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Inspiratory Capacity reference values: respond to the place of origin?

Valores de Referencia de la Capacidad Inspiratoria: ¿Responden al Lugar de Origen?

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SUMMARY: Inspiratory Capacity (IC) is a variable closely linked to functionality and physical exercise, in Chile there are reference values for IC that may over or underestimate this condition in users. Thus, the objective of this research was to determine the local values of IC for the construction of reference equations. A total of 305 volunteers participated in the evaluations, of which 161 (53 %) were women and 144 (47 %) men, from March 2019 to February 2020. All complied with the requirements of the scientific ethics committee and signed the consent; the IC was evaluated on a body plethysmograph according to American Thoracic Society and the European Respiratory Society (ATS/ERS) recommendations. The highest IC values were found in the 18-25 age range with 3.24+0.36 L for women and 4.16+0.49 L for men, respectively. The IC had a critical inflection from the range of 46 to 55 years of age (women; p=0.026 and men; p=0.012), decreasing steadily. The measured IC showed differences with respect to the values of Lisboa *et al.* (2007) and Roca *et al.* (1998) (p<0.0001 and p<0.0001 in women and p=0.0028 and p=0.0107 in men). Predictive equations were obtained for both sexs, which showed significant differences with currently used values, thus, improving the diagnosis, control, and follow-up with reference values located will allow a more appropriate management in the Maule region, Chile.

KEYWORDS: Pulmonary Function; Reference Values; Inspiratory Capacity.

INTRODUCTION

Currently in Chile, the prevalence of morbi-mortality due to causes associated with respiratory system involvement will certainly be modified by SARS CoV-2 (COVID-19), surpassing the third place it occupies in specialty consultations (Olmos *et al*., 2015). Therefore, updating the information by increasing the validity of the statistical distributions of the behavior of certain variables associated with human ventilatory movement (Kubota *et al*., 2014; Menezes *et al*., 2015; Muñoz-Cofré & del Sol, 2018) and its closer link with the possibility of physical activation, will allow a specific contribution to the monitoring and follow-up located in the region, based on values that demonstrate greater representativeness (Casanova & Celli, 2007; Gutiérrez *et al*., 2014).

Currently, one of the variables that is used and that best expresses the functional possibilities of an individual to perform physically is the Inspiratory Capacity (IC) (Casanova & Celli, 2007), which, in addition, acquires great importance for the diagnosis of a health condition determined by respiratory disease (Casanova *et al*., 2005; Vilozni *et al*., 2018, Betzalel & Efrati, 2018; Cui *et al*., 2017; Luo *et al*., 2020).

IC translates alterations in lung volumes and capacities globally, evidencing the presence of airflow limitation, and can be evaluated in conjunction with the Forced Expiratory Volume at the first second (Casanova & Celli, 2007). In turn, IC has been shown to be a good predictor of mortality (Lisboa *et al*., 2007). It has also been related to the number of hospitalization days in patients with Cystic Fibrosis (Vilozni *et al*., 2018). On the other hand, IC has considerable sensitivity for assessing changes in ventilatory 13 or pharmacological therapy (Betzalel & Efrati, 2018). In particular, the most recent reports on the sequelae

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of SARS CoV-2 (COVID-19) point to an increase in restrictive ventilatory loads (Shin *et al*., 2015; Shi *et al*., 2020), which will lead to a consequent critical decrease in IC.

Generally, the IC values used in the country and in the region are derived from external software databases that reflect socio-cultural realities different from that of our population (Casanova & Celli, 2007; Gutiérrez *et al*., 2014; Luo *et al*., 2020; Soffler *et al*., 2017). Nevertheless, there have been important efforts to generate reference data, such as those made by Lisboa *et al*. (2007) and Gutiérrez *et al*. (2014). However, there is still a gap to be considered because the studies have only validated small population segments (Casanova & Celli, 2007), leaving reasonable doubts of anthropometric and geographic origin.

Regarding the way to measure this variable, repeatable and standardized values (Miranda & Muñoz-Cofré, 2014) should be generated in laboratories, with variability levels not exceeding 5 % (Miller *et al*., 2005; Muñoz-Cofré *et al*., 2018). This does not preclude clinimetric investigation of the reliability obtained with alternative instruments such as the volume stimulator (Soffler *et al*., 2017), or by means of spirometers, which, as basic elements of the measurement of ventilatory function, are essential for the investigation, diagnosis, control, and monitoring of respiratory diseases (Gutiérrez *et al*., 2014) in the field.

To date, the facts indicate that a good part of the pulmonary function laboratories still uses reference values provided by Roca *et al*., since there are no values specific to the Chilean population (Ruppek, 2012). This is how the predictive equations for pulmonary function in the healthy Chilean population have been defined (Muñoz-Cofré & del Sol, 2018). Therefore, given the health contingency and the projected short-term sequelae, the objective of this research was to determine the local values of IC for the construction of reference equations (Maule Region - Chile), following the indications of researchers who suggest obtaining reference values from healthy subjects, with anthropometric characteristics similar to the target population (Gutiérrez *et al*., 2014).

MATERIAL AND METHOD

Participants. This cross-sectional exploratory study included healthy volunteers who were residents of the Maule Region, Chile. Participants were recruited through direct invitation and by recruitment in social networks. Once recruited, the subjects answered a health questionnaire and underwent diagnostic spirometry. Exclusion criteria were history of diabetes, cardiovascular disease, chronic respiratory disease, musculoskeletal disorders of the rib cage, and any other disease that could interfere with the performance of IC maneuvers. Before evaluation, all participants were required to read and sign an informed consent form. The recruitment and evaluation protocol were approved by the Ethics Committee of the Universidad Católica del Maule (UCM; resolution 23/2019).

Pulmonary function. Measurements were performed at the UCM Ventilatory Function-Dysfunction Laboratory from March 2019 to February 2020, by an expert kinesiologist validated in the technique (R.M.C). A Mediagraphics body plethysmograph (Platinum Elite DL® St. Paul, Minnesota USA) was used. It was calibrated before each session with a 3 L capacity & Collins syringe. The standards proposed by the ATS and ERS were followed (Wanger *et al*., 2005). Prior to the maneuver, the participants had to remain in a sedentary position. For spirometry, the subjects placed the nose clip and, while breathing through a mouthpiece, they were instructed to breathe quietly until tidal volume stability was achieved. They were then asked to perform a maximal forced inspiration until achieving Total Pulmonary Capacity (CPT) and then to exhale fast and hard. For the IC maneuver, the participants performed an inspiration to CPT and then exhaled slowly to Functional Residual Capacity (FRC) (Wanger *et al*., 2005). For both tests, the sequence was repeated until 6 acceptable maneuvers were obtained, and with a percentage of variability of 3 %, the highest value obtained was considered.

Statistical analysis. Descriptive results are expressed as means ± 1 standard deviation (SD), 25th percentile (P25 %) and 75th percentile (P75 %). SPSS version 11.5 was used (SPSS Inc., Chicago, Illinois, EE.UU.). Comparisons between both sexes and age groups were performed using Student's t-test and ANOVA for repeated samples, respectively. To generate the regression equations, the IC value was incorporated into a multiple regression model for each sex using age in years, height in centimeters, and weight in kilograms as predictors. The standard error of the estimate was generated from each equation. A $p < 0.05$ value was considered significant.

RESULTS

A total of 305 volunteers were evaluated. Of these, 161 (53 %) were women and 144 (47 %) were men. Table I shows the anthropometric and spirometry characteristics of both sexes. It can be seen that stratification by sex did not influence the age distribution. Table II shows the mean and SD of the deciles. For IC, in the case of women the highest value is observed between 18 and 25 years of age, after which there is a decrease until 46-55 years of age. Between this decade and 56-65 a statistically significant decrease is observed. In men, the highest IC value was obtained between 18 and 25 years of age. There is a significant decrease until 36-45 years of age. As in women, there is a significant decrease with the decade of 46-55 years (Fig. 1).

The prediction models for IC included age, height, and weight as predictors. They are described separately for females and males. Table III shows the proposed equations with their r^2 values of 0.541 and 0.479 for females and males, respectively. When comparing the average IC obtained *versus* the equations proposed in this study for both sexes, no significant differences were found. However, there were significant differences when compared with the references of Lisboa *et al*. (2007), and Roca *et al*. (1998), (Table IV).

Table I. Anthropometric and spirometric characteristics of the study sample.

	Male	Female	p Value
Number	144	161	
Age (years)	35.14±16.21	34.83±17.13	0.185^{MW}
Weight (kg)	76.90±8.56	62.48±9.20	<0.0001^{MW}
Height (cm)	172.6±7.15	158.5±6.70	<0.0001^{MW}
BMI (kg/m^2)	25.83±2.49	24.89±3.35	0.012^{MW}
FVC (L)	4.40±1.14	3.42±0.95	<0.0001^{MW}
FVC % Pred	103.01±1.20	101.12±0.98	-
FEV$_1$ (L/s)	3.43±1.11	2.79±0.81	<0.0001^{MW}
FEV$_1$ % Pred	102.66±1.02	100.75±1.11	-
FEV$_1$/CVF	86.12	84.39	-
FEF$_{25-75\ \%}$ (L/s)	3.74±1.13	2.82±1.03	<0.0001^{t}
FEF$_{25-75\ \%}$ Pred	100.23±1.32	101.45±1.18	-
PEF (L/s)	8.52±1.90	6.90±1.80	<0.0001^{MW}
PEF % Pred	112.93±1.58	107.58±1.99	-

BMI= Body mass index; FVC= Forced vital capacity; FEV1= volume that has been exhaled at the end of the first second of forced expiration; FEF25-75 %= forced expiratory flow 25–75 %, PEF peak expiratory flow; Pred: predicho.

Table II. Distribution of inspiratory capacity by sex and according to percentiles.

Female	**18-25**	**26-35**	**36-45**	**46-55**	**56-65**	**66-75**	**76-85**
Number	36	13	19	34	34	14	11
$P_{25\%}$	3.06	2.61	2.37	2.21	2.34	2.16	2.25
Mean	3.24	2.93	2.82	2.63	2.46	2.38	2.35
Standard Deviation	0.36	0.32	0.48	0.39	0.17	0.35	0.12
$P_{75\%}$	3.47	3.20	3.28	2.88	2.62	2.55	2.48
Male	**18-25**	**26-35**	**36-45**	**46-55**	**56-65**	**66-75**	**76-85**
Number	41	40	14	15	12	12	10
$P_{25\%}$	3.88	3.41	3.43	3.45	2.90	2.72	2.62
Mean	4.16	3.93	3.72	3.73	3.09	2.89	2.77
Standard Deviation	0.49	0.68	0.22	0.27	0.17	0.18	0.24
$P_{75\%}$	4.48	4.33	3.99	3.93	3.27	3.14	2.97

$P_{25\ \%}$: 25th percentile; $P_{\ 0}$: 75th percentile.

Table III. Proposal of predictive equations by sex.

	Coeficiente	P Value	Intervalo confianza 95%	r^2	EEM
Female					
Constant	0.088	0.916	[-1.563 -1.740]		
Age (years)	-0.014	0.0001	[-0.018 -0.010]		
Height (cm)	0.016	0.008	[0.004 0.027]		
Weight (kg)	0.013	0.002	[0.005 0.021]		
Equation	**0.088-(0.014*A)+(0.016*H)+(0.013*W)**			0.541	0.338
Male					
Constant	-2.126	0.123	[-4.839 0.587]		
Age (years)	-0.010	0.002	[-0.17 -0.004]		
Height (cm)	0.031	0.001	[0.013 0.048]		
Weight (kg)	0.014	0.031	[0.001 0.027]		
Equation	**-2.126-(0.010*A)+(0.031*H)+(0.014*W)**			0.479	0.429

A= Age; H= Height; W= Height; r^2= square r; SEM= standard error of measurement.

Table IV. Comparison of Inspiratory Capacity values according to author and sex.

	IC	Current Results	Lisboa *et al*. (2007)	Roca *et al*. (1998)
Female	2.72±0.46	2.74±0.32 Δ=0.020 P=0.284	3.00±0.51 Δ=0.080 P <0.0001	2.54±0.27 Δ=0.380 P <0.0001
Male	3.88±0.60	3.94±0.39 Δ=0.060 P=0.3781	4.08±0.65 Δ=0.200 P=0.0028	3.72±0.29 Δ=0.160 P=0.0107

IC= inspiratory capacity; Δ= difference between mean obtained versus cited author; P= p value.

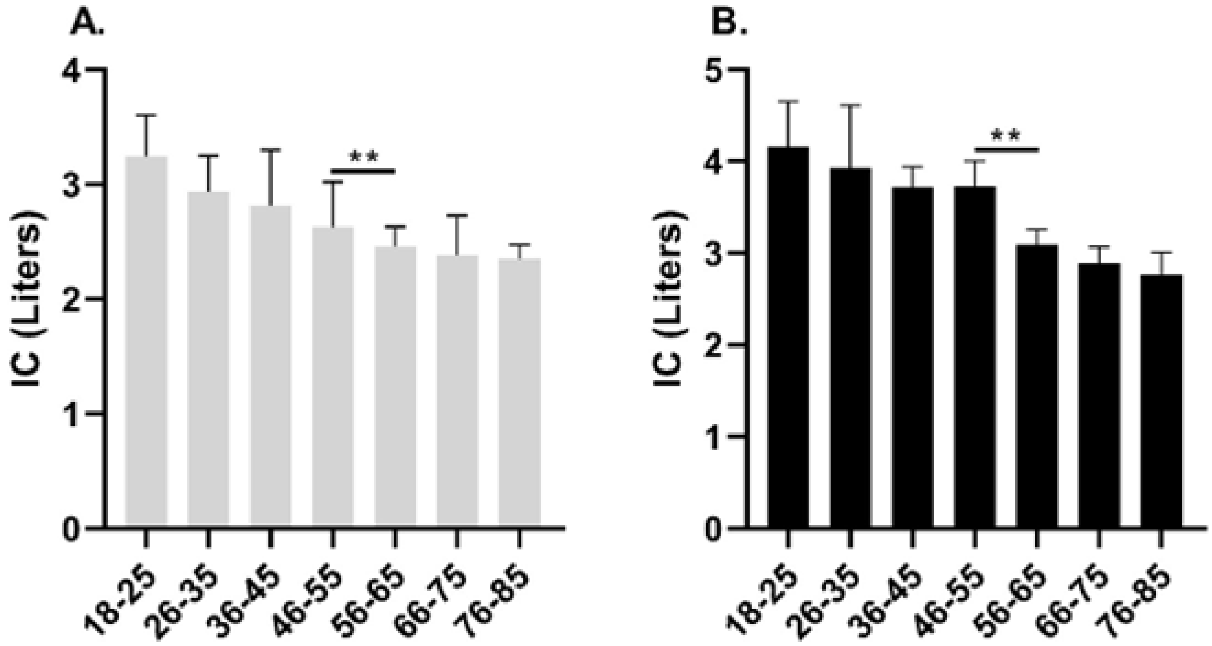

Fig. 1. Values are expressed as mean and standard deviation. The decades ranging from 18-25 to 76-85 years old. A= Female; B= Male. **: p<0.01. A statistically significant decrease is observed in the decade 46-55 years old in both female and male. Male have the highest IC values ??in all decades. There is a significant decrease until 36-45 years old of age. As in female, there is a significant decrease between the ages of 46 and 55 years old.

DISCUSSION

Having reference values that are representative of the population of Maule means increasing the validity of the comparisons referred to for the capacity to inspire and its consequent extrapolation to the capacity to exercise (Casanova & Celli, 2007). Although the general behavior of the IC results independent of sex between the different decades follows the trend described in the literature, i.e., there is a peak in the stratum ranging from 18 to 25 years of age, and from there a sustained decrease begins until the stratum ranging from 76 to 85 years of age (Sharma & Goodwin, 2006). It can be noted that the differences obtained in the stratum from 46 to 55 years of age could be due to the beginning of the definitive loss of the dynamic properties of ventilatory function in relation to the context (Lisboa *et al*., 2007). However, the main finding of the results refers to the statistically significant difference with the values of Lisboa *et al*., (2007) and Roca *et al*., (1998).

The literature warns that reference values are a current concern not only in our country, but also in all Latin America. Lessa *et al*. (2019) proposed reference values for lung volumes in white Brazilians and, at the same time, compared the results obtained with the reference values of Crapo *et al*. and Neder *et al*. Specifically, the IC was 2.35 L in women and 3.27 L in men, both values lower than those reported in the present research. Speculating, this would be due to i) the ethnic and anthropometric characteristics of both samples, ii) in the reference equations, specifically, in the male sex, height was not considered, unlike the current study where this variable had a significant contribution in the reference equation, iii) the present research used 3 % of variability for the selection of the highest value of IC, given that it is feasible to reduce the percentage of reproducibility, a situation that, at the same time, would generate greater stability of the data obtained (Muñoz-Cofré *et al*., 2018; Garrido & Muñoz-

Cofré, 2015) and iv) the presence of the statistical significance of the coefficients in the regression equations in the present study provides information on the real contribution of the variables in the final value of the IC. Finally, Lessa *et al*. (2019) did not compare the IC *versus* the values of Crapo *et al*. (1998) and Neder *et al*. In this context, the present research did find significant differences in relation to the values of Lisboa *et al*. (2007) and Roca *et al*. (1998). This would be a complement to the work of Lessa *et al*. (2019) which would reinforce the fact of the existing differences between the different ethnicities.

Ethnic differences are known to cause changes in ventilatory function in adults and children (Whittaker *et al*., 2005). For example, in some ethnic groups the proportions between leg length and body height are different, consequently, differences in chest size have also been observed (Whittaker *et al*., 2005). Although height and age are the most commonly used predictors of lung volumes, it has been suggested that other variables, such as fat-free fat mass, thoracic diameter, and trunk length may also influence the prediction of lung volumes. In this context, Muñoz-Cofré & del Sol (2018) aimed to determine whether chest measurements cause modifications in the predictive equations for IC and peak expiratory flow (PEF). In their pilot study, they evaluated 24 male subjects between 18 and 26 years of age. While in PEF the variables transverse chest diameter and mid-sternal chest circumference were statistically significant and included in their reference equation, in IC only the classic variables, weight and height, were classified (Muñoz-Cofré & del Sol, 2018). However, when comparing the results obtained by the application of the IC equation *versus* those of Roca *et al*. (1998) the results were 3.91±0.72 L *versus* 3.41±0.33 L ($p<0.001$), respectively. These results differ from those obtained in the present research, which could be explained by the smallness of the sample, both in number and age, a fact that is confirmed by the r^2 (=0.46) of the equation and that the age variable was not significant, therefore, it was not considered in the equation. This shows that, regardless of the thoracic dimensions, it is necessary to construct local reference equations with a more demanding standard, i.e., to consider representative age groups of the community and for both sexes.

Thus, the results obtained show statistically significant differences when compared with the values of Lisboa *et al*. (2007) and Roca *et al*. (1998). In detail, the IC of the participants in the present study were significantly lower than those of Lisboa *et al*. (2007). This is not of minor importance, considering that both samples are national. However, they are: i) a smaller and more specific age range, ii) a population that reported regular physical activity, a situation that has a positive impact on IC (Guenette *et al*., 2013) and iii) they performed a second assessment, a situation that reduces the learning effect. At the same time, the values obtained were significantly higher than those reported by Roca *et al*. (1998). This difference is due to the different methodologies used; the study by Roca *et al*. (1998) had i) two different plethysmographs and ii) three technicians in charge of the measurements, which could have a negative influence on the data obtained.

Morphologically, the lungs undergo a phase of growth and maturation during the first two decades of life and reach their maximum function between 20 and 25 years of age, which remains stable with a minimum change between 25 and 35 years of age, after which it begins to decrease steadily (Sharma & Goodwin, 2006). This is in agreement with the results obtained in this research, where a peak is observed in the period between 18-25 years of age and a subsequent decrease until 46-55 years of age. Although TLC remains unchanged throughout life, FRC and residual volume increase with age, resulting in a decrease in IC. Vital capacity has been reported to drop by 30 % from the age of 30 to 70 years (Ketata *et al*., 2012). However, the exact points at which these significant differences occur have not been determined. In this context, the results obtained indicate the existence of a significant difference between the 46-55 and 56-65 age groups in both sexes. This could be due to the fact that, in this group of participants, the systemic changes typical of the life cycle are accentuated, such as a decrease in muscle strength and joint mobility, together with a decrease in the distensibility of the thorax and the elastic retraction pressure of the lungs (Rodríguez & Rodríguez, 2019).

Finally, the main limitations of the study are presented in the distribution of the sample given that there is an imbalance between the age groups. In retrospect, a second test could have been included in the IC assessment to have reduced the learning effect, with the corresponding impact on the value obtained. In the meantime, the projections refer to complementing the incident aspects of exercise capacity as an indicator of the degree of dysfunction that the viral load caused by SARS CoV-2 (COVID-19) is certain to cause in ventilatory function.

In conclusion, in our country, as already mentioned, there are coexisting references for IC whose values may be above or below those reported in the present study. The contribution of the results obtained lies in the fact that they will allow to improve the relevance of the investigation, diagnosis, control, and follow-up of the contingent sequelae of respiratory diseases that they may eventually affect the inhabitants of the Maule Region.

SUÁREZ, R. C.; ESCOBAR-CABELLO, M.; PANES, V. C.; DEL SOL, M.; VALENZUELA-AEDO, F.; BRAVO, C.; CASTRO, M.; CONEI, D. & MUÑOZ-COFRÉ, R. Valores de referencia de la capacidad inspiratoria: ¿Responden al lugar de origen?. *Int. J. Morphol., 42(6)*:1474-1480, 2024.

RESUMEN: La Capacidad Inspiratoria (CI) es una variable estrechamente relacionada con la funcionalidad y el ejercicio físico. En Chile, existen valores de referencia para la CI que pueden sobreestimar o subestimar esta condición en los usuarios. Así, el objetivo de esta investigación fue determinar los valores locales de CI para la construcción de ecuaciones de referencia. Un total de 305 voluntarios participaron en las evaluaciones, de los cuales 161 (53 %) eran mujeres y 144 (47 %) hombres, desde marzo de 2019 hasta febrero de 2020. Todos cumplieron con los requisitos del Comité de Ética Científica y firmaron el consentimiento; la CI fue evaluada en un pletismógrafo corporal de acuerdo con las recomendaciones de la American Thoracic Society y la European Respiratory Society. Los valores más altos de CI estan en el rango de 18 a 25 años, con 3,24+0,36 litros (L) para mujeres y 4,16+0,49 L para hombres, respectivamente. La IC tuvo una inflexión crítica a partir del rango de 46 a 55 años de edad (mujeres; p=0,026 y hombres; p=0,012), disminuyendo de manera constante. La CI medida mostró diferencias con respecto a los valores de Lisboa *et al*. (2007) y Roca *et al*. (1998) (p<0,0001 y p<0,0001 en mujeres y p=0,0028 y p=0,0107 en hombres). Se obtuvieron ecuaciones predictivas para ambos sexos, que mostraron diferencias significativas con los valores actualmente utilizados. Por lo tanto, mejorar el diagnóstico, control y seguimiento con valores de referencia locales permitirá una gestión más adecuada en la Región del Maule, Chile.

PALABRAS CLAVE: Función pulmonar; Valores de referencia; Capacidad inspiratoria.

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