, height, and smoking status were recorded. Subjects included only divers who passed the combat diver course, but excluded those who were evaluated only once. Due to military restrictions, the number of dives, time at depth, and other parameters related to diving could not be included in the analysis.

According to national law and legislation, retrospective analyses are not required to be evaluated by a medical ethics committee. As a result of the aforementioned act and directive, informed consent is not required for retrospective (data) studies in the Netherlands. However, the methods used to handle personal details and privacy were in agreement with the guidelines of the Association of Universities in the Netherlands and the Declaration of Helsinki.

Spirometry and diffusing capacity were measured with a Masterscreen PFT Pro spirometer (Carefusion, the Netherlands) by qualified respiratory technicians according to the European Respiratory Society (ERS) Guidelines [13,14]. The PFT and diffusing data acquired at the beginning of each combat diver’s career were considered as baseline values. The aforementioned parameters were analyzed in marginal models (generalized estimating equations) using SPSS Statistics for Windows (IBM Corp.; Armonk, NY, USA: 2020, version 27.0) with age and smoking status as covariates. The normality of the data was assessed using Q-Q (quantile–quantile) plots and tested using a Shapiro–Wilk test. Differences in baseline characteristics between smokers and non-
smokers were tested using Student’s t-test or the Mann–Whitney U test where applicable. The alpha value was set at 0.05, and therefore statistical significance was assumed when \( p < 0.05 \).

3. Results

The cohort consisted of 257 SOF divers, all male, performing a total of 1612 dive medical assessments. All data, except for age at baseline and follow-up, were normally distributed.

Median follow-up after baseline was 3.9 years, the interquartile range was 1.1–7.5 years, and the maximum follow-up period was 18.8 years. Baseline results for PFT, TL\(_{\text{CO}}\), \( V_A \), K\(_{\text{CO}}\), and hemoglobin (Hb) are shown in Table 1. The cohort was divided into two groups: smokers and non-smokers. There was a significant difference between these two groups in TL\(_{\text{CO}}\), VC, and K\(_{\text{CO}}\). However, all values were within the normal range using Z-scores.

Table 1. Baseline characteristics.

|                  | Non-Smoking (n = 208) | Smoking (n = 49) | \( p \) |
|------------------|-----------------------|-----------------|--------|
| Age (years)      | 27.0 (IQR 24.0–32.0)  | 28.0 (IQR 23.0–30.0) | 0.575   |
| Height (cm)      | 183 (SD 6.2)          | 183 (SD 6.4)    | 0.854   |
| IVC (L)          | Z 0.64                | Z 0.18          | 0.868   |
| FEV\(_1\) (L)    | Z 0.09                | Z 0.61          | 0.610   |
| FEV\(_1\)/IVC    | Z –0.87               | Z –0.71         | 0.117   |
| TL\(_{\text{CO}}\) (mmol/min/kPa) | Z 0.69                | Z 0.05          | 0.004*  |
| \( V_A \) (L)    | 7.32 (SD 1.33)        | 6.70 (SD 1.90)  | 0.007*  |
| K\(_{\text{CO}}\) (mmol/min/kPa/L) | Z 0.28                | Z –0.50         | 0.118   |
| Hb (mmol/L)      | 9.29 (SD 0.78)        | 9.56 (SD 0.66)  | 0.025*  |

Inspiratory vital capacity (IVC), forced expiratory volume during the first second (FEV\(_1\)), transfer factor of the lung for carbon monoxide (TL\(_{\text{CO}}\)), alveolar volume (\( V_A \)), transfer coefficient of the lung for carbon monoxide (K\(_{\text{CO}}\)), hemoglobin (Hb). Statistically significant results using Student’s t-test are marked with an asterisk (*)

Note: Age was not normally distributed and was tested using the Mann–Whitney U test.

3.1. Pulmonary Function Tests

Table 2 shows the results of the marginal model. Age was a significant factor in the decline in IVC, FEV\(_1\), and FEV\(_1\)/IVC (i.e., a \( p \)-value < 0.05), whereas diving years did not have a significant effect. For example, the –0.024 related to age displayed under IVC (which has a \( p \)-value of 0.002) indicates that, with each year of increasing age, the IVC decreases by 0.024, and the value associated with dive years is not statistically significant.

Table 2. Generalized estimation equations.

|                  | IVC     | \( p \)  | FEV\(_1\) | \( p \)  | FEV\(_1\)/IVC | \( p \)  | TL\(_{\text{CO}}\) | \( p \)  | \( V_A \)     | \( p \)  | K\(_{\text{CO}}\) | \( p \)  |
|------------------|---------|---------|-----------|---------|--------------|---------|----------------|---------|--------------|---------|--------------|---------|
| Intercept        | 6.337   | \( 0.000^{*} \) | 5.621     | \( 0.000^{*} \) | 81.286       | \( 0.000^{*} \) | 13.185         | \( 0.000^{*} \) | 7.273        | \( 0.000^{*} \) | 1.817        | \( 0.000^{*} \) |
| Dive years       | 0.014   | 0.204   | 0.006     | 0.390   | –0.055       | 0.443   | –0.058         | 0.855   | 0.002        | 0.890   | –0.008       | 0.010   |
| Age              | –0.024  | \( 0.002^{*} \) | –0.026    | \( 0.000^{*} \) | –0.138       | \( 0.006^{*} \) | –0.048         | 0.001   | 0.002        | 0.815   | –0.007       | 0.001   |
| Non-smoking      | 0.070   | 0.446   | 0.027     | 0.708   | –0.388       | 0.539   | 1.019          | 0.000   | 0.181        | 0.088   | 0.095        | 0.010   |

Inspiratory vital capacity (IVC), forced expiratory volume during the first second (FEV\(_1\)), transfer factor of the lung for carbon monoxide (TL\(_{\text{CO}}\)), alveolar volume (\( V_A \)), transfer coefficient of the lung for carbon monoxide (K\(_{\text{CO}}\)), hemoglobin (Hb). Statistically significant results from the Wald-chi\(^2\) test are marked with an asterisk (*)
Baseline PFT results were not affected by smoking. Results are visually displayed in Figure 1a–c.

Figure 1. Cont.
Figure 1. Pulmonary function tests and diffusing capacity over time. Scatterplots of investigated parameters over time (years of diving); (a) inspiratory vital capacity (IVC); (b) forced expiratory volume during the first second (FEV1); (c) ratio of IVC/FEV1; (d) transfer factor of the lung for carbon monoxide (TLCO); (e) alveolar volume (VA); (f) transfer coefficient of the lung for carbon monoxide (KCO). Blue dots represent non-smoking datapoints, red dots are datapoints of smoking divers. Linear regression trend lines and coefficient (r²) are shown in each plot.

3.2. Diffusing Capacity

As can be derived from the data presented in Table 2, the effects of age, diving years, and smoking status on TLCO and KCO were statistically significant. VA showed no statistically significant changes over time—see Figure 1d–f.
Note that age has a statistically significant effect on almost every parameter, where dive years only affects TL\textsubscript{CO} and K\textsubscript{CO}. The values of non-smoking were also statistically significant for TL\textsubscript{CO} and K\textsubscript{CO}, and approximately 10 and 15 times larger than those of dive years.

Table 3 shows PFT and diffusing capacity values after 15 years; 18 divers (8.7%) remained in the non-smoking group. The smoking group was not analyzed as only one diver (2%) remained after 15 years.

### Table 3. Non-smoking group. PFT, diffusing capacity, and Z-scores after 15 years.

| Value                  | Value (SD)                  | Z-Score                  |
|------------------------|-----------------------------|--------------------------|
| IVC (L)                | 6.35 (SD 0.82)              | 1.308 (baseline 0.64)    |
| FEV\textsubscript{1} (L)| 4.77 (SD 0.56)              | 0.921 (baseline 0.09)    |
| FEV\textsubscript{1}/IVC | 75.7 (SD 5.4)               | −0.68 (baseline −0.87)   |
| TL\textsubscript{CO} (mmol/min/kPa) | 11.57 (SD 0.72)         | 0.610 (baseline 0.69)    |
| V\textsubscript{A} (L)   | 7.66 (SD 1.14)              | 0.671 (baseline 0.28)    |
| K\textsubscript{CO} (mmol/min/kPa/L) | 1.51 (SD 0.23)         | −0.031 (baseline 1.11)   |

None of the changes in Z-score were statistically significant relative to baseline after 15 years.

### 4. Discussion

To our knowledge, this is the first study to report long-term changes in the diffusing data of SOF divers. There was a decline in TL\textsubscript{CO} and K\textsubscript{CO}, which could be attributed to diving in this cohort. Although the decline was statistically significant, the absolute change was very small and clinically irrelevant. While a decline in pulmonary function and diffusing capacity with age is not uncommon, there seems to be an additional effect of diving with oxygen rebreathers, as shown in Table 2. However, the effect of the number of diving years was approximately 10 (K\textsubscript{CO}) and 15 (TL\textsubscript{CO}) times smaller than the effect of smoking.

The TL\textsubscript{CO} and K\textsubscript{CO} data from the generalized equations (Table 2) show that although they were significantly affected by aging and years of diving, V\textsubscript{A} was unaffected. The clinical relevance of these results seems limited as the Z-scores were well within the normal range using GLI reference values, and the decline in Z-score was not statistically significant, even after diving for 15 years. The TL\textsubscript{CO} Z-score was almost unchanged compared to baseline, the V\textsubscript{A} Z-score increased, and the K\textsubscript{CO} Z-score decreased. As TL\textsubscript{CO} was unaffected, the decline in K\textsubscript{CO} could have resulted solely from a subclinical increase in V\textsubscript{A}, which would be consistent with the improvement in IVC often seen in swimmers and divers, which is primarily due to an effect of training [7,15,16]. This would support our hypothesis that diffusing capacity is unaffected by long-term oxygen diving, and also suggests that any subclinical damage to the alveoli caused by POT is reversible.

The decline in IVC, FEV\textsubscript{1}, and IVC/FEV\textsubscript{1} over time was similar to the decline seen in the non-diving population [17,18]. Since diving years was not a significant factor in the generalized estimated equation, and the Z-scores were within the normal range, the changes in PFT should be considered to be a result of normal aging.

The possibility remains that any lung problems caused by hyperoxia over the period of a career only become manifest in later life. A follow-up on this cohort is needed to rule out any late-onset pathology.

A remarkable finding was that after 15 years of diving, only one smoking diver (2.0%) remained, as opposed to 18 (8.7%) in the non-smoking group. This difference was not statistically significant ($p = 0.111$ using a chi-square test), and the sample size was not large enough to test it with sufficient power (post hoc power analysis: 61%). Although not included in our study data, in our experience, SOF divers are in remarkably good physical condition, independent of smoking history. Additionally, the pulmonary function and diffusing capacity of the smoking group were not in the range likely to have caused clinical symptoms. We assume that other factors, such as life or career choices, led smokers to discontinue their work as SOF divers, but the data in this study cannot be used to test this
possibility. Therefore, we are inclined to regard this as a coincidental finding, but future research may reveal a relationship between smoking and length of career as an SOF diver.

Strengths and Weaknesses

To our knowledge, this is the first longitudinal analysis of the diffusing capacity of SOF divers who use oxygen rebreather systems. The data set, with over 1600 samples comprised of multiple parameters, was sufficient to produce a valid model for generalized estimation equations. These data are of interest to occupational and military physicians who assess military divers. There are, however, a few limitations to this study we would like to address.

Firstly, the population was highly biased, with only very fit male military divers. While the data are relevant to this group, the generalizability of the results cannot be assumed. Although commercial and technical divers are frequently exposed to hyperoxic conditions, their dive profiles, gas mixtures used, and dive systems are significantly different from those in the population studied here. Whether commercial or technical divers are similarly affected remains to be investigated.

Secondly, the results were interpreted using GLI reference values. Based on the associated Z-scores, the decrease in diffusing capacity is considered to be “within the normal range”. While the GLI data set is currently the best reference for interpreting PFT and diffusing capacity, it can be argued that our population is not equivalent to the general population, and interpretation should be approached with caution. However, the divers satisfied fitness requirements (such as a VO\textsubscript{2}max > 40 mL/kg/min on cycle ergometry) in their annual medical assessments after years of diving, and regularly compete in endurance sports. We therefore feel the observed decline has little clinical value. However, to explore this topic more fully, further studies of the long-term health effects are needed.

Lastly, as smoking greatly impacts pulmonary function, it is important to take this into account when evaluating diffusing capacity. In our analysis, all divers who smoked at baseline still smoked in the follow-up period, i.e., no divers stopped smoking (despite our efforts to encourage them to do so). There is a risk that some divers might have actually been smokers without reporting this during their annual medical examination, and were therefore wrongly included in the “non-smoking” group. This could have affected the results, but would likely have reduced the effect of smoking in our model. As this effect was approximately 10–15 times larger than that of diving years, we suggest this substantiates the finding that diving with oxygen systems has very little effect on diffusing capacity. In addition, SOF operators often work under challenging conditions where, for example, they are exposed to diesel fumes and other irritants. Our analysis did not correct for such operational factors, and therefore, we cannot fully exclude the possibility that they influenced the results. However, such factors would further reduce the effects attributed to diving with oxygen rebreathing systems as found in the present study.

5. Conclusions

This study reports pulmonary function and diffusing capacity data of SOF divers using oxygen rebreathers over a long period of time. The analysis showed that changes in TL\textsubscript{CO} and K\textsubscript{CO} after years of diving are statistically significant, but that the change is very small and clinically irrelevant. The effect of smoking on K\textsubscript{CO} and TL\textsubscript{CO} was estimated to be 10 and 15 times larger, respectively, than that of diving years. While further studies are required to determine long-term health effects, for example by following up after retirement, we feel that these data show that diving within current guidelines for using oxygen rebreathers has little negative effect on pulmonary health.

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Informed Consent Statement: As a result of the aforementioned act and directive, informed consent is not required for retrospective (data) studies in the Netherlands.

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