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Clinical and functional correlations of the difference between slow vital capacity and FVC

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ABSTRACT

Objective: To evaluate the relationship that the difference between slow vital capacity (SVC) and FVC (Δ SVC-FVC) has with demographic, clinical, and pulmonary function data. Methods: This was an analytical cross-sectional study in which participants completed a respiratory health questionnaire, as well as undergoing spirometry and plethysmography. The sample was divided into two groups: Δ SVC-FVC \geq 200 mL and Δ SVC-FVC < 200 mL. The intergroup correlations were analyzed, and binomial logistic regression analysis was performed. Results: The sample comprised 187 individuals. In the sample as a whole, the mean Δ SVC-FVC was 0.17 ± 0.14 L, and 61 individuals (32.62%) had a Δ SVC- $FVC \ge 200$ mL. The use of an SVC maneuver reduced the prevalence of nonspecific lung disease and of normal spirometry results by revealing obstructive lung disease (OLD). In the final logistic regression model (adjusted for weight and body mass index > 30 kg/m²), OLD and findings of air trapping (high functional residual capacity and a low inspiratory capacity/TLC ratio) were predictors of a ∆SVC-FVC ≥ 200 mL. The chance of a bronchodilator response was found to be greater in the Δ SVC-FVC \geq 200 mL group: for FEV1 (OR = 4.38; 95% CI: 1.45-13.26); and for FVC (OR = 3.83; 95% CI: 1.26-11.71). Conclusions: The use of an SVC maneuver appears to decrease the prevalence of nonspecific lung disease and of normal spirometry results. Individuals with a **DSVC-FVC** \geq 200 mL, which is probably the result of OLD and air trapping, are apparently more likely to respond to bronchodilator administration.

Keywords: Vital capacity; Plethysmography; Airway obstruction.

INTRODUCTION

American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines recommend the use of slow VC (SVC) as the denominator to calculate the Tiffeneau index.⁽¹⁾ Despite this recommendation, SVC maneuvers are not routinely used in most pulmonary function laboratories in Brazil.

VC is determined by measuring the volume of air in the lungs after a maximal inhalation and after a maximal exhalation, i.e., TLC and RV, respectively, which include lung/chest wall compliance and elastic recoil, respiratory muscle strength, alveolar collapse, and airway closure.(2-4) In individuals with no chest wall or respiratory muscle abnormalities, TLC is determined by lung elastic recoil.⁽⁵⁾ In young individuals, RV is primarily determined by static factors (chest wall elastic recoil and respiratory muscle pressure), whereas, in elderly individuals and in those presenting with airflow limitation, RV is determined by dynamic factors (expiratory flow limitation and airway closure).(3,6)

In normal individuals, VC reflects the properties of the lung parenchyma, whereas, in those with chronic obstructive lung disease, it reflects the properties of the airways.⁽⁵⁾ In patients with airflow limitation, airway

closure occurs at high lung volumes.⁽⁷⁾ During an FVC maneuver, dynamic compression and airway collapse can lead to premature airway closure, thus reducing FVC. Reduced thoracic gas compression during an SVC maneuver explains the fact that, even in healthy individuals, there is a difference between SVC and FVC (Δ SVC-FVC), which is more pronounced in patients with obstructive lung disease (OLD).⁽⁵⁾

Few studies have examined the association of ΔSVC-FVC with demographic characteristics, lung function, respiratory symptoms, and lung disease. (4,8-10) To our knowledge, there have been no studies evaluating bronchodilator response in relation to Δ SVC-FVC.

The primary objective of the present study was to examine the association of Δ SVC-FVC with demographic variables, spirometric parameters, plethysmographic parameters, bronchodilator response, and lung function, as well as to identify factors independently associated with a Δ SVC-FVC \geq 200 mL. A secondary objective was to examine the association of Δ SVC-FVC with the severity of OLD, respiratory symptoms, and clinical diagnosis, as well as to compare the spirometry results obtained with the use of FVC maneuvers alone and those obtained with the combined use of FVC and SVC maneuvers.

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METHODS

This was an analytical cross-sectional study. The study sample consisted of patients referred for pulmonary function testing between October 21, 2013 and July 28, 2015 at the *Instituto de Assistência Médica ao Servidor Público Estadual* (IAMSPE, Institute for the Medical Care of State Civil Servants), located in the city of São Paulo, Brazil. The study was approved by the Research Ethics Committee of the IAMSPE (Ruling no. 373,763, August 5, 2013).

Patients were randomly invited to participate in the study, and those who agreed gave written informed consent and completed a respiratory questionnaire,⁽¹¹⁾ which was administered by a nurse who is also a pulmonary function technician certified by the Brazilian Thoracic Association.

The inclusion criteria were being an outpatient and meeting the criteria established in studies reporting reference values for spirometry and plethysmography in Brazil.^(12,13) The exclusion criteria were having performed spirometric or plethysmographic maneuvers that failed to meet the ATS/ERS acceptability and reproducibility criteria^(14,15) and presenting with SVC < FVC.

Figure 1 shows a flow chart of the sample selection process. All participants performed SVC, FVC, and plethysmographic maneuvers (in this order) using a Collins system (Ferraris Respiratory, Louisville, CO, USA). All tests were performed by the aforementioned nurse, with participants in a sitting position and wearing a nose clip.

All tests were reviewed by the principal investigator and the coordinator of the pulmonary function laboratory. Emphasis was placed on the quality of inspiratory capacity (IC) maneuvers, which were performed in a relaxed manner after at least three stable breaths. IC was defined as the average of three reproducible measurements (a variability of ≤ 100 mL). The highest SVC value was selected from three measurements with a reproducibility of ≤ 100 mL. During FVC maneuvers, the difference between the two highest FVC and FEV₁ values was ≤ 150 mL and that between the two highest PEF values was $\leq 10\%$. The highest FVC and FEV₁ values were selected from those obtained during acceptable maneuvers, in accordance with the criterion of PEF reproducibility.^(14,16)

With regard to plethysmography, functional residual capacity (FRC) was calculated from thoracic gas volume, at the end of tidal volume exhalation. TLC and RV were calculated by the following formulas: TLC = IC + FRC and RV = TLC - SVC.⁽¹⁵⁾

The results were interpreted in accordance with the ATS/ERS criteria.⁽¹⁾ Spirometry results were considered normal when values were above the lower limit of normal; OLD was defined as an $FEV_1/(F)VC$ ratio below the lower limit of normal; nonspecific lung disease (NLD) was defined as a proportional reduction in (F) VC and FEV_1 ; and OLD with reduced (F)VC was defined as the presence of OLD associated with a reduction in (F)VC. First, we analyzed the spirometry results

obtained with the use of FVC maneuvers alone; then, we analyzed those obtained with the combined use of FVC and SVC maneuvers.

Plethysmographic variables were then analyzed. Given that specific airway conductance (sGaw) is also a parameter of airflow limitation, sGaw values of < 0.12 [with or without reduced FEV₁/(F)VC ratio] were interpreted as indicative of OLD.^(17,18) Air trapping was defined as an RV > 130%, and lung hyperinflation was defined as a TLC > 120%. All patients with reduced TLC were diagnosed with restrictive lung disease.⁽¹⁹⁾ In such cases, the use of a fixed threshold is acceptable because of decreasing dispersion of the data around the predicted equation line.⁽²⁰⁾ The difference between TLC and FVC, a theoretical measure designated forced RV (FRV), was calculated and expressed as absolute values and as a percentage of the predicted values.

OLD was classified as mild (FEV₁ \ge 60%), moderate (FEV₁ = 41-59%), or severe (FEV₁ \le 40%), in accordance with British Thoracic Society criteria.⁽²¹⁾

A subgroup of patients with OLD underwent spirometry 20 min after administration of a bronchodilator (400 µg of albuterol aerosol). A significant bronchodilator response was characterized by FVC and FEV₁ \geq 200 mL and \geq 7% of predicted; SVC \geq 250 mL and \geq 8% of predicted; and IC \geq 300 mL.⁽²²⁾

The study sample was divided into two groups: Δ SVC-FVC < 200, comprising patients in whom Δ SVC-FVC was < 200 mL (as assessed before bronchodilator administration); and Δ SVC-FVC \geq 200, comprising patients in whom Δ SVC-FVC was \geq 200 mL (as assessed before bronchodilator administration). The 200-mL threshold was used because it is higher than that used in order to assess reproducibility, as well as being higher than the mean Δ SVC-FVC values observed in healthy individuals.^(8,9,23)

Statistical analysis

All statistical analyses were performed with the IBM SPSS Statistics software package, version 21.0 (IBM Corporation, Armonk, NY, USA). Data were expressed as means and standard deviations for quantitative variables and as absolute numbers and proportions for categorical variables. Normality of data distribution was assessed with the Kolmogorov-Smirnov test with Lilliefors correction.

Functional, demographic, and clinical parameters were compared between the groups with the use of the Student's t-test (for data with normal distribution) or the Mann-Whitney U test (for data with non-normal distribution). The kappa statistic was used in order to assess the agreement between the spirometry results obtained with FVC maneuvers alone and those obtained with FVC and SVC maneuvers in combination. Categorical variables were compared by the chi-square test or Fisher's exact test.

Correlations of Δ SVC-FVC with demographic, clinical, and functional variables were analyzed with Pearson's or Spearman's correlation coefficient, the former being



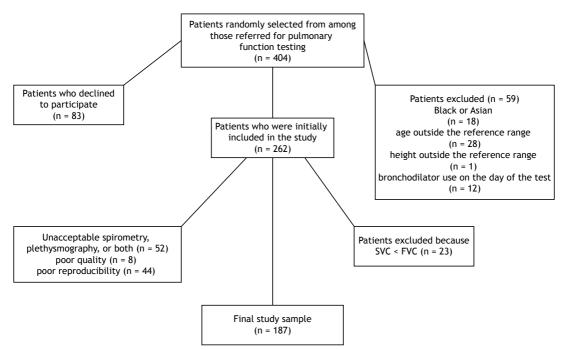


Figure 1. Flow chart of the sample selection process. SVC: slow vital capacity.

used for data with normal distribution and the latter being used for data with non-normal distribution.

Logistic regression analysis was performed to identify independent predictors of a Δ SVC-FVC \geq 200 mL. First, a single logistic regression analysis was performed to determine the OR for each demographic variable. Then, a binomial logistic regression analysis was performed to evaluate spirometric and plethysmographic parameters, crude and adjusted ORs being calculated (for the variables that were significant in the single logistic regression model) to predict a Δ SVC-FVC \geq 200 mL.

A multiple logistic regression analysis was performed to determine whether a Δ SVC-FVC ≥ 200 mL was a predictor of significant changes in spirometric parameters (FEV₁, FVC, SVC, and IC) after bronchodilator administration. It was also used in order to determine whether a Δ SVC-FVC ≥ 200 mL was predictive of normal TLC in cases in which spirometry results were indicative of NLD or of OLD with reduced FVC and a significant bronchodilator response. The level of significance was set at 5% for all analyses except the single logistic regression model, in which the level of significance was set at p < 0.20.

RESULTS

A total of 187 patients were selected (Figure 1). The general characteristics of the recruited population and a comparison between the two study groups are shown in Table 1. The mean age was 59.01 ± 12.80 years, and 126 patients (67.40%) were female. Mean height and weight were 159.90 ± 9.60 cm and 78.46 ± 18.48 kg, respectively. Mean Δ SVC-FVC was 0.17 L, a Δ SVC-FVC \geq 200 mL being observed in 61 participants (32.62%). A Δ SVC-FVC \geq 200 mL was observed in 28 (45.90%)

of the 61 male participants and in 33 (26.20%) of the 126 female participants (p = 0.007). Height and weight were higher in the Δ SVC-FVC \geq 200 group than in the Δ SVC-FVC group < 200 (p = 0.002 and p = 0.017, respectively). There were no significant differences between the two groups regarding body mass index (BMI) or clinical parameters (smoking and dyspnea). The Tiffeneau index was lower in the Δ SVC-FVC \geq 200 group than in the Δ SVC-FVC < 200 group, whereas lung volumes were higher in the former than in the latter. A Δ SVC-FVC was significantly more common in patients with OLD, regardless of the severity of airflow obstruction.

Table 2 shows the agreement between the spirometry results obtained with FVC maneuvers alone and those obtained with FVC and SVC maneuvers in combination (kappa = 0.653). Of the 73 normal spirometry results obtained when FVC maneuvers were used in isolation, 21 were reclassified as OLD when FVC and SVC maneuvers were used in combination. Of the 32 cases that were diagnosed as NLD when FVC maneuvers were used in isolation, 17 were reclassified when FVC and SVC maneuvers were used in combination. Of the 28 spirometry results interpreted as OLD with reduced FVC when FVC maneuvers were used in isolation, 8 were reclassified as OLD when FVC and SVC maneuvers were used in combination. Of the 91 cases that were diagnosed as OLD when FVC and SVC maneuvers were used in combination, only 54 had been diagnosed as OLD when FVC maneuvers were used in isolation. When normal spirometry results were excluded from the analysis, the kappa statistic was lower (0.506).

Reports of improvement in wheezing after bronchodilator administration were more common in the $\Delta \text{SVC-FVC}$



Parameter	Total sample	Group		
		Δ SVC-FVC < 200 mL	Δ SVC-FVC \geq 200 mL	
	(n = 187)	(n = 126)	(n = 61)	
Male sex	61 (32.62)	33 (26.20)	28 (45.90)	0.007*
Female sex	126 (67.40)	93 (73.81)	33 (54.10)	
Age, years	59.01 ± 12.80	59.70 ± 13.11	57.61 ± 12.11	0.300*
Height, cm	159.90 ± 9.60	158.37 ± 9.23	163.00 ± 9.70	0.002*
Weight, kg	78.46 ± 18.48	76.25 ± 16.86	83.12 ± 20.90	0.017*
BMI, kg/m ²	30.45 ± 6.40	30.26 ± 6.20	30.85 ± 6.84	0.553*
Smoking history, pack-years	18.30 ± 27.20	16.17 ± 25.82	22.70 ± 29.60	0.110**
Dyspnea, mMRC scale score	1.0 [0.0-4.0]	1.0 [0.0-4.0]	1.0 [0.0-4.0]	0.570**
FVC, L	2.83 ± 0.91	2.73 ± 0.90	3.03 ± 0.90	0.035**
FVC, % predicted	84.72 ± 17.35	85.11 ± 17.67	83.90 ± 16.79	0.666*
FEV ₁ , L	2.02 ± 0.73	1.99 ± 0.71	2.08 ± 0.76	0.418*
FEV ₁ , % predicted	75.00 ± 18.94	76.56 ± 18.44	71.87 ± 19.58	0.116*
FEV ₁ /FVC	0.71 ± 0.12	0.73 ± 0.10	0.68 ± 0.12	0.017**
PEF, L/s	6.92 ± 5.00	6.97 ± 5.87	6.82 ± 2.33	0.587**
SVC, L	3.00 ± 0.94	2.83 ± 0.91	3.35 ± 0.92	< 0.001*
SVC, % predicted	89.20 ± 17.00	87.50 ± 17.06	92.70 ± 16.50	0.049*
IC, L	2.12 ± 0.63	2.05 ± 0.62	2.26 ± 0.63	0.034*
FEV ₁ /SVC	0.67 ± 0.11	0.70 ± 0.10	0.61 ± 0.11	< 0.001**
FRC, L	2.93 ± 0.94	2.79 ± 0.90	3.21 ± 0.97	0.002**
TLC, L	5.05 ± 1.27	4.84 ± 1.22	5.47 ± 1.27	0.001**
TLC, % predicted	94.44 ±16.70	93.73 ± 16.86	95.92 ± 16.34	0.402*
RV, L	2.05 ± 0.79	2.01 ± 0.76	2.12 ± 0.86	0.185**
RV, % predicted	127.34 ± 45.00	129.17 ± 43.61	123.54 ± 47.90	0.424*
RV/TLC	0.41 ± 0.12	0.42 ± 0.11	0.39 ± 0.12	0.086*
IC/TLC	0.42 ± 0.10	0.43 ± 0.09	0.42 ± 0.09	0.495*
sGaw, L/s/cmH ₂ O	0.12 ± 0.08	0.12 ± 0.08	0.11 ± 0.07	0.380**
FRV, L	2.22 ± 0.81	2.11 ± 0.76	2.44 ± 0.85	0.02**
FRV, % predicted	155.71± 41.00	152.00 ± 36.51	163.84 ± 48.26	0.059*
∆SVC-FVC, L	0.17 ± 0.14	0.095 ± 0.052	0.321 ± 0.132	< 0.001*

Table 1. General and functional characteristics of the sample as a whole and of the two study groups.^a

 Δ SVC-FVC: difference between slow VC and FVC; BMI: body mass index; mMRC: modified Medical Research Council; SVC: slow vital capacity; FRC: functional residual capacity; IC: inspiratory capacity; sGaw: specific airway conductance; and FRV: forced residual volume. ^aValues expressed as n (%), mean ± SD, or median [minimum-maximum]. *Student's t-test. **Mann-Whitney U test.

Table 2. Agreement between the spirometry results obtained with FVC maneuvers alone and those obtained with FVC
and slow vital capacity maneuvers in combination. ^{a,b}

Functional diagnosis		FVC + SVC maneuvers			Total	kappa	р	
		Normal	OLD	OLD with reduced VC	NLD			
	Normal	52	21	0	0	73		
	OLD	0	54	0	0	54	0 (52	. 0. 001
FVC maneuvers	OLD with reduced FVC	0	8	20	0	28	0.653	< 0.001
	NLD	4	8	5	15	32		
	Total	56	91	25	15	187		

SVC: slow vital capacity; OLD: obstructive lung disease; and NLD: nonspecific lung disease. ^aValues expressed as n. ^bValues in bold indicate diagnoses that were the same regardless of the diagnostic method used.

≥ 200 group than in the Δ SVC-FVC < 200 group (p = 0.04), as assessed by the aforementioned respiratory questionnaire.⁽¹¹⁾ Of the 17 participants with a history of tuberculosis, only 1 was in the Δ SVC-FVC ≥ 200 group (p = 0.011). There were no significant differences between the two groups regarding clinical diagnosis (Table 3).

The use of Pearson's or Spearman's correlation coefficient (data not shown) showed that Δ SVC-FVC correlated positively with height, FVC (L), SVC (L), SVC (% predicted), IC (L), TLC (L), and FRV (% predicted), as well as correlating negatively with FEV₁/(F)VC, RV (% predicted), and RV/TLC.



Table 3. Clinical diagnoses based on a < 200 mL difference between slow VC and FVC in comparison with those based on a \ge 200 mL difference between slow VC and FVC.

Diagnosis	ΔSVC-FVC < 200 mL (n = 126)		$\Delta SVC-FVC \ge 200 \text{ mL}$ $(n = 61)$		p*
	n	%	n	%	
Unknown	33	26.20	16	26.23	0.566
Asthma	31	24.40	14	23.00	
COPD	15	11.80	10	16.40	
ILD	17	13.40	7	11.50	
Rhinitis	6	4.70	1	1.60	
Bronchiolitis	7	5.50	3	4.90	
Asthma + other	5	3.90	1	1.60	
COPD + other	0	0.00	2	3.30	
Other	12	9.40	7	11.50	

 Δ SVC-FVC: difference between slow VC and FVC; and ILD: interstitial lung disease. *Fisher's exact test.

Table 4. Evaluation of demographic parameters (initial model) and functional parameters (final model) predicting $a \ge 200 \text{ mL}$ difference between slow VC and FVC by logistic regression.

Initial model					
Demographic parameter	OR (95% CI)	р			
Age, years	1.348 (0.501-3.629)	0.554			
Female sex	0.774 (0.318-1.883)	0.572			
Height, cm	1.016 (0.947-1.090)	0.655			
Weight, kg	1.036 (0.983-1.091)	0.183			
BMI, kg/m ²	1.038 (0.887-1.215)	0.644			
BMI > 30 kg/m ²	5.075 (1.583-16.270)	0.006			
	Final model				
Functional parameter	Crude OR (95% CI)	Adjusted OR (95% CI)			
FVC, L	1.425 (1.015-2.002)	1.020 (0.687-1.513)			
FVC, % predicted	0.996 (0.979-1.014)	0.992 (0.974-1.011)			
FEV ₁ , L	1.190 (0.782-1.812)	0.711 (0.426-1.188)			
FEV ₁ , % predicted	0.987 (0.971-1.003)	0.980 (0.962-0.998)			
FEV ₁ /FVC	0.967 (0.940-0.994)	0.952 (0.922-0.983)			
SVC, L	1.831 (1.296-2.586)	1.399 (0.951-2.058)			
SVC, % predicted	1.019 (1.000-1.038)	1.018 (0.997-1.038)			
IC, L	1.695 (1.035-2.776)	1.014 (0.557-1.845)			
FEV ₁ /SVC	0.931 (0.902-0.960)	0.908 (0.875-0.943)			
TLC, L	1.492 (1.156-1.924)	1.282 (0.895-1.685)			
TLC, % predicted	1.008 (0.989-1.027)	1.016 (0.995-1.037)			
RV, L	1.188 (0.811-1.742)	1.201 (0.806-1.790)			
RV, % predicted	0.997 (0.990-1.004)	1.002 (0.994-1.009)			
RV/TLC	0.099 (0.007-1.400)	0.561 (0.030-10.561)			
FRC, L	1.614 (1.155-2.255)	1.532 (1.063-2.808)			
sGaw, cmH ₂ O/L/s	0.143 (0.003-8.005)	0.032 (0.000-3.000)			
IC/TLC	0.988 (0.955-1.022)	0.956 (0.917-0.998)			
FRV, L	1.692 (1.142-2.505)	1.697 (1.119-2.572)			
FRV, % predicted	1.007 (1.000-1.015)	1.000 (0.992-1.009)			
OLD _{FVC}	1.677 (0.906-3.107)	1.879 (0.948-3.723)			
OLD _{svc}	5.597 (2.543-12.322)	9.444 (3.708-24.049)			
OLD _{PLET}	2.250 (1.151-4.397)	3.225 (1.497-6.948)			

BMI: body mass index; SVC: slow vital capacity; IC: inspiratory capacity; FRC: functional residual capacity; sGaw: specific airway conductance; FRV: forced residual volume; OLD: obstructive lung disease; PLET: plethysmography.

As can be seen in Table 4, binomial logistic regression showed that weight and BMI > 30 kg/m² were predictors of a Δ SVC-FVC \geq 200 mL (p < 0.20). Crude and adjusted ORs were calculated for weight and BMI >

30 kg/m² by means of a logistic regression analysis to evaluate spirometric and plethysmographic parameters. Reduced FEV₁ (% predicted), FEV₁/FVC, FEV₁/SVC, and IC/TLC, as well as increased FRC (L) and FRV (L),



Table 5. Multiple logistic regression	analysis of bronchodilator	response for $a \ge 20$	00 mL difference between slo	ow VC
and FVC. ^a				

Parameter	OR	95% CI	Pseudo r ²	р
FEV ₁	4.38	1.45-13.26	0.112	0.009
FVC	3.83	1.26-11.71	0.090	0.018
SVC	0.63	0.38-4.91	0.040	0.630
IC	2.14	0.53-8.64	0.018	0.284
Any parameter responding positively	4.74	1.65-13.56	0.136	0.040

SVC: slow vital capacity; and IC: inspiratory capacity. ^aIn comparison with a < 200 mL difference.

were independent predictors of a Δ SVC-FVC \geq 200 mL. Increased SVC, IC, and TLC were associated with a Δ SVC-FVC \geq 200 mL, albeit only in the crude model. OLD (characterized by reduced FEV₁/SVC, reduced sGaw, or a combination of the two) was independently associated with a Δ SVC-FVC \geq 200 mL.

As can be seen in Table 5, our multiple logistic regression model showed that individuals with a Δ SVC-FVC \geq 200 mL were more likely to show a significant change in FEV₁ (OR = 4.38; 95% CI: 1.45-13.26) and FVC (OR = 3.83; 95% CI: 1.26-11.71) than were those with a Δ SVC-FVC < 200 mL. However, in cases in which spirometry results were indicative of NLD or of OLD with reduced FVC and a significant bronchodilator response, a Δ SVC-FVC \geq 200 mL failed to predict normal TLC (OR = 1.705; 95% CI: 0.333-8.721).

DISCUSSION

The use of SVC and FEV₁/SVC in the present study reduced the prevalence of NLD and of normal spirometry results by revealing airflow obstruction that can go unnoticed when only FVC and FEV₁/FVC are analyzed. Reductions in percent predicted FEV₁ and in FEV₁/(F) VC, as well as the presence of OLD, together with findings suggestive of air trapping (increased FRC and reduced IC/TLC),⁽²⁴⁾ were factors independently associated with a Δ SVC-FVC \geq 200 mL. A significant bronchodilator response was more likely to occur in cases in which the Δ SVC-FVC was \geq 200 mL.

In the present study, the spirometry results obtained with the combined use of FVC and SVC maneuvers changed the functional diagnosis that had been established with the use of FVC maneuvers alone. Of the 73 patients whose spirometry results were normal when FVC maneuvers were used in isolation, 21 were diagnosed with OLD when FVC and SVC maneuvers were used in combination. It has been reported that the prevalence of COPD in patients with mild disease is higher when assessed by FEV,/SVC than when assessed by FEV,/FVC.⁽²⁵⁾ Therefore, the FEV,/SVC ratio plays an important role in revealing airflow limitation in smokers with respiratory symptoms and impaired quality of life presenting with normal FEV,/FVC, thus contributing to an early diagnosis of COPD. However, in the present study, a Δ SVC-FVC \geq 200 mL was found to be independent of the severity of OLD, a finding that is inconsistent with those of other studies.^(4,5)

The use of SVC maneuvers in combination with FVC maneuvers changed the results of spirometry in 8 of

28 cases of OLD with reduced FVC (those 8 being reclassified as cases of OLD) and in 12 of 32 cases of NLD (those 12 being reclassified as normal cases [n = 4] or as cases of OLD [n = 8]). VC accounts for approximately 75% of TLC.⁽¹⁹⁾ A finding of normal SVC is important because it can prevent the need for plethysmography in selected cases (given the difficulty of access to the test and the associated health care costs), especially in those in which a diagnosis of restrictive lung disease is less likely. However, a ΔSVC-FVC ≥ 200 mL failed to predict normal TLC in our sample.

In our initial logistic regression model, weight and a BMI > 30 kg/m² were predictors of a Δ SVC-FVC \geq 200 mL. The association between weight and Δ SVC-FVC might be due to premature airway closure, given that there was no association with sGaw. Data from a large study suggest that Δ SVC-FVC is proportional to the increase in BMI, suggesting that obesity reduces FVC more than it does SVC; in contrast, in individuals with normal BMI and without OLD, SVC can be lower than FVC.⁽¹⁰⁾

Wang et al.⁽²⁶⁾ divided their study sample into two groups, namely those with SVC = FVC and those with SVC > FVC, and found that 65% of the sample had SVC > FVC, a finding that was more common in older individuals. In the present study, age was not associated with Δ SVC-FVC; however, the mean age of our sample was considerably high (i.e., 59 years), and it was impossible to establish a comparison with younger individuals.

Lung volumes (TLC, FRC, SVC, and IC) were predictors of a Δ SVC-FVC \geq 200 mL, although only in the crude logistic regression analysis. Markers of airflow limitation (reduced FEV₁/FVC and FEV₁/SVC) and findings of air trapping (such as increased FRC and reduced IC/TLC)⁽²⁴⁾ were independent predictors of a Δ SVC-FVC \geq 200 mL.

The magnitude of Δ SVC-FVC correlated negatively with RV and positively with FRV. This was confirmed by our logistic regression model, in which FRV (although not RV) was independently associated with the probability of a Δ SVC-FVC \geq 200 mL. This might be due to the fact that measured VC is higher during a SVC maneuver because of reduced thoracic gas compression, leading to reduced RV if we assume that TLC remains unchanged. Conversely, during a FVC maneuver, increased thoracic gas compression can result in airflow limitation, leading to reduced FVC and, consequently, increased FRV. Multiple logistic regression analysis showed that improvements in FEV₁ and FVC after bronchodilator administration were more common in the Δ SVC-FVC \geq 200 group than in the Δ SVC-FVC < 200 group. This raises the question of whether significant or nonsignificant bronchodilator response can differentiate between true obstruction and a variant of normality, respectively, in individuals with an isolated finding of Δ SVC-FVC \geq 200 mL. In the present study, no association was found between Δ SVC-FVC and OLD or restrictive lung disease/NLD.

The present study has some limitations. Strict inclusion criteria resulted in a limited sample size. In addition, there was no control group (comprising healthy

individuals); most of the study sample consisted of diseased individuals.

Future studies should determine whether Δ SVC-FVC can predict exercise-induced hyperinflation and its association with the small airways (as assessed by imaging and biochemistry).

In conclusion, the use of an SVC maneuver appears to reduce the prevalence of NLD. Although it is possible that ΔSVC -FVC is due to airflow limitation and air trapping, it might be due to dynamic compression of the airways during exercise. Individuals with a ΔSVC -FVC \geq 200 mL are more likely to have a significant bronchodilator response.

REFERENCES

- Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26(5):948-68. https://doi.org/10.1183/09031936.05.00035205
- Klingele TG, Staub NC. Alveolar shape changes with volume in isolated, air-filled lobes of cat lung. J Appl Physiol. 1970;28(4):411-4. https://doi.org/10.1152/jappl.1970.28.4.411
- Leith DE, Mead J. Mechanisms determining residual volume of the lungs in normal subjects. J Appl Physiol. 1967;23(2):221-7. https:// doi.org/10.1152/jappl.1967.23.2.221
- Chhabra SK. Forced vital capacity, slow vital capacity, or inspiratory vital capacity: which is the best measure of vital capacity? J Asthma. 1998;35(4):361-5. https://doi.org/10.3109/02770909809075669
- Brusasco V, Pellegrino R, Rodarte JR. Vital capacities in acute and chronic airway obstruction: dependence on flow and volume histories. Eur Respir J. 1997;10(6):1316-20. https://doi.org/10.1183/ 09031936.97.10061316
- Sutherland PW, Katsura T, Milic-Emili J. Previous volume history of the lung and regional distribution of gas. J Appl Physiol. 1968;25(5):566-74. https://doi.org/10.1152/jappl.1968.25.5.566
- Chan ED, Irvin CG. The detection of collapsible airways contributing to airflow limitation. Chest. 1995;107(3):856-9. https://doi.org/10.1378/ chest.107.3.856
- von Westernhagen F, Smidt U. The significance of the difference between slow inspiratory and forced expiratory vital capacity. Lung. 1978;154(4):289-97. https://doi.org/10.1007/BF02713545
- Barros AR, Pires MB, Raposo NM. Importance of slow vital capacity in the detection of airway obstruction. J Bras Pneumol. 2013;39(3):317-22. https://doi.org/10.1590/S1806-37132013000300008
- Fortis S, Corazalla EO, Wang Q, Kim HJ. The difference between slow and forced vital capacity increases with increasing body mass index: a paradoxical difference in low and normal body mass indices. Respir Care. 2015;60(1):113-8. https://doi.org/10.4187/respcare.03403
- Aguiar VA, Beppu OS, Romaldini H, Ratto OR, Nakatani J. Validity of a respiratory modified questionnaire (ATS-DLS-78) as a tool of an epidemiologic study in Brazil [Article in Portuguese]. J Pneumol. 1988;14(3):111-6.
- Pereira CA, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. J Bras Pneumol. 2007;33(4):397-406. https://doi.org/10.1590/S1806-37132007000400008
- Neder JA, Andreoni S, Castelo-Filho A, Nery LE. Reference values for lung function tests. I. Static volumes. Braz J Med Biol Res. 1999;32(6):703-17. https://doi.org/10.1590/S0100-879X1999000600006
- Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):319-38.

https://doi.org/10.1183/09031936.05.00034805

- Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. Standardisation of the measurement of lung volumes. Eur Respir J. 2005;26(3):511-22. https://doi.org/10.1183/09031936.05.0 0035005
- Sociedade Brasileira de Pneumologia e Tisiologia. Diretrizes para testes de função pulmonar. J Pneumol. 2002;28(Suppl 3):S1-S82.
- Pereira CA, Moreira MA. Pletismografia resistência das vias aéreas. In: Diretrizes para Testes de Função Pulmonar. J Pneumol. 2002;28(Suppl 3):S39-S54.
- Viljanen AA, Viljanen BC, Halttunen PK, Kreus KE. Body plethysmographic studies in non-smoking, healthy adults. Scand J Clin Lab Invest Suppl. 1982;159:35-50. https://doi. org/10.1080/00365518209168379
- Pereira CAC, Rodrigues SCS. Bases da Interpretação. In: Salge JM, Izbicki M, Rodrigues SCS, Rodrigues Junior R, editors. Série Atualização e Reciclagem em Pneumologia - SPPT: Função Pulmonar. 1st ed. São Paulo: Atheneu, 2012. p. 13-44.
- Golshan M, Amra B, Soltani F, Crapo RO. Reference values for lung volumes in an Iranian population: introducing a new equation model. Arch Iran Med. 2009;12(3):256-61.
- Esteban C, Quintana JM, Egurrola M, Moraza J, Aburto M, Pérez-Izquierdo J, et al. Classifying the severity of COPD: are the new severity scales better than the old? Int J Tuberc Lung Dis. 2009;13(6):783-90.
- Soares AL, Pereira CA, Rodrigues SC. Spirometric changes in obstructive disease: after all, how much is significant? J Bras Pneumol. 2013;39(1):56-62. https://doi.org/10.1590/S1806-37132013000100008
- Pistelli F, Bottai M, Viegi G, Di Pede F, Carrozzi L, Baldacci S, et al. Smooth reference equations for slow vital capacity and flow-volume curve indexes. Am J Respir Crit Care Med. 2000;161(3 Pt 1):899-905. https://doi.org/10.1164/ajrccm.161.3.9906006
- Zeng S, Tham A, Bos B, Jin J, Giang B, Arjomandi M. Lung volume indices predict morbidity in smokers with preserved spirometry. Thorax. 2019;74(2):114-124. https://doi.org/10.1136/ thoraxjnl-2018-211881
- Torén K, Olin AC, Lindberg A, Vikgren J, Schiöler L, Brandberg J, et al. Vital capacity and COPD: the Swedish CArdioPulmonary bioImage Study (SCAPIS). Int J Chron Obstruct Pulmon Dis. 2016;11:927-33. https://doi.org/10.2147/COPD.S104644
- Wang W, Ma D, Li T, Ying Y, Xiao W. People with older age and lower FEV1% pred tend to have a smaller FVC than VC in pre-bronchodilator spirometry. Respir Physiol Neurobiol. 2014;194:1-5. https://doi. org/10.1016/j.resp.2014.01.003