ORIGINAL ARTICLES

Reference Values for Inspiratory Capacity in Healthy Nonsmokers Over Age 50 Years

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OBJECTIVE: The role of dynamic hyperinflation in triggering dyspnea and limiting exercise capacity in patients with chronic obstructive pulmonary disease has been recognized in recent years. The degree of dynamic hyperinflation can be assessed by measuring reduction in inspiratory capacity (IC). The aim of this study was to establish reference values for IC in healthy individuals of both sexes between the ages of 50 and 87 years, as such data are scarce in the literature.

SUBJECTS AND METHODS: We studied 155 healthy volunteers (93 women) with normal spirometry. None had a prior history of respiratory, cardiovascular, or systemic diseases that might alter lung function. All were never-smokers. IC was measured during a normal, unforced inspiration to total lung capacity starting from functional residual capacity. The highest value of 6 satisfactory maneuvers was recorded. Sex, height, age, and weight were included in the regression equations. One thousand bootstrap samples for each sex were also analyzed.

RESULTS: For each sex, we found that a model including age, height, and weight produced IC prediction equations with a coefficient of determination (r^2) of 0.414 for women and 0.447 for men. The mean (SD) intrasubject coefficient of variation was 4.3% (2%) for IC measured during a single session and 5.1% (0.4%) for measurements from 5 weekly sessions.

CONCLUSIONS: Our results provide reference equations for IC that are valid for a healthy population over 50 years of age. Predicted values were similar to those recently obtained in an Italian population aged between 65 and 85 years.

Key words: *Inspiratory capacity. Reference values. Slow vital capacity.*

Valores de referencia de la capacidad inspiratoria en sujetos sanos no fumadores mayores de 50 años

OBJETIVO: En los últimos años se ha reconocido la importancia de la hiperinflación dinámica en la génesis de la disnea y de la limitación al ejercicio en la enfermedad pulmonar obstructiva crónica (EPOC), y que su magnitud puede evaluarse a través de la reducción de la capacidad inspiratoria (CI). Nuestro objetivo ha sido establecer valores de referencia de la CI en individuos sanos de ambos sexos, de entre 50 y 87 años de edad, debido a que en la literatura médica disponible prácticamente no se ofrecen tales datos.

SUJETOS Y MÉTODOS: Estudiamos a 155 voluntarios sanos (93 mujeres), que nunca habían fumado ni presentaban antecedentes de enfermedades respiratorias, cardiovasculares o sistémicas que pudieran alterar la función pulmonar, y cuya espirometría era normal. La CI se midió durante una inspiración no forzada hasta la capacidad pulmonar total a partir del valor en reposo espiratorio, y para los resultados se empleó el valor más alto de 6 maniobras satisfactorias. En las ecuaciones de regresión se incluyeron el sexo, la talla, la edad y el peso. Se empleó además el método de *bootstrapping* de 1.000 muestras para cada sexo como procedimiento de análisis.

RESULTADOS: Encontramos para cada sexo que un modelo que incorporó la edad, la talla y el peso produjo ecuaciones predictivas de CI con un coeficiente de determinación r^2 = 0,414 y 0,447 para mujeres y varones, respectivamente. El coeficiente de variación intrasujeto en una misma sesión fue (media ± desviación estándar) del 4,3 ± 2%, y en 5 sesiones separadas por una semana fue del 5,1 ± 0,4%.

CONCLUSIONES: Nuestros resultados proporcionan ecuaciones de referencia para CI válidas en población sana mayor de 50 años. Los valores predichos son semejantes a los recientemente obtenidos en población italiana de 65-85 años de edad.

Palabras clave: *Capacidad inspiratoria. Valores de referencia. Capacidad vital lenta.*

Introduction

Recent years have brought increasing evidence of the role played by dynamic hyperinflation in triggering dyspnea and limiting exercise tolerance in patients with chronic obstructive pulmonary disease (COPD), especially in severe cases.[1,2] In such patients peak expiratory flow limitation leads to progressive air trapping due to an increase in breathing rate and decrease in expiratory time during

This study was funded by the Fondecyt Project (1010993).

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Manuscript received May 31, 2006. Accepted for publication April 3, 2007.

exercise and even during activities of daily living.[2,3] In these circumstances, dynamic hyperinflation increases functional residual capacity (FRC) and, as total lung capacity (TLC) does not increase with exercise,[4] inspiratory capacity (IC) necessarily decreases. For this reason measurement of IC is being used clinically with increasing frequency to evaluate the presence of dynamic hyperinflation not only at rest, but also during exercise.[2]

Resting IC has been shown to be a predictor of maximal exercise load[3,5,6] and a good index for the evaluation of the effects of bronchodilator drugs[7-9] and of the administration of oxygen on lung hyperinflation.[10] IC expressed as a percentage of TLC (IC/TLC) has recently been shown to be a good predictor of mortality.[11,12]

The available literature provides practically no reference values for IC. We found only 2 multicenter studies in which this index was evaluated in healthy individuals between the ages of 20 and 70 years[13] and, very recently, between the ages of 65 and 85 years.[14] Due to the lack of reference values, predicted IC values have been calculated indirectly in most studies by subtracting predicted FRC from predicted TLC using mainly the normal values of the European Community for Steel and Coal.[15] Changes in IC can also be evaluated using the IC/TLC ratio. This approach assumes that TLC does not change with the various interventions or that TLC has been measured simultaneously with IC.[12]

The advantage of using IC to evaluate dynamic hyperinflation lies in the fact that it can be measured together with other parameters during spirometry and in that it can be measured during physical exercise. In view of the importance of this ratio in evaluating dynamic hyperinflation in COPD patients, the objective of the present study was to determine reference values for IC in never-smokers of both sexes between the ages of 50 and 87 years and to determine coefficients of variation during a single session and over a series of sessions spaced apart. The reference values thus obtained were compared to those estimated indirectly, that is, by subtracting FRC from TLC,[15] and with those published by Roca et al[13] and Tantucci et al.[14]

Subjects and Methods

Subjects

We studied 155 healthy never-smoking volunteers (93 women) over the age of 50 residing in Santiago de Chile who had signed informed consent to participate in the study. The population was recruited from our staff and their families, members of the Young Men's Christian Association who engaged in some type of physical fitness training, and healthy residents of geriatric institutions. The protocol was approved by our institution's ethics committee. Once recruited, the subjects answered a health questionnaire and underwent spirometry. A history of diabetes, cancer, cardiovascular disease, hypertension, respiratory disease (asthma, COPD, or tuberculosis) or any other disease that could interfere with IC maneuvers was considered an exclusion criterion, as was a history of acute respiratory infection or abdominal surgery in the 3 months prior to the study.

Lung Function Testing

A trained university nurse with considerable experience in performing spirometry carried out measurements using a Spyro Analyzer ST 250 R spirometer (Fukuda Sangyo Co, Tokyo, Japan) calibrated before each session with a 3-L syringe. A deviation of ±3% was accepted.[16]

Before IC was measured, all patients underwent spirometry according to American Thoracic Society and European Respiratory Society guidelines.[16] The reference values of Knudson et al[17] were used. Spirometry measurements were obtained with subjects in a sitting position after a 5-minute rest period. Subjects breathed through a mouthpiece while wearing a nose clip. They were instructed to breathe calmly until a stable end-expiratory level was reached. They were then to inhale normally to TLC and then exhale slowly to FRC. This sequence was repeated until 6 acceptable inspiratory maneuvers were obtained, and the highest value was selected.

The intrasubject coefficient of variation measured during a single session was calculated for all the subjects, using the 6 measurements obtained for each of them. For the intrasubject coefficient of variation in different sessions we studied 15 individuals in 5 weekly sessions.

During initial spirometry we measured slow vital capacity (SVC) in a subgroup of 108 individuals and recorded both IC and expiratory reserve volume during this maneuver. The highest IC value obtained in at least 2 reproducible maneuvers was used for comparison with IC measured during unforced breathing maneuvers without maximum exhalations.

Statistical Analysis

Descriptive data are expressed as means (SD). The Student *t* test for unpaired samples was used for comparisons between the sexes. In order to generate prediction equations for IC, multiple regression models were constructed for each sex, entering predictors used for other lung volumes, namely age (in years), height (in meters), and weight (in kilograms). The SE of the estimate of each equation was calculated.

As the number of women and men participating in the study was small, we used the bootstrapping procedure as part of our analysis. This procedure was developed in order to obtain more precise estimates when samples are small.[18-20] In our study we analyzed 1000 bootstrapped samples for each sex from the original sample of 93 women and 60 men using the SPSS statistical package, version 11.5 (Chicago, Illinois, USA). Sample selection was with replacement and subjects could thus be selected repeatedly and more than once in each sample. Regression coefficients were then estimated for IC with each of the 1000 samples of women and men. Thus, 1000 possible regression equations were obtained for each sex, each one including age, height, and weight as predictors of IC. Once the 1000 equations for each sex had been generated, the regression coefficients obtained were averaged and the resulting values were used to construct the reference equations for men and women.

Results

A total of 173 subjects were recruited, 18 of whom were excluded. Thirteen subjects who met the inclusion criteria were excluded because they were unable to perform acceptable and reproducible spirometry maneuvers. The other 5 subjects were excluded because spirometry showed mild bronchial obstruction. Of the 155 subjects studied, 93 (60%) were women and 60 (40%) were men. Table 1 shows anthropometric and lung function data for both sexes. It can be observed that stratification by sex did not influence age distribution.

Prediction Equations

Table 2 shows the prediction equations for IC generated by bootstrapping for each sex, with age, height, and weight used as predictors. Table 3 shows the average IC values for both sexes and compares them to those predicted by our equations, by the indirect method,[15] and by the equations of Roca et al[13] and Tantucci et al.[14] In the last 2 cases[13,14] the equations that included body mass index (BMI) were omitted. It can be observed that the values obtained by our equations were similar to the average measured and predicted values obtained by the equations of Tantucci et al[14] for both men and women.

Variability of Inspiratory Capacity

The mean (SD) intrasubject coefficient of variation for IC measured during a single session was 4.3% (2%), with no differences between the sexes (4.25% [1.9%] for women and 4.34% [2.1%] for men). The mean intrasubject coefficient of variation obtained for measurements from 5 weekly sessions was 5.1% (0.4%).

TABLE 1
Anthropometric Characteristics of the Study Subjects*

	Men (n=62)	Women (n=93)
Age, y	64 (8)	66 (9)
50-59	22	27
60-69	24	32
70-79	13	24
80-89	3	10
Height, cm	172 (60)	155 (50)
Weight, kg	77 (9)	67 (5)
BMI, kg/m^2	26 (3)	27 (5)
FVC, L	4.4 (0.9)	2.9 (0.5)
FVC, % predicted	114 (17)	110 (16)
FEV_1, L	3.4 (0.7)	2.2 (0.4)
FEV_1, % predicted	111 (15)	104 (19)
FEV_1/FVC, %	78 (4)	78 (5)

*Data are expressed as means (SD) or number of patients. FEV_1 indicates forced expiratory volume in 1 second; FVC, forced vital capacity; BMI, body mass index.

Comparison of Inspiratory Capacity Measurements Obtained in Isolation versus During the SVC Maneuver

The IC measurements obtained in the standard maneuvers were compared to measurements obtained during an SVC maneuver in 108 subjects for whom both were recorded simultaneously. Figure 1 shows a Bland and Altman plot of the agreement between the 2 measurements. On average, the IC obtained from the 6 maneuvers was 23 mL higher than the IC measured during the SVC maneuver (95% confidence interval, 12-34 mL). The limits of agreement were from –88 mL to 134 mL.

Discussion

The present study provides equations for predicting IC in men and women based on measurements obtained prospectively in a population of healthy non-smokers over age 50 residing in Santiago de Chile. The models included age, height, and weight with a coefficient of determination (r^2) of 0.447 for men and 0.414 for women.

The equations frequently used to predict lung volumes (FRC and TLC) include height.[13,15] Height is also therefore considered in the indirect method of predicting IC, in which the predicted FRC value is subtracted from the predicted TLC value. The equations generated in the present study include age, height, and weight. This is consistent with Tantucci et al,[14] who gave 1 equation that included age, height, and BMI for estimating a theoretical IC. BMI has also been included by other authors as a predictor for spirometric reference values.[21,22]

Our study has some possible limitations. The equations were not obtained from a population sample, but rather from healthy volunteers with a high proportion of individuals in the professions. However, socioeconomic factors have not been shown to have a marked influence on lung function.[21] Another possible limitation is the small number of individuals (especially men) over 80 years old included in the study. Nevertheless, our results are consistent with those of Tantucci et al,[14] who studied a somewhat larger and older group. We also feel that the normal

TABLE 2
Inspiratory Capacity Reference Values in Men and Women*

	Equation	r^2	SDR
Men	$-1.0106 - 0.0284 \times A + 2.2790 \times H + 0.0281 \times W$	0.447	0.513
Women	$-0.7602 - 0.0241 \times A + 2.7379 \times H + 0.0043 \times W$	0.414	0.366

*A indicates age (years); W, weight (kg); r^2, coefficient of determination; SDR, SD of the residuals; H, height (m).

TABLE 3
Comparison of the Various Prediction Equations for IC*

	Measured IC	Present Study	Roca et al[13]	Quanjer et al[15]	Tantucci et al[14]
Men	3.3 (0.7)	3.3 (0.5) Δ = –0.006 *P*=NS	3.6 (0.2) Δ = 0.288 *P*=.001	3.2 (0.4) D = –0.119 *P*=.12	3.3 (0.4) Δ = –0.002 *P*=NS
Women	2.2 (0.5)	2.2 (0.3) Δ = 0.007 *P* = NS	2.4 (0.1) Δ = 0.164 *P*<.0001	1.9 (0.2) Δ = 0.286 *P*<.0001	2.2 (0.4) Δ = 0.020 *P*=NS

*Values are expressed as means (SD). IC indicates inspiratory capacity; Δ, difference between predicted IC and measured IC; NS, not significant.
Men (n=62); mean (SD) age: 63.5 (8.4) years; height: 1.72 (0.06) m; weight: 77 (9) kg. Women (n=93); mean (SD) age: 65 (9) years; height: 1.55 (0.05) m; weight: 66 (9) kg.

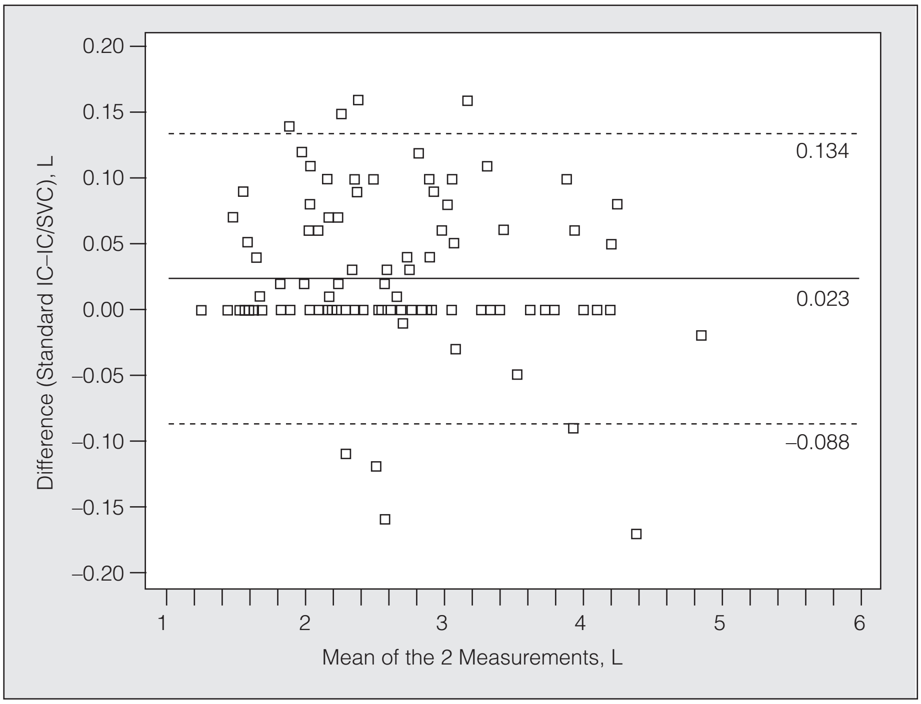

Figure 1. Bland and Altman plot of the differences between IC measured by the standard method and during an SVC maneuver plotted against the mean of the 2 measurements. IC indicates inspiratory capacity; SVC, slow vital capacity.

distribution of spirometry results we obtained for the overall sample of subjects support the validity of our results.

Sixty percent of our sample were women, but this proportion is practically identical to that of the population of Santiago de Chile in this age group (59% women and 41% men.) A preponderance of women was also observed in the PLATINO study,[24] which provided spirometric reference values for subjects over age 40 years in 5 Latin American cities.

Comparing the values obtained with the various equations (Table 3), we can see that those generated by our equations and by those of Tantucci et al[14] are practically identical to the measured values. The effect of age is reflected in both cases, as both equations predict a steady decrease in measured IC with advancing age and have markedly similar slopes, as can be seen in Figure 2. This decrease is not reflected, however, in the values predicted using the equations of Roca et al[13] and Quanjer et al,[15] whose equations did not include age.

In order to establish the reproducibility of the test we calculated the coefficient of variation. The mean intrasubject coefficient of variation for the 6 IC measurements taken during a single session was 4.3% (2%), which corresponded to a mean value of 131 mL in men and 92 mL in women. Both figures fall below the reproducibility criteria proposed by Enright et al[25] for forced vital capacity and for forced

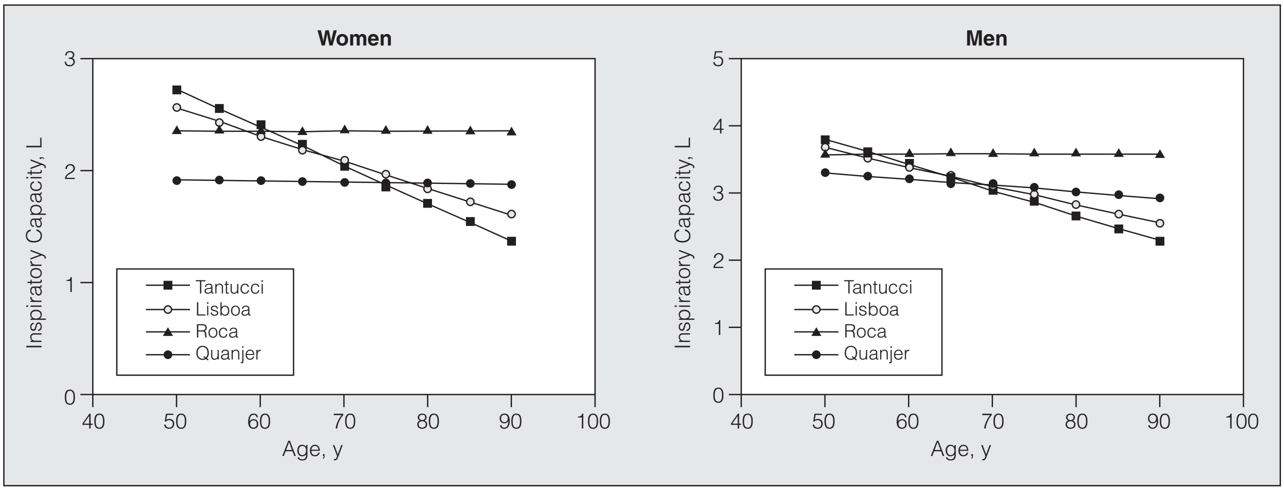

Figure 2. Comparison of inspiratory capacity values obtained for women and men with the equations of the present study (Lisboa), those of 2 previous studies (Roca et al[13] and Tantucci et al[14]), and the indirect method of subtracting predicted functional residual capacity from predicted total lung capacity using the reference values of Quanjer et al.[15] Mean heights of the present study (1.55 m for women; 1.72 m for men) and weight (66 kg for women; 77 kg men) were used.

expiratory volume in 1 second (FEV_1), ie a difference of less than 150 mL between the 2 best measurements. The coefficient of variation between sessions 1 week apart was 5.1% (0.4%), which corresponded to 167 mL in men and 112 mL in women.

With the spirometers currently available it is possible to obtain IC values during the SVC maneuver. If the spirometric maneuvers are performed correctly,[26] it is logical to assume that the values obtained will be reproducible. In the present study we have also shown that in 108 subjects these values are consistent with those obtained with the standard maneuver. We can conclude that IC could be included in an ordinary spirometry report.

In summary, we have established IC reference values in a population of healthy nonsmoking volunteers over 50 years old. These values are very similar to those recently reported by Tantucci et al[14] in a population of healthy Italian subjects older than ours. Given that the role of dynamic hyperinflation in COPD has gained increasing recognition and that IC has been shown to be a better index than FEV_1 for evaluating the effects of various bronchodilators[7-9] and for evaluating exercise capacity,[11,12] it would be advisable to include it in spirometry. The determination of IC simultaneously with SVC by ordinary spirometry (bearing in mind that end-expiratory level must remain stable) would make it possible to obtain measurements without prolonging spirometric testing.

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