Comparison of per cent predicted and percentile values for pulmonary function test interpretation

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BACKGROUND: Pulmonary function tests (PFTs) are commonly interpreted as a fraction of predicted normal values, with an abnormal test often defined as less than 80% or greater than 120% of the predicted value. However, recommendations of the American Thoracic Society/European Respiratory Society suggest using a percentile-based approach to define an abnormal test (less than the fifth or greater than the 95th percentiles).
OBJECTIVE: To compare PFT values obtained by the per cent predicted method with the percentile-based method for lung function parameters.
METHODS: Full PFTs performed between January 2000 and July 2004, at the Health Sciences Centre (Winnipeg, Manitoba) were analyzed. Using the Crapo and Gutierrez equations, per cent predicted and percentile values were calculated. An abnormal test was defined as less than 80% or greater than 120% of predicted (per cent predicted method) or as less than the fifth or greater than the 95th percentiles (percentile method). Using the percentile method as reference standard, the diagnostic test characteristics of the per cent predicted method were calculated.
RESULTS: The full PFTs of 2176 men and 1658 women were analyzed using the Crapo and Gutierrez equations. The mean (± SD) age of all subjects was 52±15 years. Per cent agreement between the two tests was more than 94% for all parameters except for reduced residual volume (88%). Per cent predicted methods had suboptimal sensitivity for abnormal total lung capacity (88% to 89%), increased residual volume (83% to 89%) and reduced diffusion capacity (89% with Crapo equations). Suboptimal specificity (83% to 86%) was observed for decreased residual volume.
CONCLUSION: The results of the per cent predicted and percentile-based approaches for PFT interpretation were similar for the majority of lung function parameters. These two methods can be used interchangeably for spirometry. However, caution may be warranted in relying solely on per cent predicted methods for assessing lung volume or diffusion capacity.

Key Words: *Abnormal PFT; PFT guidelines; Spirometry interpretation; Test characteristics*

La comparaison des prévisions en pourcentage et des valeurs percentiles pour interpréter l'exploration fonctionnelle respiratoire

HISTORIQUE : Les explorations fonctionnelles respiratoires (EFR) sont souvent interprétées comme une fraction des valeurs normales prévues, une exploration anormale étant souvent définie comme correspondant à moins de 80 % ou à plus de 120 % de la valeur prévue. Cependant, les recommandations de l'*American Thoracic Society* et de l'*European Respiratory Society* proposent d'utiliser une démarche par percentile pour définir une exploration anormale (moins du 5e percentile ou plus du 95e percentile).
OBJECTIF : Comparer les valeurs d'EFR obtenues par la méthode prédictive en pourcentage à la méthode en percentile pour établir les paramètres de la fonction pulmonaire.
MÉTHODOLOGIE : Les auteurs ont analysé les EFR complètes effectuées entre janvier 2000 et juillet 2004 au *Health Sciences Centre* de Winnipeg, au Manitoba. Au moyen des équations de Crapo et Gutierrez, ils ont calculé les pourcentages prévus et les valeurs percentiles. Ils ont défini une exploration anormale comme inférieure à 80 % ou supérieure à 120 % des prévisions (méthode de prévision en pourcentage) ou comme inférieure au 5e percentile ou supérieure au 95e percentile (méthode des percentiles). Utilisant la méthode en percentile comme norme de référence, ils ont calculé les caractéristiques d'exploration diagnostique de la méthode prédictive en pourcentage.
RÉSULTATS : Les auteurs ont analysé l'EFR complète de 2 176 hommes et 1 658 femmes au moyen des équations de Crapo et Gutierrez. Tous les sujets avaient un âge moyen (±ÉT) de 52±15 ans. L'entente en pourcentage entre les deux explorations dépassait les 94 % pour tous les paramètres sauf le volume résiduel réduit (88 %). Les méthodes de prévisions en pourcentage avaient une sensibilité sous-optimale pour la capacité pulmonaire totale anormale (88 % à 89 %), le volume résiduel accru (83 % à 89 %) et une capacité de diffusion réduite (89 % avec l'équation de Crapo). On observait une spécificité sous-optimale (83 % à 86 %) du volume résiduel décru.
CONCLUSION : Les résultats de la méthode de prévisions en pourcentage et de la méthode en percentile pour interpréter les EFR étaient similaires pour la majorité des paramètres de fonction pulmonaire. On peut utiliser ces deux méthodes de manière interchangeable pour la spirométrie. Cependant, il faudrait peut-être faire preuve de prudence lorsqu'on se fie uniquement aux méthodes de prévisions en pourcentage pour évaluer le volume pulmonaire ou la capacité de diffusion.

A pulmonary function test (PFT) is routinely used for the diagnosis and management of many pulmonary conditions. However, standardization of different parameters in a PFT is a difficult task. The American Thoracic Society (ATS) and European Respiratory Society (ERS) have jointly published standards for interpretative strategies for lung function tests (1), spirometry (2), lung volumes (3) and diffusing capacity of the lung for carbon monoxide (DLCO) (4). Despite standardization, there are many differences from laboratory to laboratory, mainly due to the different reference values used (5-9). The best reference values for a particular laboratory depend on its patient population.

PFTs are commonly interpreted in comparison with predicted normal values, based on a patient's sex, height, age and race, with the observed value expressed as a per cent of predicted. With the per cent predicted method, abnormal PFTs have been defined as less than 80% or greater than 120% of the predicted value (10,11). However, more recent recommendations of the ATS and ETS suggest a percentile-based approach to interpret PFTs (1). The percentile-based approach defines an abnormal PFT result as less than the fifth percentile or greater than the 95th percentile (1).

Although some studies have shown that for adults of average age and height, 80% of predicted is close to the fifth percentile, older and shorter adults are more likely to be classified as abnormal, and taller, younger adults are more likely to be classified as normal using the per cent predicted approach. This occurs because the scatter around the predicted value

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TABLE 1
Criteria for pulmonary function test interpretation

	Criteria for abnormality	
Parameter	Conventional	Percentile
FEV_1	<80% predicted	<5th
FVC	<80% predicted	<5th
FEV_1/FVC	<0.70 observed	<5th
TLC	<80% predicted	<5th
	>120% predicted	>95th
RV	<80% predicted	<5th
	>140% predicted	>95th
DLCO	<75% predicted	<5th

DLCO Diffusing capacity of the lung for carbon monoxide; FEV_1 Forced expiratory volume in 1 s; FVC Forced vital capacity; RV Residual volume; TLC Total lung capacity

TABLE 2
Subject age and sex distribution quintiles

	Men (n=2176)	Women (n=1658)	Total (n=3834)
Age, years (mean ± SD)	53±15	50.7±14.7	52±15
Age quintile (years), n			
18–31	209	189	398
32–45	436	404	840
46–59	707	584	1284
60–73	632	387	1019
74–88	193	96	289

is constant, regardless of the subject's age or height, and not proportional to the mean. Therefore, taller and younger adults who have higher predicted values would need to lose a larger absolute volume before being classified as abnormal according to the 80% predicted method, when they may already be below the fifth percentile (1). This has led to the recommendation that a percentile-based approach be applied, with the fifth to 95th percentiles defining the normal range (1-4).

Therefore, we explored the diagnostic test characteristics of the per cent predicted method, with the percentile method as a reference standard, using information contained in a database of all PFTs performed on individuals older than 18 years of age at the Health Sciences Centre (Winnipeg, Manitoba), between January 2000 and July 2004, with the commonly used Crapo et al (5-7) and the more recently published, Canadian, Gutierrez et al (12) reference equations.

METHODS

Data contained in the PFT database at the Health Sciences Centre, for the period between January 2000 and July 2004, were used. All PFTs were performed during standard work hours in a single pulmonary function laboratory using Collins Equipment (GS 4G and Body Box II, Warren E Collins Inc, USA). All PFTs were performed according to ATS standards for acceptability and reproducibility (13,14). Registered PFT laboratory technicians performed all PFTs. All patients referred to the laboratory underwent a series of tests including flow-volume loops, lung volumes by body plethysmography when possible and DLCO using the single-breath technique. At the end of each day, all PFT results were stored in an Excel (Microsoft Corporation, USA) database format. Although all races were included in the study, stratified data for race was not available and, therefore, correction for race was not performed.

Only one PFT per subject was included in the data collected and analyzed. All subjects included were outpatients and/or inpatients at the Health Sciences Centre. Predicted values for forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, total lung capacity (TLC), residual volume (RV) and DLCO, were calculated using Crapo et al (5-7) reference equations and the more recently published, Canadian, Gutierrez et al (12) reference equations. For percentiles, patients' observed values were converted to standardized residuals:

$$(\text{Observed} - \text{Predicted})/\text{RSD}$$

in which RSD is residual SD. If the standardized residual was less than or equal to 1.64, then the values were at or below the fifth percentile. The RSD was taken from the original papers in which the reference equations were published (5-7,12).

Generally, a test was defined as abnormal if it was less than 80% or greater than 120% of predicted, with notable exceptions for RV (greater than 140% of predicted), DLCO (less than 75% or greater than 125% of predicted) and FEV_1/FVC (less than 0.70 observed) (Table 1) using the per cent predicted method as per the conventional criteria (10,11). All of the PFTs were then reclassified using the percentile approach in which an abnormal test was defined as less than the fifth or greater than the 95th percentiles (based on ATS/ERS recommendations). The values for men and women were calculated separately.

Using the percentile method as a reference standard, the diagnostic test characteristics of the per cent predicted method for all parameters of PFT were calculated. Sensitivity and specificity were considered to be suboptimal if they were below 90%. Agreement between the per cent predicted method and percentile method was then calculated as follows:

$$\text{Agreement} = (\text{Number positive by both tests} + \text{Number negative by both tests})/\text{Total number of tests}$$

Separate analyses were performed in subgroups of patients that comprised the extremes of age and height, with respect to sex in each case. Extremes of ages were defined as younger than 25 years and older than 70 years, whereas extremes of height were defined as below 152 cm and above 173 cm for women and above 185 cm for men. Extremes of age and height were defined somewhat arbitrarily and based on the number of available subjects in each category of the data set.

RESULTS

Full PFTs including lung volumes and DLCO of 2176 male and 1658 female subjects were analyzed using Crapo et al (5-7) and Gutierrez et al (12) equations. The mean (± SD) age of the entire study cohort was 52±15 years (Table 2).

Tables 3 and 4 describe the classification of abnormal PFTs by the per cent predicted and the percentile methods using the Crapo and the Gutierrez equations for women and men, respectively. The Crapo equation classified female subjects as having decreased DLCO three times more commonly than the Gutierrez equation, using both the per cent predicted and the percentile methods.

TABLE 3
Percentage of abnormal pulmonary function tests determined by the per cent predicted and percentile methods using Crapo et al (5-7) and Gutierrez et al (12) equations for women (n=1658)

	Conventional: Per cent predicted (Crapo/Gutierrez), %*		Reference standard: Percentile (Crapo/Gutierrez), %*	
Parameter	Reduced	Increased	<5th percentile	>95th percentile
FEV_1	40.9/49.1	–	38.8/48.8	–
FVC	29.0/34.1	–	27.6/31.6	–
FEV_1/FVC†	25.1/25.1	–	29.8/27.6	–
TLC	16.2/20.5	8.3/6.7	19.8/22.9	10.5/7.0
RV	24.1/19.5	17.9/21.9	8.6/6.1	20.3/23.9
DLCO	83.1/29.7	–	92.7/28.7	–

**Per cent predicted (reduced and increased) and the percentile (<5th and >95th) values are calculated using both the Crapo and the Gutierrez equations; they are reported here in the respective columns as Crapo/Gutierrez; †Abnormal ratio is <0.70 of actual FEV_1/FVC. DLCO Diffusing capacity of the lung for carbon monoxide; FEV_1 Forced expiratory volume in 1 s; FVC Forced vital capacity; RV Residual volume; TLC Total lung capacity*

TABLE 4
Percentage of abnormal pulmonary function tests determined by the per cent predicted and percentile methods using Crapo et al (5-7) and Gutierrez et al (12) equations for men (n=2176)

	Conventional: Per cent predicted (Crapo/Gutierrez), %*		Reference standard: Percentile (Crapo/Gutierrez), %*	
Parameter	Reduced	Increased	<5th percentile	>95th percentile
FEV_1	57.2/58.5	–	54.4/54.8	–
FVC	41.7/48.1	–	35.2/47.4	–
FEV_1/FVC†	40.8/40.8	–	45.8/72.2	–
TLC	15.6/22.0	12.0/6.6	16.3/23.7	12.5/7.4
RV	14.7/19.5	30.5/26.0	7.3/6.5	36.9/28.4
DLCO	47.7/35.8	–	52.8/29.9	–

**Per cent predicted (reduced and increased) and the percentile (<5th and >95th) values are calculated using both the Crapo and the Gutierrez equations; they are reported here in the respective columns as Crapo/Gutierrez; †Abnormal ratio is <0.70 of actual FEV_1/FVC. DLCO Diffusing capacity of the lung for carbon monoxide; FEV_1 Forced expiratory volume in 1 s; FVC Forced vital capacity; RV Residual volume; TLC Total lung capacity*

Tables 5 to 7 demonstrate the diagnostic characteristics of the per cent predicted method using the percentile method as a gold standard, as suggested by the ATS/ERS guidelines, for women, men and for all PFTs combined, respectively. The specificity for a reduction in RV was suboptimal in women (83% to 86%). The sensitivity for an abnormal TLC and increased RV tended to be suboptimal in women (78% to 94%), although less so with Gutierrez than with Crapo predicted values. The performance of the per cent predicted method appeared to be much better in men, with suboptimal sensitivities for increased RV (82% to 90%), reduced DLCO (Crapo, 88%), and increased TLC (Gutierrez, 85%). In men and women combined, the specificity for reduced RV (86% to 88%), sensitivity for increased RV (83% to 89%), and sensitivity for abnormal TLC or increased RV (83% to 89%) tended to be suboptimal by both Crapo and Gutierrez predicted values. However, only the Crapo predicted values yielded suboptimal sensitivity for reduced DLCO (89%).

For women 18 to 25 years of age (n=96), suboptimal sensitivity (13% to 81%) for all parameters was found – except for increased RV by Crapo and abnormalities in RV by Gutierrez equations – as well as suboptimal specificity for reduced RV. For women older than 70 years of age (n=187), there was suboptimal specificity for FEV_1, FVC, FEV_1/FVC ratio and reduced DLCO, and suboptimal sensitivity for increased RV and reduced TLC by both equations. For women less than 152 cm in height (n=101), there was suboptimal specificity for FEV_1, FVC and reduced RV by both equations, reduced DLCO by the Gutierrez equation, and suboptimal sensitivity for FEV_1/FVC ratio by both equations. For women taller than 173 cm (n=93), there was suboptimal sensitivity for all the parameters except for reduced RV (which has suboptimal specificity) by both equations.

For men younger than 25 years of age (n=98), there was suboptimal sensitivity for all the parameters (except change in RV by both equations and FVC by Crapo's equations) and there was suboptimal specificity for reduced RV by both equations. For men older than 70 years of age (n=337), there was suboptimal specificity for FEV_1, FVC and reduced DLCO and suboptimal sensitivity for increased RV by both equations, and FEV_1/FVC ratio by the Gutierrez equation. For men taller than 185 cm (n=168), there was suboptimal sensitivity for all the parameters, except FVC and reduced RV by Crapo and FEV_1/FVC ratio, reduced RV (suboptimal specificity) and DLCO by Gutierrez equations. The study cohort did not have any male subjects shorter than 152 cm.

The per cent agreement between the two tests, for all PFTs combined, using both equations, was more than 94% for all parameters except for reduced RV (88% to 89%). For women, the per cent agreement between the two tests was more than 94% for all parameters except for reduced RV (84%) and DLCO (90%) using Crapo equations, and reduced RV (87%) using the Gutierrez equation. For men, the per cent agreement between the two tests was at least 93% for all parameters except DLCO (92%) using the Crapo equation and reduced RV (87%) using the Gutierrez equation.

TABLE 5
Diagnostic characteristics of the per cent predicted method, using the percentile method as a reference standard using Crapo et al (5-7) and Gutierrez et al (12) equations for women (n=1658)

	Crapo et al						Gutierrez et al					
Parameter	Sen, %	Spe, %	PPV, %	NPV, %	LR+	LR–	Sen, %	Spe, %	PPV, %	NPV, %	LR+	LR–
FEV_1	95	93	90	97	14	0.06	96	95	95	96	20	0.04
FVC	94	96	89	98	21	0.06	95	94	88	97	15	0.06
RV↓	100	83	36	100	6	0.00	100	86	31	100	7	0.01
RV↑	85	99	96	96	102	0.15	90	99	97	97	112	0.11
TLC↓	82	100	100	96	2172	0.18	86	99	98	96	137	0.15
TLC↑	78	100	100	98	2318	0.22	94	100	97	100	482	0.06
DLco	90	100	100	43	217	0.10	94	96	90	98	21	0.06

↓ Below normal; ↑ Above normal, for all other parameters, only below normal are presented; *DLco Diffusing capacity of the lung for carbon monoxide; FEV_1 Forced expiratory volume in 1 s; FVC Forced vital capacity; LR+ Positive likelihood ratio; LR– Negative likelihood ratio; NPV Negative predictive value; PPV Positive predictive value; RV Residual volume; Sen Sensitivity; Spe Specificity; TLC Total lung capacity*

TABLE 6
Diagnostic characteristics of the per cent predicted method, using the percentile method as a reference standard using Crapo et al (5-7) and Gutierrez et al (12) equations for men (n=2176)

	Crapo et al						Gutierrez et al					
Parameter	Sen, %	Spe, %	PPV, %	NPV, %	LR+	LR–	Sen, %	Spe, %	PPV, %	NPV, %	LR+	LR–
FEV_1	93	97	98	91	32	0.07	98	90	92	97	9	0.03
FVC	99	90	84	99	10	0.01	95	94	93	96	17	0.05
RV↓	100	92	50	100	13	0.00	100	87	33	100	7	0.00
RV↑	82	100	100	91	2264	0.18	90	92	98	96	107	0.11
TLC↓	93	100	97	99	189	0.07	90	99	97	97	93	0.11
TLC↑	94	100	98	99	357	0.06	85	100	97	98	343	0.15
DLco	88	97	97	88	32	0.12	99	91	82	99	11	0.02

↓ Below normal; ↑ Above normal, for all other parameters, only below normal are presented; *DLco Diffusing capacity of the lung for carbon monoxide; FEV_1 Forced expiratory volume in 1 s; FVC Forced vital capacity; LR+ Positive likelihood ratio; LR– Negative likelihood ratio; NPV Negative predictive value; PPV Positive predictive value; RV Residual volume; Sen Sensitivity; Spe Specificity; TLC Total lung capacity*

TABLE 7
Diagnostic characteristics of the per cent predicted method, using the percentile method as a reference standard using Crapo et al (5-7) and Gutierrez et al (12) equations for all pulmonary function tests (n=3834)

	Crapo et al						Gutierrez et al					
Parameter	Sen, %	Spe, %	PPV, %	NPV, %	LR+	LR–	Sen, %	Spe, %	PPV, %	NPV, %	LR+	LR–
FEV_1	94	95	95	94	19	0.07	97	92	93	97	12	0.03
FVC	97	93	86	99	13	0.03	95	94	92	96	16	0.05
RV↓	100	88	42	100	9	0.00	100	86	32	100	7	0.00
RV↑	83	100	99	93	204	0.17	89	99	98	96	109	0.11
TLC↓	88	100	99	97	307	0.12	88	99	97	96	107	0.12
TLC↑	88	100	99	98	594	0.12	89	100	97	99	394	0.11
DLco	89	98	99	79	34	0.11	97	93	85	99	14	0.04

↓ Below normal; ↑ Above normal, for all other parameters, only below normal are presented; *DLco Diffusing capacity of the lung for carbon monoxide; FEV_1 Forced expiratory volume in 1 s; FVC Forced vital capacity; LR+ Positive likelihood ratio; LR– Negative likelihood ratio; NPV Negative predictive value; PPV Positive predictive value; RV Residual volume; Sen Sensitivity; Spe Specificity; TLC Total lung capacity*

DISCUSSION

We compared the per cent predicted and percentile methods of PFT interpretation because the latter method has been recommended by the ATS/ERS guidelines (1). Moreover, there are no studies in the literature comparing the two methods for interpretation of lung volumes and DLco. There are only a few studies in the literature comparing the two methods for all parameters in spirometry (15,16) and FEV_1/FVC ratio (17,18). In addition, the majority of the PFT laboratories in North America use the Crapo et al (5-7) or Morris (19) equations for calculating the predicted normal values. However, these equations are dated and, therefore, are derived from PFTs performed on older PFT machines. Therefore, we compared the two interpretation strategies using the newer, Canadian, Gutierrez et al equations and the older Crapo et al equations. Although it is difficult to know whether classifying a single value as normal or abnormal makes a difference in the interpretation of a complete set of PFTs, we selected variables that we believe are of importance to clinicians in making diagnostic and therapeutic decisions. We selected a somewhat arbitrary threshold of acceptability for sensitivity and specificity (greater than 90%), but presented the actual values to allow clinicians to judge whether the degree of agreement was acceptable.

We found that both methods, per cent predicted and percentile, were comparable except for lung volumes and DLCO. In our population, the reduced specificity for a reduction in the RV of a woman translated into a positive predictive value of 31% to 36% and positive likelihood ratios of 6 to 7 (depending on the predictive equation used). In women, suboptimal sensitivity for restriction (reduction of TLC) by both methods of analysis, elevation of the TLC by Crapo's equation and an increased RV by Crapo's equation, translated into only moderate negative likelihood ratios that were generally between 0.15 and 0.22. In men, suboptimal sensitivity for increased RV by Crapo's equation and increased TLC by Gutierrez's equation translates into only moderate negative likelihood ratios of between 0.15 and 0.18. Hence, these measurements may best be corrected to percentiles. Our study supports the theoretical concern that the per cent predicted method is less accurate in subjects with extreme age or height. Therefore, the above concern should serve as a caution in the interpretation of PFTs in subjects with extreme age or height. In such subjects, it may be advisable to use the percentile method to avoid diagnostic errors.

In our study, the differences in both sexes combined appeared to be driven by the differences in the female subjects, as was observed by Aggarwal et al (16) for spirometry. Similar to our study, Aggarwal et al (16) demonstrated that subjects at extremes of ages and height had discordant results with the per cent predicted method and percentile method.

Similar to Gutierrez et al (12), but far more often, we found that reduced DLCO is more often diagnosed by using the Crapo equation, and more so in female than in male subjects. However, the discrepancy in DLCO observed in the study by Gutierrez et al (12) and in the present study, raises concerns regarding the interpretation of an abnormal DLCO measurement.

CONCLUSION

The results of the per cent predicted and percentile-based approaches to PFT interpretation are generally similar. As expected, subjects at the extremes of age and height were, however, more likely to be misclassified using the per cent predicted method. In most subjects, however, the two methods of PFT interpretation may be used interchangeably for spirometry. For TLC, increased RV and DLCO, there was suboptimal sensitivity, and for decreased RV there was suboptimal specificity. Inadequate sensitivity may lead to difficulties in detecting important disorders associated with a reduction in DLCO (eg, emphysema, interstitial lung disease and pulmonary vascular disease). Caution is warranted in relying solely on per cent predicted methods when assessing lung volumes or DLCO in all subjects, and most parameters in subjects at the extremes of age and height, for which it is likely best to correct these values using the percentile method. These results provide empirical evidence to support the ATS/ERS recommendation to use percentile-based interpretation of PFTs rather than the per cent predicted method.

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