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Reference values and repeatability of inspiratory capacity for men and women aged 65–85

C. Tantucci[a,*], V. Pinelli[a], S. Cossi[a], M. Guerini[a], F. Donato[b], V. Grassi[a], The SARA Study Group

[a]*Department of Internal Medicine, Respiratory Medicine, University of Brescia, Italy*
[b]*Department of Experimental and Applied Medicine, Chair of Hygiene, University of Brescia, Italy*

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Summary The inspiratory capacity (IC) has recently gained importance because it may signal the occurrence of dynamic hyperinflation at rest or during exercise by reflecting changes in the end expiratory lung volume (EELV). However, reliable predicted values for IC are not currently available. The aim of the study was to generate predictive equations for reference values of IC in adults aged 65–85 living in Italy and to determine its limits of the within test-session repeatability.

From the control group ($n = 429$) of the SARA study data base, 241 (161 females) never smoked, non-obese (BMI $< 30\,kg/m^2$) healthy subjects aged 65–85 who were able to correctly perform at least two manoeuvres of IC were selected.

A model that incorporated age, height and body mass index as significant predictors in either sexes produced predicting equations for IC with a coefficient of determination of $r^2 = .36$ and .34 for females and males, respectively. Ninety per cent of all the subjects were able to keep the second highest IC within 200 ml ($<9\%$) from the best IC. No significant gender difference was found for IC repeatability.

We provided the equations for deriving reliable IC reference values that can be applied in the elderly people living in southern Europe. In this population IC showed limits of the within-session repeatability similar to those accepted for other spirometric indices such as FEV_1 and FVC.

Introduction

The inspiratory capacity (IC), the maximal amount of air that can be inhaled from the end expiratory lung volume (EELV) that normally corresponds to the static functional residual capacity (FRC), has been neglected as spirometric measurement for a long time. Recently, however, it has been recognized that IC represents the volume reserve of the tidal volume and may specularly reflect the dynamic variations of EELV and FRC when the total

*Corresponding author. Tel./fax: 39 030 39 69 80.
E-mail address: tantucci@med.unibs.it (C. Tantucci).

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lung capacity (TLC) is expected to remain unchanged.

Therefore, the IC has been evaluated and found to be useful, mostly in COPD patients exhibiting expiratory flow limitation (EFL), as predictive index of exertional capacity[1,2] and dynamic increase in FRC at rest,[3,4] in different body positions, and during exercise.[5] Furthermore, in flow limited COPD patients the effectiveness of different bronchodilators has also been evaluated also in terms of volume response, looking at the IC increase.[6,7] Today, the IC is increasingly regarded as very important to determine the tolerance of exercise and signal the occurrence or change of dynamic hyperinflation in COPD as well as in other diseases.[8–10] Accordingly, in several studies predicted values of IC were used to select and compare subjects or to assess the results of a given treatment. Actually, the predicted IC can be only calculated by the difference of the theoretical values of TLC and FRC that were obtained with plethysmographic or dilutional method and in subjects aged less than 70 yr several years ago.[11] Because of these reasons, the IC reference values are poorly reliable for research and routine purposes, especially in the elderly. The prediction equations for IC values based on the population studies are surprisingly lacking in the literature. The aim of this study was to obtain appropriate reference values for IC in a sample of never smoker, healthy subjects selected from the general population living in Italy, aged 65–85. The second aim was to assess the within test-session repeatability of this parameter in the same population sample.

Materials and methods

Spirometric data were obtained from the database of the study known as ''SAlute Respiratoria nell'Anziano'' (SARA), meaning respiratory health in the elderly. SARA was a multi-centre Italian research project designed to analyse several aspects of chronic airway obstruction in the elderly and performed by 24 pulmonary and geriatric institutions distributed throughout the country between January 1996 and December 1997.[12] Subjects with a previous diagnosis of asthma or COPD, or signs and symptoms compatible with either diagnosis were defined as cases ($n = 527$). Subjects not reporting any previous diagnosis nor any sign or symptoms compatible with respiratory diseases were considered as controls ($n = 1084$). Subjects were further excluded if they had one of the following conditions: severe hepatic failure (B and C grade of the Child index), renal failure (plasma creatinine level >2 mg/ml), heart failure (NYHA >2), diabetes and arterial hypertension, severe cognitive or sensory impairment, hospitalization for any reason in the previous 6 month, or acute events in the last 2 weeks. After these exclusion criteria had been satisfied, the control group amounted to 429 subjects.[13] From this group we selected for the analysis lifetime non-smoker subjects with body mass index $<30\,kg/m^2$, without evidence of obstructive (FEV_1/FVC $>70\%$ for individuals aged <70 yr, $\geqslant 65\%$ for individuals aged 70–80 yr and $\geqslant 60\%$ for those aged >80 yr)[14,15] or restrictive ventilatory defect (VC $>80\%$ predicted) [11] and with at least two IC manoeuvres performed correctly. The final data set consisted of 241 subjects.

Spirometry

The technical characteristics of the instruments and the results of the quality control for spirometry during the SARA study have been previously described.[16] Shortly, a computerized water-sealed light-bell Stead-Wells spirometer (Biomedin, Padova, Italy) was used with an incorporated software program that assisted the operator during the test to verify on-line both acceptability and reproducibility of the spirometric manoeuvres. All the spirometric tests employed in the study fulfilled the ATS recommendations.[16] The IC measurements were obtained, while the subjects wearing a noseclip were in the seated position, during a continuous inspiratory manoeuvre starting from FRC and computed as change in lung volume from the EELV, calculated by averaging the baseline signal of at least 3 regular tidal volumes, to TLC identified as the maximal volume signal, unchanged for at least 1 s (Fig. 1). We chose the greatest IC of at least two acceptable inspiratory manoeuvres to obtain reference values and the nearest to the maximum to determine the limits of repeatability for this parameter. The IC repeatability was assessed for males, females and both combined by computing the difference between the highest and second-highest IC, either in absolute (ml) or percentage (%) terms, within the spirometry test session. Spirometry was performed by specifically trained either physicians or technicians with considerable pulmonary function testing experience who were instructed to vigorously coach the subjects during the test execution.

Statistical analysis

Descriptive analysis was performed by computing means, medians and standard deviations (SD) in men

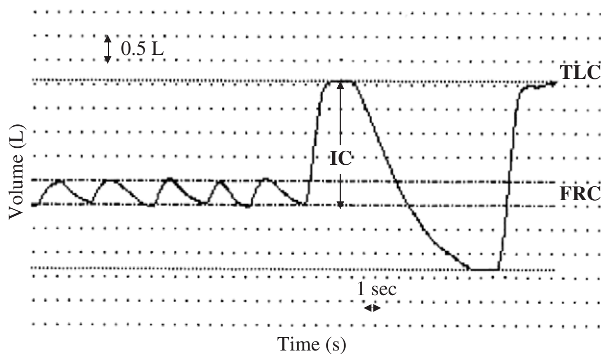

Figure 1 Example of an original spirometric tracing (volume/time) that satisfies the acceptability criteria used for measuring the inspiratory capacity (IC) (see text for explanation). TLC = total lung capacity; FRC = functional residual capacity.

Table 1 Anthropometric and functional characteristics of the subjects stratified by sex.

	Males ($n = 80$)	Females ($n = 161$)
Age (yr)	73.5±6.0	72.6±5.5
65–69, *n*	26	50
70–74, *n*	22	57
75–79, *n*	17	32
80–84, *n*	11	16
85+, *n*	4	6
Height (cm)	168±6	156±6
Weight (kg)	72.9±9.8	60.2±7.8
BMI (kg/m^2)	25.8±2.6	24.7±2.9
VC (l)	3.65±.68	2.58±.55
IC (l)	2.80±.60	2.00±.45

Data are mean±SD.

and women separately, according to each age group. Models of prediction for IC were developed, separately for males and females, by using a multiple regression analysis including initially age and height and subsequently age, height and body mass index as predictors. Difference in repeatability IC means between males and females was directly compared using the non-parametric Mann–Whitney test for independent groups. The influence of age, sex, weight, height, BMI, VC and IC values on the repeatability of the IC measurement was assessed by fitting a multiple regression model with IC difference as the dependent and all the others as explanatory variables. A squared root transformation of the IC difference was used to meet the assumptions of the normal distribution of residuals and to normalize the variance.[17] All the statistical tests were two tailed with .05 as the value to refuse the null hypothesis. The statistical analyses were performed using the STATA statistical package (Stata Statistical Software: Release 8.0 College Station; TX: Stata Corporation).

Results

Of all 241 subjects examined, 161 (67%) were female and 80 (33%) male. The age, height, weight, BMI, VC and IC (mean±SD) for males and females are reported in Table 1. The stratification of the sample for gender did not influence the age distribution (Table 1).

The models predicting IC for males and females, aged 65–85, are shown in Table 2 with age and height and with age, height and BMI as independent predictors, respectively. In each model the effect of the anthropometrical variables chosen was significant and quite similar between males and females, with greater coefficient of determination for the model including BMI in both sexes.

In Fig. 2 the values of IC obtained from the prediction equations of our model are compared with those computed by the difference between the TLC and FRC reference values for males and females of average height.

Males and females exhibited an almost identical capacity of reproducing IC within test-session when it was expressed as percent difference (Table 3). Only 10% of the all subjects were unable to keep the second highest IC within 200 ml (<9%) from the best IC. No significant gender difference was found for the IC repeatability, either in absolute or percent values. Multiple regression analysis showed that the difference between the best and the second best IC (ΔIC) was not significantly influenced by age, sex, height, BMI, IC and VC, either in absolute or percent values.

Discussion

The purpose of this study was to obtain reliable predicted values for the IC in the elderly and to determine the within-test session repeatability of this parameter in the same population. The best predicting model included age, height and BMI for both sexes with a coefficient of determination (r^2) between .34 and .36. The repeatability was similar for males and females and, expressed as absolute difference, it was within 200 ml for 90% of the all subjects.

The increasing relevance of the IC as a simple spirometric index able to indicate and follow

Table 2 Predicting models for inspiratory capacity (IC) (liter, body temperature pressure saturation).

	Coef.	Std. err.	$P>[t]$	[95% conf. interval]	
Males					
$r^2 = .24$					
Age	−.0380	.010	.000	−.058	−.018
Height	2.205	.967	.025	.280	4.131
Constant	1.889	1.948	.335	−1.991	5.768
$r^2 = .34$					
Age	−.030	.010	.003	−.050	−.010
Height	2.047	.909	.027	.237	3.858
BMI	.075	.022	.001	.031	.119
Constant	−.372	1.947	.849	−4.251	3.506
Females					
$r^2 = .31$					
Age	−.034	.005	.000	−.045	−.023
Height	2.184	.470	.000	1.256	3.113
Constant	1.043	.892	.244	−.719	2.805
$r^2 = .36$					
Age	−.030	.005	.000	−.041	−.019
Height	2.553	.465	.000	1.634	3.471
BMI	.037	.010	.000	.017	.058
Constant	−.709	.991	.475	−2.667	1.249

BMI = body mass index; coef. = coefficient of anthropometric variables.

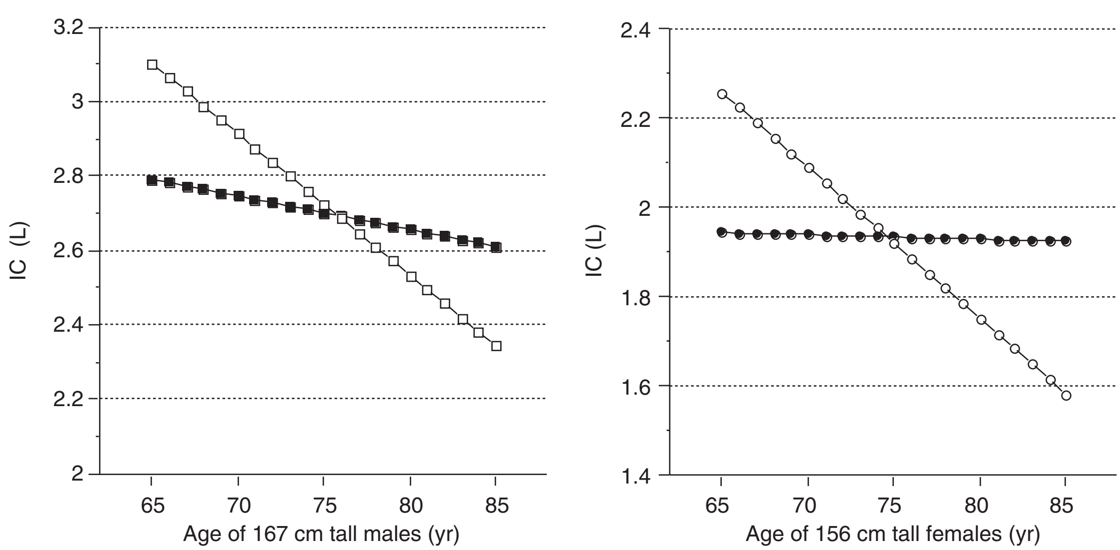

Figure 2 Comparison of predicted IC obtained by our prediction equations (white symbols) and computed by using the ECCS reference values of TLC and FRC (black symbols) (Quanjer et al.[11]) in males *(left panel, squares)* and females *(right panel, circles*) with the respective median height of our population.

changes in dynamic pulmonary hyperinflation, particularly in patients with resting, postural or exertional EFL, without measuring directly FRC by dilutional or plethysmographic method, requires the availability of reliable predicted values. In this respect, the knowledge of the expected normal IC values is relevant in the elderly people who are mostly prone to develop COPD or other cardiac or pulmonary diseases leading to dynamic pulmonary hyperinflation.

Up to now the reference values of the IC have been obtained by computing the difference

Table 3 Inspiratory capacity repeatability in males, females and combined.

	Mean	SD	Percentile		
			80th	90th	95th
Males					
ΔIC (ml)	96	80	180	210	238
ΔIC (%)	3.5	3.0	6.0	8.1	8.8
Females					
ΔIC (ml)	89	65	150	170	214
ΔIC (%)	4.4	3.2	6.8	8.6	10.2
Combined					
ΔIC (ml)	91	69	154	190	221
ΔIC (%)	4.1	3.2	6.6	8.6	9.3

between the predicted values of other functional parameters, namely TLC and FRC, that were obtained some years ago on younger populations and using indirect methods.[11] Thus, many sources of error may add on, possibly giving wrong IC reference values. Indeed, the lack of adequate theoretical values for the IC may alter the results of several studies in which the subjects were stratified according to the percent of the IC predicted values that are poorly reliable.

The centres involved in the SARA study were homogeneously distributed over the country and all subjects consecutively referring to the centres during the time period of the survey were enrolled. Hence, the examined sample can reasonably be considered as representative of the general population, even if the selection was not performed according to a random sampling procedure.[12] On the other hand, as reported in the guidelines for the selection of reference values and interpretative strategies of ATS,[18] the method for selecting the study sample used to generate reference values has little effect on either the mean value or the range of values obtained. In addition, a scrupulous effort was made to exclude all smoker and ex-smoker and obese subjects and by further reviewing all spirometric data to eliminate other 39 subjects showing relevant functional impairment.[14,15] The healthy non-smoker obese subjects (41 female and 12 male) were excluded because they usually breathe near the residual volume with a small expiratory reserve volume (ERV) and a reduced FRC. Since their TLC is normally preserved the IC results markedly increased.[10] Looking for adequate reference values in the elderly, we thought it was proper to eliminate such bias.

Therefore, despite the relatively small number of the subjects, we believe that our sample is representative of a "general" population of healthy individuals aged 65–85 living in Italy.

The coefficients of determination given by the models adopted for IC are acceptable and not dissimilar from those obtained for FEV_1 and FVC in relatively small samples of subjects in the same age range.[18]

The comparison of the predicted IC, obtained using our prediction equations with the model including age and height in two representative, male and female subjects at different age (Fig. 2), shows values that are higher at 65 and lower at 85 yr than those computed by the reference values of TLC and FRC.[11] This example clearly indicates that predicted values for IC derived from our population sample tend to decline more markedly with age in the elderly.

To individuate adequately stringent limits of repeatability (or reproducibility) for key spirometric parameters such as IC is important to give confidence about the diagnostic meaning of its change under different conditions and to facilitate the functional interpretation by the physicians interested to the IC measurement.

Ninety per cent of the women and the men were able to perform a second-best IC with variability lesser than 170 ml or 8.6% and 210 ml or 8.1%, respectively.

These values of repeatability pertain to a relatively small sample of aged people, lifetime non-smoker, free from respiratory diseases and with normal functional respiratory testing. However, the limits of IC repeatability we observed is only slightly greater than those found in a much larger sample of an unselected population aged between 20 and 90 yr for FEV_1 and FVC, either in absolute and percent terms,[19] and in accordance to the 1995 ATS recommendations for the spirometry repeatability goals for FEV_1 and FVC (<200 ml) in adults.[16]

In some previous studies smoking and lower lung function had controversial effects on the repeatability of FEV_1, slightly worsening or improving it.[20–23] A recent, above mentioned, study showed that the smoking habit increased the FEV_1 mean variability of 3.5 ml while the functional impairment, based on FEV_1 (as 10% change in percent predicted), decreased the FEV_1 mean variability of 2.6 ml, and both did not significantly affect the absolute (ml) variability of FVC. In contrast, a FEV_1 reduction of 10% of predicted, increased of about .4% and .3% the variability of the FEV_1 and FVC, respectively.[19]

Therefore, smoking and functional impairment seem to worse very little the repeatability of FEV_1 and FVC, essentially as percent difference, and the same is also expected to occur for IC.

Finally, it has to be recognized that in this relatively small sample women exceed men with a 2:1 ratio, likely because in Italy much more men than women smoked in the past, introducing in a study aimed to provide normative population data an obvious limitation which, however, might reflect a real-life phenomenon.

Although we agree that these predictive equations need to be tested and validated using other population samples in large prospective studies, and that they must not be back-extrapolated to younger subjects and applied indiscriminately to different ethnic groups, it should be stressed that no reference values are currently available for IC, while in the meantime questionable predicted values are extensively used for this parameter.

In conclusion, we provided predicting equations for IC that can be applicable to Caucasian male and female individuals older than 65 living in southern Europe to obtain the IC reference values. The limits of the within test-session repeatability of IC were less than 200 ml ($<9\%$) for 90% of the subjects studied.

Appendix. The SARA Study Group

Coordinators: V. Bellia (Palermo), F. Rengo (Napoli).

Scientific Committee Members: R. Antonelli Incalzi (Taranto), V. Grassi (Brescia), S. Maggi (Padua), G. Masotti (Florence), G. Melillo (Naples), D. Olivieri (Parma), M. Palleschi (Rome), R. Pistelli (Rome), M. Trabucchi (Rome), S. Zuccaro (Rome).

List of participating centres, principal investigator and associated investigators (the latter in brackets): (1) Div. Medicina I, Osp. Geriatrico INRCA, Ancona. D.L. Consales (D. Lo Nardo, P. Paggi). (2) Div. Geriatria, Osp. Civile, Asti. F. Goria (P. Fea, G. Araldi, R. Corradi). (3) Catt. Geront. e Geriatria, Policlinico Universitario, Bari. A. Capurso (R. Flora, S.Torres, G. Venezia, M. Mesto). (4) V Div. Geriatria, Osp. Malpigli, Bologna. S. Semeraro (L. Bellotti, A. Tansella). (5) I Div. Med. Generale, Osp. Civile, Brescia. V. Grassi (S. Cossi, M. Guerini, C. Fantoni, M. De Martinis, L. Pini). (6) Clinica Pneumologica, Fondazione 'E. Maugeri', Telese (BN). G. Melillo (R. Battiloro, C. Gaudiosi, S. De Angelis). (7) Ist. Med. Int. e Geriatria, Osp. Cannizzaro, Catania. L. Motta (I. Alessandria, S. Savia). (8) Ist. Geront. e Geriat., Osp. Ponte Nuovo, Univ. of Florence. G. Casotti (M. Chiarlone, S. Zacchei). (9) Div. Geriatria, Osp. Morgagni, Forlí. V. Pedone (D. Angelici, D. Cilla). (10) Div. Geriatria, Osp. Galliera, Genova. E. Palummeri (M. Agretti, P. Costelli, D. Torriglia). (11) G.ppo Ricerca Geriatria, Osp. Richiedei, Gussago (BS). M. Trabucchi (P. Barbisoni, F. Guerini, P. Ranieri). (12) Div. Geriatria, Osp. Generale, L'Aquila. F. Caione (D. Caione, M. La Chiara). (13) I Div. Geriatria, Osp. San Gerardo, Monza. G. Galetti (A. Cantatore, D. Casarotti, G. Anni). (14) Catt. Gerontologia e Geriatria, Univ. Federico II, Napoli. F. Rengo (F. Cacciatore, A.I. Pisacreta, C. Calabrese). (15) Ist. Med. Int., Osp. Geriatrico, Padova. G. Enzi (P. Dalla Montà, S. Peruzza, P. Albanese, F. Tiozzo). (16) Ist. Mal. App. Resp., Osp. Rasori, Parma. D. Olivieri (V. Bocchino, A. Comel, N. Barbarico). (17) Ist. Geront. e Geriatria, Policlin. Monteluce, Perugina. U. Senin (F. Arnone, L. Camilli, S. Peretti). (18) Div.Geriatria, Osp. Israelitico, Roma. S.M. Zuccaro (M. Marchetti, L. Palleschi). (19) Div. Geriatria, Osp. Gen. Addolorata, Roma. M. Palleschi (C. Cieri, F.Vetta). (20) Ist. Med. Int. e Geriatria, Policlinico Gemelli, Roma. P.U. Carbonin (F. Pagano, P. Ranieri). (21) Ist. Sem. Med. e Geriatria, Pol. Le Scotte, Siena. S. Forconi (G. Abate, G. Marotta, E. Pagni). (22) Fond. San Raffaele, Cittadella della Carità, Taranto. R. Antonelli-Incalzi (C. Imperiale, C. Spada). (23) Catt. Geront. e Geriatria, Osp. Maggiore, Milano. C. Vergani (G. Giardini, M.C. Mandrini, I. Dallera). (24) Catt. Mal. App. Resp., Osp. V. Cervello, Palermo. V. Bellia (F. Catalano, N. Scichilone, S. Battaglia).

Coordinating Center: Istituto di Medicina Generale e Pneumologia, Catt. Mal. App. Respiratorio, Università degli studi di Palermo.

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