International Journal of Gerontology 18 (2024) 179–183
https://doi.org/10.6890/IJGE.202407_18(3).0008

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Novel Bioelectrical Impedance Analysis for Bone Mineral Density Measurement in Postmenopausal Women

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ARTICLE INFO

Accepted 16 February 2024

Keywords:
dual energy X-ray absorptiometry,
whole body bone mineral density,
consistency

SUMMARY

Background: The measurement of bone mineral density (BMD) is important for determining osteoporosis. The novel bioelectrical impedance analysis (BIA) presented herein provides a new body composition measurement function: bone density measurement. The purpose of this study was to evaluate the accuracy of a novel bioimpedance method for whole-body BMD measurement in postmenopausal women in Taiwan.

Methods: Menopausal women in Taiwan were recruited as subjects. The standing foot-to-foot bioimpedance analyzer StarBIA201 (Starbia meditek Co., Taichung City, Taiwan) was used to measure whole-body bone density, and the results were compared with dual energy X-ray absorptiometry (DXA) measurements. The consistency of the 2 methods was evaluated through Pearson correlation, linear regression, and Bland-Altman analysis. Differences in whole-body BMD between groups with different obesity levels were analyzed using univariate Bonferroni-corrected analysis. A total of 74 postmenopausal women with a mean age of 66.5 ± 8.6 years, men height of 156.3 ± 4.7 cm, and mean weight of 58.6 ± 9.2 kg were included in the study.

Results: The mean whole body BMD measured by BIA (1.05 ± 0.06 g/cm^2) was significantly higher than by DXA (0.99 ± 0.13 g/cm^2). The correlation coefficient between the 2 devices for total body BMD in all subjects was 0.609. When the body mass index (BMI) was < 25 kg/m^2, BIA overestimated BMD by 0.06 g/cm^2. When the BMI was > 25 kg/m^2, BIA overestimated BMD by 0.05 g/cm^2. The limit of agreement in the Bland-Altman plots was -0.170 to 0.248 g/cm^2.

Conclusion: For postmenopausal women, BIA provides a rapid, convenient, and safe method for preliminary screening of whole-body BMD.

1. Introduction

Osteoporosis is characterized by low bone mass and microstructural degradation of bone tissue, leading to decreased bone strength and an increase in the risk of fractures.[1] Osteoporosis is responsible for 1.5 million fractures in the United States each year, including an estimated 700,000 vertebral fractures, 300,000 hip fractures, and 250,000 distal forearm fractures.[2] It is estimated that nearly 10 million people in the United States have osteoporosis, and an additional 34 million have osteopenia. According to the World Health Organization, 44 million people in the United States under the age of 50 have osteoporosis or low bone mass, accounting for 55% of the entire population. Primary osteoporosis can occur at any age, but is most common in women after menopause. Nearly four-fifths of osteoporosis patients in the United States are women.[3] Osteoporosis is a silent disease, and thus is often under-reported and under-treated, even in older adults with a recent history of low-grade traumatic fractures.[4]

Adequate bone strength is necessary to reduce the risk of fractures, and decreased bone strength may lead to fractures of the hips, vertebra, and other bones.[5,6] Osteoporosis is defined as a decrease in bone strength and bone mineral density (BMD) that occurs with age, or after menopause.[7,8] If the body does not reach its maximum bone density or mass in early age, the likelihood of developing osteoporosis is higher.[9,10] Postmenopausal osteoporosis refers to the loss of trabecular bone, accompanied by changes in body composition and estrogen level, leading to loss of body fat, muscle, and lean mass. Osteoporosis is typically asymptomatic, and is not diagnosed until a fracture occurs.[11–13] Methods for estimating BMD include single-energy X-ray absorptiometry (SXA), quantitative computed tomography (QCT), radiographic absorptiometry, and quantitative ultrasound. Computed tomography (CT) and magnetic resonance imaging (MRI) provide a large amount of measurement data; however, they are expensive, take a considerable amount of time, and CT is associated with a relatively high radiation dose. In practice, BMD is usually measured in the peripheral regions of the body using dual energy X-ray absorptiometry (DXA) and SXA. DXA measures BMD throughout the body through the lumbar spine or hip, and can effectively predict hip fractures.[14–16] As such, DXA is the standard method for assessing BMD.

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Bone quality depends on structural and material properties, including BMD, bone geometry and structure, as well as its organic composition.[17] Thus, the phase angle determined by bioelectrical impedance analysis (BIA) can be used for the prediction of sports injuries because it is directly related to the quality and vitality of human cells.[18] Notably, BMD is an important indicator of bone health.[19] Antnestest et al.[20] found that after adjusting for variables such as age, weight, lean mass, vitamin D intake, disease, fractures, and medications the phase angle determined by BIA is directly related to proximal femoral BMD, cervical BMD, and the BMD. In addition, studies have shown that the properties of bioimpedance are a linear function of body composition and bone mineral content. Measurement of whole-body single-frequency (50 KHz, 800 μA) bioimpedance in adult men and postmenopausal women showed that bioimpedance was correlated with BMD, and the correlation was higher in men than women.[21] However, it is important to note that the application of bioimpedance measurements to assess bone mineral content (BMC) or BMD involves a dual indirect estimation. Currently, bioimpedance analysis cannot directly measure or estimate BMD.

BIA is a safe, simple, and non-invasive technology. No experienced operators are required, the cost is low, and the results are highly reproducible. As BIA can be used to measure bone mineral content,[22] it has the potential to be used to measure bone density and thus become a screening tool for osteoporosis. The purpose of this study was to determine the accuracy of BIA in measuring whole-body BMD in postmenopausal women in Taiwan.

2. Methods

Data collection for this cross-sectional study was conducted between June 2021 and May 2022. All participants were informed of the objectives and risks of the study, and provided a signed consent form before participation. This study was approved by the Medical Ethics Committee of China Medical University Hospital (Number CMUH109-REC1-152). Participants were recruited from oral presentations, and posters. The inclusion criteria were postmenopausal women between the ages of 55 and 90 who could stand and walk on their own. The exclusion criteria were any prior surgery to change body composition (such as bariatric surgery). The sample size was calculated after taking into account type I ($\alpha = 0.05$) and type II errors ($\beta = 0.80$). For the linear regression analysis, a posteriori analysis indicated that at $\alpha = 0.05$ and $\beta = 0.80$, 70 women would be needed for a mean effect size of 0.50. Sample number calculations were performed using G* Power software version 3.1.9.4 (Universitat Dusselfodorf, Germany).

A 4-electrode dual-frequency StarBIA-201 foot-to-foot bioimpedance analyzer (StarBIA MediTek Co., Taichung City, Taiwan) was used. The analyzer applies resistance and reactance at 2 measurement frequencies (50 and 250 KHz) after the subject's height and age are entered in the StarBIA-201. A digital height measuring instrument (Holtain, Crosswell, Wales, UK) was used to measure the height of subjects with an accuracy of 0.1 cm. Before measurement, the subject was asked to drain urine from the bladder and stand quietly for 5 minutes before standing on the measurement platform. Through the pressure formed by the weight of the body, the soles of the 2 feet contact the 2 electrode pairs, respectively. The test takes less than 1 minute to complete.

The measurements for the study were performed from 9:00 am to 12:00 noon. It was also recommended that subjects avoid strenuous exercise 48 hours before testing, and maintain normal and regular eating habits.

Bone density measurements were performed using a GE Lunar Prodigy Advance dual-energy X-ray absorptiometer (GE Medical System Lunar, Madison, WI, USA). The scanning procedure was performed using enCORE 2011 version 13.50.0 (GE Medical System Lunar, WI, USA). During the scan, the subject lies on their back with their arms at their sides, palms facing down. Since all subjects were within the range of the scanning platform, half-body skeletal tissue assessment was not performed. All scanning and adjustments were performed by trained technicians according to the International Society for Clinical Densitometry (ISCD) standards.[23] Before each measurement, the subject's age, height, weight, sex, and race were entered into the device. The ISCD bone density measurement accuracy calculation tool version 2.1 was used to calculate the accuracy error (expressed as root mean square value and standard deviation [RMSV $\pm$ SD]), and least significant change (LSC) for each body region. In addition, the total body bone density, 0.008 g/cm^2 (RMSV $\pm$ SD), whole body bone density, 0.023 g/cm^2 (LSC), and its 0.35% coefficient of variation (CV) were calculated.

Before the test, the subjects were instructed to: (1) Change into a cotton robe and only wear underwear for the scanning; (2) Remove any accessories that may attenuate the X-ray beam, such as rings, earrings, zippers, buttons, etc.; (3) Do not ingest radionuclides or radiopaque agents within 5 days before scanning; (4) Do not ingest a large amount of caffeine or alcohol within 48 hours before the scanning; (5) Avoid moderate or high-intensity exercise 12 hours before the test; (6) Empty the bladder before the test; (7) Do not take diuretics for 7 days before scanning.

2.1. Statistical analysis

All data were presented as mean $\pm$ standard deviation (SD), and minimum and maximum values. Determination of kurtosis and asymmetry were used to assess the normality of the data (range between -2 and +2), and all data were found to have a normal distribution. The paired-t test was used to compare total body BMD measured by BIA and DXA. The correlation between BMD measured by BIA and DXA was calculated using Pearson correlation, Concordance correlation, and a p value of 0.05 was considered significant. Passing-Bablok regression and Bland-Altman plots[24] were used to analyze the consistency of the 2 methods by LOA, and the deviation was calculated as the mean of 1.96 SD of the difference between the 2 variables. Differences in whole-body BMD between BIA and DXA at different levels of body weight (normal vs. overweight BMI) were tested by using 1-factor analysis of variance (ANOVA). A simple regression analysis was performed to determine the fixed error and proportional error of BIA in BMD and DXA. All statistical analyzes were performed using SPSS version 20 software (IBM SPSS, Armonk, NY, USA).

3. Results

A total of 74 postmenopausal women were included in the study, and their characteristics are summarized in Table 1. The mean age of the subjects was 66.5 $\pm$ 8.6 years (range, 55 to 89 years). The BMI of the subjects ranged from 17.6 to 39.0 kg/m^2, and their body fat percentage ranged from 20.8 to 48.7% (Measured using DXA).

The analysis of all subjects indicated the correlation coefficient (r) between BIA and DXA for whole-body measurements was 0.609 (Figure 1). Concordnce correlation coefficient was 0.478. When the subjects were divided into those of normal weight and those that were overweight, correlation between BIA and DXA for normal weight subjects was 0.532 and for overweight subjects was 0.493. The corresponding Concordance correlation coefficients are 0.558 and 0.313, respectively.

The results of whole-body BMD measurement by BIA and DXA are shown in Table 2. The mean BMD obtained by BIA was significantly higher than that measured by DXA in normal weight and overweight subjects. The BMD measured by BIA was also higher than that measured by DXA in all subjects combined. The mean measurement error of the 2 methods was 0.039 g/cm^2. Bland-Altman plots of BMD measured by BIA and DXA are shown in Figure 2. The mean difference measured by the 2 methods was 0.039 g/cm^2, and the LOA was -0.170 to 0.248 g/cm^2. The trend equation (trend line) was y = -0.836 x + 0.835, r = 0.704. The trend equation showed that the difference in BMD measured by the 2 methods has a significant trend from positive to negative as BMD increases. Using Passing-Bablok regression analysis, DXA was comparable with BIA in estimating BMD among subjects (intercept = -1.482; slope = 2.458).

4. Discussion

Several studies have shown that age is one of the major risk factors for fractures. In postmenopausal women, changes in body composition and hormone levels lead to a decrease in BMD and ultimately osteoporosis.[25] The standard method for assessing BMD is DXA; however, DXA has some disadvantages including limited availability and high cost. Therefore, it may not be suitable for preliminary screening. Studies have shown that BIA and phase angle have a correlation with BMD of the whole body, spine, and proximal femur in middle-aged and elderly persons. Notably, lower phase angles are associated with osteoporosis.[26] Although there is a certain correlation between BMD and phase angle, the conduction pathway of the measuring electrical current does not directly pass through the bones. Many studies have pointed out that there is a significant correlation between BIVA, BIA, and BMD.[21,27] Although there are published studies on BIA or BIVA measurement and BMD, actual applications for BMD estimation are limited. This study is the first study to examine the use of BIA for whole-body BMD measurement in postmenopausal women.

The results of this study showed that there was a moderate positive correlation between total body bone density measured by BIA in the standing leg-to-leg mode and DXA for postmenopausal women. However, Bland-Altman plots showed that BIA overestimates whole-body BMD compared with DXA measurement of whole-body BMD, and the measurement difference exhibits a decreasing trend as whole-body BMD increases. Thus, there is room for improvement in the accuracy of BIA measurement of BMD compared with DXA.

With existing quantitative ultrasonography (QUS) bone density examination, the strength of the QUS weakens and the speed of

Table 1
Physical characteristics of the subject[1].

Item	BMI < 25 kg/m^2 (n = 49)	BMI ≥ 25(n = 25)	Total (n = 74)
Age (year)	65.1 ± 8.0 (55.0, 82.0)	68.0 ± 9.5 (57.0, 89.0)	66.5 ± 8.6 (55.0, 89.0)
Height (cm)	157.3 ± 5.0 (143.0, 168.0)*	154.4 ± 3.3 (149.0, 164.0)	156.3 ± 4.7 (143.0, 168.0)
Weight (kg)	52.6 ± 7.4 (41.0, 63.5)**	67.4 ± 7.6 (56.8, 93.8)	58.6 ± 9.2 (41.0, 93.8)
BMI (kg/m^2)	21.3 ± 2.8 (13.1, 24.9)**	28.2 ± 2.9 (25.5, 39.0)	24.0 ± 4.0 (17.6, 39.0)
BPF_{DXA} (%)	35.2 ± 6.3 (19.3, 45.1)**	43.0 ± 3.9 (35.6, 48.7)	38.6 ± 5.8 (20.8, 48.7)
BMC_{DXA} (kg)	1.8 ± 0.3 (1.3, 2.6)	1.9 ± 0.3 (1.4, 2.4)	1.8 ± 0.3 (1.3, 2.6)
BFM_{DXA} (kg)	18.8 ± 4.8 (6.4, 27.7)**	29.1 ± 5.1 (22.1, 45.1)	22.9 ± 6.4 (12.4, 45.1)

** p < 0.01, * p < 0.05, [1] All value are $\bar{x}$ ± SD; minimum and maximum in parentheses. The subscript DXA indicates the application of DXA measurement. BMI, body mass index; BFP, body fat percent; BMC, bone mineral content; BFM, body fat mass.

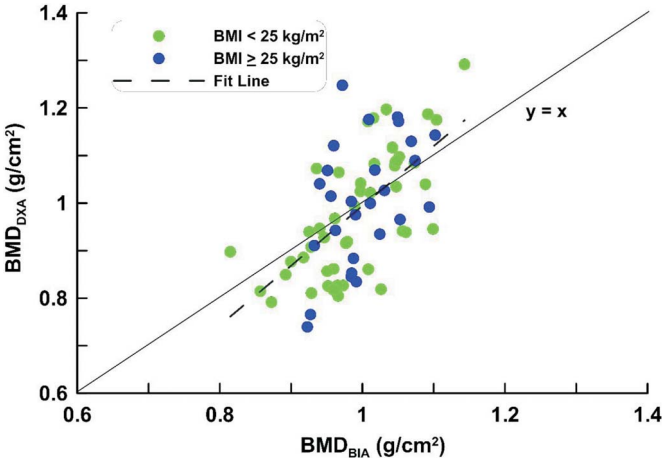

Figure 1. Distribution of whole-body BMD measured by the two devices, in which the solid black line is the equivalent line and the dotted line is the regression line (y = 0.292 x + 0.702, n = 74, r = 0.609, p < 0.05).

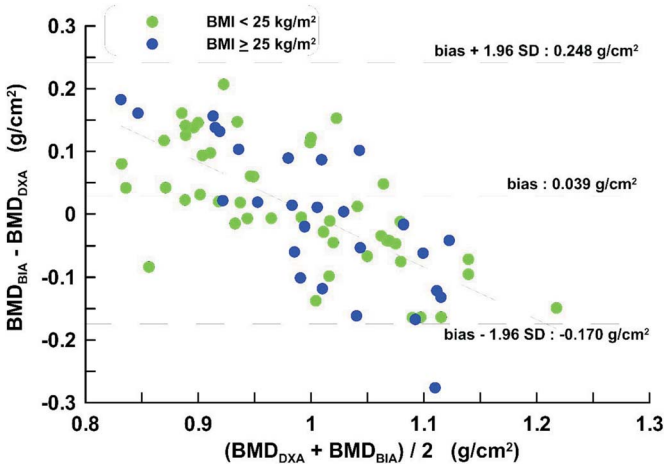

Figure 2. Bland-Altman plots of whole-body BMD measured by the two devices, where the black dotted line is the trend line (y = -0.836 x + 0.835, r = 0.704, p < 0.05).

Table 2
Bone mineral density by dual-energy X-ray absorptiometry (DXA) and by bioelectrical impedance analysis (BIA).

Method	BMI < 25 kg/m^2 (n = 49)	BMI ≥ 25 kg/m^2 (n = 25)	Total (n = 74)
BMD_{BIA}	1.04 ± 0.07 (0.81, 1.14)**	1.05 ± 0.06 (0.90, 1.09)**	1.05 ± 0.06 (0.81, 1.14)**
BMD_{DXA}	0.98 ± 0.13 (0.79, 1.29)	1.00 ± 0.13 (0.74, 1.25)	0.99 ± 0.13 (0.74, 1.25)

[1] All value are $\bar{x}$ ± SD; minimum and maximum in parentheses.
** Significant different from DXA, p < 0.001 (paired t test).

sound slows when the signal penetrates bone. The degree of slowing is related to the level of bone density. Ultrasound bone density testing is used to assess the extent of these weakenings and to modify the bone density assessment. The accuracy and reproducibility of QUS for measuring bone density are low, and it cannot effectively measure bone mass changes over a short period of time. The correlation between QUS measurement of BMD in various parts of the body and DXA ranges from r = 0.35 to 0.80.[28,29] As such, QUS is not approved for the screening, diagnosis, and tracking of osteoporosis, and its use for screening has not been recognized by the World Health Organization. Compared to QUS, BIA is more convenient, safer, cheaper, and faster, and may be more suitable BMD/osteoporosis screening.

The symptoms of osteoporosis are not obvious, and the best prevention is to include bone health care and related examinations in physical examinations or general initial screening. Otherwise, it may still be difficult to let "new of elderly patients" understand the importance of diagnostic examination and treatment. Thus, it is very important to have an effective, safe, and convenient method for measuring bone density and screening for osteoporosis.

Currently, DXA is used to measure bone density in the lumbar spine, proximal femur, and forearm bones to determine osteoporosis. Whole-body BMD measurements are mostly performed in pediatric patients. DXA has high reproducibility, and for whole-body skeletal examination the results obtained by DXA are integrated assessments. Compared with BMD of the lumbar spine, proximal femur, and forearm, whole-body BMD is less used to determine osteoporosis. However, whole-body BMD still has a certain value for determining osteoporosis. The osteoporotic process is heterogeneous, and peak bone mass and standard deviation values calculated from a population may not be suitable for ever individual. There is currently no evidence as to the best reference position for bone quality assessment.[30] In this study, the whole-body BMD of postmenopausal women had a high positive correlation with the BMD of the lumbar spine, proximal femur, and forearm bone (r = 0.78 to 0.85, data not shown in the results). The existing BIA used for the measurement or estimation of BMD still lacks substantial theoretical support. Although the indirect estimation results of whole-body BMD in postmenopausal women using the bioimpedance analyzer discussed in the study show a moderate correlation with DXA, the wide limits of agreement (LOA) and proportional errors indicate limited clinical significance and poorer predictive performance. If the device is to be employed for BMD screening, further validation studies or improvements are necessary before it can be considered a viable option for BMD screening.

This study examined postmenopausal women in Taiwan. The findings cannot be extrapolated to other groups of different ages and physiological conditions. The BIA device used in this study was a standing foot-to-foot bioimpedance composition meter with BMD measurement function. Therefore, the results cannot be inferred to other body composition analyzers of different brands, models, and other methods. The number of subjects tested in this study was limited, and larger-scale validation of postmenopausal women or other ethnic groups may be considered in the future.

The study investigates the indirectly estimated whole-body bone density using a foot-to-foot bioimpedance analyzer. Although the electrical current of the bioimpedance analyzer examined in this study only passes through the legs, and DXA provides reference values for leg bone mineral density, the bioimpedance analyzer under investigation, StarBIA201, outputs estimates for whole-body BMD. Therefore, this study does not specifically address the BMD of the legs.

5. Conclusion

BIA is simple, convenient, and safe for body composition measurement. Whole-body BMD measurement in postmenopausal women using BIA has the potential to be a screening method for osteoporosis.

Funding

This research was supported by a grant from China Medical University in Taiwan with the award number of DMR-109-083.

Conflict of interest

The authors declare non conflict of interests.

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