ORIGINAL RESEARCH

Cut-off value of FEV_1/FEV_6 as a surrogate for FEV_1/FVC for detecting airway obstruction in a Korean population

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Background: Forced expiratory volume in 1 second (FEV_1)/forced expiratory volume in 6 seconds (FEV_6) has been proposed as an alternative to FEV_1/forced vital capacity (FVC) for detecting airway obstruction. A fixed cut-off value for FEV_1/FEV_6 in a Korean population is lacking. We investigated a fixed cut-off for FEV_1/FEV_6 as a surrogate for FEV_1/FVC for detecting airway obstruction.

Materials and methods: We used data obtained in the 5 years of the Fifth and Sixth Korean National Health and Nutrition Examination Survey. A total of 14,978 participants aged ≥40 years who underwent spirometry adequately were the study cohort. "Airway obstruction" was a fixed cut-off FEV_1/FVC <70% according to the Global Initiative for Chronic Obstructive Lung Disease guidelines. We also used European Respiratory Society/Global Lung Initiative 2012 equations for the FEV_1/FVC lower limit of normal.

Results: Among the 14,978 participants (43.5% male, 56.5% female; mean age: 56.9 years for men and 57.0 years for women), 14.0% had obstructive lung function according to a fixed cut-off FEV_1/FVC <70%. Optimal FEV_1/FEV_6 cut-off for predicting FEV_1/FVC <70% was 75% using receiver operating characteristic curve analyses (area under receiver operating characteristic curve =0.989, 95% confidence interval 0.987–0.990). This fixed cut-off of FEV_1/FEV_6 showed 93.8% sensitivity, 94.8% specificity, 74.7% positive predictive value, 98.9% negative predictive value, and 0.8 Cohen's kappa coefficient. When compared with FEV_1/FVC < lower limit of normal, FEV_1/FEV_6 <75% tended to over-diagnose airflow limitation (just like a fixed cut-off of FEV_1/FVC <70%). When grouped according to age and FEV_1 (%), FEV_1/FEV_6 <75% diagnosed more airway obstruction in older participants and mild–moderate stages compared with FEV_1/FVC <70%.

Conclusion: A valid fixed cut-off for detecting airway obstruction in a Korean population is FEV_1/FEV_6 of 75%, but should be used with caution in older individuals and those with mild–moderate airway obstruction.

Keywords: chronic obstructive pulmonary disease, forced expiratory volume in 6 seconds, pulmonary function test, airway obstruction

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Introduction

COPD is the fourth leading cause of death worldwide. However, the World Health Organization predicts that it will become the third leading cause of death by 2030. According to a recent report,[1] the priority of screening spirometry in asymptomatic patients has been reduced. However, a diagnostic pulmonary function test in symptomatic patients with wheezing, dyspnea, productive cough, or cough is needed (especially in primary care clinics).[2] Until now, expensive, labor-intensive, and inconvenient

spirometry has been an obstacle in COPD diagnosis. In the United States, only 32% of COPD patients undergo spirometry within 2 years before, or 6 months after, the diagnosis has been made.[3] Previously, we showed that only 27.5% of Korean patients with airway obstruction who used COPD-related health care facilities underwent spirometry.[4]

Several studies[5–18] have demonstrated that forced expiratory volume in 6 seconds of exhalation (FEV_6), and forced expiratory volume in 1 second (FEV_1) of exhalation ratio with FEV_6, can be used as convenient and accurate surrogates for forced vital capacity (FVC) and FEV_1/FVC, respectively. Owing to its use of a 6-second expiratory maneuver, FEV_6 makes spirometry in the office easier, faster, and safer[19] than FVC measurement. This theoretical basis enables primary care physicians to use hand-held spirometric devices such as PiKo-6® (nSpire Health, Inc. Longmont, CO, USA) or COPD-6™ (Vitalograph Ltd, Ennis, Co., Clare, Ireland) without having to employ expensive spirometry tests for the screening or diagnosis of COPD, and by easily providing the values of FEV at 1 and 6 seconds of exhalation.

However, an identical cut-off value between FEV_1/FEV_6 and FEV_1/FVC cannot be used for detecting airway obstruction because FEV_6 cannot be greater than FVC. Despite this controversy, some reports have argued that FEV_1/FEV_6 can reduce the sensitivity of detecting airway obstruction, especially in elderly patients with mild airway obstruction.[20,21] Therefore, other studies[6] have submitted increased cut-off values (73%–76%) of FEV_1/FEV_6 for detecting airway obstruction to overcome these limitations.

Spirometry indices are influenced by age, height, sex, and ethnicity.[22] Therefore, discovering the cut-off value of FEV_1/FEV_6 for detecting airway obstruction in a nationwide, representative population sample in Korea is worthwhile. The purpose of the present study was to ascertain the cut-off value of FEV_1/FEV_6 in place of FEV_1/FVC for detecting airway obstruction in a Korean population.

Materials and methods
Study population
Data for the present study were obtained from 5 years of the Fifth and Sixth Korean National Health and Nutrition Examination Survey (KNHANES V–VI), which was conducted between January 2010 and December 2014. KNHANES V–VI employed a stratified, multiple-stage, clustered-probability design to select a representative sample of non-institutionalized civilians among a Korean population. These data comprised information on age, ethnicity, sex, height, weight, and pre-bronchodilator spirometry values. A Vmax 2130 Dry Rolling-seal Spirometer (SensorMedics, Yorba Linda, CA,

USA) was employed. Spirometry was undertaken by specially trained technicians according to recommendations set by the American Thoracic Society (ATS)/European Respiratory Society (ERS) in 2005.[23] Data from a total of 14,978 individuals aged >40 years who underwent complete pulmonary-function tests from KNHANES V–VI were selected for the present study. We analyzed data on FEV_1, FEV_6, and FVC from subjects with two or more acceptable spirometric performances. The study protocol was approved by the institutional review board of Severance Hospital (approval number: 4-2006-0101). Written informed consent was obtained from patients or their next of kin.

Definition of airway obstruction
All spirometric values came from pre-bronchodilator results in this study. "Airway obstruction" was defined as FEV_1/FVC <70% as a fixed cut-off point according to guidelines set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD).[24] Severity of airway obstruction was classified as: "mild" (FEV_1 ≥80% predicted, GOLD stage I), "moderate" (50%≤ FEV_1 <80% predicted, GOLD stage II), "severe" (30%≤ FEV_1 <50% predicted, GOLD stage III), and "very severe" (30%≤ FEV_1 predicted, GOLD stage IV). In addition, "normal" lung function was defined as FEV_1/FVC ≥70% and FVC ≥80% predicted. A "restrictive spirometric pattern" was defined as FEV_1/FVC ≥70% and FVC <80% predicted.

ATS/ERS guidelines recommend use of reference equations derived from a representative sample of healthy individuals to determine the lower limit of normal (LLN), taking into account that spirometry indices are influenced by age, height, sex, and ethnicity. However, an officially recognized equation to use as a reference for pulmonary function in Korea is lacking. Hence, we used equations for FEV_1/FVC LLN set by the ESR/Global Lung Initiative (GLI) in 2012. These equations were announced by an ERS/GLI taskforce, and were derived from data collected from healthy nonsmokers 3 to 95 years old from 33 countries (including Korea). ERS/GLI 2012 equations provided multiple-ethnicity values and the LLN for spirometry.[25] "Airway obstruction" by FEV_1/FVC LLN was defined as being below its LLN in the presence of a normal FEV_1/FVC.

Statistical analyses
Data were analyzed using SAS v9.2 (SAS Institute Inc., Cary, NC, USA). Baseline characteristics were summarized using numbers and percentages to describe categorical variables, and compared using the chi-squared test. Continuous variables were compared using the Student's *t*-test and are presented as the

mean ± standard deviation (SD). FEV$_1$/FEV$_6$ was determined for the highest collective sensitivity and specificity using a receiver operating characteristic (ROC) curve for detecting airway obstruction. Cohen's kappa coefficient (CKC) was used to evaluate agreement between FEV$_1$/FEV$_6$ and FEV$_1$/FVC. Positive predictive value (PPV) and negative predictive value (NPV) were calculated for the most suitable FEV$_1$/FEV$_6$ threshold for the diagnosis of FEV$_1$/FVC <70%.

Results

Study populations

Among the 14,978 participants, 6,515 (43.5%) were male and 2,104 (14.0%) had airway obstruction. A total of 1,018 (6.8%) participants were classified as having mild obstruction, 996 (6.6%) with moderate obstruction, 80 (0.5%) with severe obstruction, and ten (0.1%) with very severe obstruction according to spirometry values. Airway obstruction was more prevalent in male than in female participants (Table 1).

Spirometric diagnosis of airway obstruction

According to the airway obstruction with FEV$_1$/FVC <70%, an ROC curve was used to determine the best corresponding cut-off for FEV$_1$/FEV$_6$ (Figure 1). The area under the ROC curve was 0.989 (95% confidence interval [CI]: 0.987–0.990). The FEV$_1$/FEV$_6$ cut-off corresponding to the greatest sum of sensitivity and specificity was 75%. Table 2 shows the sensitivities and specificities of different thresholds of FEV$_1$/FEV$_6$ for prediction of FEV$_1$/FVC <70%. When choosing an FEV$_1$/FEV$_6$ cut-off of 70%, specificity reached 100% but the sensitivity dropped to 44.1%. A fixed cut-off of FEV$_1$/FEV$_6$ <76% showed high sensitivity (98.0%) and specificity (90.8%) but a low PPV (63.6%). When using a fixed cut-off FEV$_1$/FEV$_6$ of 75%, sensitivity of 93.8%, specificity of 94.8%, PPV of 74.7%, NPV of 98.9%, accuracy of 94.7%, and CKC of 0.8, (95% CI: 0.786–0.814) were obtained, suggesting very good agreement between FEV$_1$/FEV$_6$ and FEV$_1$/FVC. When using a fixed cut-off of FEV$_1$/FEV$_6$ <75%, the number of false-positive cases was 670 (5.2%) and false-negative cases was 130 (6.2%) (Table 3). In particular, false-negative cases were included in mild (n=102) and moderate (n=28) airway-obstruction groups (Table 4).

Comparison of FEV$_1$/FVC < LLN with FEV$_1$/FVC <70% or FEV$_1$/FEV$_6$ <75%

To detect airway obstruction, we compared FEV$_1$/FVC LLN with a fixed cut-off of FEV$_1$/FVC <70% or FEV$_1$/FEV$_6$ <75%. When using FEV$_1$/FVC LLN, the prevalence of obstruction was 7.2%. However, when choosing a fixed

Table 1 Baseline characteristics of the study population

	Male	Female	Total
Subject, n (%)	6,515 (43.5)	8,463 (56.5)	14,978 (100)
Age (years)	56.9±10.9	57.0 ±10.6	57.0±10.7
Age group (years)			
40–49	1,944 (29.8)	2,342 (27.7)	4,286 (28.6)
50–59	1,922 (29.5)	2,739 (32.4)	4,661 (31.1)
60–69	1,625 (24.9)	2,077 (24.5)	3,702 (24.7)
≥70	1,024 (15.7)	1,305 (15.4)	2,329 (15.5)
Height (cm)	168.4±6.0	155.4±5.8	161.0±8.7
Weight (Kg)	69.0±9.7	58.3±8.4	62.9±10.5
BMI (Kg/m^2)	24.3±2.8	24.1±3.2	24.2±3.0
Pulmonary function test			
FEV$_1$ (L)	3.11±0.66	2.33±0.45	2.67±0.67
FEV$_1$ (%, pred)	89.79±13.69	94.40±12.95	92.40±13.47
FVC (L)	4.15±0.69	2.93±0.50	3.46±0.85
FVC (%, pred)	91.52±11.65	94.10±11.57	92.98±11.67
FEV$_1$/FVC (%)	0.75±0.08	0.79±0.06	0.77±0.08
FEV$_6$ (L)	3.98±0.71	2.87±0.50	3.35±0.82
FEV$_1$/FEV$_6$ (%)	0.78±0.07	0.81±0.05	0.80±0.06
Normal	4,291 (65.9)	7,145 (84.4)	11,436 (76.4)
Restricted	688 (10.6)	750 (8.9)	1,438 (9.6)
Obstructed	1,536 (23.6)	568 (6.7)	2,104 (14.1)
GOLD stage I	740 (11.4)	278 (3.3)	1,018 (6.8)
GOLD stage II	731 (11.2)	265 (3.1)	996 (6.6)
GOLD stage III	57 (0.9)	23 (0.3)	80 (0.5)
GOLD stage IV	8 (0.1)	2 (0.0)	10 (0.1)

Notes: Data are presented as numbers (percentages) for categorical variables. Continuous variables are presented as means ± standard deviations.
Abbreviations: FEV$_1$, forced expiratory volume in 1 second; FEV$_6$, forced expiratory volume in 6 seconds; FVC, forced vital capacity; BMI, body mass index; pred, predicted; GOLD, Global Initiative for Chronic Obstructive Lung Disease.
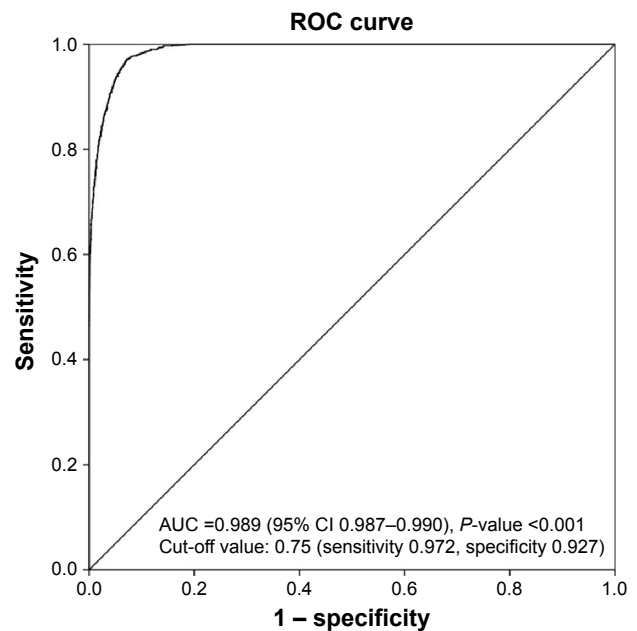

ROC curve

AUC =0.989 (95% CI 0.987–0.990), P-value <0.001
Cut-off value: 0.75 (sensitivity 0.972, specificity 0.927)

Figure 1 A receiver operating characteristic (ROC) curve showing the ability of FEV$_1$/FEV$_6$ to diagnose FEV$_1$/FVC <70%.
Notes: Area under the ROC curve is 0.989 (95% confidence interval, 0.987–0.990). The best cut-off value is 0.75 with 0.971% sensitivity and 0.927% specificity.
Abbreviations: FEV$_1$, forced expiratory volume in 1 second; FEV$_6$, forced expiratory volume in 6 seconds; FVC, forced vital capacity; AUC, area under the curve.

Table 2 Sensitivities and specificities of thresholds of FEV_1/FEV_6 for predicting FEV_1/FVC <70%

FEV_1/FEV_6 ratio	Sensitivity	Specificity	PPV	NPV	Accuracy	Kappa value (95% CI)
<70	44.1	100.0	100.0	91.6	92.2	0.576 (0.554–0.598)
<73	74.2	98.9	91.6	95.9	95.4	0.794 (0.778–0.810)
<75	93.8	94.8	74.7	98.9	94.7	0.800 (0.786–0.814)
<76	98.0	90.8	63.6	99.6	91.8	0.724 (0.710–0.738)

Note: Data are presented as percentages.
Abbreviations: FEV_1, forced expiratory volume in 1 second; FEV_6, forced expiratory volume in 6 seconds; FVC, forced vital capacity; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

cut-off of FEV_1/FVC <70% and FEV_1/FEV_6 <75%, the prevalence of obstruction was 14.1% and 17.7%, respectively. Compared with FEV_1/FVC LLN, a fixed cut-off of FEV_1/FVC <70% showed 99.0% sensitivity, 92.6% specificity, 93.1% accuracy, 51.1% PPV, and 99.9% NPV. A fixed cut-off of FEV_1/FEV_6 <75% showed 99.9% sensitivity, 88.8% specificity, 89.6% accuracy, 41.0% PPV, and 99.9% NPV (Table 5). When grouped together according to age and FEV_1 (%), a fixed cut-off of FEV_1/FEV_6 <75% was used to diagnose more airway obstruction in older individuals and those with mild–moderate stages (Table 6). With increasing age and severity of obstruction, the mean difference between FEV_1/FEV_6 and FEV_1/FVC was increasingly larger because FEV_6 was increasingly smaller than FVC.

However, with increasing age, the mean difference between FEV_1/FVC LLN and FEV_1/FVC or FEV_1/FEV_6 showed only a slight difference. With increasing severity of obstruction, the mean difference between FEV_1/FVC LLN and FEV_1/FEV_6 was larger than the mean difference between FEV_1/FVC LLN and FEV_1/FVC at mild–moderate stages of airway obstruction, but that was smaller than that at severe and very severe stages (Figures 2 and 3).

Discussion

FEV_1/FEV_6 and FEV_6 are reliable surrogates for FEV_1/FVC and FVC to identify obstruction and restriction using spirometry. However, in previous studies, the cut-off values of FEV_1/FEV_6 for detecting airway obstruction were different among LLN or fixed ratios (70%–76%).[6] LLN for FEV_1/FEV_6 is the most accurate for detecting airway obstruction, but many countries do not have pulmonary function reference equations of LLN for FEV_1/FEV_6 for local ethnic groups. Nevertheless, primary care clinicians have used handheld spirometric devices such as PiKo-6® or COPD-6™ without proper reference values for FEV_1/FEV_6. These two devices are inexpensive, and require less quality control of equipment, and no experienced personnel to carry out tests and analyses. The main purpose of the present study was to determine a fixed cut-off value for FEV_1/FEV_6 as a surrogate for FEV_1/FVC for detecting airway obstruction in a Korean population.

The present study elicited two main findings. First, a fixed cut-off for FEV_1/FEV_6 as a good surrogate for FEV_1/FVC for detecting airway obstruction in a Korean population was 75% with 93.8% sensitivity, 94.8% specificity, 74.7% PPV, 98.9 NPV, and good CKC (0.8). Second, a raised fixed cut-off value of FEV_1/FEV_6 <75% to improve sensitivity showed the tendency to over-diagnosis in the mild–moderate airflow limitation group compared with FEV_1/FVC<70% were

Table 3 Comparison of FEV_1/FEV_6 with FEV_1/FVC for diagnosing airway obstruction

	FEV_1/FEV_6[#]		Totals
	No obstruction	Obstruction	
FEV_1/FVC[§]			
No obstruction	12,204 (94.8)	670 (5.2)	12,874 (86.0)
Obstruction	130 (6.2)	1,974 (93.8)	2,104 (14.0)
Totals	12,334 (82.3)	2,644 (17.7)	14,978 (100)

Notes: Data are presented as numbers (percentages); [§]using FEV_1/FVC <70% as a fixed cut-off; [#]using FEV_1/FEV_6 as a fixed cut-off <75%; prevalence of obstruction =17.7%, Kappa value =0.80, 95% CI 0.79–0.81, P<0.001.
Abbreviations: FEV_1, forced expiratory volume in 1 second; FEV_6, forced expiratory volume in 6 seconds; FVC, forced vital capacity; CI, confidence interval.

Table 4 Comparison of FEV_1/FEV_6 with FEV_1/FVC for the diagnosis of normal, restricted, and obstruction patterns

	FEV_1/FEV_6[#]		Totals
	No obstruction	Obstruction	
FEV_1/FVC[§]			
Normal	10,862 (95.0)	574 (5.0)	11,436 (76.4)
Restricted	1,342 (93.3)	96 (6.7)	1,438 (9.6)
Obstructed	130 (6.2)	1,974 (93.8)	2,104 (14.1)
GOLD stage I	102 (10.0)	916 (90.0)	1,018 (6.8)
GOLD stage II	28 (2.8)	968 (97.2)	996 (6.6)
GOLD stage III	0 (0)	80 (100)	80 (0.5)
GOLD stage IV	0 (0)	10 (100)	10 (0.1)
Totals	12,334 (82.3)	2,644 (17.7)	14,978 (100)

Notes: Data are presented as numbers (percentages); [§]using FEV_1/FVC <70% as a fixed cut-off; [#]using FEV_1/FEV_6 as a fixed cut-off <75%.
Abbreviations: 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.

Table 5 Comparison of FEV_1/FVC LLN with $FEV_1/FVC < 70\%$ or $FEV_1/FEV_6 < 75\%$

	FEV$_1$/FVC LLN*		Totals
	No obstruction	Obstruction	
FEV$_1$/FVC[§]			
No obstruction	12,857 (99.9)	11 (0.1)	12,868 (85.9)
Obstruction	1,030 (49.0)	1,074 (51.0)	2,104 (14.1)
FEV$_1$/FEV$_6$[#]			
No obstruction	12,327 (100.0)	1 (0.0)	12,328 (82.3)
Obstruction	1,560 (59.0)	1,084 (41.0)	2,644 (17.7)
Totals	13,887 (92.8)	1,085 (7.2)	14,972 (100)

Notes: Data are presented as numbers (percentages); *lower limit of normal using ERS/GLI 2012 equations; [§]using $FEV_1/FVC < 70\%$ as a fixed cut-off; [#]using FEV_1/FEV_6 as a fixed cut-off $< 75\%$.
Abbreviations: FEV_1, forced expiratory volume in 1 second; FEV_6, forced expiratory volume in 6 seconds; FVC, forced vital capacity; LLN, lower limit of normal; ERS, European Respiratory Society; GLI, Global Lung Initiative.

observed in the mild–moderate airflow limitation group compared with FEV_1/FVC. Therefore, a raised and fixed cut-off value of $FEV_1/FEV_6 < 75\%$ should be used with caution in older individuals or those with mild–moderate airflow limitation because this cut-off value can lead to over-diagnosis rather than under-diagnosis for airway obstruction screening. A fixed ratio of cut-off led to greater over-diagnosis in patients with mild airflow limitation than LLN, but it was less-time consuming, easier, and safer for patients. Additionally, recording FEV_6 was more reproducible than FVC, less physically demanding for patients, and the results were more clear at the end of the test.[22]

In a study in Belgium, a fixed cut-off of FEV_1/FEV_6 of $< 73\%$ showed 94.4% sensitivity, 93.3% specificity, 92.2% PPV, and 95.2% NPV.[11] Jing et al showed, in a meta-analysis, that the efficacy of FEV_1/FEV_6 is not affected adversely by the choice of cut-off point,[6] but an

appropriate clinical guideline for using FEV_1/FEV_6 in place of FEV_1/FVC is needed. According to one study,[26] the cut-off value of pre-bronchodilator $FEV_1/FEV_6 < 70\%$ had 91.4% sensitivity, 100% specificity but a 91.4% PPV and 87.4% NPV in 353 Koreans aged > 65 years. However, this cut-off value of pre-bronchodilator $FEV_1/FEV_6 < 70\%$ cannot be relied upon because the data were from a small study cohort with only older participants; thus the results were not applicable to a general population. Further, a cut-off value of a fixed ratio of $FEV_1/FVC < 70\%$ cannot be applied because FEV_6 cannot be greater than FVC – otherwise, airway obstruction may be underestimated. Because an appropriate study on the cut-off of FEV_1/FEV_6 for airway obstruction in a Korean population had not been carried out, a revised clinical guideline[27] for COPD in Korea published in 2014 recommended a cut-off of FEV_1/FEV_6 of 73% for detecting airway obstruction based on studies undertaken outside Korea.[24,27]

Our study showed that 75% as a fixed value of FEV_1/FEV_6 in analyses of ROC curves was the cut-off point with the best combination of sensitivity and specificity and a good surrogate for $FEV_1/FVC < 70\%$. Prevalence of airway obstruction was 17.7% when using $FEV_1/FEV_6 < 75\%$ and 14.1% with $FEV_1/FVC < 70\%$. Rosa et al found that $FEV_1/FEV_6 < 75\%$ showed 89.0% sensitivity, 95.4% specificity, 85.2% PPV, and 96.7% NPV in pre-bronchodilator curves, results that were similar to our research.[28]

A total of 620 (5.2%) false-positive values and 130 (6.2%) false-negative values were observed (Table 3). In the subgroup analysis, 130 false-negative cases showed a mean difference of FEV_1/FVC and FEV_1/FEV_6, with a respective LLN of 4.4% (SD =2.0) and 11.4% (SD =2.1). They were

Table 6 Age and forced expiratory volume in 1 second (FEV_1) dependency of the lower limit of normal (LLN) for FEV_1/forced vital capacity (FVC) and FEV_1/forced expiratory volume in 6 seconds (FEV_6) in airway obstruction

	FEV$_1$/FVC $<$LLN	FEV$_1$/FVC $<70\%$	FEV$_1$/FEV$_6$ $<75\%$	ΔFEV$_1$/FVC*	ΔFEV$_1$/FEV$_6$[§]	Δ(FEV$_1$/FEV$_6$– FEV$_1$/FVC)[#]
	1,085 (7.2)	2,104 (14.1)	2,644 (17.7)	14,972 (100)	14,972 (100)	14,972 (100)
Age group (years)						
40–49	153 (3.6)	151 (3.5)	310 (7.2)	10.5±5.2	11.8±4.6	1.3±1.2
50–59	278 (6.0)	417 (8.9)	594 (12.7)	9.9±6.0	12.0±4.9	2.1±1.7
60–69	361 (9.8)	766 (20.7)	888 (24.0)	9.0±8.4	12.3±5.7	3.1±2.3
70~	293 (12.6)	770 (33.1)	852 (36.6)	9.7±6.6	12.6±5.3	3.7±2.8
FEV$_1$ (%)						
>80	336 (2.6)	1,018 (8.0)	1,409 (11.1)	11.0±5.1	13.9±4.2	2.1±1.8
50–80	661 (30.3)	996 (45.6)	1,144 (52.4)	3.4±8.0	7.3±6.2	3.9±2.8
30–50	78 (89.7)	80 (92.0)	81 (93.1)	−15.7±10.9	−7.5±8.1	8.2±4.1
<30	10 (100.0)	10 (100.0)	10 (100.0)	−29.8±7.9	−19.9±5.4	9.9±3.3

Notes: Data are presented as numbers (percentage) or mean ± standard deviations; *difference between LLN (%) and FEV_1/FVC (%), [§]difference between LLN (%) and FEV_1/FEV_6(%); [#]difference between FEV_1/FEV_6 (%) and FEV_1/FVC (%).
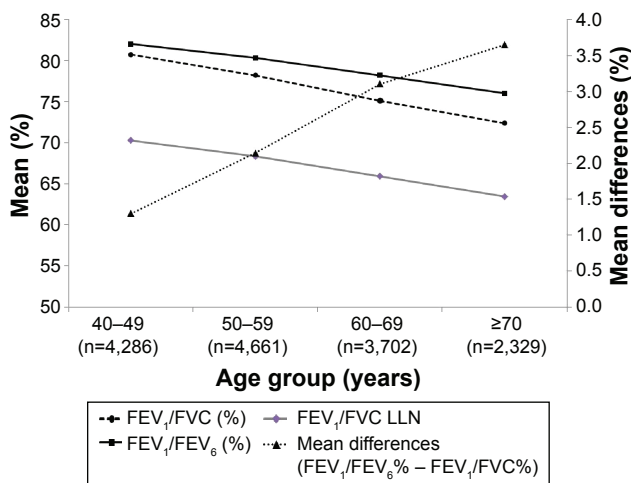
Figure 2 FEV$_1$/FVC LLN, FEV$_1$/FVC, FEV$_1$/FEV$_6$, and the mean difference between FEV$_1$/FEV$_6$ and FEV$_1$/FVC according to the age group.
Notes: With increasing age, the mean difference between FEV$_1$/FEV$_6$ and FEV$_1$/FVC was increasingly larger. However, the mean difference between FEV$_1$/FVC LLN and FEV$_1$/FVC or FEV$_1$/FEV$_6$ showed only a slight difference.
Abbreviations: FEV$_1$, forced expiratory volume in 1 second; FEV$_6$, forced expiratory volume in 6 seconds; FVC, forced vital capacity; LLN, lower limit of normal.

classified as GOLD stages I and II because reduced end-expiratory flow and expiratory time >6 seconds might have occurred in the initial stage of airflow limitation (Table 4). A total of 620 false-positive cases showed a mean difference of FEV$_1$/FVC and FEV$_1$/FEV$_6$ with a respective LLN of 4.8% (SD =2.9) and 6.8% (SD =2.8). This finding might have been due to different fixed cut-off values between FEV$_1$/FVC <70% and FEV$_1$/FEV$_6$ <75%.
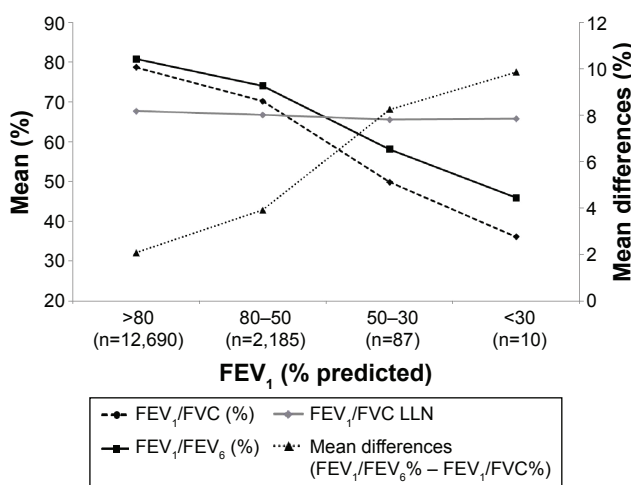

Figure 3 FEV$_1$/FVC LLN, FEV$_1$/FVC, FEV$_1$/FEV$_6$, and the mean difference between FEV$_1$/FEV$_6$ and FEV$_1$/FVC according to the FEV$_1$ (%) group.
Notes: With increasing severity of obstruction, the mean difference between FEV$_1$/FEV$_6$ and FEV$_1$/FVC was increasingly larger. The mean difference between FEV$_1$/FVC LLN and FEV$_1$/FEV$_6$ was larger than the mean difference between FEV$_1$/FVC LLN and FEV$_1$/FVC at mild–moderate stages of airway obstruction, but was smaller at severe and very severe stages.
Abbreviations: FEV$_1$, forced expiratory volume in 1 second; FEV$_6$, forced expiratory volume in 6 seconds; FVC, forced vital capacity; LLN, lower limit of normal.

The main strength of our study was that we obtained results from a representative sample of noninstitutionalized civilians among a Korean population using a stratified, multiple-stage, clustered-probability design. However, our study also had several limitations. First, lung function data from prebronchodilator spirometric values might have inadvertently included asthma patients, and hence be skewed. Carrying out postbronchodilator spirometry in a large, nationwide sample from the Korean National Health and Nutritional Examination Survey is difficult. Second, the absence of data on smoking history, previously diagnosed diseases (eg, COPD, asthma, tuberculosis, and bronchiectasis) in our study could have resulted in abnormal values for airway obstruction. So our results for detecting of airway obstruction were not limited to COPD, asthma, or other obstructive disease. Third, there were no available data on FEV$_1$/FEV$_6$ LLN because a pulmonary reference equation for FEV$_6$ for a Korean population is lacking. Hence, we could not obtain a cut-off value of FEV$_6$ in place of FVC for detecting restrictive pulmonary patterns. Finally, the fixed cut-off value of FEV$_1$/FEV$_6$ <75% should be verified with handheld spirometric devices with good repeatability, as in other studies,[18] and not only with office spirometry.

Conclusion

A fixed cut-off for FEV$_1$/FEV$_6$ as a good surrogate for FEV$_1$/FVC for detecting airway obstruction was 75% in a Korean population. However, a fixed cut-off value of FEV$_1$/FEV$_6$ <75% should be used with caution in older individuals and in those with mild–moderate airflow obstruction.

Author contributions

Kyung Soo Chung contributed to the study design, analysis and interpretation of data, and writing of the manuscript. Ji Ye Jung, Moo Suk Park, Young Sam Kim, Se Kyu Kim, and Joon Chang contributed to the study design, analyses and interpretation of data, and critically revised the manuscript. Joo Han Song, contributed to the study design, analyses and interpretation of data, and writing of the manuscript.

Disclosure

The authors report no conflicts of interest in this work.

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