



# Trabajo Original

Valoración nutricional

# Validity of bioelectric impedance analysis for body composition assessment in interstitial lung disease patients

Validación del análisis de bioimpedancia eléctrica para la evaluación de la composición corporal en pacientes con enfermedad pulmonar intersticial

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# Abstract

**Background:** changes in body composition (BC) are common in interstitial lung disease, which leads to an increased risk of complications and infections, and are associated with poor quality of life and worse outcomes. BC assessment is important to identify malnutrition and sarcopenia. However, gold-standard techniques are not available in all clinical settings.

Aims: this study aimed to evaluate the agreement and reliability of body composition estimated by bioelectric impedance analysis (BIA) and measured using dual-energy X-ray absorptiometry (DEXA) in women with interstitial lung disease.

**Methods:** this is a cross-sectional study. BC (fat mass and appendicular skeletal muscle mass) were assessed using BIA multifrequency and DEXA in standardized conditions. Agreement and reliability between techniques were evaluated using Bland-Altman plots and the intraclass correlation coefficient (ICC).

#### Keywords:

Interstitial lung disease. Appendicular skeletal muscle mass. Body composition. Fat mass. **Results:** a total of 50 women were evaluated. No differences were observed for FM (BIA,  $25.8 \pm 10.2$  kg and DEXA,  $26.3 \pm 10.0$  kg, p = 0.77) and ASMM (BIA,  $14.1 \pm 2.7$  kg and DEXA,  $13.9 \pm 2.3$  kg, p = 0.83). Based on ICC, good reliability was observed for FM (ICC, 0.98) and ASMM (ICC, 0.93).

**Conclusion:** BC estimated by BIA showed good agreement and reliability with DEXA measurements. In the absence of this method, BIA can replace the DEXA technique for body composition assessment.

Received: 15/08/2023 • Accepted: 15/01/2024

Acknowledgments: we gratefully acknowledge all of the involved physicians, nurses, and dietitians for their dedication to the present study.

Funding: this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest: OPIA has previously received honoraria and/or paid consultancy from Fresenius Kabi, Baxter, BBraun, and InBody Co. GAGR, GRAL, ADA, RDZ, BRI report no conflicts of interest.

Artificial intelligence: the authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

García del Valle-Alegría GR, Osuna-Padilla IA, Gómez-Rodríguez AL, Alarcón-Dionet A, Rodríguez-Díaz Z, Buendía-Roldán I. Validity of bioelectric impedance analysis for body composition assessment in interstitial lung disease patients. Nutr Hosp 2024;41(4):810-814 DOI: http://dx.doi.org/10.20960/nh.04882

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### Resumen

Introducción: los cambios en la composición corporal son comunes en la enfermedad pulmonar intersticial, lo cual incrementa el riesgo de complicaciones e infecciones, además de asociarse a peor calidad de vida y peores desenlaces clínicos. La evaluación de la composición corporal es importante para identificar la desnutrición y la sarcopenia, sin embargo, las técnicas consideradas "estándar de oro" no se encuentran disponibles en todos los entornos clínicos.

**Objetivo:** este estudio tiene por objetivo evaluar la validez y concordancia de los parámetros de composición corporal obtenidos por análisis de bioimpedancia eléctrica (BIA) en comparación con la técnica de absorciometría de rayos X de doble energía (DEXA) en mujeres con enfermedad pulmonar intersticial.

Métodos: estudio transversal donde se midió la composición corporal (masa grasa y masa muscular apendicular esquelética) utilizando un equipo de bioimpedancia eléctrica multifrecuencia y DEXA en condiciones estandarizadas. Se evaluó la concordancia y validez entre las técnicas utilizando gráficos Bland-Altman y el coeficiente de correlación intraclase (CCI).

#### Palabras clave:

Enfermedad pulmonar intersticial. Masa muscular apendicular esquelética. Composición corporal. Masa grasa. **Resultados:** se evaluaron un total de 50 mujeres. No se observaron diferencias en los valores de masa grasa (BIA:  $25,8 \pm 10,2$  kg y DEXA:  $26,3 \pm 10,0$  kg, p = 0,77), ni en los de masa muscular apendicular esquelética (BIA:  $14,1 \pm 2,7$  kg y DEXA:  $13,9 \pm 2,3$  kg, p = 0,83). Acorde a los valores del CCI, se observa una validez buena para los valores de masa grasa (CCI: 0,98) y de masa muscular apendicular esquelética (CCI: 0,93). **Conclusión:** la composición corporal estimada por BIA muestra una buena concordancia y validez con el resultado obtenido por DEXA en mujeres con enfermedad pulmonar intersticial. En ausencia de este método, la BIA puede utilizarse para la valoración de la composición corporal en este grupo de pacientes.

# INTRODUCTION

Interstitial lung diseases (ILD) are a heterogeneous group of pulmonary disorders characterized by various degrees of inflammation and/or fibrosis that are characterized by dyspnea. increased metabolic requirements, depression, and anxiety (1,2). These symptoms, in addition to the use of certain drugs such as corticosteroids and immunosuppressives agents, are associated with vomiting, diarrhea, nausea, anorexia, and dysgeusia (3). Due to these complications, changes in body composition (BC) are common in this population (4), which leads to an increased risk of complications and infections, and are associated with poor quality of life (5) and predicts hospitalization (6). Additionally, fat mass (FM), fat-free mass (FFM, includes lean soft tissue and bone mineral density), and appendicular skeletal muscle mass (ASMM, includes lean soft tissue in legs and arms) were associated with diverse outcomes such as exercise capacity, disease severity (7.8), and increased mortality (9-11). In chronic obstructive pulmonary disease (COPD) patients, low muscle mass and sarcopenia is associated with reduced FEV<sub>1</sub> (12).

Dual-energy X-ray absorptiometry (DEXA) is considered a gold standard for BC assessment, but this method is expensive and not available in all clinical settings (13). Bioelectric impedance analysis (BIA) estimates the FM and FFM through the resistance and reactance measurement (14) and has been proposed as a safe and low-cost alternative (13). Accuracy between both methods was studied in cystic fibrosis, breast cancer, heart failure, and liver disease (15-19) populations and reports high variability between techniques using mono-frequency or multi-frequency BIA devices. There is a lack of evidence about BC assessment using BIA multifrequency and their agreement with DEXA in the ILD population.

This study aimed to evaluate the agreement and reliability of body composition estimated by BIA and DEXA in women with ILD.

#### **METHODS**

# STUDY POPULATION

This is a cross-sectional analysis from an institutional cohort of women patients with ILD in the Institute of Respiratory Diseases (INER) diagnosed according to the American Thoracic Society/European Respiratory Society (ATS/ERS) 2013 guidelines (1). This study protocol was reviewed and approved by the Institutional Review Board of the National Institute of Respiratory Diseases.

## DATA COLLECTION

Demographic and clinical information, including age and drug prescription, were collected from patient records.

#### **BODY COMPOSITION ASSESSMENT**

Patients were instructed to wear lightweight clothing and to avoid food intake 8 h previous to DEXA and BIA scans. Previous procedures, participants removed all metal jewelry from the body. Once removed, body weight and height were measured (SECA 769, Germany). Body mass index (BMI) was calculated and classified using World Health Organization criteria (14). Height and weight measurements were inputted into the BIA and DEXA devices.

DEXA measurements were made using a total-body scanner (Lunar Prodigy Advance, GE Healthcare, UK) with the participant in the supine position according to manufacturer recommendations. System quality assurance protocols were performed daily by the manufacturer's instructions. Regional lean mass, total- FM in kilograms, and percentage were calculated using enCORE 2010 software using scan modes (thick, standard, or thin) suggested by the software. At the end of the scan, all BC analyses were thoroughly checked for random measurement errors (i.e., regions of interest errors or metal artifacts) and were manually adjusted for the region of interest for regional BC estimations (arms, legs, and trunk). All scans were performed by a single certified technician to decrease the potential introduction of interoperator differences. ASMM was calculated as the sum of the lean mass in the legs and arms.

BIA was performed with the patient in a supine position after the DEXA scan using a multi-frequency device (InBody S10<sup>®</sup>, In-Body Co., Ltd., Seoul, Korea) according to the manufacturer's guidelines. This instrument uses eight tactile electrodes, with four in contact with the palm and thumb of both hands and the other four in contact with the anterior and posterior aspects of the sole of both feet. A total of 30 impedance measurements are obtained using 6 different frequencies (1 kHz, 5 kHz, 50 kHz, 250 kHz, 500 kHz, 1000 kHz) at the 5 following segments of the body: right and left arms, trunk, right and left legs. Data output (phase angle-PhA-, ASMM, and FM), as calculated by using the manufacturer's algorithm, were recorded from the machine output.

# STATISTICAL ANALYSIS

Data analysis was performed using the Stata V14 software package. Normality was evaluated with the Shapiro-Wilk test. Data are expressed as means and standard deviations (SD) or median and interguartile range (IQR). A Bland Altman analysis was performed to evaluate the agreement of both methods (DEXA and BIA), including an analysis with the Student's t-test for the means to assess the differences in the real and estimated measurements compared with zero. Intraclass correlation coefficient (ICC) was evaluated, which calculates reliability between the body composition estimated by BIA and the measured by DEXA. Reliability was defined as good (> 0.75), moderate (0.5 to 0.75), and poor (< 0.5). A posteriori power analysis for the sample was performed and showed that the analyzed sample size is sufficient to detect a correlation > 0.90between methods with a power of 80 %. A significance level of p < 0.05 was set.

#### RESULTS

Fifty women with ILD diagnosis were included, 58 % of cases were secondary to autoimmune disease; all patients were receiving immunosuppressant treatment (mycophenolate mofetil or azathioprine), some with steroids or nintedanib. The mean age was  $60.8 \pm 11$  years (minimum 27, maximum 83 years).

The phase angle for the total sample was  $5.2 \pm 0.9^{\circ}$ . Demographic characteristics are summarized in table I.

According to the BMI, 30 % of the sample had overweight and 32 % obesity. No statistical differences were observed for BC results between both techniques. BIA underestimates FM (25.8  $\pm$  10.2 kg) in comparison to DEXA (26.3  $\pm$  10.0 kg) without statistical significance (p = 0.77) (Table II). Oppositely, ASMM was overestimated (14.1  $\pm$  2.7 kg) by BIA vs DEXA (13.9  $\pm$  2.3) (p = 0.83). Based on ICC, good reliability was observed for FM (ICC, 0.98) and ASMM (ICC, 0.93) (Fig. 1).

# Table I. Demographic, nutritional and pulmonary functional characteristics

|   | n = 50   |  |  |  |  |
|---|--|--|--|--|--|
| Age, years  | 61 ± 11  |  |  |  |  |
| <i>Diagnosis, n (%)</i><br>Hypersensitivity pneumonitis<br>Interstitial lung disease secondary to auto-<br>immune disease   | 21 (42)<br>29 (58)   |  |  |  |  |
| Treatment, n (%)<br>AZA<br>MMF<br>MMF + prednisone<br>MMF + nintedanib<br>MMF + nintedanib + prednisone<br>MMF + MTX + prednisone<br>MTX + AZA + prednisone<br>MTX + prednisone | 2 (4)<br>13 (26)<br>25 (50)<br>3 (6)<br>4 (8)<br>1 (2)<br>1 (2)<br>1 (2) |  |  |  |  |
| Body composition  |  |  |  |  |  |
| Body mass index<br>< 18.5 kg/m <sup>2</sup><br>18.5-24.9 kg/m <sup>2</sup><br>25-29.9 kg/m <sup>2</sup><br>> 30 kg/m <sup>2</sup>   | 3 (6 %)<br>16 (32 %)<br>15 (30 %)<br>16 (32 %)                           |  |  |  |  |
| Weight (kg)   | 61.1 ± 14.1  |  |  |  |  |
| Phase angle (°)   | 5.2 ± 0.9  |  |  |  |  |
| <i>Fat mass (kg)</i><br>DEXA<br>BIA   | 26.3 ± 10.0<br>25.8 ± 10.2   |  |  |  |  |
| <i>Fat free mass (kg)</i><br>BIA  | 35.2 ± 5.1   |  |  |  |  |
| <i>Appendicular skeletal muscle mass (kg)</i><br>DEXA<br>BIA  | 13.9 ± 2.3<br>14.1 ± 2.7   |  |  |  |  |

AZA: azathioprine; MMF: mycophenolate mofetil; MTX: methotrexate. Mean ± standard deviation.

| skeletal muscle mass in patients with interstitial lung disease |               |               |        |      |  |
|---|---------------|---------------|--------|------|--|
|   | Bland-Altman* | 95 % CI       | t-test | ICC  |  |
| ASMM kg   | 0.19          | -1.59 to 1.89 | 0.77   | 0.93 |  |
| FM kg   | -0.41         | -3.4 to 2.58  | 0.83   | 0.98 |  |

Table II. Agreement between the estimated and measured fat mass and appendicularskeletal muscle mass in patients with interstitial lung disease

CI: confidence interval; ICC: intraclass correlation coefficient; ASMM: appendicular skeletal muscle mass; FM: fat mass. \*Analysis of differences (estimated body composition by BIA – body composition by DEXA).

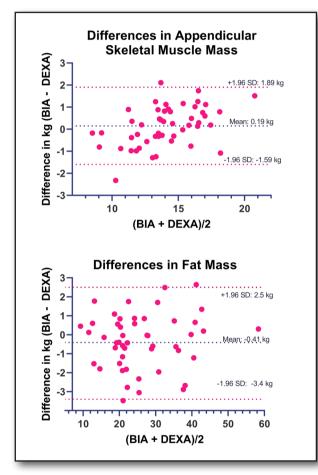


Figure 1.

Bland-Altman plots for differences in appendicular skeletal muscle mass and fat mass between BIA and DEXA.

#### DISCUSSION

In this sample of outpatient women with ILD, BC assessment using BIA shows good agreement and reliability for ASMM (mean difference of 0.19 kg and ICC = 0.93) and FM (mean difference of -0.41 kg and ICC = 0.98).

A study conducted by McLester in a healthy population found an underestimation of FM percentage and an overestimation of FFM using BIA in comparison to DEXA (20). Discrepancy data were reported in clinical populations; in cystic fibrosis patients, Ziai et al. found that BIA underestimated FM (-10.2 %) and overestimated FFM (8.04 %) (16). Grover et al report a good agreement between DEXA and BIA for FM (mean difference BIA-DEXA = 1.18, 95 % CI: 0.54 to 1.81 kg) and FFM (mean difference BIA-DEXA = -1.16, 95 % CI: -2.21 to -1.11 kg) assessment in patients with cirrhosis (15). Both suggested that BIA can be used for monitoring purposes but, for an accurate measurement of BC, DEXA is an irreplaceable tool. Shah et al. found differences in measurements between DEXA and BIA techniques in patients with heart disease, where BIA underestimates FM (mean difference BIA-DEXA = -5.1, 95 % CI: -11.7 to 1.5 kg) and overestimates lean mass (mean difference BIA-DEXA = 5.5, 95 % Cl: -1.3 to 12.3 kg) (19). Saito et al. report a low agreement between BIA and DEXA for ASMM (mean difference = -1.19, 95 % Cl: -1.47 to -0.91) in heart failure hospitalized patients, and poor agreement in diagnosing low ASMM (Cohen's kappa coefficient: 0.294, 95 % CI: 0.17 to 0.42) (17). In patients with breast cancer, Bell et al. found that BIA overestimated FFM (mean difference BIA-DEXA 4.1  $\pm$  3.4 kg) using DEXA as the gold standard (18). The clinical characteristics of this study are different from those of ILD patients, which can explain the differences in agreement and reliability observed in our sample. Considering these results, an assessment of agreement and concordance of BIA with gold-standard methods is recommended before the incorporation of this technique into routine clinical care and nutritional monitoring.

Our study compared ASMM and FM measured by BIA and DEXA in patients with ILD. ASMM could be a better indicator than FFM when BIA is applied. In women with ILD, BIA can replace DEXA to estimate ASMM and FM to assess and monitor nutritional status and to identify patients who should benefit from a nutritional intervention. However, some factors can affect the accuracy of BC results such obesity, edema, pleural effusion, or chronic kidney disease (21).

PhA derived from BIA is another nutritional marker that is related to poor quality of body mass cells and cell membrane integrity (22). During a pro-inflammatory state, PhA responds over the lower capacitance of damaged cell membranes. This indicator was studied in other clinical conditions, such as cirrhosis (23), chronic kidney disease (24), or COPD (12). In the ILD context, it could be used as a biomarker of higher degrees of inflammation (22); however, more studies were needed to assess the validity and associations of PhA with other clinical outcomes in men and woman with ILD. The limitations of this study consist of the number of participants, as they were only fifty women, so it makes it difficult to extrapolate our results to all women and the male population with ILD. Additionally, this study was conducted in a heterogenous sample, and inflammation status was not assessed; it may be an opportunity to consider future research on inflammation biomarkers to correlate with BC.

#### CONCLUSION

Body composition estimated by BIA showed good agreement and reliability with DEXA measurements. In the absence of this method, BIA can replace the DEXA technique for body composition assessment in women with interstitial lung disease.

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