

ORIGINAL ARTICLE

Defining obstructive ventilatory defect in 2015

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Introduction: There is no clear consensus as to what constitutes an obstructive ventilatory defect (OVD): Is it $FEV_1/FVC < \text{lower limit of normal (LLN)}$ or < 0.70 (respectively, physiological and operational definitions)?

Aim: To determine, according to the two definitions, the percentage of subjects having an OVD among them explored in a lung function exploration laboratory.

Population and methods: This is a retrospective study including 4,730 subjects aged 17–85 years. Subjects were divided according to the presence [physio (+) or operat (+)] or absence [physio (–) or operat (–)] of an OVD, and into younger (< 45 years, $n = 2,076$), older (≥ 45 years, $n = 2,654$), smokers ($n = 1,208$), and non-smokers ($n = 3,522$) groups.

Results: For the total sample, the younger and older groups [mean \pm SD of age (years), respectively, 46.7 ± 14.1 ; 33.9 ± 7.4 , and 56.8 ± 9.1], the ‘physiological definition’ detected, respectively, 13.46, 43.22, and 5.09% more OVD than the ‘operational one’ ($p < 0.05$). In addition, the operational definition, compared with the physiological one, overdiagnosed OVD in 2.33 and 0.44% of smokers and non-smokers, respectively, and underdiagnosed it in 4.46% and 29.72% of smokers and non-smokers, respectively ($p < 0.05$). Compared with the group ‘physio (–), operat (+)’, the ‘physio (+), operat (–)’ one was younger (74.2 ± 4.7 years vs. 40.9 ± 10.3 years) and had significantly higher FEV_1 ($62 \pm 13\%$ vs. $78 \pm 17\%$) and FVC ($71 \pm 15\%$ vs. $93 \pm 19\%$).

Conclusion: The frequency of OVD much depends on the criteria used for its definition.

Keywords: *obstructive ventilatory defect; FEV₁/FVC; fixed threshold; lower limit of normal; spirometry; guideline*

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The prevalence of bronchial asthma and chronic obstructive pulmonary disease (COPD) is constantly increasing worldwide including African countries (1, 2). These two chronic diseases, often having in common an obstructive ventilatory defect (OVD), should be diagnosed more accurately by using spirometry (3, 4). However, there is no clear consensus as to what constitutes an OVD.

On the one hand, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) (5) opted for a ‘physiological definition’ based on a first-second forced expiratory volume/forced vital capacity (FEV_1/FVC) ratio below the lower limit of normal (LLN) range. On the other hand, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) opted for an ‘operational definition’ based on a fixed threshold value of 0.70 ($FEV_1/FVC < 0.70$) (3).

The last definition was recently criticised in an open letter addressed to GOLD committee members (6–10). The main criticism was that the FEV_1/FVC ratio declines with increasing age and height, even in healthy lifelong non-smokers, whose LLN drops below a ratio of 0.70 from about 45 years of age (6–10). Therefore, the use of a fixed threshold value causes up to 50% overdiagnosis (misclassification) above that age (6–10). Authors and signatories of the open letter have asked GOLD committee members to abandon the ‘operational method’ in favour of the ‘physiological’ one (6–10).

The lack of a clear worldwide consensus about OVD definition could be a source of confusion and/or misdiagnosis for clinicians and respiratory researchers. This is the case in Africa, where the ‘operational definition’ is widely applied (11–15). For example, a recent paper

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published in the *Libyan Journal of Medicine* (11) was criticised (16) since authors have opted for the use of a fixed threshold of 0.70 to define the OVD.

Recently, the ATS/ERS in a paper entitled ‘Research Questions in COPD’ have recommended studies that evaluate the impact of age on the importance of identifying an OVD (17). Thus, the aim of the present study is to highlight, on a large sample, the potential errors engendered by applying the ‘operational definition’ instead of the ‘physiological’ one.

Population and methods

Study design

It is a retrospective study including anthropometric and spirometric data ($n = 4,516$ records) from a local team’s previous published studies during the last 10 years (18–34). Some included data ($n = 214$ cases) were prospectively evaluated during January and February of 2015.

The Tunisian population comprises people of mainly Arab, Berber, and Turkish descent (26).

Inclusion and non-inclusion criteria

Only reproducible spirometric data of subjects aged more than 17 years were considered for analysis.

Collected data

Quantity of used cigarettes and/or narghile [respectively, in packets-years (PY) and narghiles-years (NY)], age (years), height (m), weight (kg), body mass index (BMI, kg/m^2), FEV_1 (L,%), FVC (L,%), and FEV_1/FVC (absolute value).

Smoking status (smoker/non-smoker)

The subject was qualified as a smoker when the cigarette or narghile use was ≥ 5 PY or NY, respectively, or when the sum of cigarette and narghile use was ≥ 5 (20, 26).

Spirometric measurements

All spirometric measurements were performed according to the ATS/ERS 2005 guidelines (35–37). Local spirometric norms were applied (20, 26, 38).

Applied definitions

Subjects were divided into seven groups of 10-year age ranges, into two groups of younger (< 45 years) or older (≥ 45 years) subjects (6–10, 39), and into two groups of smokers and non-smokers. According to the presence or absence of an OVD, subjects were divided into six groups:

Group I: Physiological definition ‘physio (+)’: $\text{FEV}_1/\text{FVC} < \text{LLN}$.

Group II: Operational definition ‘operat (+)’: $\text{FEV}_1/\text{FVC} < 0.7$.

Group III: ‘physio (+), operat (–)’: $\text{FEV}_1/\text{FVC} < \text{LLN}$ and $\text{FEV}_1/\text{FVC} \geq 0.70$.

Group IV: ‘operat (+), physio (–)’: $\text{FEV}_1/\text{FVC} < 0.70$ and $\text{FEV}_1/\text{FVC} \geq \text{LLN}$.

Group V: ‘physio (+), operat (+)’: $\text{FEV}_1/\text{FVC} < \text{LLN}$ and $\text{FEV}_1/\text{FVC} < 0.70$.

Group VI: ‘physio (–), operat (–)’: $\text{FEV}_1/\text{FVC} \geq \text{LLN}$ and $\text{FEV}_1/\text{FVC} \geq 0.70$.

Statistical analyses

Quantitative and qualitative data were expressed, respectively, as mean \pm SD and as number (%). Chi-square test was used to compare percentages of included subjects between Groups I and II. Parametric (t -test) and non-parametric (Mann–Whitney U) tests were used to compare anthropometric and spirometric data between Groups III and VI. Analyses were carried out using Statistica statistical software (Statistica Kernel version 6; Stat Software, Maisons-Alfort, France). Significance was set at the 0.05 level.

Results

Anthropometric and spirometric data of 4,730 subjects were retained. Table 1 presents their data divided according to age ranges. Compared with the ‘physio (+)’ group, the ‘operat (+)’ group included significantly lower percentages of subjects (total samples data) only in age ranges < 55 years. For the total sample (17–85 years), compared with the ‘physiological definition’, the ‘operational definition’ gives a significantly lower percentage of subjects having OVD, respectively, 19.15% vs. 16.57%. Thus, the ‘physiological definition’ detected 13.46% more OVD than the ‘operational definition’.

For both younger ($n = 2,076$) and older ($n = 2,654$) groups [mean \pm SD of age (years): 33.9 ± 7.4 and 56.8 ± 9.1 , respectively], compared with the ‘physiological definition’, the ‘operational definition’ gives statistically significant lower percentages of subjects having OVD, respectively, 9.59% vs. 5.44% and 26.64% vs. 25.28%. Thus, the ‘physiological definition’ detected 43.22 and 5.09% more OVD than the ‘operational definition’, respectively, in younger and older groups.

Table 2 presents the anthropometric and spirometric data of included subjects divided according to OVD definitions (Groups III – VI). Compared with the ‘operat (+), physio (–)’ group, the ‘physio (+), operat (–)’ group was younger, had significantly higher FEV_1 and FVC, and included higher percentages of females and non-smokers. Among the 784 subjects ‘operat (+)’ (Table 1), 14 (2%) were ‘physiol (–)’ (Table 2). Among the 906 subjects ‘physio (+)’ (Table 1), 136 (15%) were ‘operat (–)’ (Table 2).

Figure 1 shows the step-by-step distribution of included subjects with respect to OVD definitions [operat ‘+’ (Fig. 1a); operat ‘–’ (Fig. 1b)] and smoking status. Depending on the OVD definitions and smoking status, each subgroup was distinguished in different cells (A_1 – A_2 ; B_1 – B_4). The analysis of Fig. 1 revealed the following:

1. Among the 557 smokers ‘operat (+)’ [$B_1 + B_3$ (Fig. 1a)], 13 were ‘physiol (–)’ [B_3 (Fig. 1a)], and

Table 1. Anthropometric and spirometric data of included subjects divided according to age ranges (n = 4,730)

Age range (years)	Anthropometric data					FEV ₁		FVC		FEV ₁ /FVC	Group I	Group II	Probability
	Sex	Age (year)	Height (m)	Weight (kg)	BMI	(L)	%	(L)	%	Absolute value	(FEV ₁ /FVC < 0.70)	(FEV ₁ /FVC < LLN)	
17–25	M (n = 189)	21.5 ± 2.1	1.75 ± 0.07	71 ± 12	23.2 ± 3.3	4.27 ± 0.53	89 ± 10	4.97 ± 0.65	90 ± 10	0.86 ± 0.05	0 (0.00)	6 (3.19)*	0.0169
	F (n = 111)	21.0 ± 1.9	1.65 ± 0.08	61 ± 10	22.6 ± 3.6	3.40 ± 0.60	90 ± 12	3.86 ± 0.67	88 ± 11	0.88 ± 0.05	0 (0.00)	0 (0.00)	1
	T (n = 300)	21.3 ± 2.0	1.71 ± 0.09	68 ± 12	23.0 ± 3.4	3.95 ± 0.70	90 ± 11	4.56 ± 0.85	89 ± 10	0.86 ± 0.05	0 (0.00)	6 (2.00)*	0.0141
25–35	M (n = 556)	30.0 ± 2.8	1.74 ± 0.07	78 ± 14	25.6 ± 4.0	4.00 ± 0.62	88 ± 11	4.85 ± 0.77	92 ± 11	0.82 ± 0.06	17 (3.05)	47 (8.45)*	0.003
	F (n = 182)	30.5 ± 2.9	1.65 ± 0.08	68 ± 12	25.2 ± 4.0	3.30 ± 0.91	94 ± 17	3.91 ± 0.91	95 ± 17	0.84 ± 0.05	3 (1.64)	8 (4.39)	0.2641
	T (n = 738)	30.1 ± 2.8	1.72 ± 0.08	75 ± 14	25.5 ± 4.0	3.82 ± 0.71	90 ± 13	4.62 ± 0.90	93 ± 13	0.83 ± 0.06	20 (2.71)	55 (7.45)*	0.003
35–45	M (n = 768)	40.1 ± 2.7	1.71 ± 0.07	80 ± 14	27.2 ± 4.3	3.51 ± 0.69	84 ± 15	4.37 ± 0.77	90 ± 13	0.80 ± 0.07	84 (10.93)	118 (15.36)*	0.0199
	F (n = 270)	39.8 ± 2.7	1.62 ± 0.08	73 ± 12	27.8 ± 4.3	3.00 ± 0.71	94 ± 19	3.61 ± 0.85	95 ± 18	0.83 ± 0.06	9 (3.33)	20 (7.40)*	0.0334
	T (n = 1038)	40.1 ± 2.7	1.69 ± 0.09	78 ± 14	27.4 ± 4.3	3.38 ± 0.73	86 ± 16	4.17 ± 0.86	91 ± 15	0.81 ± 0.07	93 (8.58)	138 (13.29)*	0.036
45–55	M (n = 870)	49.6 ± 2.8	1.71 ± 0.06	78 ± 14	26.6 ± 4.5	2.93 ± 0.88	75 ± 21	3.83 ± 0.83	84 ± 16	0.75 ± 0.13	197 (22.64)	229 (26.32)	0.1459
	F (n = 484)	49.5 ± 3.0	1.59 ± 0.08	73 ± 11	28.7 ± 4.2	2.57 ± 0.61	89 ± 17	3.11 ± 0.75	91 ± 17	0.82 ± 0.06	12 (2.47)	20 (4.13)	0.0685
	T (n = 1354)	49.6 ± 2.8	1.67 ± 0.09	76 ± 13	27.4 ± 4.5	2.80 ± 0.81	80 ± 21	3.58 ± 0.88	86 ± 17	0.77 ± 0.11	209 (15.43)	249 (18.38)*	0.0356
55–65	M (n = 458)	58.7 ± 2.7	1.68 ± 0.07	75 ± 14	26.7 ± 4.7	2.44 ± 0.87	67 ± 23	3.30 ± 0.84	78 ± 18	0.72 ± 0.14	157 (34.27)	162 (35.37)	0.7503
	F (n = 256)	58.8 ± 2.8	1.58 ± 0.08	71 ± 12	28.2 ± 4.5	2.26 ± 0.61	87 ± 19	2.74 ± 0.72	88 ± 18	0.82 ± 0.09	16 (6.25)	19 (7.42)	0.6465
	T (n = 714)	58.7 ± 2.7	1.65 ± 0.09	74 ± 14	27.2 ± 4.7	2.38 ± 0.79	74 ± 23	3.10 ± 0.84	82 ± 18	0.76 ± 0.14	173 (24.22)	181 (25.35)	0.6605
65–75	M (n = 328)	68.5 ± 2.6	1.67 ± 0.07	71 ± 12	25.5 ± 4.4	1.71 ± 0.78	54 ± 25	2.59 ± 0.84	67 ± 21	0.64 ± 0.14	197 (60.06)	190 (57.92)	0.6027
	F (n = 104)	68.1 ± 2.3	1.56 ± 0.09	65 ± 11	26.9 ± 3.9	1.99 ± 0.71	87 ± 24	2.44 ± 0.80	89 ± 21	0.81 ± 0.10	9 (8.65)	9 (8.65)	1
	T (n = 432)	68.4 ± 2.6	1.64 ± 0.09	69 ± 12	25.8 ± 4.4	1.78 ± 0.77	62 ± 28	2.55 ± 0.83	73 ± 23	0.68 ± 0.15	206 (47.68)	199 (46.06)	0.5561
75–85	M (n = 129)	77.9 ± 2.7	1.64 ± 0.06	69 ± 10	25.5 ± 3.8	1.47 ± 0.63	62 ± 17	2.30 ± 0.56	72 ± 18	0.62 ± 0.17	83 (64.34)	78 (60.46)	0.5087
	F (n = 25)	78.4 ± 2.3	1.48 ± 0.04	62 ± 7	28.3 ± 2.9	1.38 ± 0.23	80 ± 14	1.58 ± 0.28	74 ± 15	0.87 ± 0.05	0 (0.00)	0 (0.00)	1
	T (n = 154)	78.0 ± 2.7	1.62 ± 0.08	68 ± 9	25.9 ± 3.8	1.46 ± 0.58	64 ± 27	2.18 ± 0.59	66 ± 18	0.66 ± 0.18	83 (53.89)	78 (50.64)	0.5985
17–85	M (n = 3298)	46.7 ± 14.4	1.71 ± 0.07	76 ± 14	26.2 ± 4.4	3.07 ± 1.09	76 ± 22	3.94 ± 1.10	84 ± 17	0.76 ± 0.12	735 (22.28)	830 (25.16)*	0.0041
	F (n = 1432)	46.6 ± 13.4	1.60 ± 0.08	70 ± 12	27.4 ± 4.5	2.69 ± 0.79	90 ± 18	3.23 ± 0.93	91 ± 18	0.83 ± 0.07	49 (3.42)	76 (5.30)*	0.0064
	T (n = 4730)	46.7 ± 14.1	1.67 ± 0.09	75 ± 14	26.6 ± 4.5	2.96 ± 1.02	90 ± 22	3.72 ± 1.10	86 ± 18	0.78 ± 0.12	784 (16.57)	906 (19.15)*	0.0114

BMI, body mass index in kg/m²; F, Female; FEV₁, first-second forced expiratory volume; FVC, forced vital capacity; LLN, lower limit of normal; M, male; T, total sample. Quantitative data are mean ± SD. Groups I and II data are number (%). *Probability (chi-square) < 0.05: 'FEV₁/FVC < 0.70' vs. 'FEV₁/FVC < LLN'.

Table 2. Anthropometric and spirometric data of included subjects divided according to OVD definitions ($n = 4,730$)

		Group III 'physio (+), operat (-)'	Group IV 'physio (-), operat (+)'	Group V 'physio (+), operat (+)'	Group VI 'physio (-), operat (-)'
		FEV ₁ /FVC < LLN and FEV ₁ /FVC ≥ 0.70 ($n = 136$)	FEV ₁ /FVC < 0.70 and FEV ₁ /FVC ≥ LLN ($n = 14$)	FEV ₁ /FVC < 0.70 and FEV ₁ /FVC < LLN ($n = 770$)	FEV ₁ /FVC ≥ 0.70 and FEV ₁ /FVC ≥ LLN ($n = 3,810$)
Sex	Male	109 (80)	14 (100)*	721 (94)	2,454 (64)*
	Female	27 (20)	0 (0)*	49 (16)	1,356 (36)*
Smoking status	Smoker	39 (29)	13 (93)*	544 (71)	544 (14)*
	Non-smoker	97 (71)	1 (7)*	226 (29)	3,266 (86)*
Age	(year)	40.9 ± 10.3	74.2 ± 4.7 ^a	57.8 ± 11.9	44.5 ± 13.4 ^b
Height	(m)	1.71 ± 0.09	1.67 ± 0.02 ^a	1.69 ± 0.07	1.67 ± 0.09 ^b
Weight	(kg)	79 ± 16	75 ± 6	70 ± 14	75 ± 14 ^b
BMI	(kg/m ²)	26.8 ± 4.6	26.7 ± 2.0	24.8 ± 4.6	27.0 ± 4.4 ^b
FEV ₁	(L)	3.13 ± 0.78	1.68 ± 0.33 ^a	1.73 ± 0.84	3.21 ± 0.87 ^b
	(%)	78 ± 17	62 ± 13 ^a	48 ± 20	87 ± 16 ^b
FVC	(L)	4.37 ± 1.07	2.49 ± 0.49 ^a	2.99 ± 1.10	3.85 ± 1.04 ^b
	(%)	93 ± 19	71 ± 15 ^a	71 ± 22	89 ± 15 ^b
FEV ₁ /FVC (absolute value)		0.71 ± 0.01	0.67 ± 0.00 ^a	0.56 ± 0.10	0.83 ± 0.05 ^b

BMI, body mass index; FEV₁, first-second forced expiratory volume; FVC, forced vital capacity; OVD, obstructive ventilatory defect; LLN, lower limit of normal. Data are mean ± SD, except for sex and smoking status, where data are number (%). ^aProbability (Mann-Whitney *U* test) < 0.05: Group III vs. Group IV. ^bProbability (*t*-test) < 0.05: Group V vs. Group VI. *Probability (chi-square) < 0.05: Group III vs. Group IV or Group V vs. Group VI.

among the 227 non-smokers 'operat (+)' [B2 + B4 (Fig. 1a)], only one was 'physiol (-)' (B4 (Fig. 1a)). Thus, the 'operational definition' overdiagnosed OVD in 2.33% of smokers and in 0.44% of non-smokers.

- Among the 583 smokers 'physiol (+)' [B1 (Fig. 1a) + B1 (Fig. 1b)], 26 were 'operat (-)' [(B1 (Fig. 1a) + B1 (Fig. 1b)) - (B1 + B3 (Fig. 1a))], and among the 323 non-smokers 'physiol (+)' [B2 (Fig. 1a) + B2 (Fig. 1b)], 96 were 'operat (-)' [(B2 (Fig. 1a) + B2 (Fig. 1b)) - (B2 + B4 (Fig. 1a))]. Thus, the 'operational definition' underdiagnosed OVD in 4.46% of smokers and in 29.72% of non-smokers.

Discussion

The present study, involving 4,730 adults, shows that the percentage of subjects having an OVD is recommendation dependent, especially in the age ranges < 55 years. For the total sample (17–85 years), the younger (< 45 years) and the older (≥ 45 years) groups, the 'physiological definition' detected, respectively, 13.46, 43.22, and 5.09% more OVD than the 'operational definition'. In addition, the 'operational definition', compared with the 'physiological definition', overdiagnosed OVD in 2.33 and 0.44% of smokers and non-smokers, respectively, and underdiagnosed it in 4.46% and 29.72% of smokers and non-smokers,

respectively. Therefore, a subject could be diagnosed as having or not having an OVD depending on which definition was applied.

Brief history of OVD spirometric definitions

In 1983, the ERS defined OVD as FEV₁/FVC < 88 and < 89% of its predicted value, respectively, in males and females (40). In 1991, the ATS defined it as FEV₁/FVC < LLN (41). In 1994, BTS opted for the use of a fixed threshold (FEV₁/FVC < 0.70 and FEV₁ < 80% of its predicted value) (42). In 2000, Viegi et al. (43) defined it as an FEV₁/FVC < 0.70. In 2001, GOLD adopted the BTS definition (44). In 2005, the ATS/ERS opted for the 'physiological definition' using the LLN concept (5), but slow vital capacity replaced FVC. In 2012, a new definition (FEV₁/FVC < *z*-score) was proposed by the Global Lung Initiative (GLI) (45). All these definitions continue to be used around the world; hence, a worldwide clear consensus is needed (17, 39).

Table 3 displays results of some studies (46–51) with a similar aim to the present one.

Discussion of the methodology

Study design

Like some other studies having similar aims (46, 49–54), the present one was retrospective. It was better to opt for

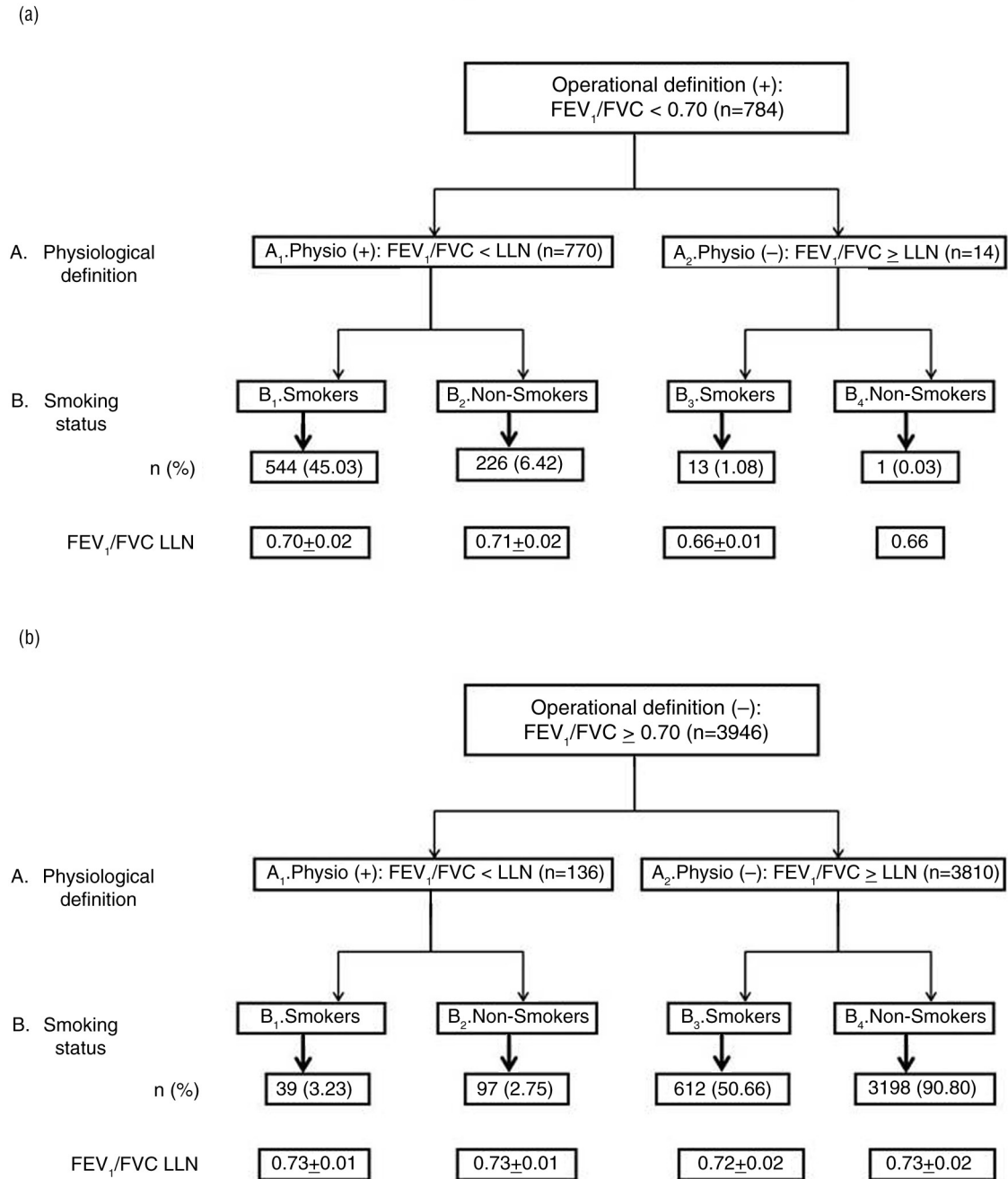


Fig. 1. Distribution of included subjects with respect to obstructive ventilatory defect definitions and smoking status: (a) operational definition 'negative'; (b) operational definition 'positive'.

FEV₁, first-second forced expiratory volume; FVC, forced vital capacity; LLN, lower limit of normal; *n*, number; %: percentage of smokers with OVD; FEV₁/FVC LLN values are mean \pm SD.

a prospective study as done by some authors (47, 48). However, such studies require more time and human and economic resources (55, 56). In the present study, 5% of data were prospectively evaluated. In this prospective subgroup ($n=214$), similar results were found [statistically significant difference between the percentage of

subjects with an OVD according to the 'physiological' 30.4% vs. the 'operational' (22.9%) definitions]. It was better to collect subjects' medical data especially those about COPD and/or asthma (47, 48, 53). However, it seems that the diagnosis of COPD is also recommendation dependent, as shown in a recent local study (21).

Table 3. Results of some studies aiming to compare the OVD operational and physiological definitions

First author	Miller (49)	Lau (48)	Szanto (51)	Roberts (50)	Aggarwal (46)	Present study
Year of study	NR	2001–2003	2001–2002	2003–2004	1999–2008	2006–2015
Country	United Kingdom USA New Zealand	Hong Kong	Sweden	USA	India	Tunisia
Study design	Retrospective	Prospective	Retrospective	Retrospective	Retrospective	Retrospective/partially prospective
Sample size (male/female)	11,413 (6,026/5,387)	525 (525/0)	574 (226/348)	1,503 (796/707)	27,307 (27,307/0)	4,730 (3,298/1,432)
Inclusion criteria	White adults	Smokers Ex-smokers	NR	NR	Male Age > 15 years	Age > 17 years
Exclusion criteria	Non-white Lack of cooperation	Asthma COPD Pulmonary tuberculosis Lung fibrosis Spinal abnormalities History of pleurodesis or chest tube insertion or thoracic surgery Acute illness (past 3 months) Respiratory tract infection (past 4 weeks)	Lack of cooperation	Inaccurate tests Uninterpretable tests	Age ≤ 15 years	Lack of cooperation
Applied spirometric guidelines	ATS/ERS 2005 (35)	ATS-1995 (61)	ATS-1995 (61)	ATS-1995 (61)	ATS-1995 (61) ATS/ERS-2005 (35)	ATS/ERS-2005 (35)
Applied spirometric norms	European norms (40) USA norms (62)	Local norms (63)	ECSC (40) Local norms (64–66)	Local norms (62, 67–69)	Local norms (70)	Local norms (20, 26, 38)
Age ranges (years)	20–92	20–80	60–93	14–95	15–95	17–85
Percentages of subjects with an OVD						
Operational definition	38	19	23	40	37	17
Physiological definition	32	14	10	37 (69) to 43 (74)	33	19
Significant difference between definitions	Yes	Yes	Yes	No	Yes	Yes

COPD, chronic obstructive pulmonary disease; ECCS, European-Community for Coal and Steel; OVD, obstructive ventilatory defect; NR, not reported.

Sample main characteristics

As carried out in some studies (46, 48–50), the present one included samples with a large age range (17–85 years). Szanto et al. (51) have opted for an elderly group aged ≥ 60 years. It is interesting to perform similar studies in children and adolescents who also need a clear consensus concerning OVD definition (45).

Discussion of the results

In the present study, the ‘physiological definition’ detected significantly 13.46% more OVD than the ‘operational definition’ (Table 1). On the one hand, this result was contrary to what was previously published, where the ‘physiological definition’ compared with the ‘operational definition’ significantly underdiagnosed OVD by 4% (46), 5% (48), and 6% (49) (Table 3). On the other hand, the present result was intermediate to the one published by Roberts et al. (50), where the differences between the two definitions were about -3 to 3%, depending on the applied spirometric norms. It is important to note that the differences reported by Roberts et al. (50) were not statistically significant (Table 3). The present study result cannot be compared with the one of Szanto et al. (51) (reporting a difference of 13% in favour of the ‘operational definition’) since they have studied only elderly subjects (Table 3). Some plausible explanations of the results’ divergence could be study design [retrospective vs. prospective (55, 56)], sample size (57) [low, e.g., $< 2,000$ (48, 50, 51) vs. high, e.g., $> 4,000$ (46, 49)], applied inclusion and exclusion criteria (58–60) [e.g. comorbidities (48)], applied spirometric guidelines [old (46, 48, 50, 51) (ATS-1995 (61)) vs. new (46, 49) (ATS/ERS-2005 (35))], and age ranges [large (46, 48–50) vs. narrow (51)].

The following sections will discuss the advantages and disadvantages of the two most applied definitions to diagnose OVD.

Operational definition

The advantage of the ‘operational definition’ (3) is that the diagnosis of OVD is made by reference to one easy to remember number (0.70), avoiding the use of reference values and calculations (43). Its use by general practitioners or specialists of other disciplines could be justified by its simplicity (43). These qualities lend it to practical use in the detection of COPD in any country (31). In addition, the use of the ‘operational definition’ is associated with increased death risk, whereas using the ‘physiological definition’ is not (71). The profile of subjects ‘operat (+), physio (–)’ is characterised by the predominance of males and smokers; the advanced age of included subjects; and lower FEV₁, FVC, and FEV₁/FVC (Group IV, Table 2).

However, the ‘operational definition’, the main objective of which is to favour screening, has its limits. First, the argument that the fixed cut-off of 0.70 is easy to remember cannot be justified because even inexpensive pocket spirometers compute the predicted FEV₁ and FEV₁/FVC,

as well as the LLN (72). Secondly, ignoring that FEV₁/FVC ratio changes with age (38, 50, 73) probably leads to and underestimates the OVD prevalence in the young subjects and overestimates its prevalence in the elderly subjects (74, 75). Thirdly, the fixed ratio does not delimit mild airways obstruction and its use introduces an important age and sex bias (39). However, the present study does not confirm the above hypothesis since in both younger and older groups, compared with the ‘physiological definition’, the ‘operational definition’ gives statistically significant lower percentages of subjects having OVD, respectively, 9.59% vs. 5.44% and 26.64% vs. 25.28%.

The use of a fixed threshold value for OVD diagnosis is based on the same reasoning for the diagnosis of other chronic diseases, such as diabetes or hypertension where it is conventional that using fixed cut points works well (72), so that a fixed threshold for FEV₁/FVC should work equally well (76). However, the normal levels of blood pressures and glycaemia are maintained within a narrow range of the target value by physiological regulation systems. There is no such system that controls the level of FEV₁/FVC and the absence of such a target value for FEV₁/FVC should therefore be accepted (72).

Physiological definition

Interpretation of spirometry data is usually based on comparisons of parameters measured in an individual patient or subject with reference values based on healthy subjects (77). Values below the LLN, defined by the 95% confidence interval, are considered as abnormal (5, 54, 77). The use of the LLN is an appropriate method to interpret spirometry data, since the clinical question is whether the calculated FEV₁/FVC ratio is reduced (5, 41, 54). Problems arise, however, when FEV₁/FVC lie near its LLN (5, 77). In this case, a literal interpretation of the functional defect is too simplistic and could fail to properly describe the functional status and other tests, such as the reversibility one, should be performed (5, 77). The ‘operational definition’, compared with the ‘physiological definition’, underestimated the OVD in 122 subjects (2.6%) (Table 1). The profile of subjects ‘physio (+), operat (–)’ is characterised by the predominance of females and non-smokers; the middle age of included subjects; and higher FEV₁, FVC, and FEV₁/FVC (Group III, Table 2).

One limitation to the application of the ‘physiological definition’ could be a lack of reference values for many countries, especially the low-income ones, such as some African countries (5). A Medline search performed on 12 September 2015 and applying the following keywords (‘reference equations’ and ‘spirometry’ and ‘Africa’ and ‘adult’), found 15 papers with norms published for only a few African countries (Tunisia, Algeria, South Africa, Sudan, Rwanda, Togo, Tanzania, Senegal, Ethiopia, and Ivory Coast). Another limitation is that errors in interpretation (with respect to both overestimation and underestimation

of ventilatory defects) can occur if inappropriate reference equations are used (20, 26). In Europe and some other countries, the GLI reference equations are presently recommended (45). These reference equations have been expanded to include preschool children, and the LLN has been more precisely defined, using *z*-scores (45). Similar analyses are underway to update the spirometry reference equations for use in Africa with, for example, the project 'Paediatric and Adult African Spirometry (PAAS)' working group.

Implications for research

As advised by the ATS/ERS (5, 17), there is a need for more research related to OVD definition. Specifically, there is a need for higher quality prospective studies that could more clearly identify an unambiguous consensus on what constitutes an OVD taking account of the smoking status of subjects.

In conclusion, the prevalence of OVD very much depends on the criteria used for its definition. The present study provides powerful support for the view that the 'physiological definition' should be applied in order to avoid the risk of misdiagnosing a part of the population as free from pulmonary disease. The reasons of simplicity and ease of remembrance, advanced for the 'operational definition' seem unimportant compared with the objective of being able to properly detect OVD, especially in smokers (47). An OVD definition based on LLN derived from an appropriate spirometric reference equation would diminish the rate of misinterpretations. It will bring pulmonary medicine more in line with other medical disciplines and facilitate the correct interpretation of spirometry defects (49). Schooling societies and scientific organisations, such as GOLD (www.goldcopd.com/, accessed 12 September 2015), are recommended to return to evidence-based medicine and revise their guidelines.

Authors' contributions

ZA and SR conceived the study, participated in its design, collected spirometric data, performed the statistical analysis, coordinated the study and helped to draft the manuscript. HBS conceived the study, participated in its design, performed the statistical analysis, coordinated the study, and approved the final version.

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