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## ORIGINAL RESEARCH



# Body composition in patients with obesity-related heart failure with preserved ejection fraction: A comparison study

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## Abstract

**Background:** Appendicular lean mass index is a major determinant of cardiorespiratory fitness in patients with obesity-related heart failure with preserved ejection fraction (HFpEF). Moreover, appendicular lean mass index can be used to diagnose sarcopenia and sarcopenic obesity in this population. We aimed to validate the ability of segmental single-frequency bioelectrical impedance analysis (SF-BIA) to assess body composition compared with dual-energy x-ray absorptiometry (DXA) in patients with HFpEF and obesity, with a focus on appendicular lean mass index for its critical role in diagnosing sarcopenia and sarcopenic obesity.

**Methods:** We analyzed 62 euvolemic patients from a heart failure outpatient clinic with persistent obesity-related HFpEF (83.8% women, 60.8 ± 2.8 years of age). We used DXA and segmental SF-BIA.

Hannah Salmons and Syed Imran Ahmed contributed equally to this work.

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**Results:** Strong correlations were found between segmental SF-BIA and DXA for appendicular lean mass index ( $r = 0.897$ ), appendicular fat mass index ( $r = 0.864$ ), fat mass ( $r = 0.968$ ), fat mass percentage ( $r = 0.867$ ), fat-free mass ( $r = 0.954$ ), fat-free mass percentage ( $r = 0.852$ ), fat mass index ( $r = 0.97$ ), and fat-free mass index ( $r = 0.88$ ) (all  $p < 0.001$ ), without significant proportional bias for all parameters, except for appendicular fat mass index.

**Conclusions:** Segmental SF-BIA-measured body composition shows strong correlations, appropriate agreements, and no proportional bias compared with DXA. Segmental SF-BIA should be considered in patients with obesity-related HFpEF.

#### KEYWORDS

BIA, body composition, DXA, heart failure, HFpEF, obesity

## INTRODUCTION

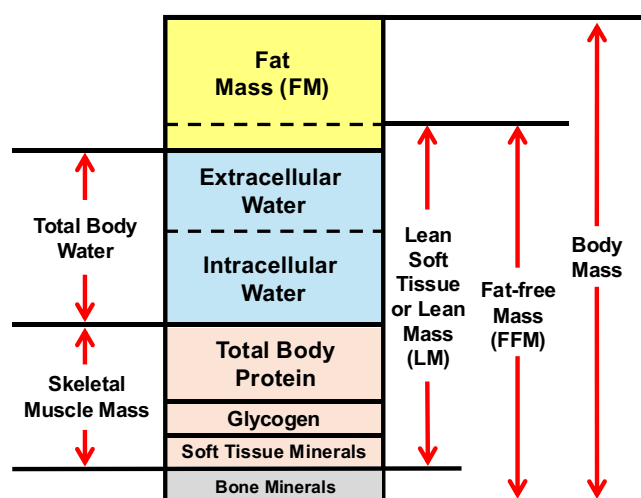
Patients with obesity-related heart failure with preserved ejection fraction (HFpEF) are characterized by excess fat mass that negatively impacts cardiorespiratory fitness and quality of life.<sup>1-5</sup> The exclusive reliance on body mass index (BMI) may lead to misclassification of these individuals, whereas those with higher BMI but with greater lean mass (defined as bone-free fat-free mass) may present a more favorable cardiorespiratory fitness.<sup>6,7</sup> A recent meta-analysis of 27 studies confirmed that reduced cardiorespiratory fitness measured as peak oxygen consumption in patients with heart failure is heavily driven by reduced whole-body lean mass and appendicular lean mass.<sup>8</sup> Moreover, lean mass, but not fat mass, is an independent predictor of long-term survival in patients with HFpEF.<sup>9</sup> When reduced lean mass is paired with excess adiposity characteristic of obesity (ie, sarcopenic obesity), prognosis is further worsened in patients with HFpEF.<sup>6,10-12</sup> Taken together, this substantiates the limitations of BMI, which does not allow for differentiation between body composition compartments. Importantly, although fat-free mass and lean mass are often used interchangeably, they provide information on different body composition compartments, with lean mass being the best surrogate to estimate skeletal muscle mass given that it excludes bone mineral content from fat-free mass (Figure 1).

Considering the growing use and efficacy of medications for chronic weight management in patients with obesity-related HFpEF,<sup>13</sup> which results in a reduction of fat mass and lean mass, assessing body composition in this population is essential.<sup>14,15</sup> The reduction in lean mass potentially leads to an increased long-term risk for sarcopenia and sarcopenic obesity.<sup>16,17</sup>

Despite the well-established role of body composition in patients with obesity-related HFpEF, its assessment outside of clinical research is rarely implemented because of the challenges associated with the available tools that can accurately estimate fat mass and lean mass compartments. Dual-energy x-ray absorptiometry (DXA) is one of the accepted reference methods for assessing whole and segmental body composition and diagnosing sarcopenia and sarcopenic obesity. DXA-

measured appendicular lean soft tissue, which is the bone-free fat-free mass of the arms and legs, is the same compartment we refer to as “appendicular lean mass.” Although body composition analysis can improve HFpEF risk stratification, there are several barriers to routine implementation of DXA in the clinical setting, such as cost, time, weight limit, radiation exposure, lack of portability, and need for skilled personnel for the segmental analysis.<sup>18,19</sup> This highlights the need to identify alternative tools to routinely assess whole and segmental body composition in this population.

Segmental single-frequency bioelectrical impedance analysis (SF-BIA) is a noninvasive tool that provides an estimation of body composition quantity and quality. It may represent a more accessible, portable, and cost-effective method to estimate whole and segmental body composition, including appendicular lean mass index, without risk of exposure to radiation. We have previously shown that in



**FIGURE 1** Schematic of body composition compartments that includes the differentiation between fat-free mass, lean mass (or lean soft tissue), and skeletal muscle mass. The sum of lean mass of arms and legs describes appendicular lean mass. Lean mass divided by height<sup>2</sup>, allows to calculate appendicular lean mass index ( $\text{kg}/\text{m}^2$ ).

patients with obesity-related HFpEF, SF-BIA-derived fat mass index (fat mass/height<sup>2</sup>) provides a valid alternative to DXA-derived fat mass index<sup>4</sup> and that in patients with heart failure with reduced ejection fraction, this particular segmental SF-BIA approach is a suitable alternative for assessing appendicular lean mass index as compared with DXA-assessed appendicular lean mass index.<sup>6</sup> This segmental SF-BIA algorithm, however, has not been validated against DXA in patients with obesity-related HFpEF, which would ultimately allow its implementation in both clinical and research practices.<sup>6,20</sup>

The aim of this study is to validate a segmental SF-BIA method against the reference standard DXA in patients with obesity-related HFpEF. Our primary outcome was appendicular lean mass index measured by SF-BIA analysis and DXA because of its significant diagnostic and prognostic value in identifying sarcopenia and sarcopenic obesity. We hypothesized that there is a difference between resting appendicular lean mass index measured by segmental SF-BIA and DXA.

## METHODS

We conducted a prospective comparison study approved by the Virginia Commonwealth University Institutional Review Board (20016253, approved on May 17, 2019) in adult individuals from the Virginia Commonwealth University heart failure outpatient clinic. Patients were stable, symptomatic, and euvoletic at physical examination conducted by a cardiologist, were persistent and previously diagnosed HFpEF (New York Heart Association [NYHA] class II and III, left ventricular ejection fraction >50% documented in the prior 12 months, and no recent hospitalizations for acute decompensated heart failure or changes in medication in the prior month) had obesity (BMI  $\geq$  30 kg/m<sup>2</sup> or fat mass >25% for men and >35% for women), and underwent body composition analysis. Patients with known secondary causes of HFpEF (eg, valvular heart disease, hypertrophic cardiomyopathy, or pericardiac disease) were excluded. All patients provided written informed consent. Demographic and medical history data were either self-reported or obtained by the electronic medical record. Physical examination and anthropometrics were collected by the study team.

We compared DXA (Lunar iDXA, encore 2011 software, version 13.60.033; GE HealthCare) and a segmental SF-BIA (50 kHz) device (Quantum V, RJL Systems) as body composition determinants. There were no restrictions on food intake, fluid intake, and physical activity before the visit. SF-BIA and DXA were conducted on the same day of the study visit. For SF-BIA measurements, patients were asked to lie flat on a hospital bed, and device-specific electrodes purchased from RJL Systems were placed on both hands and feet in a standard eight-polar configuration. Briefly, two electrodes were placed on each hand and each foot, for a total of eight electrodes, following device manufacturer instructions. SF-BIA were conducted by different operators of the study team, including dietitians, physicians, exercise physiologists, and supervised trainees. All operators were required to undergo at least one 30-min training on how to conduct the assessment and observed at least five assessments conducted by a body composition expert. The first five independent assessments were also conducted under the supervision of a

body composition expert. Patients underwent the DXA scan while lying in a supine position on the scanning table, remaining still with arms at their sides and legs extended, in accordance with standardized imaging protocols. A single operator conducted all DXA scans.

DXA scans provided lean mass and fat mass in kilograms and percentage of body weight. Segmental body composition was assessed using Lunar iDXA regional body tissue quantitation system. The segmental SF-BIA device software provides estimates of whole-body and segmental fat-free mass, lean mass (bone-free fat-free mass), and fat mass. The predictive equation used by the segmental SF-BIA for the estimate of right arm, left arm, right leg, and left leg have been described in Table S1, as provided by the device manufacturer.

For both assessments, appendicular lean mass was obtained by summing the lean mass of both arms and legs, and appendicular fat mass was obtained by summing the fat mass of both arms and legs. We then calculated appendicular lean mass index (kg of lean mass in limbs/height<sup>2</sup>) and appendicular fat mass index (kg of fat mass in limbs/height<sup>2</sup>) for both methods. We further calculated fat mass index (kg of fat mass/height<sup>2</sup>) and fat-free mass index (kg of fat-free mass/height<sup>2</sup>). We used transthoracic Doppler echocardiography to measure resting left ventricular ejection fraction and venipuncture to measure glomerular filtration rate, high-sensitivity C-reactive protein, and N-terminal pro-B-type natriuretic peptide (NT-proBNP).

Clinical characteristics were presented as number (percentage) or mean (standard deviation [SD]). Correlations between DXA and SF-BIA for appendicular lean mass index (kg/m<sup>2</sup>), appendicular fat mass index (kg/m<sup>2</sup>), fat mass (kg), fat mass percentage, fat-free mass (kg), fat-free mass percentage, fat mass index, and fat-free mass index were assessed using Pearson correlation coefficients to quantify the strength of agreement between SF-BIA and DXA body composition measurements.

The degree of agreement between appendicular lean mass index measured by segmental SF-BIA and DXA were visualized with the Bland-Altman plot. We also determined the degree of agreement between the other body composition measurements via the Bland-Altman plot. The Bland-Altman plot produces upper and lower limits of agreement that allow for a subjective decision whether the agreement between measured and predicted resting energy expenditure is acceptable. The Bland-Altman plot emphasizes clinical significance and allows for assessment of the magnitude of disagreement, both error and bias. But the Bland-Altman plot ignores statistical inference. We therefore conducted simple linear regression to assess proportional bias in SF-BIA measurements compared with DXA. We also analyzed differences between SF-BIA and DXA using Wilcoxon signed-rank test for paired samples. Statistical analysis was performed using SPSS 28 (IBM Corp), and statistical significance was set at  $p < 0.05$ .

## RESULTS

### Baseline characteristics

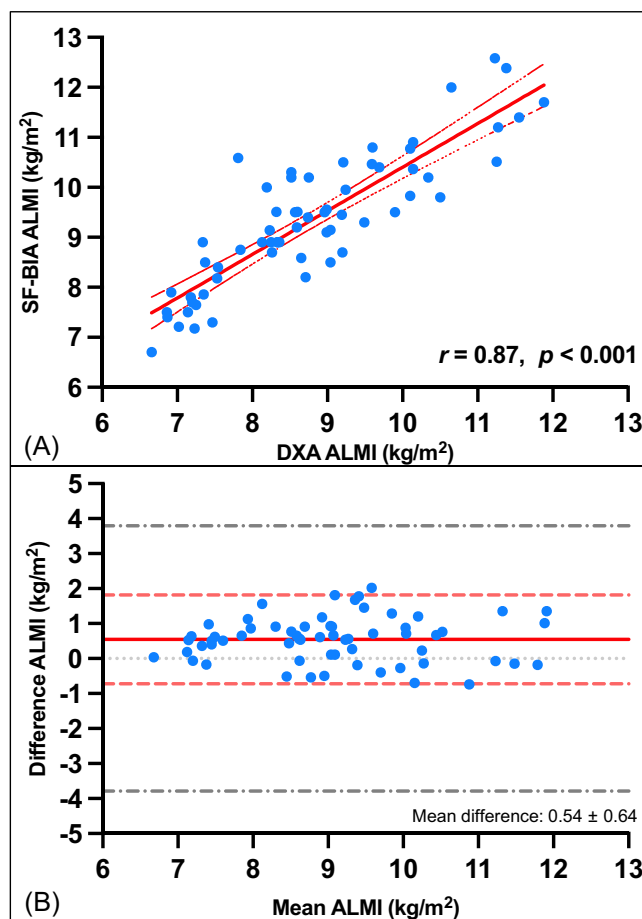
We included 62 patients with obesity-related HFpEF; 83.8% self-identified as women and 58% as Black/African American.

**TABLE 1** Baseline characteristics.

Demographic variable	N = 62
Age, mean (SD), y	60.8 (12.8)
Women n (%)	52 (83.8)
Black, n (%)	36 (58)
Functional class and comorbidities, n (%)	
NYHA class 2	52 (83.8)
NYHA class 3	10 (16.1)
Ischemic heart disease	11 (17.7)
Prior percutaneous intervention	8 (12.9)
Prior coronary artery bypass grafting	3 (4.8)
Prior cerebrovascular event	1 (1.6)
Diabetes	31 (50.0)
Hyperlipidemia	54 (87.1)
Tobacco use	2 (3.2)
Hypertension	56 (90.3)
Peripheral vascular disease	3 (4.8)
Chronic kidney disease	3 (4.8)
Chronic obstructive pulmonary disease	3 (4.8)
Obstructive sleep apnea	27 (43.5)
Anthropometrics, mean (SD)	
Weight, kg	101.6 (18.8)
Height, m	1.65 (0.1)
Body mass index, kg/m <sup>2</sup>	36.6 (5.4)
Waist circumference, cm	112.7 (13.3)
Vital signs, mean (SD)	
Heart rate, bpm	71.1 (10.8)
Systolic blood pressure, mm Hg	127.7 (12.7)
Diastolic blood pressure, mm Hg	68.3 (10.4)
Echocardiographic parameters, mean (SD)	
Left ventricular ejection fraction, %	58.7 (4.2)
Biomarkers, mean (SD)	
Glomerular filtration rate, ml/min/1.73 <sup>2</sup>	77.2 (19.3)
High-sensitivity C-reactive protein, mg/L	4.58 (5.1)
NT-proBNP, pg/ml	217.2 (307.9)

Abbreviations: NYHA, New York Heart Association; NT-proBNP, N-terminal pro-b-type natriuretic peptide; SD, standard deviation.

Mean (SD) age was 60.8 (12.8) years, BMI was 36.6 (5.4) kg/m<sup>2</sup>, left ventricular ejection fraction was 58.7% (4.2%), NT-proBNP was 217.2 (307.9) pg/ml, and 52 (83.8%) and 10 (16.2%) patients were classified as NYHA class II and III, respectively (Table 1).



**FIGURE 2** (A) Correlation of appendicular lean mass index (kg/m<sup>2</sup>) between DXA and SF-BIA measurement. (B) Bland-Altman plot with limits of agreements and maximum allowed difference of appendicular lean mass index (kg/m<sup>2</sup>) between SF-BIA and DXA measurement. Dotted gray lines indicate maximum allowed difference, dotted red lines indicate limits of agreements, and solid red line indicates mean difference between SF-BIA and DXA measurements. ALMI, appendicular lean mass index; DXA, dual-energy x-ray absorptiometry; SF-BIA, single-frequency bioelectrical impedance analysis.

### Segmental body composition: Appendicular lean mass index and appendicular fat mass index

Appendicular lean mass index values were strongly correlated between SF-BIA and DXA ( $r = 0.897$ ,  $p < 0.001$ ). Linear regression showed lack of proportional bias ( $\beta = 0.003$ , standard error [SE] = 0.06,  $p = 0.96$ ), and Bland-Altman analysis indicated limits of agreement from  $-0.72$  to  $1.82$  kg/m<sup>2</sup>, with all values within the allowed difference range of  $-3.8$  to  $3.8$  kg/m<sup>2</sup> (Figure 2A,B).

Appendicular fat mass index values showed a strong correlation ( $r = 0.864$ ,  $p < 0.001$ ) but a significant proportional bias ( $\beta = -0.34$ , SE = 0.068,  $p < 0.001$ ), with limits of agreement from  $-3.2$  to  $1.1$  kg/m<sup>2</sup> and the maximum allowed difference to range from  $-5.0$  to  $5.0$  kg/m<sup>2</sup>. Table 2 describes the differences of the values between SF-BIA- and DXA-measured segmental body composition compartments.

**TABLE 2** Body composition compartments measured with segmental SF-BIA and DXA.

Body composition compartment	SF-BIA, mean (SD)	DXA, mean (SD)	Difference (BIA-DXA), mean (SD)	95% CI		<i>p</i> value <sup>a</sup>
				Lower	Upper	
Appendicular lean mass index, kg/m <sup>2</sup>	9.3 (1.3)	9.3 (1.4)	0.5 (0.6)	0.3344	0.6905	0.558
Appendicular fat mass index, kg/m <sup>2</sup>	6.6 (1.5)	7.7 (2.1)	-1.0 (1.1) <sup>a</sup>	-1.3898	-0.7906	<0.001
Fat-free mass, kg	58.6 (10.7)	55.2 (11.2)	3.4 (3.5) <sup>a</sup>	2.2229	4.0742	<0.001
Fat mass, kg	44.8 (12.2)	47.3 (12.5)	-2.5 (3.0) <sup>a</sup>	-3.7097	-2.0417	<0.001
Fat-free mass, % BW	57.0 (5.8)	53.6 (6.0)	3.4 (3.2) <sup>a</sup>	2.4194	4.1611	<0.001
Fat mass, % BW	43.5 (6.3)	45.5 (5.9)	-2.5 (3.0) <sup>a</sup>	-3.3312	-1.6752	<0.001
Fat-free mass index, kg/m <sup>2</sup>	21.3 (2.5)	20.0 (2.5)	1.4 (1.3) <sup>a</sup>	0.8640	1.5060	<0.001
Fat mass index, kg/m <sup>2</sup>	16.2 (4.1)	17.1 (4.1)	-0.9 (1.1) <sup>a</sup>	-1.5180	-0.4220	<0.001

Abbreviations: BW, body weight; CI, confidence interval; DXA, dual-energy x-ray absorptiometry; SF-BIA, single-frequency bioelectrical impedance analysis; SD, standard deviation.

<sup>a</sup>*p*-value < 0.05 (Wilcoxon signed rank test).

### Whole-body composition: fat mass, fat-free mass, fat mass index, and fat-free mass index

SF-BIA-measured whole-body fat mass (kg) showed a strong, significant correlation with DXA-measured fat mass ( $r = 0.97$ ,  $p < 0.001$ ; Figure 3A). Linear regression showed a lack of proportional bias ( $\beta = -0.026$ ,  $SE = 0.032$ ,  $p = 0.416$ ), and Bland-Altman analysis resulted in limits of agreement between  $-8.4$  and  $3.4$  kg, with a maximum allowed difference ranging from  $-34.0$  to  $34.0$  kg (Figure 3B). Fat mass percentage measured with SF-BIA correlated strongly with DXA ( $r = 0.867$ ,  $p < 0.001$ ), with a lack of proportional bias ( $\beta = -0.003$ ,  $SE = 0.066$ ,  $p = 0.967$ ) (Figure 3C), limits of agreement between  $-8.4\%$  and  $3.4\%$ , and a maximum allowed difference from  $-16.7\%$  to  $16.7\%$  (Figure 3D).

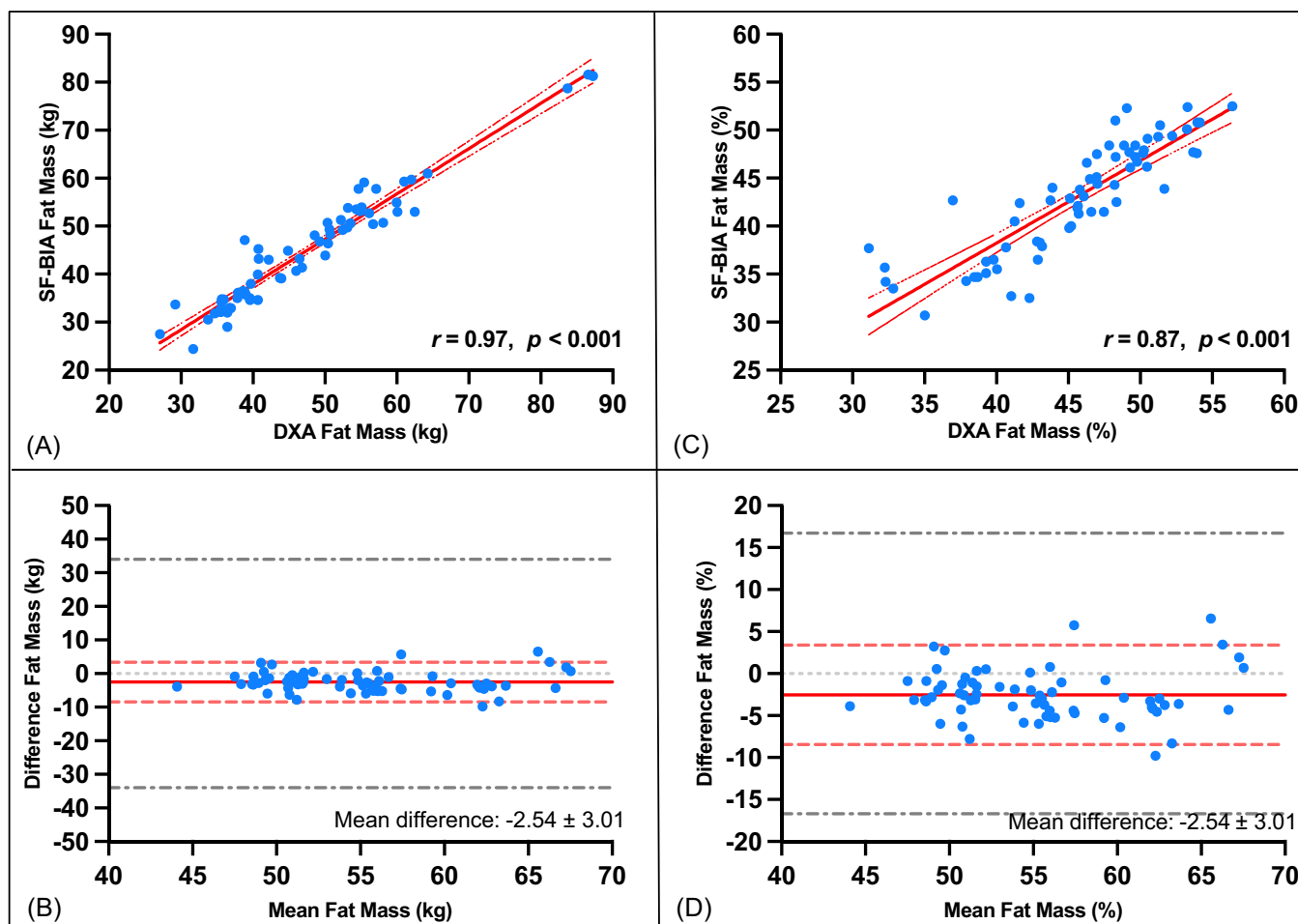
Similarly, whole-body fat-free mass (kg) measured by SF-BIA strongly correlated with that by DXA ( $r = 0.954$ ,  $p < 0.001$ ), and regression analysis showed no evidence of proportional bias ( $\beta = -0.052$ ,  $SE = 0.04$ ,  $p = 0.194$ ) (Figure 4A), with limits of agreement between  $-3.5$  and  $10.2$  kg and maximum allowed difference of  $-30.2$  and  $30.2$  kg (Figure 4B). For fat-free mass percentage, the correlation was also strong ( $r = 0.852$ ,  $p < 0.001$ ), with no significant bias ( $\beta = -0.03$ ,  $SE = 0.071$ ,  $p = 0.669$ ) (Figure 4C). Bland-Altman limits of agreement ranged between  $-2.5$  and  $9.3$  kg, and the maximum allowed difference from  $-17.0\%$  to  $17.0\%$  (Figure 4D).

Whole-body fat-free mass index values measured by SF-BIA showed a strong, statistically significant correlation with DXA ( $r = 0.88$ ,  $p < 0.001$ ) (Figure 5A). Linear regression analysis indicated minimal bias ( $\beta = -0.013$ ,  $SE = 0.063$ ,  $p = 0.838$ ), and Bland-Altman analysis displayed limits of agreement between  $-1.2$  and  $4.0$  kg/m<sup>2</sup>, without any points outside the allowed range ( $-6.8$  to  $6.8$  kg/m<sup>2</sup>) (Figure 5B). Whole-body fat mass index values also demonstrated a strong correlation ( $r = 0.97$ ,  $p < 0.001$ ) (Figure 5C). Regression analysis showed no evidence of proportional bias ( $\beta = -0.028$ ,  $SE = 0.078$ ,  $p = 0.721$ ), and limits of agreement were calculated between  $-3.1$  and  $1.3$  kg/m<sup>2</sup>, without outliers beyond the maximum allowed difference ( $-11.2$ ,  $11.2$  kg/m<sup>2</sup>) (Figure 5D). Table 2 summarizes the differences and related 95% confidence intervals between SF-BIA-measured and DXA-measured whole-body composition compartments.

### DISCUSSION

In this study, we found that segmental SF-BIA using the RJL Systems Quantum V device is a suitable alternative to DXA for measurement of whole and segmental body composition in patients with obesity-related HFpEF. Except for appendicular fat mass index, which is rarely used in research and clinical practice, all body composition compartments measured by the SF-BIA device presented a strong correlation without any evidence of proportional bias against DXA, a well-accepted reference standard tool to assess body composition; however, except for appendicular lean mass index, the other body composition measures presented significant differences at Wilcoxon signed-rank test, for which we reported the sizes and directions.

Overall, our results support that SF-BIA remains a suitable alternative to DXA in patients with obesity-related HFpEF. This is of particular clinical relevance because body composition plays a crucial role in determining cardiorespiratory fitness, quality of life, as well as survival in HF.<sup>10,21–26</sup> Moreover, up to 50% of patients with heart failure have a reduced appendicular lean mass index, which portends to a worse prognosis. An accurate assessment of appendicular lean mass index, a surrogate for skeletal muscle mass, also allows for the diagnosis of sarcopenia and sarcopenic obesity.<sup>27–29</sup> Particularly, sarcopenic obesity has recently received intense scrutiny because of the pivotal role of weight loss in patients with obesity-related HFpEF. In fact, despite the short-term beneficial effects of weight loss in this population,<sup>11,30,31</sup> fat mass loss is typically accompanied by a loss of skeletal muscle mass. Moreover, in patients undergoing energy restriction-induced weight loss, long-term weight regain in the form of fat mass is common, ultimately leading to a greater long-term risk for sarcopenic obesity.<sup>21,32</sup> In patients treated with medications for chronic weight management, weight regain is less common unless medication is interrupted; however, because of their powerful weight loss effects, whether the loss of skeletal muscle mass results in long-term detrimental effects is largely unknown.<sup>33</sup> This is mainly

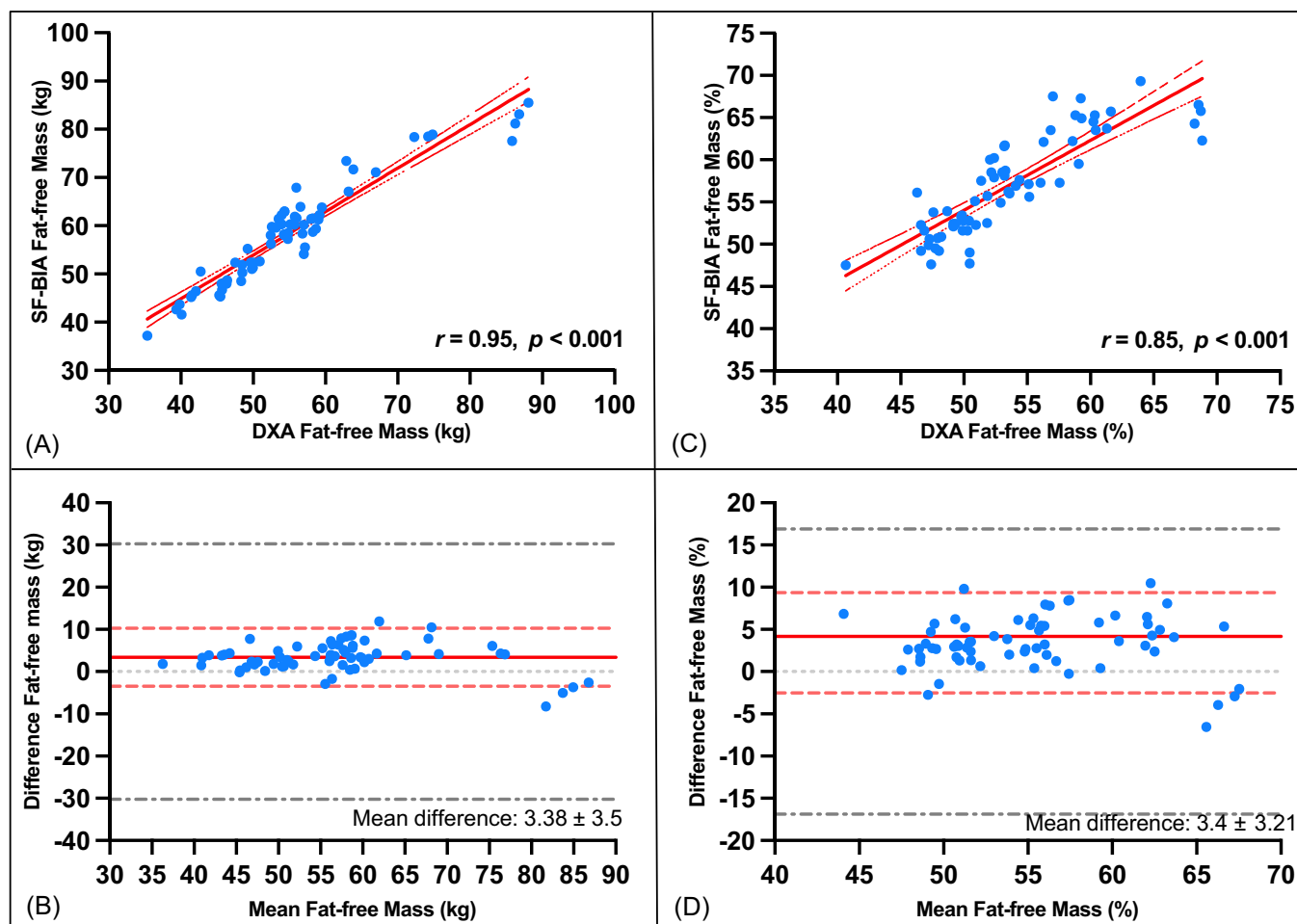


**FIGURE 3** (A) Correlation of fat mass (kg) between DXA and SF-BIA measurement. (B) Bland-Altman plot with limits of agreement and maximum allowed difference of fat mass (kg) between SF-BIA and DXA measurement. (C) Correlation of fat mass percentage between DXA and SF-BIA measurement. (D) Bland-Altman plot with limits of agreement and maximum allowed difference of fat mass percentage between SF-BIA and DXA measurement. Dotted gray lines indicate maximum allowed difference, dotted red lines indicate limits of agreements, and solid red line indicates mean difference between SF-BIA and DXA measurements. DXA, dual-energy x-ray absorptiometry; SF-BIA, single-frequency bioelectrical impedance analysis.

because of the complexity of implementing available tools, such as DXA, resulting in the lack of body composition assessment in most pharmacologic trials in patients with obesity-related HFpEF.

In addition to providing an estimate of the quantity of body composition compartments, such as appendicular lean mass index, this SF-BIA method also allows for the estimation of skeletal muscle quality in the form of phase angle, ultimately providing insights on both quantity and quality of body composition. Skeletal muscle quality is also a strong predictor for cardiorespiratory fitness assessed as peak oxygen consumption in patients with obesity-related HFpEF; however, its assessment remains challenging. We have previously reported that phase angle, purported to be a surrogate measure for cellular membrane integrity and body cell mass, is an independent predictor for peak oxygen consumption in patients with obesity-related HFpEF, in which greater phase angle values were associated with more favorable cardiorespiratory fitness and exercise time.<sup>34</sup>

The results of this study help identify alternative tools, filling an important and urgent gap in clinical and research practices. The RJL Systems Quantum V SF-BIA device offers a cost-effective and more accessible alternative to DXA for assessing body composition in patients with obesity-related HFpEF. Moreover, DXA uses the differential attenuation of two x-ray energies to perform multi-compartment assessments. The radiation dose from DXA is small (5–7  $\mu$ Sv) but not insignificant, adding to the list of barriers to its broad implementation. Finally, the segmental body composition assessment with DXA usually requires a trained operator. In contrast to DXA, SF-BIA is radiation-free because it relies on differences of conductivity to assess body composition, passing a low-voltage current between electrodes to measure body water, which is then used to estimate fat-free mass as well as fat mass.<sup>19</sup> Moreover, SF-BIA requires only a few minutes of training because the segmental assessment is automatically estimated by the device and its related software. Also, SF-BIA can be safely used in individuals with



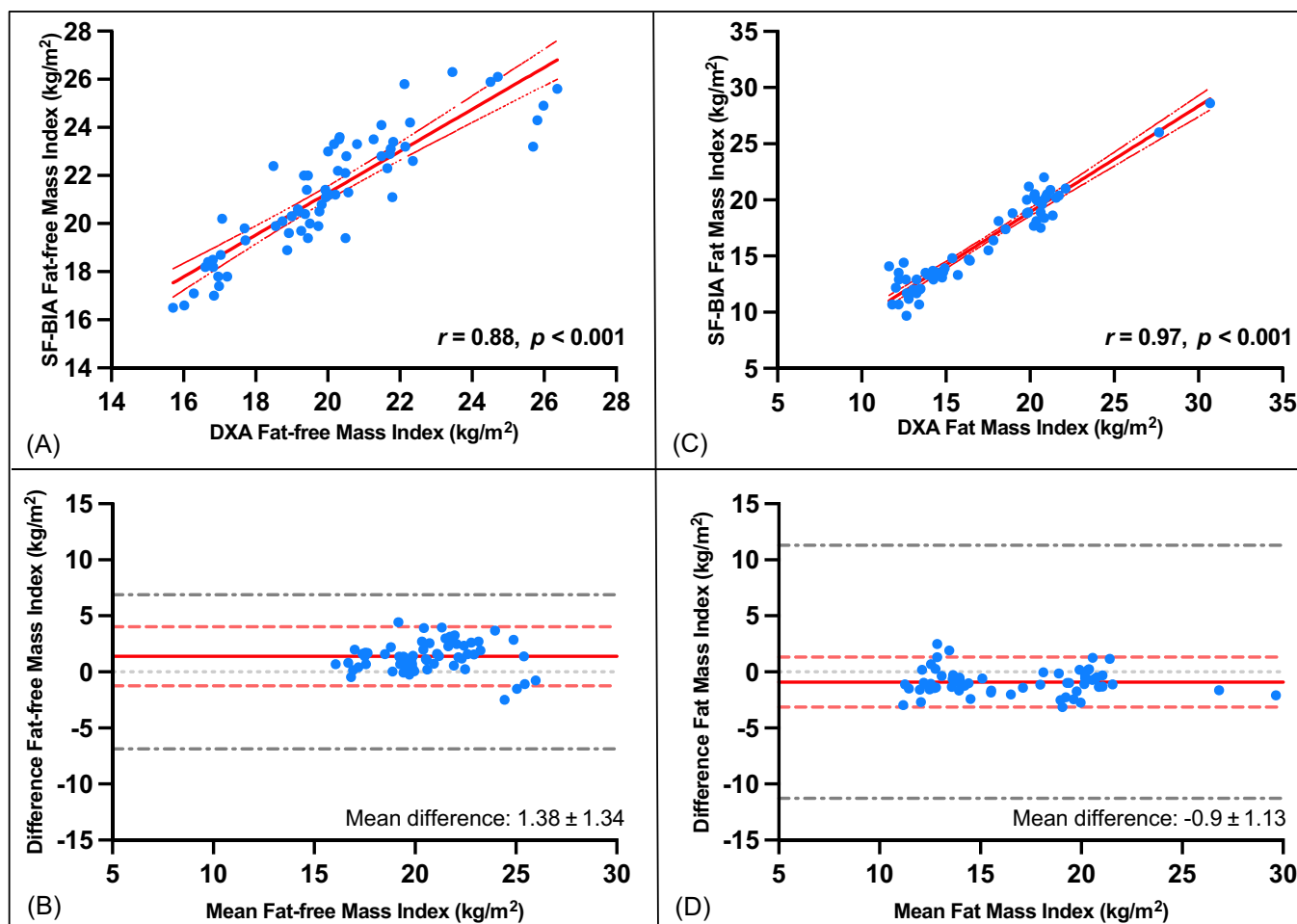
**FIGURE 4** (A) Correlation of fat-free mass (kg) between DXA and SF-BIA measurement. (B) Bland-Altman plot with limits of agreement and maximum allowed difference of fat-free mass (kg) between SF-BIA and DXA measurement. (C) Correlation of fat-free mass percentage between DXA and BIA measurement. (D) Bland-Altman plot with limits of agreement and maximum allowed difference of fat-free mass percentage between SF-BIA and DXA measurement. Dotted gray lines indicate maximum allowed difference, dotted red lines indicate limits of agreements, and solid red line indicates mean difference between SF-BIA and DXA measurements. DXA, dual-energy x-ray absorptiometry; SF-BIA, single-frequency bioelectrical impedance analysis.

implantable devices.<sup>35-37</sup> The current findings support the use of the SF-BIA approach to measure body composition in HFpEF.

Our study is not without limitations. Our population was largely composed of self-identified Black women, which represents, however, most patients with HFpEF, particularly in a metropolitan area of Richmond, Virginia, where recruitment for this study occurred. Whether these findings can be replicated in a different population could not be ascertained, and future studies are clearly needed to confirm our results. Moreover, our study intentionally targeted individuals with obesity; therefore, whether these findings could be replicated in patients with HFpEF, but without obesity, remains unknown. Typically, the use of SF-BIA has been questioned in individuals with obesity because of their extracellular water expansion; however, we cannot exclude the possibilities that specifically in HFpEF, the accuracy of SF-BIA would be different than what is reported in our study in patients without obesity. Importantly, our patients were considered euvoletic at physical examination

completed by a cardiologist; whether these results could be replicated in patients with fluid expansion is unknown. Such validation studies across different populations and fluid status will ultimately allow for the universal implementation of SF-BIA in patients with HFpEF. Finally, the reason for proportional biases for appendicular fat mass index are unclear. We could speculate that patients with HFpEF might present a disproportionate amount of fat mass in the extremities compared with the populations enrolled in the initial validation studies used to develop the predictive equations that SF-BIA relies on for the assessment of body composition (Table S1).

In conclusion, we propose that the segmental SF-BIA approach we evaluated is a practical, cost-effective, radiation-free alternative to DXA for accurately assessing whole-body, but most importantly segmental body composition, particularly appendicular lean mass index, in patients with persistent obesity-related HFpEF. As such, we advocate for its use in clinical trials, but also in clinical practice, to identify body composition phenotypes (ie, sarcopenia and sarcopenic



**FIGURE 5** (A) Correlation of fat-free mass index (kg/m<sup>2</sup>) between dual-energy x-ray absorptiometry (DXA) and single-frequency bioelectrical impedance analysis (SF-BIA) measurement. (B) Bland-Altman plot with limits of agreement and maximum allowed difference of fat-free mass index (kg/m<sup>2</sup>) between SF-BIA and DXA measurement. (C) Correlation of fat mass index between DXA and SF-BIA measurement. (D) Bland-Altman plot with limits of agreement and maximum allowed difference of fat mass index between SF-BIA and DXA measurement. Dotted gray lines indicate maximum allowed difference, dotted red lines indicate limits of agreements, and solid red line indicates mean difference between SF-BIA and DXA measurements. DXA, dual-energy x-ray absorptiometry; SF-BIA, single-frequency bioelectrical impedance analysis.

obesity) and to determine body composition compartments affected by a given intervention, whether it be lifestyle or behavioral or pharmacologic (ie, medications for chronic weight management). This is of critical importance, especially in the setting of interventions resulting in a large weight loss (ie, with modern incretin-mimetic agents), to truly determine the proportion of appendicular lean mass index compared with the overall changes in body weight.

#### AUTHOR CONTRIBUTIONS

**Hannah Salmons:** Investigation; writing—original draft; software; methodology; formal analysis; writing—review and editing. **Syed Imran Ahmed:** Investigation; writing—original draft; methodology; software; formal analysis; writing—review and editing. **Hayley E. Billingsley:** Investigation; methodology; software; formal analysis; writing—review and editing. **Alexander Reavey-Cantwell:** Investigation; writing—review and editing; software. **Roshanak Markley:** Investigation; writing—original draft; writing—review and editing. **Michele Golino:** Investigation;

writing—original draft; writing—review and editing; methodology. **Marco Giuseppe Del Buono:** Investigation; writing—original draft; writing—review and editing; methodology. **Juan Ignacio Damonte:** Investigation; writing—original draft; writing—review and editing; methodology. **Sebastian Pinel:** Investigation; methodology; writing—original draft. **R. Lee Franco:** Investigation; writing—original draft; methodology; writing—review and editing; software. **Antonio Abbate:** Conceptualization; investigation; writing—original draft; methodology; writing—review and editing. **Carrie P. Earthman:** Conceptualization; writing—original draft; writing—review and editing; methodology. **Salvatore Carbone:** Conceptualization; investigation; funding acquisition; writing—original draft; methodology; validation; visualization; writing—review and editing; software; formal analysis; project administration; resources; supervision; data curation.

#### CONFLICT OF INTEREST STATEMENT

None declared.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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