Short Communication

Effect of changing from the National Health and Nutritional Examination Survey III spirometry reference range to that of the Global Lung Initiative 2012 at Gold Coast Hospital and Health Service

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Abstract: The categorisation of lung disease into obstructive ventilatory defect (OVD) and tendency to a restrictive ventilatory defect (TRVD) patterns using spirometry is used to guide both prognostication and treatment. The effectiveness of categorisation depends upon having reference ranges that accurately represent the population they describe. The Global Lung Initiative 2012 (GLI 2012) has spirometry reference ranges drawn from the largest sample size to date. This study aimed to determine whether using spirometry reference ranges from the new GLI 2012 dataset, compared to the previously used National Health and Nutritional Examination Survey III (NHANES III) dataset, resulted in a change in diagnosis between OVD, TRVD and normal ventilatory pattern (NVP). Spirometry data were collected from 301 patients, aged 18–80 years, undergoing investigation at the Gold Coast Hospital and Health Service (GCHHS) throughout February and March 2014. OVD was defined as a forced expiratory volume in 1 second (FEV_1) divided by forced vital capacity (FVC) less than lower limit of normal (LLN). TRVD was defined as $FEV_1/FVC \geq LLN$, $FEV_1 < LLN$, and $FVC < LLN$. The LLN values were determined by equations from the GLI and NHANES datasets. Spirometry interpreted using the NHANES III equations showed: 102 individuals (33.9%) with normal spirometry, 136 (45.2%) with an OVD pattern, 52 (17.3%) with a TRVD pattern, and 11 (3.7%) with a mixed pattern. When the spirometry data were interpreted using the GLI 2012 equations 2 (0.7%) individuals changed from OVD to NVP, 2 (0.7%) changed from NVP to OVD and 14 (4.7%) changed from TRVD to NVP. Using the GLI 2012 reference range resulted in a change in diagnosis of lung disease in 5.9% of the individuals included in this study. This variance in diagnosis when changing reference ranges should be taken into account by clinicians as it may affect patient management.

Keywords: Respiratory function tests; spirometry reference equation

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Introduction

Spirometry is a vital tool in the diagnosis and monitoring of respiratory disorders. It is interpreted by comparing measured values to a reference range. Abnormal results are defined as falling outside the lower limits of normal of the reference range. The reference range should ideally approximate as closely as possible to the local population as matched by age, height, sex and ethnicity (1).

The Gold Coast Hospital and Health Service (GCHHS) pulmonary function testing (PFT) laboratories had previously used equations from the National Health and Nutritional Examination Survey III (NHANES III) spirometry dataset to assess individuals aged 18 to 80 years. These equations are based on spirometry results collected in North America between 1988 and 1994 from 2,281 healthy, non-smoking Caucasians aged between 8 and 80 years of age (2). The NHANES III reference equations were chosen for use as they had been drawn from the largest dataset previously available that matched the predominately Caucasian population of Gold Coast, Australia (3).

In 2012 a European Respiratory Society (ERS) task force called the Global Lung Initiative (GLI) released spirometry reference equations that were based on spirometry results collected worldwide from 55,428 healthy, non-smoking Caucasians aged 3 to 95 years (4). The purpose of the new dataset was to provide a continuous spirometry reference range that spanned all ages so as to improve the continuity of diagnosis and care for patients with respiratory disorders. As the GLI 2012 equations were derived from the largest spirometry dataset to date, including data from the NHANES III study, they are likely to be the equations favoured by many lung laboratories.

Since publication of the GLI 2012 spirometry reference equations multiple studies (5-7) have been performed to identify whether changing from the NHANES III to the GLI 2012 equations resulted in a change in diagnosis between obstructive ventilatory defect (OVD), tendency to a restrictive ventilatory defect (TRVD) and normal ventilatory patterns (NVPs). The purpose of this study was to determine if transitioning from the NHANES III to the GLI 2012 equations at the GCHHS PFT laboratories resulted in a change of diagnosis for the individuals tested.

Methods

Spirometry data were collected from patients undergoing investigation at the GCHHS PFT laboratories throughout February and March 2014. These data were then analysed using the NHANES III and GLI 2012 equations to determine a diagnosis of OVD, TRVD or NVP. The results were then evaluated to determine if a change in an individual's diagnosis had occurred when transitioning between equations. This study was approved by the GCHHS Human Research Ethics Committee (HREC/14/QGC/35).

All patients between the ages of 18 and 80 years who underwent spirometry testing at GCHHS PFT laboratories in the given time period were included in the analysis. Sensormedics VMAX testing software available at the GCHHS PFT laboratories was used to generate predicted spirometry values from the NHANES dataset. Software available on the Spirexpert website (6,8) was used to generate predicted spirometry values from the GLI 2012 dataset.

OVD was defined as a forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) < lower limit of normal (LLN). TRVD was defined as FEV_1/FVC ≥ LLN, FEV_1 < LLN, and FVC < LLN. Mixed ventilatory defect (MVD) pattern was defined as FEV_1/FVC < LLN, FEV_1 < LLN, and FVC < LLN. Severity of OVD and TRVD was graded using the American Thoracic Society (ATS) and ERS 2005 guidelines (1). Severity of OVD was defined as the percentage of predicted FEV_1: mild >70%, moderate 60–69%, moderately severe 50–59%, severe 35–49% and very severe <35%. Severity of TRVD was defined as the percentage of predicted FVC: mild >70%, moderate 50–70% and severe <50%.

Results

A total of 349 patients were investigated at the GCHHS PFT laboratories throughout February and March 2014. Individuals were excluded if they were >80 years of age (n=19) or <18 years of age (n=25). Test results where patients were not fully able to complete the assessment were also excluded (n=4). The total number of patients included in the final analysis was 301 comprised of 158 males and 143 females.

When the NHANES III equations were applied to the spirometry data from the 301 individuals included in the study the number diagnosed with each ventilatory pattern was: 102 (34%) with a NVP, 136 (45%) with an OVD, 52 (17%) with a TRVD, and 11 (4%) with a MVD. When the GLI 2012 equations were applied the number of individuals diagnosed with each ventilatory pattern was: 116 (39%) with a NVP, 136 (45%) with an OVD, 38 (13%) with a TRVD and 11 (4%) with a MVD. These results are shown in *Table 1* with additional breakdown of diagnosis by sex.

Of the 147 patients diagnosed as having an OVD using the NHANES equations (including the 11 with a MVD) the grading of severity was: 39 (27%) with a mild defect, 20 (14%) with moderate defect, 30 (20%) with a moderately severe defect, 40 (27%) with a severe defect, and 18 (12%) with a very severe defect. Of the 147 patients diagnosed as having an OVD using the GLI 2012 equations (including the 11 with a MVD) the grading of severity was: 37 (25%)

Table 1 Spirometry interpretation: comparing National Health and Nutritional Examination Survey III (NHANES III) to Global Lung Initiative 2012 (GLI 2012) reference equations

Spirometry interpretation	Reference equation	
	NHANES III	GLI 2012
Males, n [%]		
Normal	49 [16]	53 [18]
OVD	71 [24]	73 [24]
TRVD	31 [10]	25 [8]
MVD	7 [2]	7 [2]
Total males	158 [52]	158 [52]
Females, n [%]		
Normal	53 [18]	63 [21]
OVD	65 [22]	63 [21]
TRVD	21 [7]	13 [4]
MVD	4 [1]	4 [1]
Total females	143 [48]	143 [48]
Total sample, n [%]		
Normal	102 [34]	116 [39]
OVD	136 [45]	136 [45]
TRVD	52 [17]	38 [13]
MVD	11 [4]	11 [4]
Total sample	301 [100]	301 [100]

n represents number of individuals with each diagnosis as determined by the given reference equations. Percentages are calculated as: number of individuals with each diagnosis divided by the total number of individuals in their entire given reference group. OVD, obstructive ventilatory defect; TRVD, tendency to a restrictive ventilatory defect; MVD, mixed ventilatory defect.

Table 2 Severity of obstructive ventilatory defect (OVD): comparing National Health and Nutritional Examination Survey III (NHANES III) to Global Lung Initiative 2012 (GLI 2012) reference equations

OVD severity	Reference equation	
	NHANES III	GLI 2012
Males, n [%]		
Mild	23 [16]	24 [16]
Moderate	8 [5]	9 [6]
Moderately severe	15 [10]	13 [9]
Severe	22 [15]	22 [15]
Very severe	10 [7]	12 [8]
Total males	78 [53]	78 [53]
Females, n [%]		
Mild	16 [11]	13 [9]
Moderate	12 [8]	14 [10]
Moderately severe	15 [10]	12 [8]
Severe	18 [12]	19 [13]
Very severe	8 [5]	9 [6]
Total females	69 [47]	69 [47]
Total sample, n [%]		
Mild	39 [27]	37 [25]
Moderate	20 [14]	23 [16]
Moderately severe	30 [20]	25 [17]
Severe	40 [27]	41 [28]
Very severe	18 [12]	21 [14]
Total sample	147 [100]	147 [100]

n represents number of individuals with each severity grading within their entire given reference group. Percentages are calculated as: number of individuals with each severity grading divided by the total number of individuals in their entire given reference group.

with a mild defect, 23 (16%) with a moderate defect, 25 (17%) with a moderately severe defect, 41 (28%) with a severe defect, and 21 (14%) with a very severe defect. These results are shown in *Table 2* with additional breakdown of OVD severity grade by sex.

Of the 63 patients diagnosed as having a TRVD with the NHANES III equations the grading of severity was: 24 (38%) with a mild defect, 33 (52%) with a moderate defect and 6 (10%) with a severe defect. Of the 49 patients diagnosed as having a TRVD with the GLI 2012 equations the grading of severity was: 11 (23%) with a mild defect, 33 (67%) with a moderate defect, and 5 (10%) with a severe defect. These results are shown in *Table 3* with additional breakdown of TRVD severity grade by sex.

Transitioning from the NHANES III to the GLI 2012 equations resulted in a change in diagnosis in a total of 18 individuals (6.0%). The diagnosis changed from an OVD to a NVP for 2 individuals (0.7%), from a NVP to an OVD for 2 individuals (0.7%), and from a TRVD to a NVP for 14 individuals (4.7%). There was change in the proportion

Table 3 Severity of tendency to a restrictive ventilatory defect (TRVD): comparing National Health and Nutritional Examination Survey III (NHANES III) to Global Lung Initiative 2012 (GLI 2012) reference equations

TRVD severity	Reference equation	
	NHANES III	GLI 2012
Males, n [%]		
Mild	11 [17]	6 [12]
Moderate	23 [37]	23 [47]
Severe	4 [6]	3 [6]
Total males	38 [60]	32 [65]
Females, n [%]		
Mild	13 [21]	5 [10]
Moderate	10 [16]	10 [20]
Severe	2 [3]	2 [4]
Total females	25 [40]	17 [35]
Total sample, n [%]		
Mild	24 [38]	11 [22]
Moderate	33 [52]	33 [67]
Severe	6 [10]	5 [10]
Total sample	63 [100]	49 [100]

n represents number of individuals with each severity grading within their entire given reference group. Percentages are calculated as: number of individuals with each severity grading divided by the total number of individuals in their entire given reference group.

of individuals in nearly every grade of severity in both the OVD and the TRVD groups when transitioning from the NHANES III to the GLI 2012 equations. These changes did not show a propensity to either increase or decrease the severity of the grading.

Discussion

The GLI 2012 equations were derived from the largest spirometry dataset to date, with data collected from 26 countries including Australia (4). Spirometry data from a sample population at GCHHS was in fact provided for the GLI 2012 report. The GLI 2012 spirometry reference equations have been endorsed internationally by the ERS, the ATS, the American College of Chest Physicians, the Australian and New Zealand Society of Respiratory Science and the Asian Pacific Society of Respirology (9). Given their wide acceptance it is likely that the GLI 2012 equations will become the reference range of choice in countries where a Caucasian population predominates.

Linares-Perdomo *et al.* (5) noted significant differences in the predicted LLN for both FEV_1 and FEV_1/FVC when changing from the NHANES III to the GLI 2012 equations. They noted this to be most prominent in older and taller or shorter individuals, with the differences being large enough to result in possible differences in clinical management. Brazzale *et al.* (6) reported a 2.2% reduction in diagnosis of OVD and a 5.3% reduction in a diagnosis of TRVD when changing equations. Quanjer *et al.* (7) found a reduction in diagnosis of OVD in 1.2% of males and 2.5% of females when changing equations. This group also found a reduction in diagnosis of TRVD in 5.5% of males and 4.7% of females. This previously observed reduction in the number of individuals with a diagnosis of TRVD when changing from the NHANES III to the GLI 2012 equations was also noted in our study.

The aim of our study was to assist clinicians in anticipating changes in diagnosis of ventilatory defect and classification of severity if the GLI 2012 equations were to be introduced. If spirometry data are analysed using the new equations then there is likely to be a reduction in the number of patients diagnosed with TRVD. This is accounted for by the lower value for FVC LLN seen within the GLI 2012 dataset. It is important to note that spirometry is not diagnostic for restrictive ventilatory defects without static lung volumes. For this reason the terminology 'tendency to a restrictive ventilatory defect' (TRVD) is used throughout this article (10). In our study half of the individuals whose diagnosis changes from TRVD to NVP still had a total lung capacity below the LLN.

A clear advantage of changing to the GLI 2012 dataset is that it is drawn from individuals aged from 3 to 95 years compared to the NHANES III dataset that is drawn from individuals aged 8 to 80 years. This improves the consistency of disease monitoring in childhood as it reduces the need to transition between dataset equations. It also ensures that the results are more representative of individuals aged over 80 years (11).

The GLI 2012 dataset is likely to provide the spirometry equations of choice to many clinicians working in predominately Caucasian populations given its larger cohort size, broader age range and wide acceptance from several international respiratory organisations. When transitioning to these equations clinicians should be aware of the possibility of a reduction in diagnosis of TRVD, as demonstrated in our study.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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