

# Diagnosis of airway obstruction in the elderly: contribution of the SARA study

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**Background:** The choice between lower limit of normal or fixed value of forced expiratory volume in one second/forced vital capacity ratio ( $FEV_1/FVC$ )  $< 0.70$  as the criterion for confirming airway obstruction is an open issue. In this study, we compared the criteria of lower limit of normal and fixed  $FEV_1/FVC$  for diagnosis of airway obstruction, with a focus on healthy elderly people.

**Methods:** We selected 367 healthy nonsmoking subjects aged 65–93 years from 1971 participants in the population-based SARA (Salute Respiratoria nell’Anziano, Italian for “Respiratory Health in the Elderly”) study, analyzed their spirometric data, and tested the relationship between spirometric indices and anthropometric variables. The lower limit of normal for  $FEV_1/FVC$  was calculated as the fifth percentile of the normal distribution for selected subjects.

**Results:** While  $FEV_1$  and FVC decreased significantly with aging, the relationship between  $FEV_1/FVC$  and age was not statistically significant in men or women. The lower limit of normal for  $FEV_1/FVC$  was 0.65 in men and 0.67 in women. Fifty-five participants (15%) had  $FEV_1/FVC < 0.70$  and would have been inappropriately classified as obstructed according to the Global Initiative for Obstructive Lung Disease, American Thoracic Society/European Respiratory Society, and Canadian guidelines on chronic obstructive pulmonary disease. By applying different  $FEV_1/FVC$  thresholds for the different age groups, as previously proposed in the literature, (0.70 for  $<70$  years, 0.65 for 70–80 years, and 0.60 for  $>80$  years) the percentage of patients classified as obstructed decreased to 6%. No subjects older than 80 years had an  $FEV_1/FVC < 0.60$ .

**Conclusion:** The present results confirm the inadequacy of  $FEV_1/FVC < 0.70$  as a diagnostic criterion for airway obstruction after the age of 65 years.  $FEV_1/FVC < 0.65$  and  $<0.67$  (for men and women, respectively) could identify subjects with airway obstruction in such a population. Further reduction of the threshold after 80 years is not justified.

**Keywords:** aging, airflow obstruction, chronic obstructive pulmonary disease, forced expiratory volume, lung function tests, spirometry

## Introduction

The most appropriate way to diagnose airway obstruction is currently the subject of heated debate.<sup>1–10</sup> Most national and international chronic obstructive pulmonary disease (COPD) guidelines recommend to use a forced expiratory volume in one second/forced vital capacity ratio ( $FEV_1/FVC$ ) of 0.70 as a suitable threshold value to define the presence of an obstructive ventilatory defect. Commonly used guidelines include those of the Global Initiative for Obstructive Lung Disease (GOLD),<sup>11</sup> the American Thoracic Society/European Respiratory Society,<sup>12</sup> the British Thoracic

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Society,<sup>13</sup> the Canadian Thoracic Society,<sup>14</sup> and the National Institute for Health and Clinical Excellence.<sup>15</sup>

However, there is evidence that the fixed cut-off value of 0.70 for FEV<sub>1</sub>/FVC becomes less specific in males aged > 40 years and females > 50 years, implying a risk of overestimation of airway obstruction. This is due to an age-related decline in pulmonary volumes, particularly in FEV<sub>1</sub>, which is observed even in healthy people with no history of exposure to noxious particles or gases.<sup>16–19</sup> Proposed strategies for reducing the misclassification of airway obstruction include use of the lower limit of normal for FEV<sub>1</sub>/FVC, calculated as the fifth percentile of the normal distribution in a healthy population,<sup>20–22</sup> or the use of different FEV<sub>1</sub>/FVC thresholds for different age groups (eg, 0.70 for subjects aged < 70 years, 0.65 for those aged 70–80 years, and 0.60 for those aged > 80 years).<sup>19</sup>

On this basis, a group of colleagues involved in respiratory research and/or the diagnosis and treatment of lung diseases recently wrote an open letter to members of the GOLD committee inviting them to change the method by which airway obstruction is defined and asking for retraction of the fixed ratio in favor of the lower limit of normal.<sup>1</sup>

The aim of the present study was to provide additional information for determination of the most appropriate spirometric criteria for confirming airway obstruction in the elderly, by describing lung function and calculating the lower limit of normal for FEV<sub>1</sub>/FVC in healthy nonsmoking elderly subjects (age > 65 years) who participated in the Italian multicenter SARA (acronym of Salute Respiratoria nell'Anziano, Italian for "Respiratory Health in the Elderly") study. The degree of potential misclassification relative to use of 0.70 or other proposed fixed thresholds for FEV<sub>1</sub>/FVC was also evaluated.

## Materials and methods

We performed a cross-sectional analysis of data from the SARA study, the design of which, along with technical characteristics of instruments as well as training of operators and results of quality control of spirometry, have been described in detail elsewhere.<sup>23</sup> Briefly, the study involved 24 pulmonary or geriatric institutions distributed throughout Italy. A total of 1971 subjects aged 65–100 years were recruited as consecutive outpatients referred between January 1996 and December 1997 to the participating centers (see Appendix). The study design was approved by the ethics committee of the University of Palermo. Patients gave their written consent to participate in the study.

Lung function was measured using an identical fully computerized water-sealed Stead-Wells spirometer

(Baires System, Biomedin, Padua, Italy) by specifically trained and certified personnel supervised by a rigorous real-time control of acceptability and repeatability<sup>23</sup> according to American Thoracic Society recommendations.<sup>24</sup> FVC maneuvers were performed with the patient sitting. The largest FVC and FEV<sub>1</sub> were selected from a minimum of two acceptable tests. The FEV<sub>1</sub>/FVC ratio was calculated on the basis of the highest values of individual parameters obtained in the acceptable curves for each subject. Analyses were conducted only on patients with good repeatability of the above-mentioned indices (difference between two best values < 150 mL).<sup>25</sup>

Of the 1870 subjects who performed spirometry, we selected only those without any previous or present diagnosis or any sign or symptom suggestive of respiratory diseases according to the modified International Union against Tuberculosis and Lung Disease bronchial symptoms questionnaire.<sup>25,26</sup> Current smokers and previous smokers with a smoking exposure > 5 pack/year were excluded, since the <5 pack/year smoking exposure was not significantly associated with decreased lung function.<sup>27</sup> Additional exclusion criteria were: severe hepatic failure; severe renal failure; severe cardiac failure; cognitive and/or sensory impairment severe enough to affect a multidimensional assessment; severe kyphoscoliosis with occiput wall distance (distance between the occiput and the wall when the patient stands with heels and shoulder against the wall with the back straight) > 10; occurrence of a major psychosocial event (eg, bereavement) within the past 6 months; and hospitalization for any reason within the past 6 months. We further excluded individuals who had hypertension (diastolic pressure  $\geq$  90 mmHg and/or systolic pressure  $\geq$  160 mmHg), diabetes, and/or major electrocardiographic abnormalities.

Statistical analyses were performed using SPSS (SPSS Inc, Chicago, IL) and Stata (Stata Corporation, College Station, TX) software packages. Regression models were used for testing the relationship between spirometric indices and anthropometric variables. Based on the recommendations from the American Thoracic Society/European Respiratory Society task force,<sup>22</sup> the lower limit of normal for FEV<sub>1</sub>/FVC was estimated as the fifth percentile of its frequency distribution. To evaluate the effect of aging on spirometric measures independently of body height, FEV<sub>1</sub> and FVC were normalized for height at the third power.<sup>28,29</sup>

## Results

After applying the above-mentioned selection criteria, our final data set consisted of 367 healthy, nonsmoking subjects.

One hundred and one subjects were excluded for lack of availability of lung function testing, a further 709 subjects because of a history of respiratory disease, 445 for significant smoking exposure ( $>5$  pack/year), 262 for inadequate quality of spirometry, and 87 for the above-mentioned additional exclusion criteria.

Tables 1 and 2 show anthropometric and functional data for the sample and distribution of the participants according to age and gender. Although the most advanced ages were less represented, a total of 73 subjects aged 80 years and over were included. The sample consisted of 314 never-smokers (85.6%) and 53 former-smokers with a smoking exposure from 0.15 to 5 pack-years (mean  $\pm$  standard deviation,  $2.75 \pm 1.5$ ).

As shown in Figure 1, the values of  $FEV_1/FVC$  showed a normal frequency distribution. The mean  $FEV_1/FVC$  was  $0.75 \pm 0.6$  in males and  $0.78 \pm 0.6$  in females, whereas the corresponding fifth percentiles were 0.65 and 0.67, respectively, in males and females.  $FEV_1$  and FVC significantly decreased with age ( $r = -0.38$  and  $-0.35$ ;  $P < 0.001$ ), while  $FEV_1/FVC$ , was not significantly correlated with age or height in either gender group over the considered range of age (lowest  $P = 0.103$ ). As a consequence, there was no rationale to develop reference equations for  $FEV_1/FVC$ , with age or height as independent variables in this restricted range of age. Figure 2 shows the decline in  $FEV_1$  and FVC with increasing age observed in the study sample in men and women, after normalization for height.

In the sample of healthy subjects, 15% had a  $FEV_1/FVC < 0.70$ , and would have been inappropriately classified as obstructed according to GOLD criteria. Table 3 describes the proportion of participants with the ratio  $< 70$  in the different age groups. By applying the  $FEV_1/FVC$  thresholds proposed by Hardie et al<sup>19</sup> for different age groups (ie, 0.70 for  $<70$  years, 0.65 for 70–80 years, and 0.60 for  $>80$  years), the percentage of obstructed subjects decreased to 6% (men 11%, women 4%). In particular, the proportion of subjects

**Table 1** Anthropometric and functional characteristics of the study sample, with data expressed as the mean  $\pm$  standard deviation

	Women	Men
Age, years	73.3 $\pm$ 6.2	74.2 $\pm$ 6.9
Height, cm	154.8 $\pm$ 7.0	167.8 $\pm$ 6.4
Weight, kg	63.1 $\pm$ 11.2	73.7 $\pm$ 11.2
$FEV_1$ , mL	1907 $\pm$ 474	2694 $\pm$ 586
LVC, mL	2532 $\pm$ 595	3688 $\pm$ 736
FVC, mL	2456 $\pm$ 604	3618 $\pm$ 743

**Abbreviations:**  $FEV_1$ , forced expiratory volume in one second; FVC, forced vital capacity; LVC, lung volume change.

**Table 2** Distribution of subjects according to gender and age group, with data presented as n (%)

Age (years)	Females	Males
All	246 (67.0)	121 (33.0)
65–69	77 (31.3)	35 (28.9)
70–74	76 (30.9)	34 (28.1)
75–79	50 (20.3)	22 (18.2)
$\geq 80$	43 (17.5)	30 (24.8)

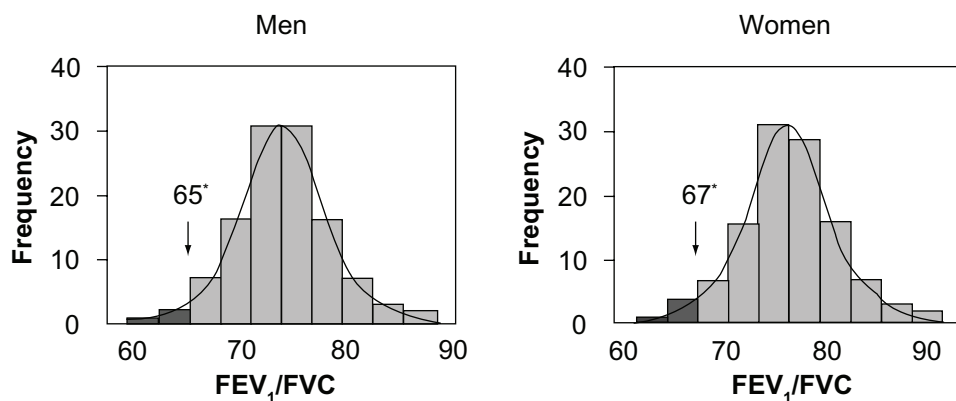
aged 65–70 years with a ratio below 0.70 was 11% (men 16%, women 8%); the proportion of subjects between 70 and 80 years of age with the ratio below 0.65 was 5% (men 12%, women 2%), whereas none of the subjects aged 80 years or more had  $FEV_1/FVC < 0.60$ .

## Discussion

This study provides additional evidence helpful for determining the most appropriate spirometric criteria to define airway obstruction in elderly subjects. The fifth percentile of  $FEV_1/FVC$  observed in the considered sample of healthy subjects aged  $> 65$  years was lower than 0.70 in both men and women, thus confirming the inadequacy of this threshold for  $FEV_1/FVC$  after the age of 65 years. Moreover, the findings of the present study suggest that, in such a population,  $FEV_1/FVC < 0.65$  and  $< 0.67$  (for males and females, respectively) could represent valid criteria that are simple to use and incorporate the known physiological decline in lung function with aging.

The present findings are in agreement with observations made by other authors,<sup>16–18</sup> who have emphasized that the use of the  $FEV_1/FVC$  threshold proposed by GOLD leads to a risk of overdiagnosis of COPD in geriatric subjects. Furthermore, the current results suggest that the inaccuracy of using a threshold of 0.70 for  $FEV_1/FVC$  already exists in subjects aged 65 years and older. This differs to some extent from what has been suggested by the most recent GOLD guidelines<sup>11</sup> (that recognize some imprecision of the threshold of 0.70 for  $FEV_1/FVC$  in people over 70 years of age) and by Medbo et al,<sup>10</sup> who suggested the use of a threshold of  $FEV_1/FVC < 0.65$  in subjects over the age of 70 years on the basis of prebronchodilator spirometry data from a population-based study in Norway.

Interestingly, in our study, the rate of decline in the  $FEV_1/FVC$  ratio with aging was not statistically significant in men or women older than 65 years, because of a concomitant decline in both  $FEV_1$  and FVC. Thus, in contrast with the findings of Hardie et al,<sup>19</sup> our results do not support the need to decrease the lower limit of normal for  $FEV_1/FVC$  to



**Figure 1** Distribution and fifth percentile of FEV<sub>1</sub>/FVC by gender (Caucasian Southern Europeans > 65 years).

**Note:** Asterisks indicate the 5th percentile.

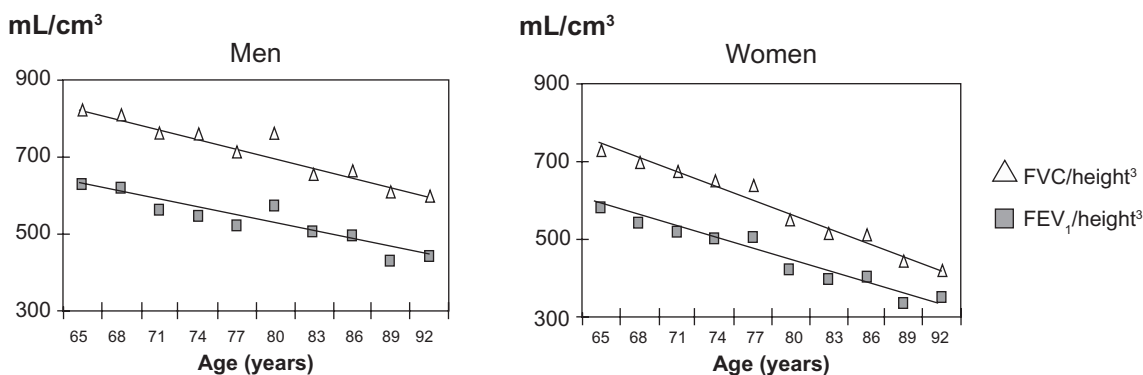
**Abbreviations:** FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity.

0.60 in elderly subjects (>80 years). For the same reason, no predictive equation for FEV<sub>1</sub>/FVC could be derived; accordingly, the mean value and the fifth percentile of FEV<sub>1</sub>/FVC from this healthy population can be used as the predicted value and lower limit of normal, respectively, for people aged 65 years and over.

All reference equations derived from samples with a wide age range describe a progressive decline in the FEV<sub>1</sub>/FVC ratio with aging; the age-related decrease involves both FEV<sub>1</sub> and FVC, seems to be nonlinear, and accelerates with aging.<sup>30-32</sup> In 1982, Crapo et al<sup>33</sup> found that between 20 and 70 years of age, vital capacity decreases to approximately 75% of the best values achieved previously. According to the present observations, presumably in the oldest people the decline of vital capacity accelerates more than in the younger age groups and such a decline is similar to the reduction of FEV<sub>1</sub>, so that the FEV<sub>1</sub>/FVC ratio could undergo minimal variations in the last decades. Recently, Langhammer et al<sup>34</sup> and Falaschetti et al<sup>35</sup> observed that FEV<sub>1</sub>/FVC reaches a near plateau phase

in elderly subjects. The authors emphasized that, although the sample consisted of subjects with a wide range of height and age, the extremes did not influence the equations.

In a reference study specifically designed for elderly residents in Madrid (age range 65–85 years), Garcia et al<sup>36</sup> found a significant relationship between FEV<sub>1</sub>/FVC and age in men and between FEV<sub>1</sub>/FVC, age and height in women. Even in this study, the predicted equation for FEV<sub>1</sub>/FVC had a very low R<sup>2</sup> (0.048 and 0.083 for men and women, respectively) and the authors highlighted the strong negative relationship of FVC with age. By applying predictive equations recently derived from Kuster et al<sup>37</sup> in a Swiss population, the lower limit of normal for FEV<sub>1</sub>/FVC does not show important decreases with aging; for example, in men with a height of 170 cm, the lower limit of normal for FEV<sub>1</sub>/FVC ranges from 0.66 at the age of 65 years to 0.64 for people aged 95 years. All these results support a position in favor of almost stable predicted values and lower limits of normal for FEV<sub>1</sub>/FVC in elderly people aged 65 years and over.



**Figure 2** Decline of FEV<sub>1</sub> and FVC with aging, normalized for height.<sup>3</sup>

**Abbreviations:** FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity.

**Table 3** Proportion of healthy elderly subjects with FEV<sub>1</sub>/FVC ratio < 0.70 in different age groups, with data presented as n (%)

	Age (years)		All n = 367
	65–79 n = 294	≥80 n = 73	
FEV <sub>1</sub> /FVC ≥ 0.70	254 (86)	59 (81)	313 (85)
FEV <sub>1</sub> /FVC < 0.70	28 (10)	8 (11)	36 (10)
FEV <sub>1</sub> % ≥ 80			
FEV <sub>1</sub> /FVC < 0.70	12 (4)	6 (8)	18 (5)
FEV <sub>1</sub> % < 80			

**Abbreviations:** FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity.

A clear position in favor of the fixed threshold of FEV<sub>1</sub>/FVC < 0.70 has been recently reported by other authors, with the claim that it is easy to use, thus helping to remove barriers to widespread use of spirometry.<sup>3,6–8</sup> Probably the use of the two lower fixed values for the elderly, suggested by data from the SARA study, does not add elements of particular complexity for physicians involved in interpretation of pulmonary function tests. However, this approach would diminish the number of false diagnoses of COPD, with significant cost savings due to reduction of inappropriately prescribed drugs. Thus, more resources could be redirected to primary prevention of COPD (smoking cessation) and treatment of more severe COPD.

Authors advocating retaining FEV<sub>1</sub>/FVC < 0.70 often quote the results of Mannino et al, who found that such a threshold is very good for identifying patients at risk of death and COPD-related hospitalizations.<sup>38</sup> However, although this indicates that FEV<sub>1</sub>/FVC < 0.70 may recognize a proportion of individuals at risk, it does not mean that this is the best way to diagnose the disease. On the other hand, Vas Fragoso et al<sup>39</sup> found elevated risk of death and respiratory symptoms in adults with FEV<sub>1</sub>/FVC less than the lower limit of normal. Sorino et al<sup>40</sup> recently confirmed that FEV<sub>1</sub>/FVC less than the lower limit of normal, FEV<sub>1</sub>/FEV<sub>0</sub> less than the lower limit of normal, and FEV<sub>1</sub> less than the lower limit of normal are all significant predictors of all-cause and cardiopulmonary mortality in older individuals. The strongest spirometric predictor of all-cause mortality remains the appropriately named vital capacity, because the majority of deaths in adult smokers, with or without COPD, are caused by cardiovascular disease.

Two recent studies investigated subjects in between the two definitions of airway obstruction (ie, FEV<sub>1</sub>/FVC < 0.70 but ≥ lower limit of normal), showing that their clinical profile is characterized by relevant comorbid disease and poor health-related quality of life, but similar exercise, frequency

of exacerbations, and indices of systemic effects.<sup>41,42</sup> The investigators emphasized that these subjects might be at risk and should be followed carefully; we should be aware that fewer than one in five smokers with mild airway obstruction ever develop clinically important COPD, and that today we are not yet able to identify which smokers will be rapid fallers.<sup>2,4</sup>

The present study has some limitations. First, the cohort was recruited for a cross-sectional investigation, whereas the effect of aging on respiratory function would be better assessed in a longitudinal study. It is plausible that FEV<sub>1</sub>/FVC decreases significantly even after the age of 65 years, but this can be less reliable when derived by a cross-sectional observation of older people. In fact, they could represent individuals who had higher spirometric values at a younger age, and FEV<sub>1</sub>/FVC similar to those of younger subjects at the time of recruitment. Second, subjects participating in the SARA project were not randomly selected from the population, but consisted mainly of subjects with nonrespiratory illnesses attending outpatient clinics; this might have resulted in some selection bias, although it would not explain the higher pulmonary volumes than in other studies. The authors wish to emphasize that FEV<sub>1</sub>/FVC less than the lower limit of normal should not be the only criterion used for diagnosis of airway obstruction, but should always be combined with evaluation of FEV<sub>1</sub> as percent of predicted. Indeed, patients with severe airflow limitation could have an important reduction both in FEV<sub>1</sub> and FVC, with a sustained FEV<sub>1</sub>/FVC ratio. Thus, in doubtful cases, measurement of residual volume and total lung capacity is recommended.

In conclusion, the present findings confirm the inadequacy of FEV<sub>1</sub>/FVC < 0.70 for diagnosis of airway obstruction in elderly people, and we propose other easy to remember thresholds for FEV<sub>1</sub>/FVC after 65 years of age, ie, 0.65 in men and 0.67 women. Further studies are needed to assess both the classificatory and prognostic properties of such a threshold as well as epidemiological surveys to confirm it.

## Disclosure

The authors report no conflicts of interest in this work.

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## Appendix

### Respiratory Health in the Elderly study group

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