Validation of FEV_6 in the elderly: correlates of performance and repeatability

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ABSTRACT

Background: Forced expiratory volume in 6 s (FEV_6) has been proposed as a more easily measurable parameter than forced vital capacity (FVC) to diagnose airway disease using spirometry. A study was undertaken to estimate FEV_6 repeatability, to identify correlates of a good quality FEV_6 measurement and of volumetric differences between FEV_6 and FVC in elderly patients.
Methods: 1531 subjects aged 65–100 years enrolled in the SA.R.A project (a cross-sectional multicentre non-interventional study) were examined. FEV_6 was measured on volume-time curves that achieved satisfactory start-of-test and end-of-test criteria. Correlates of FEV_6 achievement were assessed by logistic regression.
Results: Valid FEV_6 and FVC measurements were obtained in 82.9% and 56.9%, respectively, of spirometric tests with an acceptable start-of-test criterion. Female sex, older age, lower educational level, depression, cognitive impairment and lung restriction independently affected the achievement of FEV_6 measurement. Good repeatability (difference between the best two values <150 ml) was found in 91.9% of tests for FEV_6 and in 86% for FVC; the corresponding figures in patients with airway obstruction were 94% and 78.4%. Both FEV_6 and FVC repeatability were affected by male sex and lower education. Male sex, airway obstruction and smoking habit were independently associated with greater volumetric differences between FEV_6 and FVC.
Conclusions: In elderly patients, FEV_6 measurements are more easily achievable and more reproducible than FVC although 1/6 patients in this population were unable to achieve them.

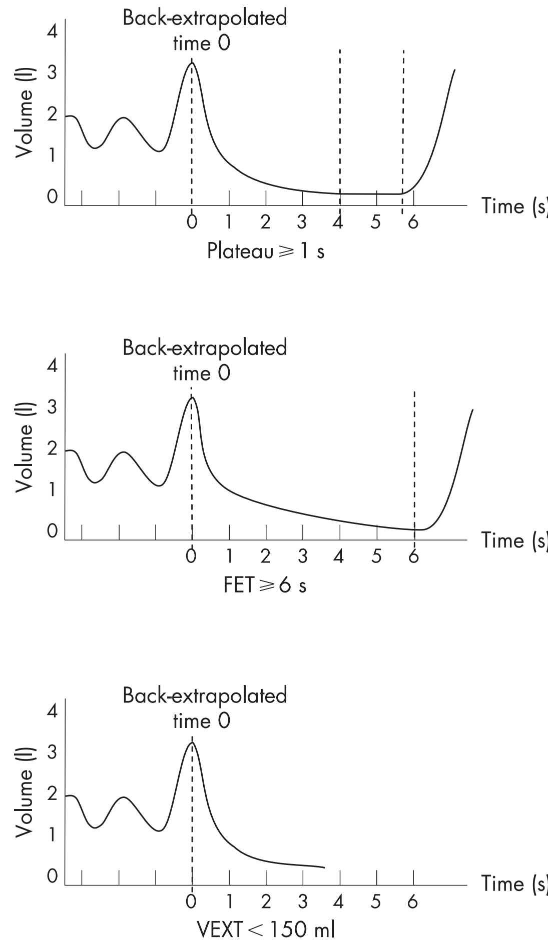
Spirometry is the most frequently performed respiratory function test and has a primary diagnostic role in the elderly since many factors (co-morbidity, blunted sensitivity to dyspnoea, polypharmacy) variously confound or conceal the clinical expression of respiratory disorders in this age group.[1 2] However, performing a reliable spirometric test involves strict patient cooperation to satisfy current guidelines for acceptability and repeatability.[3] A vigorous physical effort and, occasionally, the prolongation of expiration for up to 20 s are needed to obtain complete lung emptying to measure forced vital capacity (FVC). Unfortunately, elderly subjects or patients with severe respiratory diseases quite frequently cannot make such an effort.[4 5] For this reason, there is an increasing interest in more easily measurable spirometric parameters that could replace FVC in the elderly. Among these, forced expiratory volume in 6 s (FEV_6) has been shown to be able to predict lung function decline in adult smokers[6] and to be a reliable surrogate for FVC in the spirometric diagnosis of airway obstruction and restriction.[7–12] Reference equations and lower limits of normality for FEV_6 and for FEV_1/FEV_6 have recently been produced in selected populations.[13–16] However, to date no study has focused on the factors related to a good quality FEV_6 and to the correlates of volumetric differences between FEV_6 and FVC in elderly patients.

We analysed the spirometric findings obtained in the Italian multicentre SAlute Respiratoria nell'Anziano, Respiratory Health in the Elderly (SA.R.A) study to identify factors that influence the achievement of an acceptable FEV_6 measurement and to assess FEV_6 repeatability. We also attempted to quantify the differences between the best FEV_6 and FVC, as well as between the best FEV_1/FEV_6 and FEV_1/FVC, and to search for inherent explanatory factors.

METHODS

Analysed data were derived from a sample of 1971 subjects aged 65–100 years enrolled in the SA.R.A. multicentre case-control study. Details on the recruitment criteria, studied population and diagnostic procedures are available elsewhere.[1] Spirometric tests were not performed in 101 subjects because of early interruption of expiration, physical impairment, inability to understand the instructions, lack of collaboration and refusal; 1870 spirometric measurements were therefore obtained and retained for analysis. Briefly, the sample included 1054 subjects (56.4%) with normal spirometric parameters (429 healthy and 625 with non-respiratory diseases), 509 subjects (27.2%) with an obstructive pattern and 307 (16.4%) with a restrictive pattern (for criteria see below).

Spirometric tests were performed according to the guidelines of the American Thoracic Society (ATS).[17] A rigorous quality control programme was implemented throughout the study; the results have been published elsewhere.[1] Spirometric flow-volume curves were considered acceptable if they had extrapolated volume (VEXT) <5% of the FVC or 0.150 l (start-of-test criterion) and a forced expiratory time (FET) $\geqslant$6 s or an obvious plateau in the volume-time curve (end-of-test criterion) in the absence of cough, glottis closure or other significant interruptions of the manoeuvre. In accordance with the recommendations of the ATS,[17] we did not exclude curves which did not satisfy the repeatability criteria in order to avoid the exclusion of data in which an abnormal lung function causes a greater coefficient of variation than in normal subjects. There are different proposed surrogate measures of FVC such as FVC_6



VEXT	< 150 ml
FET	⩾6 s
Plateau	⩾1 s
Measurable FEV_1, FVC_6, FEV_6, FVC	

VEXT	< 150 ml
FET	⩾6 s
Plateau	Any
Measurable FEV_1, FVC_6, FEV_6	

VEXT	< 150 ml
FET	⩾2 s
Plateau	Any
Measurable FEV_1, FVC_6	

Figure 1 Volume-time curves of valid sessions for the measurement of maximum volume exhaled at any time during the first 6 s (FVC_6), volume forcefully exhaled at exactly 6 s after back-extrapolated time 0 (FEV_6) and forced vital capacity (FVC). VEXT, extrapolated volume; FET, forced expiratory time; FEV_1, forced expiratory volume in 1 s.

(maximum volume exhaled at any time during the first 6 s)[13] or FEV_6 (volume forcefully exhaled at exactly 6 s after back-extrapolated time 0). We chose the latter because it is the measure proposed by the ATS and the European Respiratory Society (ERS)[3] and has been shown to be a reliable surrogate of the FVC.[7–12] Figure 1 shows examples of valid sessions for the measurement of FVC_6, FEV_6 and FVC. FEV_1 and FEV_6 were measured on all acceptable curves. FVC was measured only on curves with an end-expiratory plateau ⩾1 s, ie, an end expiratory phase ⩾1 s with a volume change lower than the minimal detectable volume of 0.026 litres.[18]

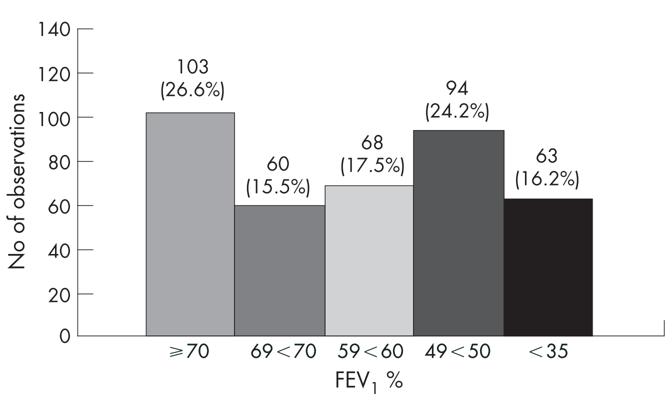


Figure 2 Severity of airways obstruction on the basis of forced expiratory volume in 1 s (FEV_1) % predicted among subjects with FEV_1/forced vital capacity (FVC) less than lower limit of normal.

We defined airways obstruction as FEV_1/FVC below the lower limit of normal (LLN: mean − 1.645*SD) of the SA.R.A. study reference population[19] and restriction as FVC below LLN with normal or increased FEV_1/FVC.[18] Severity of airways obstruction was evaluated on the basis of FEV_1 expressed as % predicted[3]: mild (⩾70%), moderate (60–69%), moderately severe (50–59%), severe (35–49%), very severe (<35%) (fig 2).

The following data that might affect the quality of measurements were collected: sociodemographic characteristics (sex, age, instruction level), smoking habit, spirometric index of airway obstruction (FEV_1 and FVC % predicted), anthropometric characteristics (body mass index (BMI), waist/hip ratio, occiput wall distance), mood state (15-item Geriatric Depression Scale (GDS)[20]), cognitive function (Mini Mental State Examination (MMSE)[21]) and physical performance (Barthel's index,[22] 6 min walking test (6MWT)[23]).

FEV_6 and FVC repeatability were estimated by calculating the difference between the two highest values of the index obtained from each subject. A few subjects with a difference >1000 ml were considered outliers and not included in the analysis (N = 10 for FEV_6 and N = 18 for FVC). Repeatability was also expressed using mean differences and 95% agreement limits according to the method of Bland and Altman.[24] The analysis of intraindividual FEV_6 repeatability was carried out in subjects with at least two valid FEV_6 measurements (VEXT <150 ml and FET ⩾6 s; n = 1345). FEV_6 repeatability was compared with the repeatability of FVC calculated in a subset of 1135 subjects with two or more valid FVC measurements (VEXT <150 ml and plateau ⩾1 s).

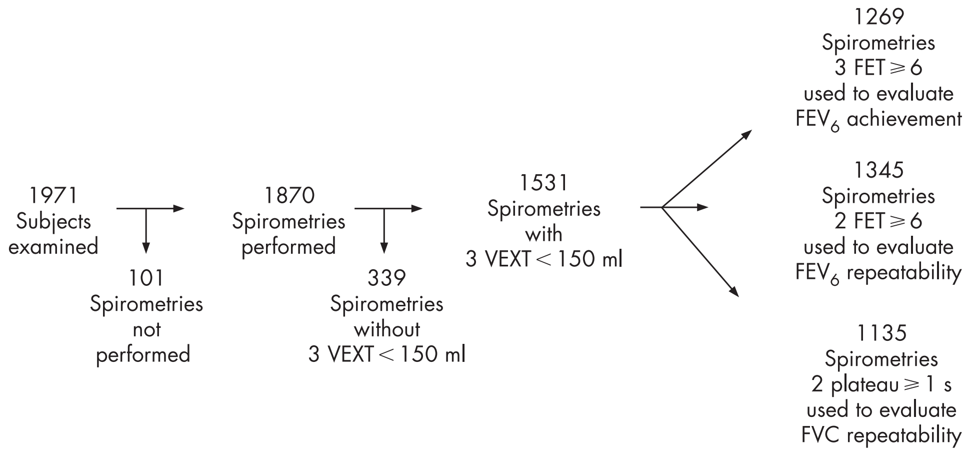


Figure 3 Pathway used for the selection of tests. VEXT, extrapolated volume; FET, forced expiratory time; FEV_6, volume forcefully exhaled at exactly 6 s after back-extrapolated time 0; FVC, forced vital capacity.

Analysis of data

Differences between groups were analysed using Pearson χ^2 for dichotomous variables and the Student *t* test or Mann-Whitney test for continuous variables, as appropriate. Multivariable logistic analysis or linear regression was used for the identification of independent correlates of outcomes. Variables entered in the models were chosen on the basis of univariable analysis results. Independent variables were considered statistically significant if the odds ratio (OR) was different from 1 and if the 95% confidence interval (CI) did not include 1.

Table 1 Main characteristics of the study sample*

	Men	Women
Number of subjects	785	746
Age (years)		
Mean	73.85	73.53
SD	6.46	6.24
Range	65–100	65–98
Instruction level		
≤5 years	463 (59.0%)	498 (66.8%)
>5 years	322 (41.0%)	248 (33.2%)
Smoking habit		
NS	542 (72.7%)	136 (17.3%)
CS	80 (10.7%)	121 (15.4%)
FS	124 (16.6%)	528 (67.3%)
GDS		
≤5	628 (80.0%)	474 (63.5%)
>5	157 (20.0%)	272 (36.5%)
MMSE		
≤23	103 (13.1%)	125 (16.8%)
>23	682 (86.9%)	621 (83.2%)
BMI (kg/m²)		
Mean	26.2	26.7
SD	3.8	5.2
Range	15.3–38.6	15.4–41.1
Obesity rate (BMI >30)	118 (15.0%)	167 (22.4%)
Spirometric pattern		
Obstructive	388 (25.3%)	
Restrictive	272 (17.8%)	
Normal	871 (56.9%)	

*Subjects who performed spirometric measurements with a satisfactory start of test criterion (extrapolated volume (VEXT) <150 ml).
SD, standard deviation; GDS,15-item Geriatric Depression Scale; MMSE, Mini Mental State Examination; NS, non-smokers; CS, current smokers; FS, former smokers; BMI, body mass index.

All the analyses were performed using Epi Info (CDC, Atlanta, Georgia, USA and WHO, Geneva, Switzerland) and Stata (Stata Corporation, College Station, Texas, USA) software packages.

RESULTS

FEV_6 achievement

Among the 1870 subjects who performed spirometry, 1531 (81.9%) obtained VEXT <150 ml in at least three curves and 1485 (79.4%) obtained FET ≥6 s in at least three curves. Among the 1531 subjects with VEXT <150 ml in at least three curves, 1269 (82.9%) obtained FET of ≥6 s in at least three curves and 871 (56.9%) attained a plateau of end expiration ≥1 s in at least three curves (fig 3).

The main demographic and clinical characteristics of the 1531 subjects with a positive start-of-test criterion are shown in table 1. Most of the subjects had a lower educational level and were former or current smokers. Nutritional status (as reflected by BMI) was, on average, good. Mood depression, corresponding to a GDS score >5, was found in 20% of men and 36.5% of women, while cognitive impairment affected about one participant out of seven.

The mean FEV_1% was 86.5% (5th and 95th percentiles 37.3% and 126.6%, respectively), while the mean FEV_1/FVC% was 64.2% for men (5th and 95th percentiles 34.6% and 89.1%, respectively) and 74.4% for women (5th and 95th percentiles 52.9% and 89.1%, respectively). Most of the patients with airways obstruction were men, and obstruction was severe or very severe in over 40% of them.

Table 2 compares the characteristics of people who could or could not achieve a valid FEV_6 measurement. Older people and those with a lower educational level, a restrictive respiratory pattern and physical or neuropsychological impairment were less likely to achieve a valid FEV_6. According to results from a multivariable logistic model, female sex, older age, lower educational level, depression, cognitive impairment and restrictive spirometric pattern were all independently and negatively correlated with the achievement of a valid FEV_6 measurement (table 3).

Intraindividual FEV_6 and FVC repeatability

The mean (SD) difference between the two best values of FEV_6 was 62 (84) ml (coefficients of variation 1.35%). The number of spirometric measurements with a difference between the two best values of FEV_6 <150 ml was 1236 (91.9%). In the subset of

Table 2 Characteristics of participants who did or did not achieve three valid FEV_6 measurements

	Without 3 FEV_6 measurements	With 3 FEV_6 measurements	p Value
Total (n = 1531)†	262 (17.1%)	1269 (82.9%)	
Age (years)*	76.4 (7.4)	73.2 (6.0)	<0.001
Respiratory function			
Obstructed (n = 388)†	46 (17.5%)	342 (26.9%)	<0.01
Normal (n = 871)†	144 (55.0%)	727 (57.3%)	
Restricted (n = 272)†	72 (27.5%)	200 (15.8%)	
Smoking habit			
Non-smokers (n = 679)†	146 (55.7%)	533 (42.0%)	<0.001
Current or former smokers (n = 852)†	115 (44.3%)	737 (58.0%)	
Sex			
Women (n = 746)†	154 (58.8%)	592 (46.6%)	<0.001
Men (n = 785)†	108 (41.2%)	677 (53.4%)	
Spirometric parameters			
FEV_1 (% predicted)*	87.5 (27.5)	86.3 (26.8)	0.505
FVC (% predicted)*	82.5 (21.4)	92.3 (19.5)	<0.001
FEV_1/FVC*	77.4 (13.9)	7.8 (13.9)	<0.001
Educational level			
⩽5 years (n = 961)†	203 (77.5%)	758 (59.7%)	<0.001
>5 years (n = 570)†	59 (22.5%)	511 (40.3%)	
GDS*	5.0 (3.7)	3.7 (3.3)	<0.001
MMSE*	25.3 (4.1)	27.2 (3.2)	<0.001
Barthel score*	91.7 (10.7)	94.1 (6.8)	<0.001
6MWT (m)*	282 (138)	333 (123)	<0.001
BMI (kg/m²)*	26.3 (5.0)	26.6 (4.5)	0.166
Waist-hip ratio*	0.95 (0.1)	0.94 (0.1)	0.612
Occiput wall distance (cm)*	5.6 (4.6)	5.8 (4.5)	0.376

Values are *mean (SD) or †n (%).
FEV_6, volume forcefully exhaled at exactly 6 s after back-extrapolated time 0; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GDS, Geriatric Depression Scale; MMSE, Mini Mental Status Examination; 6MWT, 6 min walking test; BMI, body mass index.

subjects who had two or more measurable FVC values, the mean (SD) difference between the two best values was 72 (87) ml (coefficients of variation 1.21%), while the number of spirometric measurements with a difference between the two best values of FVC <150 ml were 976 (86% of the total). The repeatability of FEV_6 was high even in subjects with airway obstruction (<150 ml in 94% of tests), whereas the repeatability of FVC in the same group was lower (78.4%). Table 4 shows the mean differences between the two best FEV_6 and FVC measurements, together with 95% agreement limits and centile distribution stratified by gender.

Table 3 Factors negatively influencing achievement of valid FEV_6 measurement: multivariable logistic analysis on 1531 subjects with a satisfactory start-of-test criterion

	Odds ratio	p Value	95% confidence interval
Older age (every 5 years)	1.42	<0.001	1.25 to 1.59
Female sex	1.58	0.022	1.08 to 2.31
Lower education*	1.77	0.001	1.25 to 2.51
Depression†	1.54	0.045	1.12 to 2.13
Cognitive impairment‡	1.61	0.009	1.09 to 2.37
Spirometric restriction§	1.98	<0.001	1.37 to 2.86

FEV_6, volume forcefully exhaled at exactly 6 s after back-extrapolated time 0.
Also corrected by smoking habit, Barthel index and 6 min walking test.
*Lower education: ⩽5 years.
†Depression: Geriatric Depression Scale (GDS) >5.
‡Cognitive impairment: Mini Mental Status Examination (MMSE) <24.
§Spirometric restriction: forced vital capacity (FVC) < lower limit of normal (LLN) and forced expiratory volume in 1 s (FEV_1)/FVC ⩾LLN.

Several factors were associated with poor FEV_6 repeatability in the univariable analyses (table 5). Only male sex (OR 1.04; 95% CI 1.11 to 2.68) and lower educational level (OR 1.76; 95% CI 1.08 to 2.85) remained associated with lack of repeatability of FEV_6 in a multivariable model corrected for age, cognitive function, Barthel index and 6 MWT.

Differences between the largest FVC and FEV_6, between FEV_1/FEV_6 and FEV_1/FVC, and correlates of differences

Among the 871 spirometric measurements with three acceptable curves and a plateau of ⩾1 s in at least three curves, the mean (SD) difference between FVC and FEV_6 was 182 (171) ml (range 0–1279). The mean (SD) difference between FEV_1/FEV_6 and FEV_1/FVC was 4.14 (3.10)% (range 0–17%). As expected, the difference between FVC and FEV_6 increased as the absolute values of FVC increased (fig 4). In a linear multivariable regression, male sex, airway obstruction and smoking habit emerged as independent correlates of a larger difference between FVC and FEV_6 and between the best FEV_1/FEV_6 and FEV_1/FVC ($p<0.001$). The difference between FVC and FEV_6 was 0 in 23 subjects but exceeded 1000 ml in 5 subjects, all characterised by severe obstruction (mean (SD) FEV_1/FVC 35.2 (9.0)%). The positive relationship between the difference FVC-FEV_6 and the degree of airway obstruction was confirmed by the significant correlation shown in fig 5.

DISCUSSION

The findings of our study indicate that, in elderly subjects, FEV_6 measurements are more easily achieved and are more reproducible than FVC. The potential implication of this result is evident, since

Table 4 Characteristics of FEV_6 and FVC repeatability

	Mean	95% agreement limits	Percentiles 5th	10th	25th	50th	75th	90th	95th
FEV_6 repeatability (ml)									
Men	68.5	−126.0 to 262.0	3	6	18	40	80	146	205
Women	55.8	−79.4 to 191.0	3	6	15	35	71	118	159
FVC repeatability (ml)									
Men	96.2	−254.6 to 447.0	3	9	24	60	125	200	271
Women	69.4	−315.7 to 454.5	3	6	19	42	80	139	182

FEV_6, volume forcefully exhaled at exactly 6 s after back-extrapolated time 0; FVC, forced vital capacity.
Mean (SD) FEV_6: 3016 (777) ml for men, 2341 (560) ml for women.
Mean (SD) FVC: 3187 (611) ml for men, 2323 (812) ml for women.

FEV_6 was obtained in more than 80% of spirometric measurements with acceptable start-of-test criteria whereas a reliable FVC measurement was obtained in <60% of tests.

To our knowledge, this is the first study to address the factors that influence the achievement and repeatability of FEV_6 measurements in the elderly. Factors that negatively affected attainment of an expiration of at least 6 s, which is the only end-of-test requirement for FEV_6, were female sex, older age, lower educational level, depression, cognitive impairment and a restrictive spirometric pattern. The mechanism by which age affects the achievement of FEV_6 is unclear. In older subjects, airway closure occurs at lung volumes above functional residual capacity, impairing the FEV_6 manoeuvre. In fact, some studies have shown that the decline in lung function accelerates with age.[25–29] Our results support this explanation: among people aged 77 years or older (corresponding to the 75th percentile of age distribution), 75% of participants achieved an acceptable FEV_6 compared with 83% in the entire sample (data not shown). However, since even the most accurate multivariable analysis could miss important explanatory variables, older age might also be considered a "summary index" of conditions hampering the achievement of FEV_6.

The cooperation of the patient is an essential requirement for a reliable test: cognitive impairment is a well recognised negative correlate for achieving FEV_6.[1 30–32] Conversely, depressed mood has not previously been recognised as a negative correlate for achieving any spirometric measure. Lack of motivation to perform the spirometric manoeuvre might underlie the negative relationship between depression and achievement of FEV_6. The fact that less educated subjects achieved a satisfactory FEV_6 measurement less frequently than more educated subjects probably reflects education-related differences in the ability to understand and perform the spirometric manoeuvre.

Table 5 Characteristics of participants with and without FEV_6 repeatability <150 ml

	FEV_6 repeatability ⩾150 ml	FEV_6 repeatability <150 ml	p Value
Total (n = 1345)†	109 (8.1%)	1236 (91.9%)	
Age (years)*	74.8 (6.2)	73.1 (6.0)	0.004
Respiratory function			
Obstructed (n = 352)†	21 (19.3%)	331 (26.8%)	0.150
Restricted (n = 222)†	23 (21.1%)	199 (16.1%)	
Normal (n = 771)†	65 (59.6%)	706 (57.1%)	
Smoking habit			
Non-smokers (n = 568)†	44 (40.4%)	524 (42.4%)	0.591
Current or former smokers (n = 777)†	65 (59.6%)	712 (57.6%)	
Sex			
Women (n = 631)†	40 (36.7%)	591 (47.8%)	0.026
Men (n = 714)†	69 (63.3%)	645 (52.2%)	
Spirometric parameters			
FEV_1 (% predicted)*	86.9 (26.5)	88.1 (26.7)	0.770
FVC (% predicted)*	88.9 (18.4)	92.0 (19.6)	0.107
FEV_1/FVC*	69.9 (14.7)	67.9 (13.7)	0.104
Educational level			
⩽5 years (n = 821)†	82 (75.2%)	739 (59.8%)	0.001
>5 years (n = 524)†	27 (24.8%)	497 (40.2%)	
GDS*	4.1 (3.6)	3.7 (3.3)	0.301
MMSE*	25.9 (4.4)	27.2 (3.1)	<0.001
Barthel score*	91.6 (13.1)	94.1 (6.6)	0.001
6MWT (m)*	304.4 (130.1)	334.5 (122.9)	0.020
BMI (kg/m^2)*	25.9 (3.8)	26.6 (4.3)	0.086
Waist-hip ratio*	1.01 (0.10)	1.00 (0.05)	0.208
Occiput wall distance (cm)*	5.9 (4.2)	5.7 (4.5)	0.659

Values are *mean (SD) or †n (%).
FEV_6, volume forcefully exhaled at exactly 6 s after back-extrapolated time 0; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GDS, Geriatric Depression Scale; MMSE, Mini Mental Status Examination; 6MWT, 6 min walking test; BMI, body mass index.

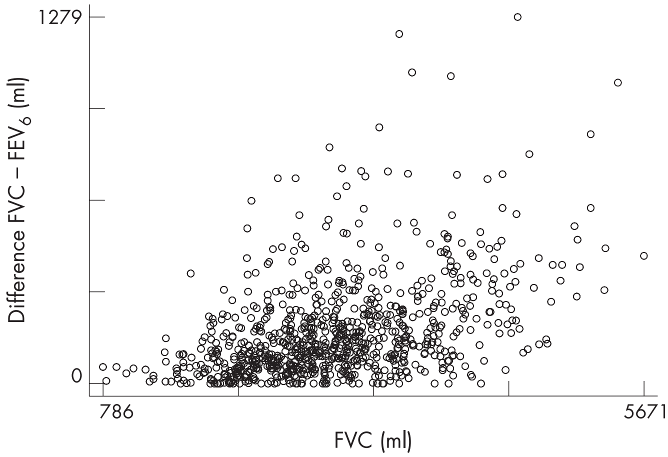


Figure 4 Relationship between the difference between forced vital capacity and the volume forcefully exhaled at exactly 6 s after back-extrapolated time 0 (FVC − FEV_6) and FVC.

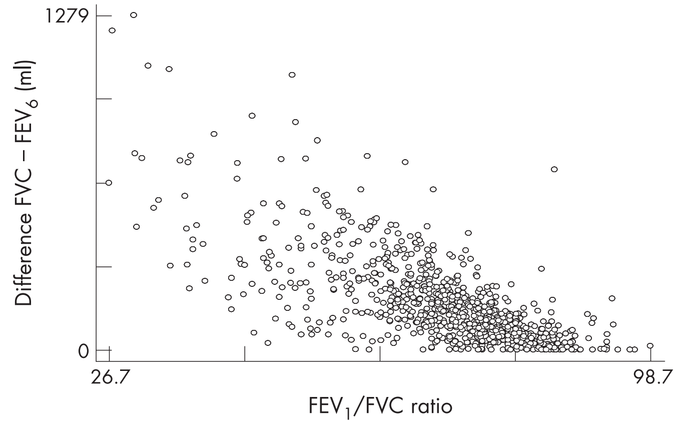


Figure 5 Relationship between the difference between forced vital capacity and the volume forcefully exhaled at exactly 6 s after back-extrapolated time 0 (FVC − FEV_6) and forced expiratory volume in 1 s (FEV_1)/FVC.

Patients with a restrictive functional pattern had difficulties in performing a measurable FEV_6 manoeuvre; in 64/272 the FVC manoeuvre lasted <6 s. It is conceivable that patients with a restrictive pattern have less air to expire and therefore need less time to do it. Furthermore, restrictive lung diseases are frequently associated with increased lung stiffness which could make the expiration explosive and therefore shorter. Our sample included only patients with a mild to moderate restrictive respiratory pattern, and it is conceivable that a greater proportion of patients will not achieve a FET ⩾6 s and a measurable FEV_6 in samples including severely restricted patients. Our findings are indirectly supported by the observation of Vanderwoorde *et al*[8] that FEV_6 had lower sensitivity for a diagnosis of a restrictive pattern than for a diagnosis of an obstructive pattern.

Women achieved FEV_6 less frequently than men. This could be explained by the fact that women tend to have lower levels of FVC than age-matched men. Smaller lungs could complete emptying in <6 s more easily, and therefore women are more likely to achieve an adequate plateau, thus allowing FVC to be measured, even if the manoeuvre is interrupted before the FEV_6 can be measured. In the SA.R.A. population, 24.2% of women with FET <6 s had a plateau compared with 9.1% of men ($p<0.001$). Our results therefore indicate that FEV_6 might not be a suitable surrogate for FVC in elderly women and in people with a restrictive pattern. A possible solution to the problem could be to re-define FEV_6 as the largest volume exhaled anytime during the first 6 s (ie, FVC_6 referred to above[13]). This could be obtained in a larger number of subjects, including mainly women and patients with spirometric restriction.

Our results confirm the findings of Swanney *et al*[7] that FEV_6 measurement was more reproducible than FVC. The repeatability of both FEV_6 and FVC were affected by male sex and lower education. Since men have larger lung volumes than women, and because FEV_6 is obviously less than FVC, it seems logical that FVC and FEV_6 should have different criteria for reproducibility and these should also be gender-specific. To express reproducibility as a percentage of the best value instead of using the cut-off point of 150 ml could be a possible solution.

In our study the mean difference between the best FEV_6 and FVC was 182 ml, while Demir *et al*[33] reported a mean (SD) difference of 95 (121) ml in 5114 adult patients of mean (SD) age 49.95 (15.48) years and Enright *et al*[6] found that, on average, the FEV_6 was 112 ml smaller than the FVC in adult smokers. A potential reason for this discrepancy could be our decision to calculate FVC only when a 1 s plateau was reached, thus excluding curves in which FVC could be underestimated because of an early interruption of expiration. The possibility that the observed differences could be linked to different male/female ratios between study samples can also be excluded: indeed, the proportion of women in our sample was 53.7% compared with 53.6% in the study by Demir *et al*. In the sample studied by Enright *et al*, only 37.5% were women; however, given that the difference between FVC and FEV_6 is higher in men, the greater fraction of men in the sample studied by Enright *et al* would be expected to increase rather than to decrease such difference.

On the other hand, the severity of airway obstruction was directly related to the difference between FVC and FEV_6. The expiration time is, on average, proportional to the severity of airway obstruction and, thus, the proportion of FVC expired in the first 6 s is expected to decrease in parallel with FEV_1. Interestingly, all subjects having a difference between FVC and FEV_6 of more than 1 litre were among those with the most severe obstruction. Demir *et al*[33] also found a greater difference between FVC and FEV_6 in patients with airway obstruction. Similarly, Enright *et al*[6] found that the difference between the two spirometric indices was, on average, 6–9% larger in smokers with more severe airway obstruction. In comparison with previous studies[6,33] our sample consisted of subjects with less severe airway obstruction (mean FEV_1 86.5%), whereas Demir *et al* reported a mean FEV_1 of 72.9 (24.4)% predicted and in the study by Enright *et al* the mean (SD) FEV_1 was 74.8 (9.5)% predicted in men and 74.9 (9.3)% predicted in women. Our study therefore emphasises the inverse relationship between FEV_1% predicted and the difference between FVC and FEV_6 by confirming it in a population with less severe airway obstruction.

We found that, in addition to airway obstruction, male sex and smoking habit were positive correlates of the difference between FVC and FEV_6. The greater lung volumes and the resulting expiration times in men and the risk of airway disease in smokers are possible explanations for these findings.

This study has some limitations. First, we defined restriction according to spirometric evidence, but only the measurement of total lung capacity can provide a definitive diagnosis.[34] However, this limitation would have a greater effect on a study assessing the diagnostic accuracy of FEV_6 than on our study which aimed to identify factors associated with achieving a satisfactory measurement of FEV_6. Second, in our study FVC was considered reliable only if the subject reached a plateau ⩾1 s. This criterion is very restrictive and excludes the operator's option considered a possible alternative by the ATS/ERS statements.[3] At any rate, it seems an acceptable choice for the sake of standardisation since, in a multicentre study, it would not have been possible to evaluate the subjective terms of judgement adopted by individual operators. Third, we cannot exclude the possibility that, in selected cases, we might have observed glottis closure and not a true plateau. Finally, a high proportion of our patients with chronic obstructive pulmonary disease had severe or very severe obstruction (over 40% of them had FEV_1 <50% predicted). As suggested elsewhere,[18 35 36] we identified airways obstruction using the LLN of FEV_1/FVC of our reference population of elderly people,[19] which was lower than the classic 70%, thus reducing the proportion of people with mild obstruction.

In conclusion, FEV_6 can be a valid alternative to FVC in the identification of airway obstruction in elderly patients because the spirometric manoeuvre is easy to perform and it satisfies the criteria for repeatability and diagnostic accuracy. However, very old poorly educated and cognitively impaired subjects, women and patients with a restrictive respiratory pattern have more difficulty in achieving a satisfactory FEV_6. The measurement of FEV_6 therefore represents an important step forward with regard to FVC, although it may not be the ideal surrogate for FVC in subjects who are very old and frail.

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