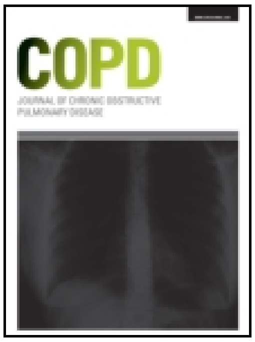

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ORIGINAL RESEARCH

The Diagnostic Importance of a Reduced FEV_1/FEV_6

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Abstract

Background: On spirometry the FEV_1/FEV_6 ratio has been advocated as a surrogate for the FEV_1/FVC. The significance of isolated reductions in either the FEV_1/FEV_6 or FEV_1/FVC is not known. ***Methods***: First-time adult spirograms (n = 22,837), with concomitant lung volumes (n = 12,040), diffusion (n = 14,154), and inspiratory capacity (n = 12,480) were studied. Four groups were compared. 1) Only FEV_1/FEV_6 reduced (n = 302). 2) Only FEV_1/FVC reduced (n = 1158). 3) Both ratios reduced (n = 6593). 4) Both ratios normal (n = 14,784). ***Results***: In patients with obstructed spirometry (either a reduced FEV_1/FVC and/or FEV_1/FEV_6), 3.8% only had a reduced FEV_1/FEV_6, while 14.4% only had a reduced FEV_1/FVC. The mean FEV_1 was lower when both ratios were reduced. The group with only a reduced FEV_1/FEV_6, compared to only the FEV_1/FVC reduced, had a lower FEV_1, FVC, BMI, Expiratory Time, and IC (p values < 0.0001). DL_{CO} was also lower ($p = 0.005$), and the FEV_1/FVC and RV/TLC were higher (p values < 0.0001). When the patients with only a reduced FEV_1/FEV_6 had a subsequent spirogram, 60% had a reduced FEV_1/FVC when their mean expiratory times were 3.5 seconds longer. Ninety percent of this group had strong clinical evidence of airways obstruction. ***Conclusions***: The FEV_1/FEV_6 is not as sensitive as the FEV_1/FVC for diagnosing airways obstruction, but in the presence of a normal FEV_1/FVC, subjects have greater physiologic abnormalities than when only the FEV_1/FVC is reduced. The FEV_1/FEV_6 ratio should not replace the FEV_1/FVC as the standard for airways obstruction, but there is benefit including this measurement to identify individuals with greater air trapping and diffusion abnormalities.

Keywords: Airway obstruction, FEV_1/FEV_6, Pulmonary function test, Spirometry, Timed vital capacity

This study was presented (in part) as a slide presentation at the ACCP, San Diego, CA, 2009.

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Abbreviations

ATS	American Thoracic Society
BMI	Body Mass Index
CI	Confidence Interval
COPD	Chronic Obstructive Lung Disease
DL_{CO}	Diffusing Capacity
ERS	European Respiratory Society
FEV_1	Forced Expiratory Volume in 1 second
FEV_6	Forced Expiratory Volume in 6 seconds
FVC	Forced Vital Capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
IC	Inspiratory Capacity
LLN	Lower Limit of Normal
OR	Odds Ratio
RV	Residual Volume
SVC	Slow Vital Capacity
TLC	Total Lung Capacity.

Introduction

Since the publication of the National Health and Nutrition Examination Survey (NHANES) III data in 1999, creating the first reliable predicted equations for the FEV1/FEV6 ratio, with a defined lower limit of normal (LLN) for multiple races, there have been a number of studies arguing the importance of this value for diagnosing airways obstruction (1). The National Lung Health Education Program consensus statement in 2000 advocated the use of the FEV_6 and FEV_1/FEV_6 as a replacement for the FVC and FEV_1/FVC for the diagnoses of airways obstruction (2).

The reasoning was that measuring the volume at 6 seconds is a more consistent endpoint across a broad patient population, is easier to perform, and is associated with less patient discomfort. Although a number of studies promote the use of the FEV_1/FEV_6 as an alternative or substitute for detecting airways obstruction (3–9), there also have been voices of caution regarding its sensitivity compared to the FEV_1/FVC (10–14).

A systematic review of the literature (11 studies) by Jing et al. looked at the relationship of the FEV_1/FEV_6 to the FEV_1/FVC. In spite of reporting a wide range in the sensitivity of the FEV_1/FEV_6 ratio, varying from 73% to 97%, and specificity ranging from 70% to 100%, they supported using this ratio as valid alternative for the FEV_1/FVC (3). The purpose of our study was to establish the prevalence of discordant abnormalities of these two ratios in our large institutional pulmonary function lab, and determine if there may be a physiological explanation for these differences using additional lung volume measurements and diffusing capacity.

Methods

This study was performed with the permission of the Institutional Review Board for Henry Ford Hospital, Detroit, Michigan. The authors had no conflicts of interests. Data were collected from the pulmonary division database of pulmonary function tests performed over 8 years. Only Vmax equipment and software was used for testing, though different versions were used. Spirometry, lung volumes, and diffusion measurements were performed using Legacy, Spectra, and Encore systems (from CareFusion). The tests were performed by a core group of pulmonary function technicians with experience testing almost 50,000 patients during the study period.

Senior staff pulmonologists, on a daily basis would evaluate each test for quality control issues, i.e., examining flow volume loops, volume time curves, expiratory times, consistency of efforts, and achieving zero airflow. Testing protocols adhered to guidelines for calibration and testing recommended by the ATS, and most recently updated by the ATS and ERS (15–19). Spirometers were calibrated daily using a 3 L syringe. Maximum efforts were made to achieve reproducibility of 3% between the two best test efforts, zero flow, and maximum expiratory effort and times. In the real world setting, patients with respiratory diseases experience discomfort, and may have trouble achieving these goals, especially on first time testing, and could improve with training after given bronchodilators or on future tests. The spirogram with the best FEV_1+FVC effort was reported and it was on this trial that the FEV_6 was also selected.

Plethysmography was performed using variable pressure technique calibrating daily according to manufacturer's guidelines and monthly using biological controls, with equipment meeting published standards recommended by the ATS/ERS. Manufacturer frequency response was verified. Patients were seated comfortably and allowed time for thermal drift. Patients were coached to achieve panting frequencies between 0.5 and 1.0 Hz while holding hands against cheeks. A minimum of 3 efforts were obtained. The order of ERV and VC maneuvers may have been adjusted based on the severity of underlying lung disease and degree of dyspnea the patient was experiencing. Nitrogen was also calibration daily according to manufacturer's guidelines, and monthly using biological controls achieving an N2 concentration <1.5% for at least 3 successive breaths while closely examining for air leaks.

Diffusion calibration was performed internally prior to each patient test. Manufacturer's guidelines were again followed closely as well as using frequent biological controls. Using a single breath technique, a minimum of 2 acceptable efforts was collected with averaging of results. The goal was to achieve a breath hold of >10 sec, and VC capacity within 85% of the best FVC maneuver in <4 seconds. At least 4 minutes elapsed between each effort, up to 10 minutes in more severely impaired patients.

Patients younger than the age of 20 were excluded to confine results to adults with reliable predicted values. A very small number of tests with expiratory times less than 6 seconds were also excluded since the purpose of this study was to examine the clinical significance of abnormalities related to the FEV_6. Only Caucasians and African-Americans were included because of the small number of subjects in the other racial groups and the lack of well defined lower confidence limits of normal. Patients self-selected their race from an institutional approved list of accepted ethnic groups. Though post-bronchodilator spirometry is often advocated to evaluate, diagnose, and classify COPD, we reviewed an institutional database in which testing was performed for all possible diagnoses. Often post-bronchodilator studies were not ordered with initial testing. Exclusively examining only post-bronchodilator studies would have underestimated the number of our patients with airways obstruction due to asthma if they had reversibility after bronchodilators, and we wanted to examine all patients with airway obstruction.

Lung volume measurements were performed primarily by plethysmography, but N2 washout values were used of if plethysmography could not be performed.

The volumes studied were inspiratory capacity (IC), total lung capacity (TLC), residual volume (RV), and RV/TLC. If the patient did not have a recent hemoglobin value within the previous month, or had recent significant changes in their medical status, a finger stick hemoglobin was obtained whenever possible. In only a small percentage of cases was a non-hemoglobin corrected diffusing capacity (DL_{CO}) used for analysis.

The use of tobacco was self-reported by the patient during the entering of demographic data by the lab technician.

Patients were categorized into 4 groups (Table 1) using strict NHANES III 95% lower confidence limits of normal for the FEV_1/FEV_6 and the FEV_1/FVC:

1) A reduced FEV_1/FEV_6 with normal FEV_1/FVC.
2) A reduced FEV_1/FVC with normal FEV_1/FEV_6.
3) Both ratios reduced.
4) Both ratios normal.

We then identified the patients who had simultaneous lung volumes and DL_{CO} to look for physiologic characteristics unique to each of these groups. To adjust for demographic differences in race, sex, age, and height when making comparisons between groups, percent predicted values were compared. Crapo predicted volumes (TLC, RV, RV/TLC, IC) were used for Caucasians, and corrected for African-Americans according to ATS/ERS guidelines (TLC × 0.88, RV × 0.93, and RV/TLC × 1.05) (20). The Miller et al. non-smoking equations were used for diffusion-predicted values and corrected by 0.93 for African Americans (21).

The patients in our group that only had an isolated reduction of the FEV_1/FEV_6 ratio, were further evaluated by searching for those subjects who had spirometry at a future date. The clinical diagnosis of these 302 patients was determined by carefully reviewing their medical records for diagnoses of airways obstruction, conditions for which they were being treated, and also to more accurately obtain their smoking history.

The open source, R-statistical package (r-project.org) version 2.8.0, was utilized for data analysis with two-sample t-test and chi-square test used for significance testing, with 95% CI of the group differences reported for comparisons of continuous and dichotomous data, respectively.

Results

Table 1 shows the breakdown of the numbers of the individual pulmonary functions tests performed during the study period. Of the 43,630 patient tests analyzed, 22,837 were first-time spirograms with 12,040 having concomitant lung volumes, and 14,154 having simultaneous DL_{CO}. 12,480 had IC measured as either part of a slow vital capacity (SVC) maneuver during lung volume measurements or SVC ordered as a separate test. The greater number of subjects who had DL_{CO} compared to lung volumes is due to ordering staff only requesting diffusion with spirometry, and not volumes.

Caucasians were more likely to have obstruction when both ratios were reduced (OR = 1.15, 95% CI 1.08, 1.22, $p < 0.05$) and when only the FEV_1/FEV_6 was reduced (OR = 1.68, 95% CI 1.30, 2.18, $p < 0.05$).

Table 1. Database Characteristics of the 4 Groups Studied

	# of Patients	Only FEV_1/FEV_6 reduced	%	Only FEV_1/FVC reduced	%	Both Ratios reduced	%	Both Ratios Normal	%
Total Adult Database	43,630	582		2,243		14,549		26,256	
1st Time Spirometry	22,837	302		1,158		6,593		14,784	
African-American	8,392	78	0.9	424	5.1	2,271	27.1	5,619	67.0
Caucasian	14,445	224	1.6	734	5.1	4,322	29.9	9,165	63.4
Female	12,965	173	1.3	579	4.5	3,450	26.6	8,763	67.6
Male	9,872	129	1.3	579	5.9	3,143	31.8	6,021	61.0
Smokers*	7,312	106	35.1	414	35.8	2,750	41.7	4,042	27.3
With Volumes	12,040	154		649		3,197		8,040	
African-American	4,407	34	0.8	225	5.1	1,054	23.9	3,094	70.2
Caucasian	7,633	120	1.6	424	5.6	2,143	28.1	4,946	64.8
With DLCO	14,154	174		742		3,891		9,347	
African-American	5,097	39	0.8	261	5.1	1,295	25.4	3,502	68.7
Caucasian	9,057	135	1.5	481	5.3	2,596	28.7	5,845	64.5
With Inspir Capacity	12,480	166		665		3,348		8,301	
African-American	4,457	34	0.8	226	5.1	1,072	24.1	3,125	70.1
Caucasian	8.023	132	1.6	439	5.5	2,276	28.4	5,176	64.5

Ethnic and smoking distribution of groups studied.
* Smoking history obtained at time of demographic information prior to testing.

Table 2. Mean of Variables of 4 Study Groups ± Standard Deviation

	Only FEV_1/FEV_6 reduced	Only FEV_1/FVC reduced	Both Ratios reduced	Both Ratios Normal
# Patients	302	1,158	14,549	26,253
Expir Time (sec) ± SD	8.1 ± 1.5	14.8 ± 3.7	12.9 ± 4.1	10.0 ± 2.7
Age (yrs) ± SD	62.3 ± 16.5	62.5 ± 12.6	61 .9 ± 14.3	57.8 ± 14.7
BMI ± SD	28.7 ± 8.7	30.6 ± 6.9	28.5 ± 7.4	31.9 ± 8.1
FEV_1 %Pred ± SD	71.0 ± 19.2	76.3 ± 16.3	56.2 ± 19.2	86.3 ± 18.3
FVC %Pred ± SD	79.6 ± 21.4	90.3 ± 19.1	79.7 ± 20.1	87.3 ± 18.4
FEV_1/FVC % ± SD	68.3 ± 3.6	64.7 ± 4.0	53.6 ± 10.9	77.0 ± 5.7
FEV_6 %Pred ± SD	81.3 ± 21.6	83.8 ± 18.0	72.8 ± 19.7	87.2 ± 18.3
FEV_1/FEV_6 % ± SD	69.9 ± 3.3	72.9 ± 5.0	60.8 ± 8.8	79.9 ± 4.6
RV %Pred ± SD	1 16.4 ± 32.0	114.3 ± 30.5	145.1 ± 49.6	98.3 ± 28.9
TLC %Pred ± SD	95.3 ± 17.3	100.0 ± 16.3	106.4 ± 19.5	92.7 ± 16.7
RWTLC %Pred ± SD	122.4± 24.8	113.8 ± 22.2	134.8 ± 30.7	106.0 ± 22.0
Insp Cap %Pred ± SD	79.2 ± 25.2	92.4 ± 22.2	79.8 ± 24.8	93.3 ± 24.3
DLCO %Pred ± SD	72.1 ± 22.1	76.6 ± 18.3	65.2 ± 21 .4	78 .9 ± 18.7

This table shows the mean values analyzed in each of the 4 study groups along with their standard deviations.

In addition, males were more likely to have both ratios reduced (OR = 1.29, 95% CI 1.22, 1.36, $p < 0.05$). Tobacco use was more likely if both ratios were reduced (OR = 1.83, 95% CI 1.73, 1.95, $p < 0.05$). The groups with only a reduced FEV_1/FEV_6 or FEV_1/FVC had similar reported tobacco use.

Table 2 shows the mean values of the variables examined in the 4 groups studied, along with their standard deviations. There appeared to be differences in almost all the mean variables analyzed between the 4 study groups. Using the mean values in Table 2, we performed pair-wise comparisons of the 3 groups with a reduced FEV_1/FEV_6 and/or a reduced FEV_1/FVC. Table 3 shows the differences between the mean values in Table 2 for the 3 groups in which the FEV_1/FVC and/or FEV_1/FEV_6 ratios were reduced below their 95% lower limit of normal, along with their *p*-values. There were significant differences between all groups for almost all of the variables analyzed.

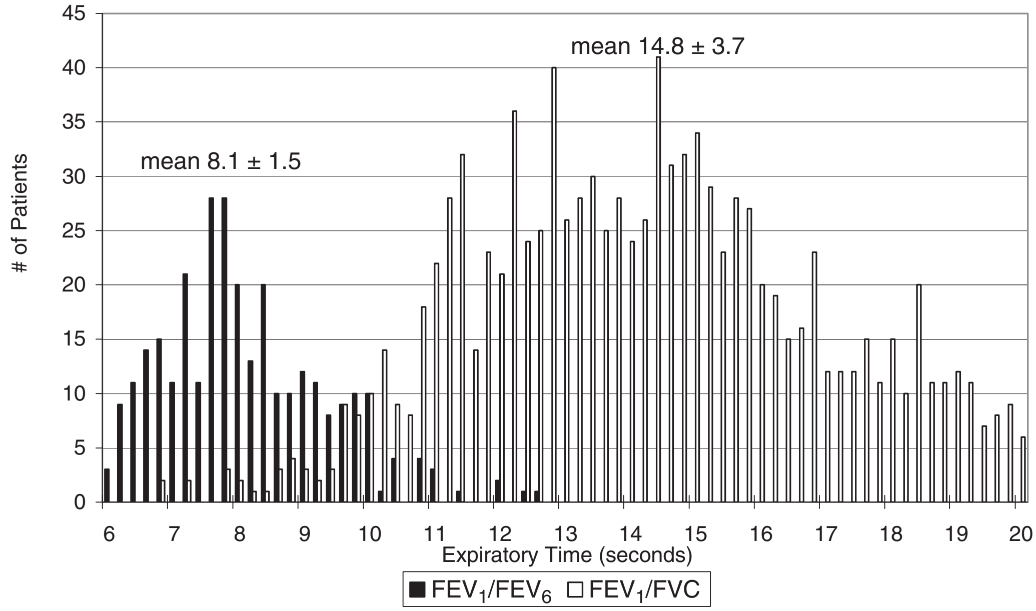
The ages of the 3 groups with reduced ratios were similar. The group with only a reduced FEV_1/FEV_6 had a lower BMI than if only the FEV_1/FVC was reduced (28.7 ± 8.7 vs. 30.6 ± 6.9, $p < 0.0001$), but similar to when both ratios were reduced (28.5 ± 7.4).

Spirometry revealed significant differences in the mean FEV_1 and FEV_1/FVC between the 3 groups with reduced ratios ($p < 0.0001$). The lowest values occurred when both ratios were reduced indicating a greater

Table 3. Differences Between Mean Values Studied

	Only FEV_1/FEV_6 reduced minus Only FEV_1/FVC reduced		Only FEV_1/FEV_6 reduced minus Both ratios reduced		Only FEV_1/FVC reduced minus Both ratios reduced	
Expir Time (s)	−6.7	p < 0.0001	−4.8	p < 0.0001	1.9	p < 0.0001
Age (yrs)	−0.2	p = 0.8489	0.4	p = 0.6060	0.6	p = 0.1778
BMI %	−2.0	p < 0.0001	0.2	p = 0.6155	2.2	p < 0.0001
FEV_1 %Pred	−5.2	p < 0.0001	14.8	p < 0.0001	20.1	p < 0.0001
FVC %Pred	−10.7	p < 0.0001	−0.1	p = 0.9581	10.7	p < 0.0001
FEV_1/FVC %	3.6	p < 0.0001	14.7	p < 0.0001	11.1	p < 0.0001
FEV_6 %Pred	−2.5	p = 0.0373	8.5	p < 0.0001	17.6	p < 0.0001
FEV_1/FEV_6	−3.1	p < 0.0001	9.0	p < 0.0001	12.1	p < 0.0001
RV %Pred	2.2	p = 0.4276	−28.7	p < 0.0001	−30.9	p < 0.0001
TLC %Pred	−4.7	p = 0.0018	−11.1	p < 0.0001	−6.4	p < 0.0001
RWTLC %Pred	8.5	p < 0.0001	−12.5	p < 0.0001	−21.0	p < 0.0001
Insp Cap %Pred	−13.1	p < 0.0001	−0.6	p = 0.7522	12.6	p < 0.0001
DLCO %Pred	−4.5	p = 0.0050	6.9	p < 0.0001	11.4	p < 0.0001

Pair-wise comparisons of differences in mean values for the 3 groups that had reduced ratios of either the FEV_1/FEV_6 or the FEV_1/FVC or if both ratios were reduced.



This figure demonstrates the difference in the distribution of the expiratory times between the 2 groups when only the FEV_1/FEV_6 is reduced or only the FEV_1/FVC is reduced.

Figure 1. Expiratory Times if Only FEV_1/FEV_6 or FEV_1/FVC is Obstructed.

degree of airway obstruction (FEV_1 = 56.2% predicted, FEV_1/FVC = 53.6%).

Comparing the 2 milder groups of obstruction (only the FEV_1/FEV_6 or only the FEV_1/FVC reduced), when only the FEV_1/FEV_6 was reduced, the FEV_1 was significantly lower (71.0% vs. 76.3%, $p < 0.0001$), as well as the FVC (79.6% vs. 90.3%, $p < 0.0001$), but the FVC was comparable to the more impaired group in which both ratios were reduced (79.6% vs. 79.7%, $p = .958$).

Not unexpectedly, the TLC and RV/TLC, measures of hyperinflation and air trapping, were highest when both ratios were reduced. But when only the FEV_1/FEV_6 was reduced, the RV/TLC was significantly higher compared to the group in which only the FEV_1/FVC was reduced (122.4% vs. 113.8%, $p < 0.0001$), and significantly lower than when both ratios were reduced (134.8%, $p < 0.0001$).

The IC, also useful in monitoring air trapping, corresponded to the above findings. In the group in which only the FEV_1/FEV_6 was reduced, the IC was lower than if only the FEV_1/FVC was reduced ($p < 0.0001$), and similar to when both ratios were reduced ($p = 0.7522$). The differences in DL_{CO} were also highly significant. When only the FEV_1/FEV_6 was reduced, the DL_{CO} was lower than if only the FEV_1/FVC was reduced (72.1% vs. 76.6%, $p < 0.005$), but higher than if both ratios were reduced (65.2%, $p < 0.0001$).

One of the most striking findings between all of our obstructed groups was the differences in mean expiratory times. The group in which only the FEV_1/FEV_6 was reduced had a significantly shorter mean expiratory time (8.1 sec) than all the other groups ($p < 0.0001$), with the greatest difference occurring between the groups in which only the FEV_1/FEV_6 or only the FEV_1/FVC was reduced (Fig. 1). For this reason, we searched the database to find how many of the patients in this group had future repeat spirometry. Of 100 patients identified (Table 4), 60% demonstrated a reduced FEV_1/FVC on subsequent testing. This group of 60 patients showed a significantly longer mean expiratory time increase (test2 minus test1) than the 40 patients in whom the FEV_1/FVC remained within the confidence limits of normal (3.5 seconds longer vs. 1 second, $p < 0.0001$).

Reviewing the medical records of the 302 patient with only a reduction in the FEV_1/FEV_6 (Table 5), 45.4% had a clinical diagnosis of COPD, 29.8% asthma, and 2.7% other obstructive diseases (tracheal stenosis, bronchiectasis) and were being treated for these conditions. Though another 11.9% did not have an obstructive diagnosis listed, they had significant smoking histories (>15 pack-years) and almost all of them were on bronchodilator therapy and/or were being managed for advanced stages of lung cancer. It is noted that only 4% had a diagnosis consistent with a restrictive process with 2.7% having diagnosis of both obstructive and restrictive disease.

Discussion

The literature reports a wide range in sensitivity and specificity regarding the usefulness of substituting the FEV_1/FEV_6 for the FEV_1/FVC. Half favor doing so, while half urge caution. This study highlights that though both these ratios are measurements of airways obstruction,

Table 4. Of the 302 patients with only a reduced FEV_1FVC_6, 100 of them (below) had future repeat spirograms

	Repeat Spirometry Results		
	Reduced FEV_1/FVC	Normal FEV_1/FVC	P
# of patients (total of 100)	60	40	
1st Test ExpTime (sec)	7.9	8.2	
Repeat Test Exp Time (sec)	11.4	9.2	
Change (sec)	3.5	1.0	$p < 0.0001$

This table demonstrates when the group of patients with only a reduced FEV_1/FEV_6 ratio had a significantly longer mean expiratory time, their FEV_1/FEV_6 ratio dropped below the 95% LLN.

Table 5. Diagnoses of subjects with only a reduced FEV_1/FEV_6 ratio (302 subjects)

	n	%
COPD	137	45.4%
Asthma	90	29.8%
Other obstructions*	8	2.7%
No obstruction, but smoked > 1 5 pk yr	36	11.9%
	Total	89.7%
Other Diagnostic Categories		
Total smokers > 15 pk yr	198	65.6%
Only restriction Dx §	12	4.0%
Restriction + Obstruction†	8	2.7%

This table indicates that of the 302 subjects with only a reduced FEV_1/FEV_6 ratio, 90% had strong clinical evidence to indicate they were not false positives for airways obstruction.

* Tracheal obstruction, bronchiectasis

§ Sarcoid (5), ALS (2), effusions (3), lobectomy (2)

† Sarcoid (5), effusions (1), fibrosis (2)

there appears to be physiologic reasons for their discordance.

Our results indicated that if only the FEV_1/FEV_6 is reduced, when compared to the group with only a reduced FEV_1/FVC ratio, this group had a higher TLC and RV/TLC, with a lower IC, DL_{CO}, FEV_1, and FVC. In addition, the FVC, BMI and IC in this group were similar to the group that had both ratios reduced suggesting a greater degree of air trapping with the relatively shorter expiratory times masking a reduction in the FEV_1/FVC. This finding is further supported by looking at future tests on these subjects and finding that with a longer expiratory time, their FEV_1/FVC ratios decreased below the confidence limit of normal (Table 4).

Because 90% of the subjects with only a reduced FEV_1/FEV_6 (Table 5) had strong clinical evidence for having airways disease (reviewing their medical records), this supports that these subjects are not the 5% of the normal population that falls outside the 95% lower limit of normal. A chart review of the 1,158 patients with only a reduced FEV_1/FVC was not performed since this value is considered the standard for defining airways obstruction on spirometry.

Table 6 shows that if we substituted the FEV_1/FEV_6 ratio for the FEV_1/FVC, as some have recommended, out of our total patients with a reduced ratio (airways obstruction), based on spirometry alone we would ultimately have misclassified 1158 subjects (14.4% of 8053 subjects). In contrast, using both ratios together, we would have included another 4% of patients who had greater physiologic abnormalities than when only the FEV_1/FVC was reduced. Our results were not too dissimilar from a recent review.

Five of those studies used the GOLD guidelines of an $FEV_1/FVC < 70\%$ and $FEV_1/FEV_6 < 70\%$ to define obstruction (4,5,8,9,10,22), even though the GOLD document has no guidelines for interpreting the FEV_1/FEV_6 ratio. Furthermore, using the criteria of an FEV_1/FVC ratio < 70% as defining obstruction is increasingly discouraged. Hansen et al. have pointed out the problem using the GOLD consensus opinion of creating a cutoff of 70% for the lower limit of normal for an FEV_1/FVC ratio. We know that predicted values and lower limits of normal decline with age, qualifying the GOLD conclusion that obstruction worsens with age (23).

Our study looked at all patients with airway obstruction, not just patients at risk for COPD. Recent COPD studies advocate using only post-bronchodilator spirometry (5,12,13), which could lead to erroneous conclusions if one is also evaluating patients for possible asthma, by normalizing airway obstruction after bronchodilator therapy. Hanson et al, stated that the significance of an isolated reduction in the FEV_1/FEV_6 is not known (14).

It appears too simplistic to try to replace the FEV_1/FVC ratio with the FEV_1/FEV_6, attempting to find a substitute, especially if screening patients who have a milder degree of airways obstruction. Though using only the FEV_1/FVC ratio will be more inclusive for finding airways obstruction, it can miss identifying a small number of patients as having normal airflows that have more pronounced abnormalities in lung volumes and diffusion. Figure 1 shows how these 2 milder subgroups separate out from each other based on their expiratory times, supporting our premise that these groups may differ by greater air trapping in the group with only reduced

Table 6. Breakdown of patients with one or both ratios reduced.

	Both Ratios Reduce	Only FEV_1/FVC Reduced	Only FEV_1/FEV_6 Reduced	Total With Reduced Ratios
# of Obstructed Patients	6,593	1,158	302	8,053
% of Obstructed Patients	81.90%	14.30%	3.80%	100.00%

Distribution of total pateints with obstruction based on a reduced FEV_1/FEV_6 and/or reduced FEV_1/FVC.

FEV_1/FEV_6. Although we did not selectively examine the flow volume curves of these subjects, we may have found that this subgroup had a higher number of subjects that did not actually achieve zero flow on spirometry even with expiratory times meeting ATS criteria.

The authors believe that the FEV_1/FEV_6 ratio should not be used as a substitute for the FEV_1/FVC ratio. We recognize that including this value on spirometry could potentially increase the occurrence of a false positive result (the 5% of the normal population that falls outside the normal 95% LLN). However, since 90% of this group had strong clinical support for having an obstructive disease that would have been missed only using the FEV_1/FVC, the benefit may outweigh the risk. This abnormality should make one more carefully scrutinize a clinically symptomatic patient with the additional measurements of lung volumes and diffusion. And in particular, it could identify patients for repeat future spirometry with concentrated efforts on achieving a more prolonged expiratory time to >11 seconds.

Conclusion

When this FEV_1/FEV_6 is reduced, with a normal FEV_1/FVC ratio, it may identify a group with a greater degree of physiologic abnormalities than if only the FEV_1/FVC is reduced. And substituting the FEV_1/FEV_6 for the FEV_1/FVC in a large pulmonary population can result in a significant reduction in the diagnosis of airways obstruction on spirometry in patients with milder obstruction.

Declaration of Interests

Zachary Q. Morris, MD was responsible for the design of the study, creation of the database, writing of programs to extract data, and writing of the manuscript. Najia Huda, MD was responsible for research and assisted in manuscript preparation. Robert R. Burke, MD was responsible for statistical analysis and assisted in manuscript preparation. The authors have no conflicts of interests to disclose.

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