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ORIGINAL RESEARCH

Use of the forced-oscillation technique to estimate spirometry values

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Purpose: Spirometry is sometimes difficult to perform in elderly patients and in those with severe respiratory distress. The forced-oscillation technique (FOT) is a simple and noninvasive method of measuring respiratory impedance. The aim of this study was to determine if FOT data reflect spirometric indices.

Patients and methods: Patients underwent both FOT and spirometry procedures prior to inclusion in development (n=1,089) and validation (n=552) studies. Multivariate linear regression analysis was performed to identify FOT parameters predictive of vital capacity (VC), forced VC (FVC), and forced expiratory volume in 1 second (FEV_1). A regression equation was used to calculate estimated VC, FVC, and FEV_1. We then determined whether the estimated data reflected spirometric indices. Agreement between actual and estimated spirometry data was assessed by Bland–Altman analysis.

Results: Significant correlations were observed between actual and estimated VC, FVC, and FEV_1 values (all $r>0.8$ and $P<0.001$). These results were deemed robust by a separate validation study (all $r>0.8$ and $P<0.001$). Bias between the actual data and estimated data for VC, FVC, and FEV_1 in the development study was 0.007 L (95% limits of agreement [LOA] 0.907 and −0.893 L), −0.064 L (95% LOA 0.843 and −0.971 L), and −0.039 L (95% LOA 0.735 and −0.814 L), respectively. On the other hand, bias between the actual data and estimated data for VC, FVC, and FEV_1 in the validation study was −0.201 L (95% LOA 0.62 and −1.022 L), −0.262 L (95% LOA 0.582 and −1.106 L), and −0.174 L (95% LOA 0.576 and −0.923 L), respectively, suggesting that the estimated data in the validation study did not have high accuracy.

Conclusion: Further studies are needed to generate more accurate regression equations for spirometric indices based on FOT measurements.

Keywords: forced expiratory volume in 1 second, forced-oscillation technique, forced vital capacity, spirometry, vital capacity

Introduction

Pulmonary function testing is used to evaluate respiratory mechanics and physiology in children and adults suspected of having respiratory disease. Spirometry is the most commonly used pulmonary function test and has the advantage of being readily available in both inpatient and outpatient settings. Diagnosis of COPD requires spirometry. Spirometry can be used to evaluate other obstructive pulmonary diseases, including asthma and restrictive pulmonary disease, such as interstitial lung disease (ILD). Unfortunately, spirometry can sometimes be difficult to perform in elderly and/or cognitively impaired patients and those with severe respiratory distress, because it requires maximum effort during forced expiratory maneuvers.[1] Therefore, there is a need for physiologically accurate and easily performed methods of assessment of pulmonary mechanics in these patient populations.

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The forced-oscillation technique (FOT) is a simple, non-invasive procedure that measures respiratory impedance.[2] Because FOT does not require the forced expiratory maneuvers needed to generate spirometry data, it can be performed easily in pediatric patients[3,4] and adults who are unable to perform spirometry.[2,5] It has been reported that FOT measurements may be more sensitive than forced expiratory volume in 1 second (FEV_1) for measuring the effects of bronchodilator drugs in patients with COPD and asthma.[6–8] Further, FOT measurements have been used to assess abnormal function in the distal airway, even in the setting of normal spirometry.[9,10] Finally, it has been reported that breath changes in reactance at 5 Hz (X5) might be associated with severity of ILD and physiologic abnormality.[11]

Although several reports have analyzed the value of FOT in assessment of pulmonary disease, it remains unclear whether FOT measurements can predict specific spirometric indices, such as vital capacity (VC), forced VC (FVC), and FEV_1. Previous reports have shown significant correlations between spirometric indices and FOT measurements in patients with asthma,[12] COPD,[13] and ILD.[11,14] However, the correlation coefficients were relatively low, and each report included only a small number of patients.

The aim of the present study was to evaluate the relationship between FOT measurements and spirometry data in both healthy subjects and patients with various respiratory diseases. To this end, we generated regression equations for VC, FVC, and FEV_1 based on FOT measurements and used them to calculate estimated VC, FVC, and FEV_1 values. We then determined whether the estimated data reflected spirometric indices.

Patients and methods

Study population

The development data set consisted of 1,708 consecutive patients who simultaneously underwent FOT measurements and spirometry at Ehime University Hospital between January 1, 2010 and December 31, 2015. The validation data set consisted of 1,287 subjects who simultaneously underwent FOT measurements and spirometry at Sumitomo Besshi Hospital between April 1, 2013 and March 31, 2016. FOT measurements had been performed routinely to some degree in patients who visited the respiratory division of each of the participating institutions.

Subjects were excluded if they were unable to perform spirometry at the time of the FOT measurements, if they were aged younger than 17 years, or if they were not Japanese. Subjects whose spirometry performance did not meet American Thoracic Society (ATS)/European Respiratory Society (ERS) spirometry criteria[15] were also excluded.

The study protocol was approved by the ethical committees of Ehime University Hospital and Sumitomo Besshi Hospital. The need for patient consent was waived, in view of the retrospective nature of the study. Our manuscript data was deidentified, and did not require patient consent to review.

Forced oscillometry

Respiratory impedance was measured using a commercially available multifrequency FOT device (MostGraph-01; Chest MI, Tokyo, Japan) as previously reported[12–14] and following standard recommendations.[16,17] Briefly, oscillatory signals generated by a loudspeaker at 0.25-second intervals were applied to the respiratory system through a mouthpiece during tidal breathing at rest. Mouth pressure and flow signals were measured, and the values of resistance and reactance to the oscillatory frequency were obtained. During the procedure, the subjects used a nose clip with the cheeks firmly supported while sitting with the neck in a comfortable, neutral posture. We measured resistance at 5 Hz (R5), resistance at 20 Hz (R20), X5, and resonant frequency (Fres) where the reactance crossed zero and the elastic and inertial forces were equal in magnitude and opposite in direction. The low-frequency reactance area (ALX), which is the integral of reactance from R5 to Fres, was also measured. Each oscillatory index was expressed in the whole-breath, inspiratory, and expiratory phases. The oscillatory index in the whole-breath phase was used. FOT was performed prior to spirometry.

Spirometry

Spirometry was performed according to the method described in the ATS/ERS guidelines.[15] Pulmonary function indices, including VC, FVC, and FEV_1, were measured by spirometry. The indices were calculated as percentages of predicted normal values. Predicted normal values for VC, FVC, and FEV_1 were calculated using the equation devised by the Japanese Respiratory Society, as previously reported.[18]

Definition

All patients with ILD were diagnosed in accordance with the clinical criteria established by the current ATS/ERS guidelines.[19] Diagnoses of asthma were based on clinical history and historical evidence of reversible airway obstruction. COPD and chronic bronchitis were diagnosed according to Global Initiative for Obstructive Lung Disease criteria.[20] Acute bronchitis was diagnosed based on a previously reported definition.[21] Diagnosis of sarcoidosis was based

on clinical findings and histologic evidence of noncaseating epithelioid cell granuloma after excluding known causes of granulomatous disease according to the ATS/ERS/World Association of Sarcoidosis and Other Granulomatous Disorders guidelines.[22]

Calculation of estimated VC, FVC, and FEV_1

In the development study, we identified parameters predictive of VC, FVC, and FEV_1 using anthropometric variables (age, sex, height, body weight) with and without FOT indices. Using the results, we determined two types of regression equations and calculated the estimated VC, FVC, and FEV_1.

Equation 1 for estimated VC, FVC, and FEV_1 was: L = numeric constant + age × (regression coefficient of age) + sex (1 if female, 2 if male) × (regression coefficient of sex) + height (cm) × (regression coefficient of height) + body weight (kg) × (regression coefficient of body weight).

Equation 2 for estimated VC, FVC, and FEV_1 was: L = numeric constant + age × (regression coefficient of age) + sex (1 if female, 2 if male) × (regression coefficient of sex) + height (cm) × (regression coefficient of height) + body weight (kg) × (regression coefficient of body weight) + R5 × (regression coefficient of R5) + R20 × (regression coefficient of R20) + X5 × (regression coefficient of X5) + Fres × (regression coefficient of Fres) + ALX × (regression coefficient of ALX).

In this analysis, we generated equations for VC, FVC, and FEV_1 including all predictive variables uniformly (equation 1 for all anthropometric variables and equation 2 for all anthropometric variables and FOT indices), whether these variables were statistically significant predictors or not.

Validation study

Using a separate validation data set (obtained from Sumitomo Besshi Hospital), we sought correlations between spirometry and MostGraph-01 data. In addition, the equations derived from the development study were evaluated by determining the correlation coefficients between the actual and estimated data.

Statistical analysis

Results are reported as mean ± SD. Correlations between variables were determined using Pearson's correlation coefficient. Correlation statistics were interpreted as slight (<0.2), fair (0.2–0.4), moderate (0.4–0.6), substantial (0.6–0.8), or almost perfect (>0.8) agreement.[23] Multivariate linear regression analysis was used to identify parameters predictive of VC, FVC, and FEV_1, with age, sex, height, body weight, R5, R20, X5, Fres, and ALX included as independent variables. The bias of the equations was expressed as the mean difference between the estimated data and the actual data (estimated data – actual data). The root-mean-square-error (RMSE) was calculated as the square root of (sum of squared errors of the estimate/n). The agreement between the equations was evaluated by Bland–Altman plots using 95% limits of agreement (LOA), which were calculated as average difference ± two SDs. The 95% CIs were computed for all variables. All tests were two-tailed, and a P-value <0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS version 22 for Windows (IBM, Armonk, NY, Japan).

Results

Clinical characteristics of patients in the development study

Of the 1,708 subjects identified, 1,608 underwent spirometry at the same time as MostGraph-01 examination. a total of 502 subjects with suboptimal spirometry data, 13 aged younger than 17 years, and four who were not Japanese were excluded, leaving data from 1,089 subjects (615 male, 474 female) for inclusion in the final analysis (Figure 1). The characteristics of the study subjects are presented in Table 1. The majority of patients in the development study had malignant lung tumors, asthma, COPD, or ILD.

Correlations between spirometry and MostGraph-01 data in the development study

Statistically significant correlations were observed between most spirometry and MostGraph-01 parameters (Table 2). However, FEV_1/FVC showed modest correlations with all MostGraph-01 parameters. R5 and R20 showed fair or moderate correlations with VC, %VC, FVC, %FVC, FEV_1, and $\%FEV_1$. X5, Fres, and ALX demonstrated moderate or substantial correlations with VC, %VC, FVC, %FVC, FEV_1, and $\%FEV_1$.

Calculation of estimated VC, FVC, and FEV_1

We identified parameters predictive of VC, FVC, or FEV_1, with age, sex, height, and body weight with and without FOT parameters as independent variables. Multivariate linear regression analysis using only anthropometric variables showed that almost all parameters correlated significantly

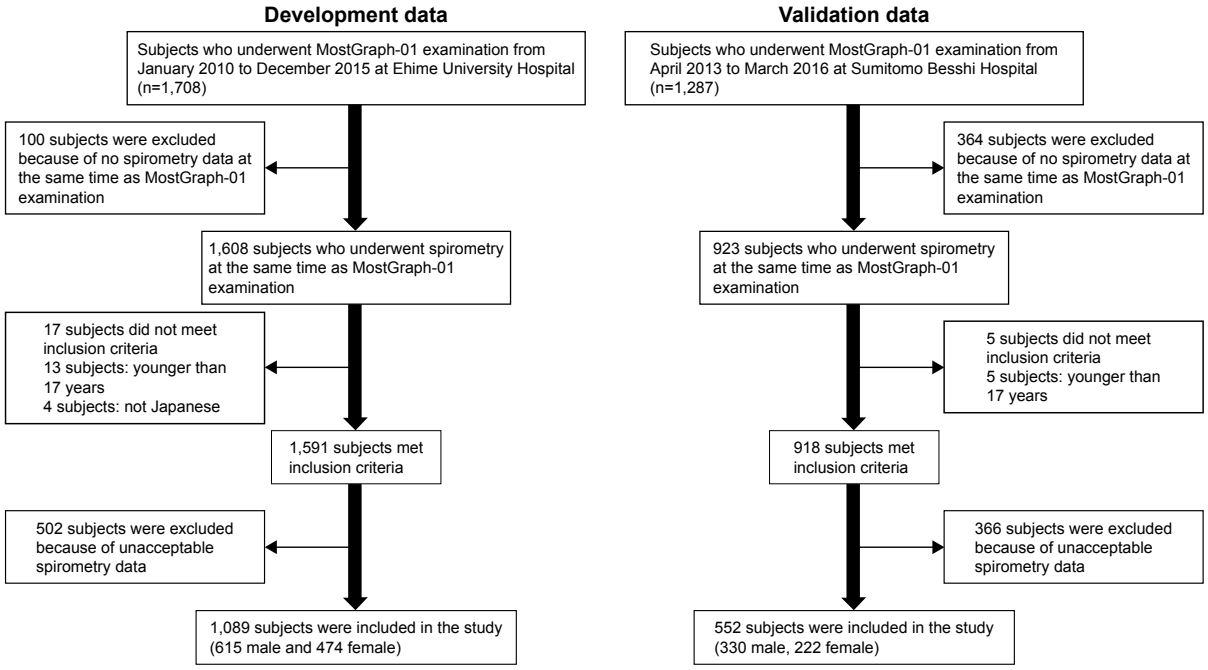

Figure 1 Recruitment flowchart for study participants.

with VC, FVC, and FEV_1, with the exception of body weight with FVC and FEV_1. Multivariate analysis including the FOT parameters also showed that almost all parameters correlated significantly with VC, FVC, and FEV_1, with the exception of X5 and FEV_1 (Tables 3–5). Based on these results, we generated regression equations, and calculated the estimated VC, FVC, and FEV_1:

Equation 1

$$\text{Estimated VC} = -4.003 - \text{age} \times 0.020 + \text{sex} \times 0.382 + \text{height} \times 0.047 + \text{weight} \times 0.004$$

$$\text{Estimated FVC} = -4.060 - \text{age} \times 0.021 + \text{sex} \times 0.371 + \text{height} \times 0.048 + \text{weight} \times 0.003$$

$$\text{Estimated FEV}_1 = -1.413 - \text{age} \times 0.026 + \text{sex} \times 0.207 + \text{height} \times 0.030 + \text{weight} \times 0.001$$

Equation 2

$$\text{Estimated VC} = -0.011 - \text{age} \times 0.015 + \text{sex} \times 0.539 + \text{height} \times 0.026 + \text{weight} \times 0.007 + \text{R5} \times 0.268 - \text{R20} \times 0.388 + \text{X5} \times 0.365 - \text{Fres} \times 0.149 + \text{ALX} \times 0.062$$

$$\text{Estimated FVC} = 0.112 - \text{age} \times 0.016 + \text{sex} \times 0.526 + \text{height} \times 0.026 + \text{weight} \times 0.006 + \text{R5} \times 0.269 - \text{R20} \times 0.403 + \text{X5} \times 0.325 - \text{Fres} \times 0.154 + \text{ALX} \times 0.058$$

$$\text{Estimated FEV}_1 = 2.410 - \text{age} \times 0.021 + \text{sex} \times 0.318 + \text{height} \times 0.011 + \text{weight} \times 0.004 + \text{R5} \times 0.157 - \text{R20} \times 0.306 + \text{X5} \times 0.012 - \text{Fres} \times 0.135 + \text{ALX} \times 0.022$$

Correlations between actual and estimated VC, FVC, and FEV_1

We observed statistically significant correlations between actual and estimated VC, FVC, and FEV_1 in the analyses using equations 1 and 2 (all $P<0.001$; Figure 2A–F; Table 6). Estimated VC, FVC, and FEV_1 derived from equation 2 demonstrated almost perfect correlation with actual VC (r=0.867), FVC (r=0.867), and FEV_1 (r=0.857), while estimated VC, FVC, and FEV_1 derived from equation 1 demonstrated substantial correlation with actual VC (r=0.745), FVC (r=0.741), and FEV_1 (r=0.711). In addition, estimated VC, FVC, and FEV_1 using equation 2 had smaller RMSE values than those obtained using equation 1. The Bland–Altman plots are shown in Figure 3. The bias of equation 1 was 0.075 L for VC, 0.058 L for FVC, and −0.095 L for FEV_1. The 95% LOAs for equation 1 were 1.279 and −1.129 L for VC, 1.281 and −1.166 L for FVC, and 0.963 and −1.152 L for FEV_1. In contrast, the bias of equation 2 was 0.007 L for VC, −0.064 L for FVC, and −0.039 L for FEV_1. The 95% LOAs for equation 2 were 0.907 and −0.893 L for VC, 0.843 and −0.971 L for FVC, and 0.735 and −0.814 L for FEV_1.

Table 1 Characteristics of study subjects. Results reported as mean ± SD

Parameters	Development data	Validation data
Subjects, n	1,089	552
Sex, n, male/female	615/474	330/222
Age, years	63±15	58±18
Height (cm)	160.4±8.9	162.2±8
Body weight (kg)	58.9±11.9	60.5±11.7
Smoking (never/current/past/unknown)	420/153/449/67	216/83/180/73
Diagnosis, n		
Normal	73	31
Malignant lung tumors	381	30
Asthma	202	202
COPD	170	79
ILD	156	38
Bronchitis (acute or chronic)	53	100
Mediastinal tumor	52	0
Sarcoidosis	36	2
Pleural or chest-wall disease	21	6
Mycosis	10	4
Tbc or old Tbc	13	5
NTM	11	3
Other	51	87
Pulmonary function tests		
VC (L)	3.03±0.9	3.15±0.9
%VC (%)	90.2±18.3	88.9±17
FVC (L)	3.02±0.91	3.12±0.92
%FVC (%)	93.2±19.3	91.4±18.2
FEV_1 (L)	2.24±0.75	2.35±0.85
$\%FEV_1$ (%)	87.6±21.6	85.4±22.2
FEV_1/FVC	0.74±0.12	0.74±0.12
MostGraph-01 data		
R5	3.58±1.42	3.09±1.22
R20	2.93±1.04	2.40±0.91
X5	−0.64±0.9	−1.05±1.18
Fres	8.31±3.75	10.63±4.28
ALX	3.56±7.36	6.31±9.61

Abbreviations: ALX, low-frequency reactance area; FEV_1, forced expiratory volume in 1 second; Fres, resonant frequency; FVC, forced vital capacity; ILD, interstitial lung disease; NTM, nontuberculous mycobacteriosis; R5, resistance at 5 Hz; R20, resistance at 20 Hz; Tbc, tuberculosis; VC, vital capacity; X5, reactance at 5 Hz.

Validation study

Based on the development-study results, we evaluated the validity of equation 2 in the validation study. After exclusion of subjects with suboptimal spirometry data, the validation study comprised 552 subjects (330 male, 222 female; Figure 1). The characteristics of these patients are shown in Table 1.

There were statistically significant correlations between all spirometry and MostGraph-01 parameters (Table 2). FEV_1/FVC showed slight or moderate correlations with all MostGraph-01 parameters. R5 and R20 showed slight or fair correlations with VC, %VC, FVC, %FVC, FEV_1, and $\%FEV_1$. X5, Fres, and ALX demonstrated moderate or substantial correlations with VC, %VC, FVC, %FVC, FEV_1, and $\%FEV_1$.

Using equation 2 derived from the development data set, we calculated estimated VC, FVC, and FEV_1 for all patients in the validation data set, and assessed correlations between actual and estimated VC, FVC, and FEV_1 values. We observed statistically significant correlations between actual and estimated VC, FVC, and FEV_1 values (all $P<0.001$; Figure 2G–I, Table 6). Estimated VC, FVC, and FEV_1 demonstrated almost perfect correlation with actual VC ($r=0.891$), FVC ($r=0.889$), and FEV_1 ($r=0.897$). However, the bias between estimated and actual data for VC, FVC, and FEV_1 was −0.201 L, −0.262 L, and −0.174 L, respectively. The 95% LOAs were 0.62 and −1.022 L for VC, 0.582 and −1.106 L for FVC, and 0.576 and −0.923 L for FEV_1 (Figure 3).

Discussion

This study evaluated the hypothesis that FOT measurements correlate significantly with spirometry data. We used FOT

Table 2 Correlations between spirometry and MostGraph-01 data

Parameters	VC	%VC	FVC	%FVC	FEV_1	$\%FEV_1$	FEV_1/FVC
Development study							
R5	−0.525*	−0.377*	−0.537*	−0.399*	−0.543*	−0.418*	−0.16*
R20	−0.478*	−0.28*	−0.488*	−0.303*	−0.465*	−0.31*	−0.089
X5	0.489*	0.565*	0.499*	0.577*	0.548*	0.594*	0.26*
Fres	−0.551*	−0.647*	−0.562*	−0.657*	−0.622*	−0.677*	−0.286*
ALX	−0.402*	−0.489*	−0.413*	−0.504*	−0.473*	−0.544*	−0.284*
Validation study							
R5	−0.362*	−0.224*	−0.357*	−0.221*	−0.354*	−0.27*	−0.183*
R20	−0.337*	−0.186*	−0.33*	−0.178*	−0.329*	−0.23*	−0.176*
X5	0.544*	0.565*	0.557*	0.573*	0.602*	0.617*	0.423*
Fres	−0.633*	−0.682*	−0.648*	−0.689*	−0.716*	−0.746*	−0.509*
ALX	−0.497*	−0.525*	−0.511*	−0.535*	−0.565*	−0.591*	−0.435*

Note: *$P<0.001$.

Abbreviations: ALX, low-frequency reactance area; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; Fres, resonant frequency; R5, resistance at 5 Hz; R20, resistance at 20 Hz; X5, reactance at 5 Hz; VC, vital capacity.

Table 3 Regression coefficients for parameters predictive of vital capacity

Parameters	Unstandardized coefficients		95% CI		*P*-value
	β	SE	Low	High	
Anthropometric parameters only					
Age	–0.02	0.001	–0.023	–0.017	<0.001
Sex	0.382	0.056	0.273	0.491	<0.001
Height	0.047	0.003	0.040	0.053	<0.001
Body weight	0.004	0.002	0.00007	0.007	0.046
Anthropometric and FOT parameters					
Age	–0.015	0.001	–0.017	–0.013	<0.001
Sex	0.539	0.044	0.453	0.624	<0.001
Height	0.026	0.003	0.021	0.031	<0.001
Body weight	0.007	0.001	0.004	0.01	<0.001
R5	0.268	0.047	0.175	0.361	<0.001
R20	–0.388	0.058	–0.502	–0.273	<0.001
X5	0.365	0.093	0.183	0.547	<0.001
Fres	–0.149	0.012	–0.172	–0.126	<0.001
ALX	0.062	0.008	0.045	0.078	<0.001

Abbreviations: ALX, low-frequency reactance area; FOT, forced-oscillation technique; Fres, resonant frequency; R5, resistance at 5 Hz; R20, resistance at 20 Hz; SE, standard error; X5, reactance at 5 Hz.

Table 5 Regression coefficients for parameters predictive of forced expiratory volume in 1 second

Parameters	Unstandardized coefficients		95% CI		*P*-value
	β	SE	Low	High	
Anthropometric parameters only					
Age	–0.026	0.001	–0.028	–0.023	<0.001
Sex	0.207	0.049	0.111	0.303	<0.001
Height	0.03	0.003	0.024	0.036	<0.001
Body weight	0.001	0.002	–0.002	0.005	0.382
Anthropometric and FOT parameters					
Age	–0.021	0.001	–0.023	–0.019	<0.001
Sex	0.318	0.038	0.244	0.392	<0.001
Height	0.011	0.002	0.007	0.016	<0.001
Body weight	0.004	0.001	0.002	0.007	<0.05
R5	0.157	0.041	0.077	0.237	<0.001
R20	–0.306	0.05	–0.405	–0.208	<0.001
X5	0.012	0.08	–0.145	0.169	0.88
Fres	–0.135	0.01	–0.155	–0.115	<0.001
ALX	0.022	0.007	0.008	0.036	<0.05

Abbreviations: ALX, low-frequency reactance area; FOT, forced-oscillation technique; Fres, resonant frequency; R5, resistance at 5 Hz; R20, resistance at 20 Hz; SE, standard error; X5, reactance at 5 Hz.

measurements to develop regression equations to estimate VC, FVC, and FEV_1, and compared estimated values with spirometry values. Our results demonstrated that estimated VC, FVC, and FEV_1 correlated significantly with actual data in both the development and validation studies. However, the estimated data in the validation study still did not show high accuracy. To our knowledge, this is the first study of whether FOT indices predict spirometry parameters.

Table 4 Regression coefficients for parameters predictive of forced vital capacity

Parameters	Unstandardized coefficients		95% CI		*P*-value
	β	SE	Low	High	
Anthropometric parameters only					
Age	–0.021	0.001	–0.024	–0.018	<0.001
Sex	0.371	0.057	0.26	0.482	<0.001
Height	0.048	0.003	0.041	0.054	<0.001
Body weight	0.003	0.002	–0.001	0.007	0.148
Anthropometric and FOT parameters					
Age	–0.016	0.001	–0.018	–0.014	<0.001
Sex	0.526	0.044	0.44	0.613	<0.001
Height	0.026	0.003	0.021	0.032	<0.001
Body weight	0.006	0.001	0.003	0.009	<0.001
R5	0.269	0.048	0.175	0.363	<0.001
R20	–0.403	0.059	–0.518	–0.287	<0.001
X5	0.325	0.094	0.141	0.508	<0.05
Fres	–0.154	0.012	–0.178	–0.131	<0.001
ALX	0.058	0.008	0.042	0.075	<0.001

Abbreviations: ALX, low-frequency reactance area; FOT, forced-oscillation technique; Fres, resonant frequency; R5, resistance at 5 Hz; R20, resistance at 20 Hz; SE, standard error; X5, reactance at 5 Hz.

Previous reports have shown that some FOT parameters are associated with spirometry values. A significant correlation of $\%FEV_1$ and FEV_1/FVC values with R_{rs} and X_{rs} parameters has been demonstrated in patients with asthma.[12] In addition, significant correlations have been found between breath changes in X5 and %FVC, $\%FEV_1$, and FEV_1/FVC in patients with COPD.[13] In patients with ILD, it has been reported that X5, Fres, and ALX correlate with %FVC and $\%FEV_1$.[14] Sugiyama et al also reported a significant inverse correlation between breath changes in X5 and %VC.[11] However, correlation coefficients in these previous reports showed only fair–moderate agreement. Shirai and Kurosawa reported that FOT is not a surrogate test for spirometry, because the tests are not identical.[16] Consistently with previous reports, the present study demonstrated that most FOT indices are significantly correlated with spirometric indices, but the correlation is only fair–moderate. Therefore, other parameters that reflect spirometry more accurately are required.

In order to solve this problem, we generated regression equations to estimate VC, FVC, and FEV_1 based on FOT measurements. First, we compared the accuracy of an equation built on anthropometric values and FOT indices (equation 2) with that of an equation using anthropometric values alone (equation 1). Estimated VC, FVC, and FEV_1

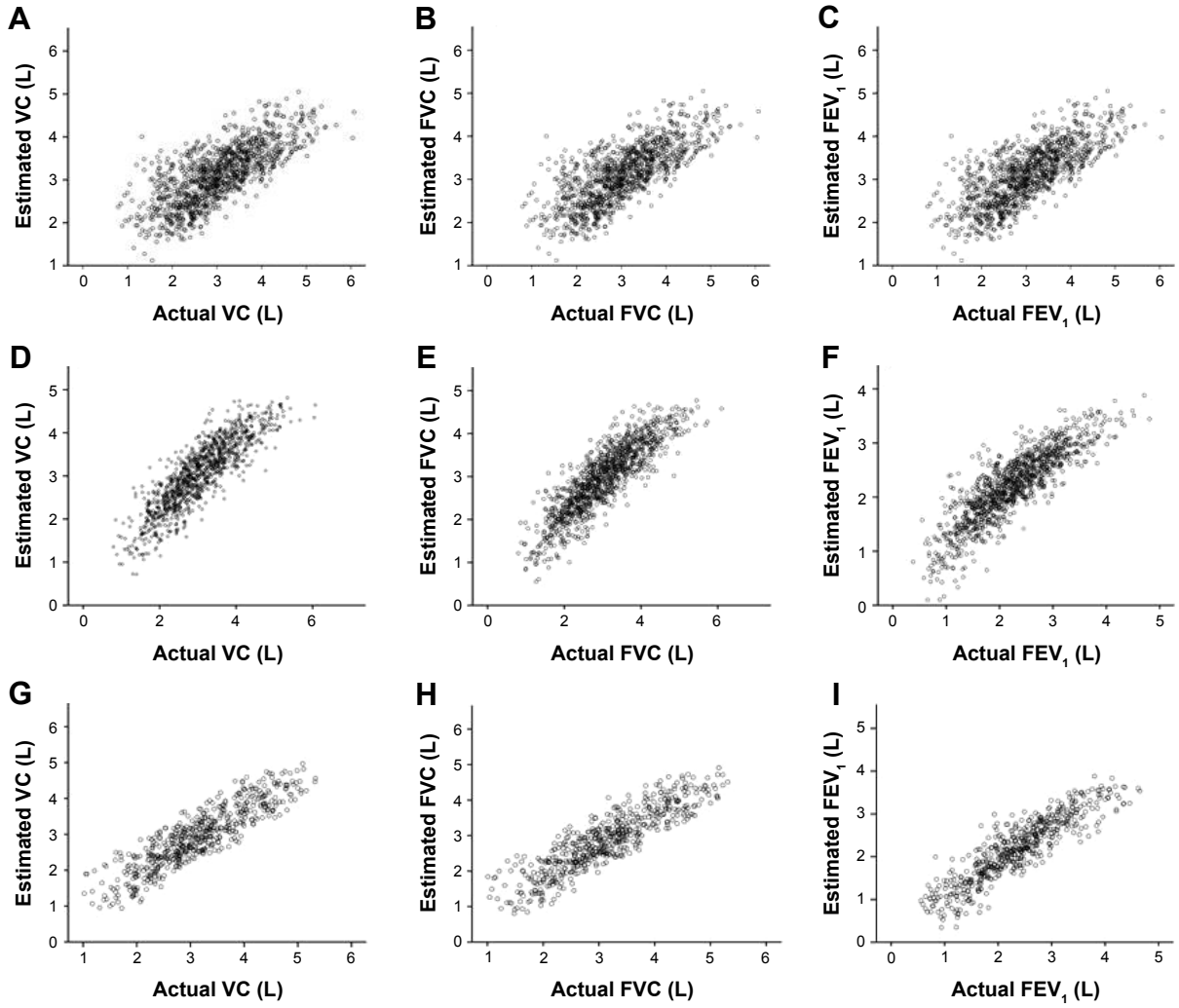

Figure 2 Correlations between actual and estimated VC, FVC, and FEV_1 in the development and validation study.
Notes: Estimated data obtained using equation 1 (**A**–**C**) and equation 2 (**D**–**F**) in the development study. Using equation 2, we calculated estimated data in the validation data set (**G**–**I**).
Abbreviations: VC, vital capacity; FVC, forced VC; FEV_1, forced expiratory volume in 1 second.

Table 6 Correlations between actual and estimated data, and performance of estimation equations

	r (95% CI)	*P*-value	Bias (95% CI)	RMSE
Development study				
Equation 1				
VC	0.745 (0.717–0.77)	<0.001	0.075 (0.039–0.111)	0.606
FVC	0.741 (0.713–0.767)	<0.001	0.058 (0.021–0.094)	0.614
FEV_1	0.711 (0.68–0.739)	<0.001	−0.095 (−0.126, −0.063)	0.537
Equation 2				
VC	0.867 (0.851–0.881)	<0.001	0.007 (−0.02–0.034)	0.45
FVC	0.867 (0.851–0.881)	<0.001	−0.064 (−0.091, −0.037)	0.458
FEV_1	0.857 (0.84–0.872)	<0.001	−0.039 (−0.062, −0.016)	0.389
Validation study				
VC	0.891 (0.872–0.907)	<0.001	−0.201 (−0.236, −0.167)	0.457
FVC	0.889 (0.87–0.905)	<0.001	−0.262 (−0.3, −0.227)	0.5
FEV_1	0.897 (0.879–0.912)	<0.001	−0.174 (−0.205, −0.142)	0.411

Note: Bias (estimated data – actual data) expressed as means and 95% CIs.
Abbreviations: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; RMSE, root-mean-square error; VC, vital capacity.

derived from equations 1 and 2 correlated significantly with actual VC, FVC, and FEV_1. However, correlation coefficients for VC, FVC, and FEV_1 using equation 2 were higher than those using equation 1. Estimated VC, FVC, and FEV_1 using equation 2 had lower RMSE than values obtained using equation 1. Bland–Altman plots showed that 95% LOAs for equation 2 were less broad than those of equation 1. These results suggest that adding the FOT indices as independent variables increased the ability of an equation to estimate VC, FVC, and FEV_1.

Next, we assessed the accuracy of equations derived from the development study in a separate data set. Estimated VC, FVC, and FEV_1 correlated significantly with actual VC, FVC, and FEV_1, and the correlation coefficients for each parameter demonstrated almost perfect agreement in the validation study. However, as shown in Table 6 and Figure 3, mean differences

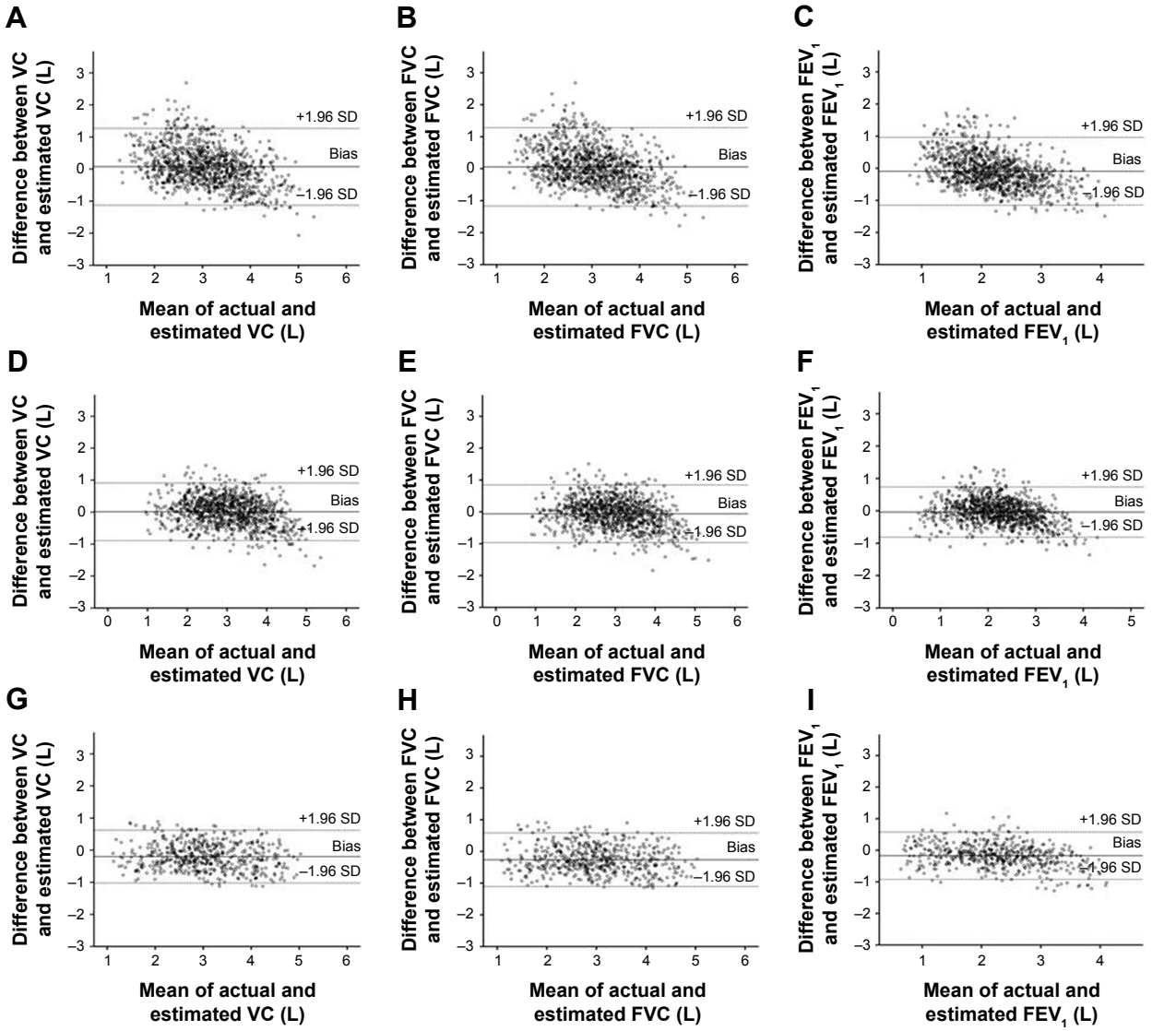

Figure 3 Bland–Altman plot comparing actual and estimated VC, FVC, and FEV_1.
Notes: Estimated data obtained using equation 1 (**A**–**C**) and equation 2 (**D**–**F**) in the development study. Using equation 2, we calculated estimated data in the validation data set (**G**–**I**). Bias of equations expressed as mean difference between estimated data and actual data (estimated data – actual data).
Abbreviations: VC, vital capacity; FVC, forced VC; FEV_1, forced expiratory volume in 1 second.

between the estimated data and actual data in the validation study were not small. The regression equations in the present study may be incomplete. However, spirometry is sometimes difficult to perform in elderly patients, those with cognitive impairment, and those with severe respiratory distress.[1] A previous report that evaluated the quality of spirometry in subjects aged 65 years or older showed that spirometry was performed correctly by only 415 of 1,242 patients (33.4%).[24] The method used to assess pulmonary function in our study may be a useful approach in such patients.

Limitations

There are several limitations to this study. First, the development and validation studies were retrospective in nature. Second, no children were evaluated. Third, we used the MostGraph-01, but not the MasterScreen IOS-J (CareFusion, San Diego, CA, USA) to measure respiratory impedance. It has been reported that these devices do not necessarily generate identical impedance values, and differences between the devices should be taken into consideration when evaluating clinical data.[25] Fourth, this study included only Japanese subjects. Further studies are needed to evaluate whether our findings can be extrapolated to other populations. Fifth, our analysis used the oscillatory index in the whole-breath phase, but not the inspiratory or expiratory phases, even though it has been reported that breath changes in FOT data may be useful in assessing respiratory diseases.[11,13,26] Sixth, we used raw FOT values in subjects of various ages. This is because

definitive predictive equations have not yet been established. Reference values for MostGraph-01 measurements in middle-aged and elderly Japanese individuals have now been published.[27] However, in that study, 44.8% of the population had abnormal spirometric findings, and it was unclear how many subjects had abnormal chest-radiography findings. Therefore, it is uncertain if the findings of that study can be used as reference values for MostGraph-01 measurements. Seventh, in the present study, we evaluated whether it is possible to generate regression equations for spirometry data based on FOT measurements in both healthy subjects and patients with various respiratory diseases. However, the estimated data in the validation study still did not demonstrate high accuracy. The present analyses including the healthy subjects and patients with various respiratory diseases might be one of the reasons the estimated data were less accurate. If we had generated regression equations for spirometric indices for each respiratory disease, estimated data might have been more accurate.

Conclusion

Our findings suggest that while there is a significant correlation between estimated spirometry values derived from FOT measurements and actual values, estimated values are still not identical to actual values. Further studies are needed to generate more accurate regression equations for spirometric indices based on FOT measurements.

Data sharing statement

Our manuscript data are freely available upon request.

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Disclosure

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