

Modern assessment of pulmonary function in divers cannot rely on old reference values

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Abstract

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Introduction: Pulmonary function testing (PFT) is an important part of dive medical examinations. Depending on the standard used to assess fitness to dive, different reference sets and fixed cut-off points are used. Reference values are part of an ongoing debate regarding the validity and accuracy related to different age groups, sex and ethnic backgrounds. The Global Lung Initiative (GLI) has provided an all-age reference set which corrects for sex and ethnicity (GLI-2012); this has had substantial impact on pulmonary medicine.

Method: We present an algorithm that can be used to standardise analysis of PFT in divers using the GLI-2012 reference set. Differences in the analysis of PFT between the ECSC/ERS-1993 and the GLI-2012 reference values are illustrated by means of three case reports.

Conclusion: Using a valid database of reference values increases accuracy and might prevent additional medical investigations and/or incorrect assessment of fitness to dive. Although our algorithm needs further evaluation to ensure its validity, the preliminary results are promising. Whatever algorithm is used, we urge dive medical physicians to consider using valid reference sets when analysing PFT for assessment of fitness to dive.

Introduction

Diving requires substantial adaptation in human physiology. Without these necessary changes, immersion and/or breathing hyperbaric mixtures may lead to significant and potentially life-threatening injuries. Especially existing pathology in the areas of ENT and cardiopulmonary fitness may cause severe problems when an individual is exposed to hyperbaric conditions; the latter being the second most common cause of lethal diving accidents, after faulty procedures and panic.^{1,2}

Although occupational safety laws and medical assessment of fitness to dive are nowadays common, this was not always the case. For example, after numerous injuries and deaths when building the pillars of the Brooklyn Bridge, the first legislation to protect employees from occupational health damage was established in 1909.³ Today, many (inter-) national recommendations exist regarding safe diving procedures and fitness to dive.^{4–8}

Assessment of occupational divers, such as commercial or military divers, should include pulmonary function testing (PFT). The results of PFT are compared to a reference set, such as those of the European Community for Steel and Coal (ECSC), the European Respiratory Society

(ERS), the National Health and Nutrition Examination Survey (NHANES) or the American Thoracic Society (ATS).^{9,10} Although reference tables can focus on sports, commercial or military diving, many standards have similar recommendations regarding cardiopulmonary fitness. Small differences exist between the main fitness-to-dive standards, most, but not all of which specify a fixed cut-off point for parameters such as forced vital capacity (FVC), forced expiratory volume in one second (FEV₁) and the FEV₁/FVC ratio (Table 1).

There are other standards available than those presented in Table 1 and there are even more reference sets.¹¹ Despite revisions over time, the various reference tables have remained a topic of discussion in pulmonary medicine. For example, many lacked accuracy for ethnic groups other than Caucasians, African and Mexican Americans, and some were unable to properly correct for age and sex.¹² In 2008 the Global Lung Initiative (GLI) was established by the ERS and ATS to develop all-age reference equations with correction for sex and ethnic background. In 2012 the first results were published and were rapidly endorsed worldwide in pulmonary medicine and other fields of practice.^{13,14}

Compared to any of the previous reference sets, one of the most important changes is the definition of a ‘normal’

Table 1

Overview of pulmonary function test (PFT) criteria from different standards; FVC – forced vital capacity; FEV₁ – Forced expiratory volume in 1 sec; FEF₂₅₋₇₅ – Forced expiratory flow at 25–75% of the pulmonary volume; PEF – Peak expiratory flow

Standard	Recommended PFT	Suggested lower limit
EDTC ⁴	FVC, FEV ₁ , FEV ₁ /FVC	Not specified
ADC ⁵	FVC, FEV ₁ , FEF ₂₅₋₇₅	> 75%
BTS ⁶ /MA1 ⁷	FVC, FEV ₁ , PEF FEV ₁ /FVC	> 80% > 70%
ADivP-1 ⁸	Not specified, other than PFT should be performed	Not specified

value. Previously, an expected value was reported as a fixed number, whereas in the GLI-2012 it is described as the Z-score from the mean. This means there is a normal distribution of expected values instead of a single expected value. This approach allows easy comparison with the reference group and more accurate assessment of pulmonary function.¹⁵ For example, a Z-score of ± 1.64 indicates a value is ± 1.64 standard deviations (SD) from the mean and, therefore, outside the 90% confidence interval (CI), excluding 5% at the extremes of the normal distribution, whilst a Z-score of ± 1.96 places a value outside the 95% CI, excludes 2.5% at each end of a normal distribution. These values are translated into the upper and lower limits of normal (ULN and LLN, respectively). A ULN-95 indicates that a value is above the Z-score of 1.64 and a LLN-2.5 puts a value below the Z-score of -1.96.

The cut-off point of any test influences the predictive value. If a test is too stringent, many individuals will be flagged positive while there are no significant problems (false positive). On the other end of the spectrum, a cut-off value that is too low may fail to identify persons with pathology (false negative). Depending on the setting in which a medical test is utilized, the cut-off point must be chosen wisely. Preferably, a diagnostic test has a high negative predictive value to ensure that no cases are incorrectly regarded as pathologic. However, a test used for screening purposes has, preferably, a high positive predictive value to ensure that no cases are missed. Although the lower limit for fitness to dive has yet to be determined, it stands to reason that a pulmonary function within the 90% CI in a healthy individual without clinical signs of pulmonary disease can be regarded as normal. This is similar to pulmonary screening in the Netherlands, both in general practice and in hospital analysis by a pulmonary specialist.

In this paper we present three people who were assessed for fitness to dive at the Royal Netherlands Navy (RNLN) Diving Medical Centre. We compare the ECSC/ERS-1993 reference set with the GLI-2012 reference set. Although medical ethical approval was not required, our methods for handling data and privacy are in line with the Declaration of

Helsinki and national laws. Additionally, changes in policy regarding fitness to dive are in agreement with the Surgeon General of the Ministry of Defence. To provide the proper context for the cases, we first describe the algorithm used to evaluate these cases.

Royal Netherlands Navy algorithm to interpret PFT in divers

The RNLN Diving Medical Centre has developed an algorithm in cooperation with pulmonary specialists from the Military Hospital (Figure 1). With regard to PFT, we feel that an individual should be considered fit to dive when the main spirometric parameters (FVC, FEV₁, FEV₁/FVC) are within the 90% CI (Z-score of ± 1.64) and there are no signs of pathology in the history or physical examination. If a person's PFT is outside the 95% CI (Z-score ± 1.96), we refer the person to a pulmonary specialist and review their fitness to dive case-by-case afterwards. Note that we refrain from analysing FEF₂₅₋₇₅, since these values have no impact on clinical decision-making.¹⁶

When FVC, FEV₁ or FEV₁/FVC are outside the 90% CI, but within the 95% CI (i.e., a Z-score between ± 1.64 and ± 1.96), further assessment is required, even if there are no signs and symptoms of pathology. For instance, a lower than normal FVC could be the result of anatomical anomalies, such as bullae or blebs. Ventilatory dead-space can be assessed using body plethysmography or high-resolution computed tomography (HR-CT). A decreased FEV₁ or FEV₁/FVC might be the result of bronchoconstriction, which is a risk factor for intrapulmonary air-trapping and can lead to pneumothorax or arterial gas embolism.

The FEV₁ or FEV₁/FVC could be decreased for several weeks after a pulmonary stressor, albeit a common viral infection or exposure to non-specific agents (such as dust, which is a relevant factor in deployed military forces). In case of a low FEV₁ or FEV₁/FVC (LLN 2.5), that person is (temporarily) unfit to dive and PFT is repeated after at least six weeks. Additional testing (next paragraph) is delayed until the PFT is normalised. When the PFT has normalised, we regard the decrease as temporary and non-significant.

Bronchospasm should be investigated using bronchial challenge or exercise tolerance testing.¹⁷ Note that the Dutch guidelines regarding fitness to dive in occupational divers recommend routine screening for bronchospasm. A methacholine challenge test is performed at the initial dive medical assessment, subsequent assessments do not require further testing for bronchial hyper-reactivity unless indicated. This can be different in other nations or when screening recreational divers. It stands to reason that any history of bronchospasm should prompt further investigation in all divers. The goal of bronchial challenge testing is to evaluate hyperreactivity. A subject is exposed to an increasing dose of an irritable substance, such as histamine or methacholine, and performs several flow-volume curves

Figure 1

Algorithm for analysis of pulmonary function testing (PFT) using the GLI-2012.

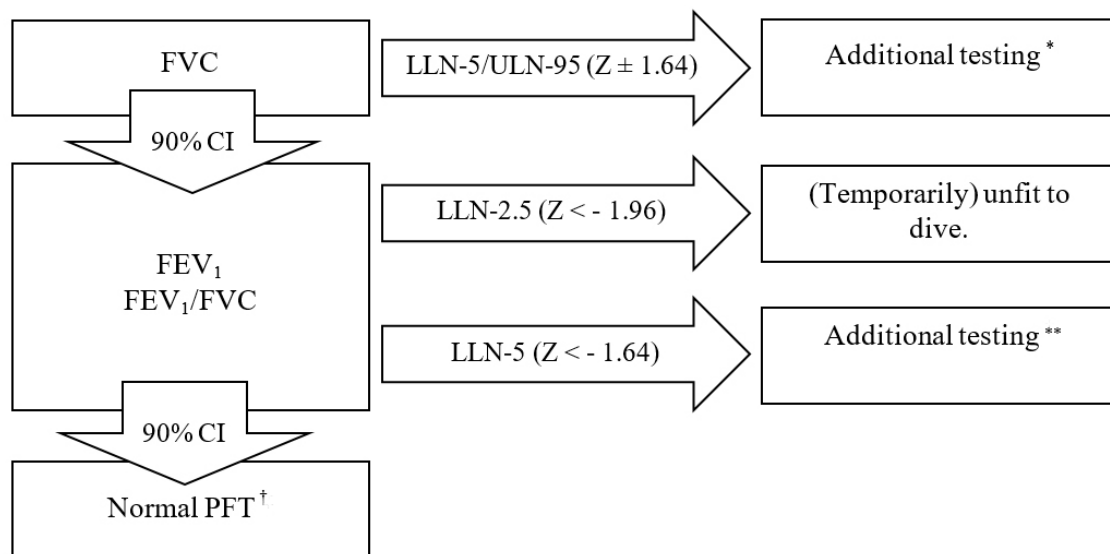
A PFT with parameters outside the 90% CI could be caused by recent respiratory tract infection or exposure to irritating non-specific agents. Repeating the PFT after several weeks should be considered. Furthermore, a variation in FVC or FEV₁ of ≥ 10% compared to the previous PFT should trigger further evaluation.

* Whole-body plethysmography, high-resolution computed tomography or referral to a pulmonary specialist.

** Testing for reversibility using a beta-sympatomimetic drug (i.e., salbutamol), methacholine challenge (if not done previously), exercise challenge testing, or referral to a pulmonary specialist.

† A PFT should never be evaluated in isolation and should always be complemented by taking a thorough history and physical examination. Absence of symptoms and/or signs of pathology and a PFT within the 90% CI should be considered normal.

FVC – Forced vital capacity; FEV₁ – Forced expiratory volume in 1 second; CI – confidence interval;
 ULN – upper limit of normal; LLN – lower limit of normal.



before being exposed to a higher dose. When the FEV₁ decreases ≥ 20% compared to the original spirometry, the test is aborted and the subject is given a beta-sympathomimetic drug (i.e., salbutamol) to counter the bronchoconstriction. Discussion continues regarding what the highest dose of the irritant should be. Because histamine and methacholine are chemically different substances, the concentration-effect dose also differs slightly. Our institute used to test with a histamine dose up to 16 mg·ml⁻¹, but currently tests up to 9.8 mg·ml⁻¹. The provocative dose (in case of histamine) or concentration (in case of methacholine) when this 20% reduction is reached, is reported as the PD₂₀ or PC₂₀ respectively.¹⁸ Alternative tests, such as exercise challenge or cold air testing, can give further insight into the origin of the bronchial hyperreactivity.¹⁷

In any case, after thorough evaluation (possibly by a pulmonary specialist) an individual can be declared fit to dive with regard to his/her pulmonary function. When similar spirometric parameters are found in subsequent medical assessments, no further evaluation is required and that person is considered fit to dive. When FVC or FEV₁ varies more than 10% compared with a previous measurement, this could be a sign of developing pathology and should trigger additional analysis.

Case 1

A 46-year-old, male, caucasian Navy diver (height 192 cm) came for his yearly medical assessment. Other than a history of smoking for thirteen years, which he had quit more than ten years previously, his medical history was unremarkable. He was known for having a large vital capacity (defined as an FVC ≥ 120% of the ECSC/ERS-1993 reference group). According to the previous Navy algorithm, which was similar to the that described in Figure 1, he had to undergo additional medical investigations, such as body plethysmography and HR-CT. The rationale behind these additional investigations is that large lungs (with a large residual volume) could be caused by structural anatomical anomalies.¹⁹

The results from the PFT of this diver are shown in Table 2. With the ECSC/ERS-1993 reference set, the FVC is ≥ 120% of predicted; although the literature is inconclusive, some authors attribute this to a higher residual volume or alveolar distention.^{20,21} Other authors attribute this larger than normal FVC to natural selection, or repeated exposure to hyperbaric conditions.²²⁻²⁴ According to previous Royal Netherlands Navy standards, this would mean that this individual would have to undergo additional investigations.

Table 2

Pulmonary function tests for the three example cases; FVC - forced vital capacity (L); FEV₁ - forced expiratory volume in 1 sec (L·sec⁻¹); see text for more details

Parameter	Observed	ECSC/ERS-1993 (%)	GLI-2012 (Z-score)
Case 1			
FVC	7.28	132	1.49
FEV ₁	5.46	124	1.21
FEV ₁ /FVC (%)	75	-	-0.57
Case 2			
FVC	5.94	108	-0.18
FEV ₁	4.06	93	-1.03
FEV ₁ /FVC (%)	68	-	-1.45
Case 3			
FVC	5.77	112	1.27
FEV ₁	4.26	106	-0.03
FEV ₁ /FVC (%)	74%	-	-1.84

However, when compared to the new GLI reference table, it shows that this individual has larger lungs than average, but well within the 90% CI. Therefore, we deemed this candidate's PFT to be normal and did not perform additional medical investigations. This person was declared fit to dive.

Case 2

A 50-year old, healthy, non-smoking, male, caucasian Navy diver (height 193 cm) who had been a RNLN diver for 21 years was assessed for fitness to dive. His spirometric parameters are shown in Table 2. Bronchial challenge testing was performed at the beginning of his career and showed no reduction in FEV₁ (PD₂₀ > 16 mg·ml⁻¹). In retrospect, his FEV₁/FVC had decreased over the years. A decrease in FVC or FEV₁ is frequently reported when a person has been diving for several years.²³⁻²⁷ Even though this diver was physically active with a significant exercise tolerance and had no clinical signs of pulmonary dysfunction, he would have been declared unfit to dive owing to his FEV₁/FVC ratio of 68%. However, when compared to the GLI reference tables, the Z-score of his FEV₁/FVC ratio is -1.45; although this is at the lower end of the 'normal' spectrum it is, again, well within the 90% CI. Because FEV₁/FVC is known to decline over the years, it stands to reason that assessment should take 'healthy ageing' into account. We declared this person fit to dive.

Case 3

A 21-year-old, non-smoking, caucasian female (height 184 cm) with no medical history presented for her initial medical assessment to work in a recompression chamber; her PFTs are presented in Table 2. She was healthy, physically active and reported no pulmonary complaints. When comparing her results with the current fitness to dive standards, she would have been declared fit to dive. However, her FEV₁/FVC of 74% is too low for young females and is outside the 90% CI range. Further assessment

using a histamine challenge showed profound bronchial hyperreactivity with a PC₂₀ FEV₁ of 3.07 mg·ml⁻¹. The PFT and bronchial hyperactivity met the criteria for a diagnosis of asthma. She was referred to a pulmonary specialist for further assessment and considered to be unfit to dive.

Discussion

Interpretation of pulmonary function in dive medical assessments requires a valid reference set. This may help to minimize potential risk of diving accidents (false negative) and can avoid unnecessary additional medical examination (false positive). The GLI-2012 is a valid all-age reference table with correction for sex and ethnicity.^{13,14} This fits the increasing demand of personalised medicine, in which physiological ageing and differences between ethnicity and sex are accounted for.

These three cases illustrate that the interpretation of PFT may change substantially when using a different dataset.¹⁴ Case 1 would have been subjected to additional examination, including exposure to radiation as well as additional costs. Because Case 2 shows a physiological decrease in pulmonary function due to ageing, this person would have been deemed unfit to dive using the ECSC/ERS-1993 standards, resulting in considerable impact on this diver's career. Case 3 might have been declared fit to dive using the old standards, even though her FEV₁/FVC is within the lowest 5% of the population. In general, using the lower limit of normal as defined by the GLI-2012 means that younger individuals should have slightly higher PFT values to be considered fit to dive, whereas lower PFT values due to ageing can be accepted in older divers. However, pulmonary assessment of fitness to dive cannot rely solely on PFT and should always be used to complement a thorough medical history.

All current fitness-to-dive standards use percentages of expected values. Interpreting the FEV₁/FVC as a percentage (i.e., above or below 70%) introduces a considerable margin

of error.¹³ In young individuals, an FEV₁/FVC of 75% could be a sign of obstructive lung disease, whereas an FEV₁/FVC of 65% in elderly persons is physiological. Even though healthy ageing includes a decline of lung function, there is probably a lower limit at which diving is considered safe; however, this lower limit has not yet been determined.

Interpretation of a Z-score is slightly more abstract than a percentage relative to the 'normal value'. It requires an extensive dataset, which might be difficult to implement in the software of older PFT devices. To help the clinician with assessment of lung function using the GLI-2012 dataset, several software solutions are freely available online (www.lungfunction.org). Currently the GLI-2012 reference set includes FVC, FEV₁, FEV₁/FVC and FEF₂₅₋₇₅; however, additional values are expected to be added in the coming years. Moreover, reference values for TL_{CO} have recently been published.²⁸

Even though a detailed history, physical examination and PFT can generate important information regarding fitness to dive, it will not necessarily prevent pulmonary barotrauma. In a study of barotrauma in a large cohort of healthy subjects participating in submarine ascent training,²⁹ there were 10 pulmonary barotrauma cases, one fatal, in 115,090 ascents. Either ascent training is safe or fitness-to-dive assessment has minimised the potential risk of injury. Conversely, abnormal PFTs have not been shown to be predictive of pulmonary barotrauma, although sufficient evidence is probably impossible to generate since many divers will be disqualified for diving when an abnormal PFT is found.

An important remaining question is: which PFT values can be accepted when determining a person's fitness to dive. Our centre has used the algorithm described here to assess occupational divers since 2015. During this period we have assessed more than 900 divers, submariners and hyperbaric technicians. Our intention is to evaluate and publish the data on the safety and cost-effectiveness of these assessments. Although our algorithm may require some modification, the preliminary results are promising. We have deemed several individuals fit to dive using the GLI-2012 standards, whereas these persons would have been declared unfit using the ECSC/ERS-1993 standards. Conversely, we have referred a few individuals to a pulmonary specialist for analysis and have identified pathology, such as airtrapping found on HR-CT, which we would not have identified using the ECSC/ERS-1993 standards and current fitness-to-dive standards.

PFT is part of both the initial and subsequent annual medical assessment of occupational divers in the Netherlands by regulation. However, its contribution to dive safety has been questioned.³⁰ Occasionally an annual PFT in physical fit and healthy divers brings additional information to light which could not have been gained by a thorough history. What frequency, and which examinations, should be performed to optimize dive safety remain to be determined.

Conclusion

Irrespective of the chosen algorithm and lower limit, every physician who is faced with evaluating pulmonary function should be using the most appropriate reference tables available for their population. In the field of pulmonary medicine, the introduction of the GLI-2012 standard has made a considerable positive impact on the assessment of pulmonary function testing. The GLI-2012 is an all-age reference table with correction for sex and ethnicity. We recommend that, in the development of fitness to dive standards, the concepts of upper and lower limits of normal should be adopted, and the use of fixed cut-off points for parameters such as FVC, FEV₁ and FVC/FEV₁ should be avoided.

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