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ORIGINAL RESEARCH

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Effect of obesity on sexual functioning among gynecologic cancer patients receiving radiotherapy

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Abstract

Background: Both obesity and sexual dysfunction are common in gynecologic cancer patients. We aimed to examine the effect of obesity on sexual functioning in gynecologic cancer patients receiving radiotherapy and explore the difference by obesity measures. **Methods**: In this secondary analysis of a prospective observational study, obesity was measured by body mass index (BMI) and body fat percentage (BFP). BFP was estimated using the Clinica Universidad de Navarra-Body Adiposity Estimator. Sexual functioning and physical and emotional well-being were assessed pre-radiotherapy by Female Sexual Function Index and Functional Assessment of Cancer Therapy-General. Sexual functioning was reassessed at six months post-radiotherapy. We used generalized linear models to examine the effect of obesity on sexual functioning and mediation analysis to identify the indirect effect of obesity on sexual functioning through physical and emotional well-being. **Results**: The 54 eligible gynecologic cancer (24 cervical and 30 endometrial) patients were Black (48.1%), in a married/domestic partnership (51.9%), and had a history of prior treatment (59.3%). Patients without obesity reported slightly worse sexual functioning than those with obesity pre-radiotherapy (BMI-based obesity $p = 0.012$, BFP-based obesity $p = 0.033$), but regardless of obesity, patients showed extremely poor sexual functioning, which continued post-radiotherapy. After adjusting for cancer type and history of prior treatment, we found no association between obesity and sexual functioning pre-radiotherapy. However, BFP-based obesity had a negative effect on the changes in sexual functioning from pre- to post-radiotherapy ($p = 0.013$) while BMI-based obesity had no effect. The effect of obesity on sexual functioning was mediated by neither physical nor emotional well-being. **Conclusions**: Obesity, when measured by BFP, was associated with delayed recovery of sexual functioning in women with gynecologic cancer after radiotherapy. Further work with rigorous measurement of obesity could help provide definitive evidence of the association between obesity and sexual functioning in this population.

Keywords

Sexual function; Obesity; Body mass index; Body fat percentage; Gynecologic cancer; Radiotherapy

1. Introduction

Approximately 1.5 million women worldwide are diagnosed with gynecologic cancer each year, with 73% having uterine corpus and cervix cancers [1]. In the United States, the incidence rates of uterine corpus cancer, particularly endometrial cancer have been increasing since 2007 [2], potentially associated in part with increasing obesity rates, a known risk factor for the disease [3]. Gynecologic cancer and its treatment often impair sexual functioning, defined as an ability to experience physical and psychological pleasure from sexual activity [4]. Up to 89% of women with gynecologic cancer report poor sexual functioning [5–7], with the highest rates among those receiving radiotherapy. Pelvic radiotherapy, an important treatment for endometrial and cervical cancer, often leads to genital toxicities, such as vaginal dryness, narrowing, and shortening [8, 9]. These toxicities can persist after treatment, significantly compromising sexual functioning [8, 10]. Identifying patients at higher risk for long-term impairment in sexual functioning after radiotherapy is crucial for timely and effective intervention.

Given the high prevalence of obesity and the longer life expectancy of cancer survivors [1], understanding the impact of obesity on quality of life during cancer survivorship has become increasingly important. However, research on how obesity affects sexual functioning after cancer treatment remains limited. Although obesity is a well-known risk factor for sexual dysfunction [11, 12], existing studies involving gy-

necologic cancer patients are mostly cross-sectional, and have found mixed findings on the association between obesity and sexual functioning (*i.e.*, positive, negative, or no associations) [13]. Obesity has been linked to poorer physical and emotional well-being [14], which may negatively impact sexual functioning [10]. Obesity may delay healing of damaged tissues and exaggerate inflammation, including in the genital area [15, 16]. This inflammation could potentially prevent the recovery of sexual functioning after radiotherapy. For example, although acute vaginal toxicities usually resolve within six months [17], endometrial cancer patients with obesity reported no increase in sexual functioning at 6 months post-radiotherapy, unlike those without obesity [5, 15, 18].

The purpose of this study was to examine the effect of obesity on sexual functioning among gynecologic cancer patients receiving radiotherapy. We investigated (1) the effect of obesity (obese *vs.* non-obese) on sexual functioning pre-radiotherapy, including its indirect effects through physical and emotional well-being, and (2) the effect of obesity on changes in sexual functioning from pre- to post-radiotherapy. Although obesity is commonly defined as body mass index (BMI) $\geq$30 kg/m^2, BMI may underestimate obesity, particularly in women who tend to have higher body fat at similar BMIs [19]. Thus, we also explored body fat percentage (BFP) as a complementary measure of obesity to examine its association with sexual functioning in women with gynecologic cancer.

2. Materials and methods

2.1 Study design

This study was a secondary analysis using an existing dataset from a prospective observational study about the vaginal microbiome of gynecologic cancer patients treated with radiotherapy [20].

2.2 Data source and study sample

The primary findings from the parent study were previously published [20], including recruitment and data collection procedures. We analyzed deidentified data at two time points: baseline (pre-radiotherapy) and 6 months after the completion of radiotherapy (post-radiotherapy). The study participants were $\geq$18 years of age, diagnosed with endometrial or cervical cancer, had a plan of curative radiotherapy (external beam radiation therapy or vaginal brachytherapy, or both), English-speaking, and free from evidence of metastases, other primary cancers, uterine sarcomas, and comorbidities that might cause severe vaginal toxicities (*e.g.*, uncontrolled type 2 diabetes, sexually transmitted diseases). None of the participants had used antibiotics, corticosteroids, or hormone replacement therapy within the 4 weeks prior to baseline assessment. Our sample included 54 patients whose pre-radiotherapy data of both obesity and sexual functioning were available.

2.3 Study variables

To define obesity, we used both BMI and BFP. BMI was calculated using body weight and height pre-radiotherapy. BMI-based obesity was defined as a BMI $\geq$30 kg/m^2. BFP refers to the proportion of body fat mass relative to total body mass. Because a direct measure of BFP was not available in the dataset, we estimated BFP using the Clinica Universidad de Navarra-Body Adiposity Estimator, called CUN-BAE. This predictive equation [21] is: $\text{BFP} = -44.988 + (0.503 \times \text{age}) + (10.689 \times \text{sex}) + (3.172 \times \text{BMI}) - (0.026 \times \text{BMI}^2) + (0.181 \times \text{BMI} \times \text{sex}) - (0.02 \times \text{BMI} \times \text{age}) - (0.005 \times \text{BMI}^2 \times \text{sex}) + (0.00021 \times \text{BMI}^2 \times \text{age})$, in which sex is "1" for female and "0" for male, and age is in years. BFP-based obesity was defined differently by age groups (>39% for women aged 20–39 years, >40% for women aged 40–59, and >42% for women aged 60 or older [22].

The level of sexual functioning was the total score of the Female Sexual Function Index (FSFI), and we used both pre- and post-radiotherapy FSFI total scores. FSFI is a self-report questionnaire assessing six domains of female sexual functioning (desire, arousal, lubrication, orgasm, satisfaction and pain) [23]. FSFI total scores are the sum of the six domain scores, raining from 2 to 36, with the higher scores representing better sexual functioning. FSFI total scores $\leq$26.55 indicate sexual dysfunction [24].

The levels of physical and emotional well-being were measured by the relevant subscale scores of the Functional Assessment of Cancer Therapy-General (FACT-G). FACT-G is a self-report questionnaire about cancer patients' multidimensional quality of life [25]. The physical well-being subscale consists of seven items (*e.g.*, pain, nausea, fatigue), and the emotional well-being subscale consists of six items (*e.g.*, sadness, anxiety, nervousness). Subscale scores range from 0 to 28 for physical well-being and 0 to 24 for emotional well-being, with higher scores representing better physical and emotional well-being.

Other variables included patient demographics (*e.g.*, age, race, marital status), cancer type and stage, and the history of prior treatment (*i.e.*, chemotherapy or surgery before radiotherapy). While cancer type, stage, and treatment data were extracted from medical records, all the other variables were from self-reports.

2.4 Statistical analyses

Before analysis, we examined missing patterns to perform imputation. For patients with incomplete FSFI, if no more than 50% of the item of each domain were missing, we replaced the missing values of each domain with the mean of the remaining item scores of the same domain [26]. No other missing imputation was performed.

To examine the effect of obesity on sexual functioning pre-radiotherapy, we first performed Mann-Whitney U tests due to the skewed distribution of FSFI total scores. To further examine the effect of obesity on sexual functioning, including its indirect effects through physical and emotional well-being, we implemented ordinary least squares regression-based "multiple" mediation models, where the two potential mediators were tested at the same time to consider any interactions between mediators. For this mediation analysis, we used the PROCESS tool, a statistical macro developed by Hayes [27]. This tool allowed us to test the mediation models based on 5000 bootstrap samples. Using the percentile bootstrapping

method, we could provide more accurate confidence intervals even though the normality and homoscedasticity assumptions were not satisfied [27].

To examine the effect of obesity on the changes in sexual functioning from pre- to post-radiotherapy, we used generalized linear mixed models. Because generalized linear mixed models can handle repeatedly measured data with missing observations based on missing-at-random [28], we could include all 54 patients in our analysis, including 24 whose post-radiotherapy FSFI scores were not available in the dataset. To test whether obesity affected the changes in sexual functioning "within" patients pre-radiotherapy while allowing variability "between" patients (*i.e.*, differences in intercepts for FSFI total scores), generalized linear mixed models were fitted with random intercepts. For random effects, a scaled identity variance-covariance structure was assumed as the random effect had only one level. By using a log-link function that allows the "mean" of the outcome values to be log-transformed, the results could be more easily interpreted. This method is as opposed to fitting a log-normal model that first log-transforms the outcome values of each patient and then calculates the mean of logs.

Covariates that were adjusted in the final models (*e.g.*, cancer type, prior treatment) were selected based on statistical associations with both obesity and sexual functioning. These associations were analyzed using nonparametric tests (*i.e.*, Mann-Whitney U tests, Kruskal-Wallis test, Chi-square tests, or spearman correlation analysis), depending on the variables. We found no multicollinearity in our fitted multivariate models (variance inflation factors <2). To explore the use of two different obesity measures (BMI *vs.* BFP), we repeated all these analyses twice, first using BMI-based obesity and then BFP-based obesity, as the predictor. Power analysis using G*Power version 3.1 [29] (Heinrich-Heine-University Düsseldorf, Düsseldorf, NRW, Germany) indicated a power of 93% with a medium effect size (0.25) at a significance level of 0.05, based on the approach to repeated measures analysis of variance within-between interaction. All statistical analyses were performed using SPSS version 29.0 (IBM, Armonk, NY, USA). Tests with a p-value < 0.05 were determined to be significant.

3. Results

3.1 Patient characteristics

Table 1 summarizes demographic and clinical characteristics of patients by obesity and its measure pre-radiotherapy. The median age at baseline was 56.5 years (interquartile range (IQR): 45.8–66.3), ranging from 29–82. About 60% were non-White patients, including Black (n = 26, 48.1%), Asian (n = 4, 7.4%), and biracial (n = 2, 3.7%; White and American Indian/Alaska Native, Black/African American and Asian) although three (5.6%) patients chose not to answer. More than half were diagnosed with endometrial cancer (n = 30, 55.6%) and had received prior treatment, either surgery (n = 24, 44.4%), chemotherapy (n = 1, 1.9%), or both (n = 7, 13.0%). The median scores of physical and emotional well-being pre-radiotherapy were 22.0 (IQR: 15.1–26.5) and 18.5 (IQR: 15.3–21.8), respectively. Of the 20 patients who completed post-radiotherapy assessment, most received vaginal brachytherapy with (n = 11, 55.0%) or without (n = 6, 30.0%) external beam radiation therapy while three (15.0%) received external beam radiotherapy alone.

3.2 The status of obesity and sexual functioning and their associations with patient characteristics

Based on BMI, 26 patients (48.1%) were classified as being obese, but BFP classified more patients as obese (n = 33, 61.1%). The median FSFI total scores were 6.2 (IQR: 4.4–18.7) pre-radiotherapy and 13.8 (IQR: 6.2–20.33) post-radiotherapy (Fig. 1). Based on the FSFI cutoff score of 26.55, most patients had sexual dysfunction pre- (n = 45, 83.3%) and post-radiotherapy (n = 17, 85.0%). Cancer type and prior treatment were significantly associated with both obesity and sexual functioning pre-radiotherapy and were thus adjusted for in the multivariate analysis (**Supplementary Table 1**). Endometrial cancer patients were more likely to be obese (76.9% *vs.* 23.1% based on BMI; 72.7% *vs.* 27.3% based on BFP) and reported higher levels of sexual functioning (median (IQR) = 12.3 (22.4) *vs.* 4.9 (5.2), $p = 0.002$), compared to cervical cancer patients. Patients who had received prior treatment were more likely to be obese (73.1% *vs.* 26.9%, $p = 0.046$) and reported higher levels of sexual functioning (median (IQR) = 7.5 (17.6) *vs.* 5.2 (7.0), $p = 0.039$) compared to those who had not.

3.3 The effect of obesity on sexual functioning pre-radiotherapy

Bivariate analyses showed that obesity was positively associated with sexual functioning pre-radiotherapy. Patients with obesity reported slightly higher FSFI total scores than those without obesity, no matter whether obesity was measured by BMI (median = 8.0 *vs.* 5.6, $p = 0.012$) or BFP (median = 8.0 *vs.* 5.5, $p = 0.033$).

After adjusting for cancer type and prior treatment, we found no association between obesity and sexual functioning pre-radiotherapy, regardless of obesity measure, as there was no significant "total" effect of obesity on sexual functioning based on mediation analysis (Fig. 2). Specifically, obesity had no effect on sexual functioning directly or indirectly through physical and emotional well-being although physical well-being was significantly associated with sexual functioning.

3.4 The effect of obesity on sexual functioning post-radiotherapy

In bivariate analyses, we found no association between obesity and sexual functioning post-radiotherapy, regardless of obesity measure. For multivariate analyses, we fitted generalized linear mixed models, adjusting for cancer type and prior treatment. As we found a significant interpatient variability in sexual functioning in the adjusted models (*i.e.*, variance in intercepts), this interpatient variability was also adjusted (Table 2). When obesity was measured by BFP, obesity had a negative effect on the changes in sexual functioning from pre-

TABLE 1. Sample characteristics by obesity and its measure pre-radiotherapy.

		Obesity measure					
		Body mass index			Body fat percentage		
Variable	Total (N = 54)	Obese (n = 26)	Non-obese (n = 28)	*p*	Obese (n = 33)	Non-obese (n = 21)	*p*
Age, yr	56.5 (45.8–66.3)	63.0 (46.3–71.3)	51.5 (45.3–61.8)	0.065	60.0 (50.6–69.5)	51.0 (42.0–64.0)	0.065
Race							
Black/African American	26 (48.1)	14 (53.8)	12 (42.9)		17 (51.5)	9 (42.9)	
White	19 (35.2)	9 (34.6)	10 (35.7)	0.623[a]	10 (30.3)	9 (42.9)	0.640
Other	9 (16.7)	3 (11.5)	6 (21.4)		6 (18.2)	3 (14.3)	
Marital status							
Married/domestic partnership	28 (51.9)	10 (38.5)	18 (64.3)	0.058	11 (33.3)	17 (81.0)	0.001
Never married/divorced or separated/widowed	26 (48.1)	16 (61.5)	10 (35.7)		22 (66.7)	4 (19.0)	
Cancer type							
Cervical	24 (44.4)	6 (23.1)	18 (64.3)	0.002	9 (27.3)	15 (71.4)	0.001
Endometrial	30 (55.6)	20 (76.9)	10 (35.7)		24 (72.7)	6 (28.6)	
FIGO cancer stage							
I	28 (51.9)	18 (69.2)	10 (35.7)		22 (66.7)	6 (28.6)	
II	15 (27.8)	5 (19.2)	10 (35.7)	0.046	6 (18.2)	9 (42.9)	0.023
III	11 (20.4)	3 (11.5)	8 (28.6)		5 (15.2)	6 (28.6)	
Prior treatment history							
None	22 (40.7)	7 (26.9)	15 (53.6)	0.046	10 (30.3)	12 (57.1)	0.050
Chemotherapy	8 (14.8)	5 (19.2)	3 (10.7)	0.460[a]	6 (18.2)	2 (9.5)	0.461[a]
Surgery	31 (57.4)	19 (73.1)	12 (42.9)	0.025	22 (66.7)	9 (42.9)	0.085
Physical well-being, FACT-G subscale score (n = 53)	22.0 (15.1–26.5)	22.0 (14.6–26.0)	22.1 (15.5–27.8)	0.436	22.5 (14.3–26.0)	22.0 (16.0–27.5)	0.749
Emotional well-being, FACT-G subscale score (n = 52)	18.5 (15.3–21.8)	18.0 (15.5–22.0)	19.0 (15.0–22.0)	0.975	18.5 (16.0–22.0)	18.0 (14.3–20.0)	0.450

Data are presented as n (%) (for categorical variables) or median (interquartile range) (for continuous variables). Comparisons were conducted by Mann-Whitney U tests (for continuous variables) or Chi-square tests (for categorical variables). [a]*Fisher's exact test. FACT-G, Functional Assessment of Cancer Therapy-General; FIGO, International Federation of Gynecology and Obstetrics.*

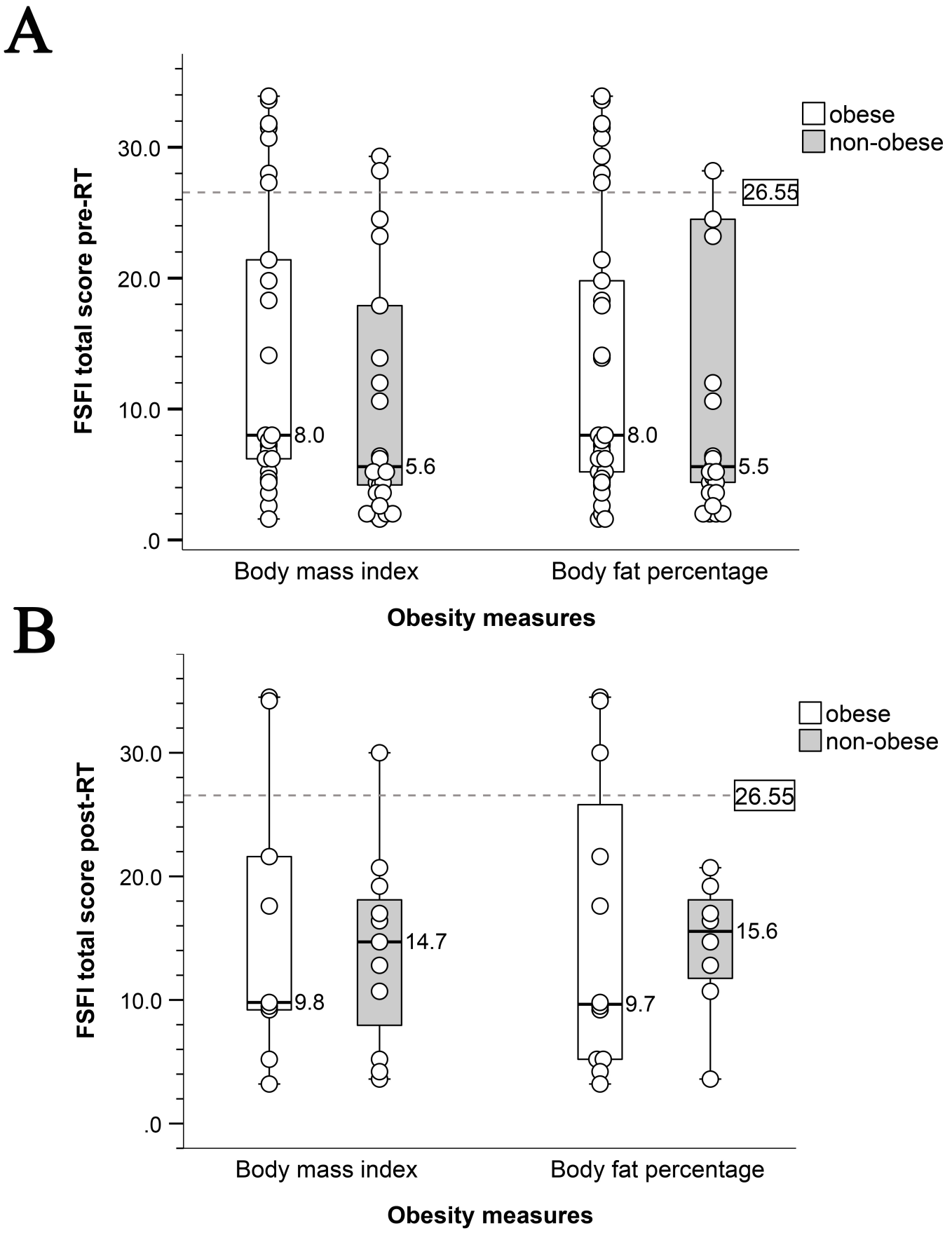

FIGURE 1. Sexual functioning by obesity and its measures. (A) Pre-radiotherapy (n = 54). (B) Post-radiotherapy (n = 20). The dotted grey horizontal line indicates the cutoff score for sexual dysfunction (*i.e.*, FSFI total scores ≤26.55). FSFI, Female Sexual Function Index (the higher, the better); RT, radiotherapy.

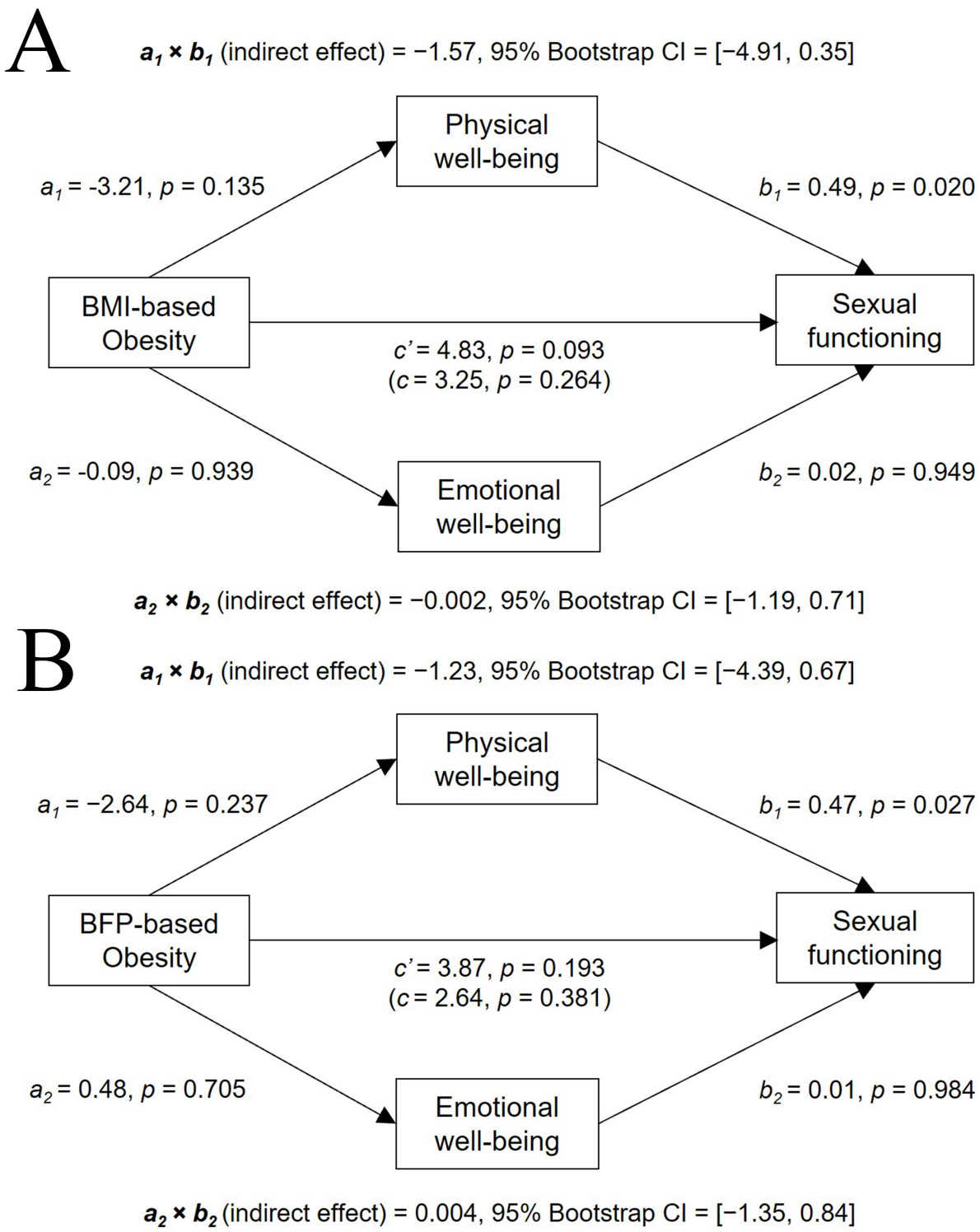

FIGURE 2. Mediation models of the effects of obesity on sexual functioning through physical and emotional well-being pre-radiotherapy. (A) BMI-based obesity. (B) BFP-based obesity. Data from 52 patients were available for analysis. Mediation models were tested after adjusting for cancer type and prior treatment. Unstandardized coefficients from ordinary least square regression-based mediation models are denoted as *a*, *b*, *c* and *c'*, where total effect (*c*) = direct effect (*c'*) + physical well-being specific indirect effects ($a_1 \times b_1$) + emotional well-being specific indirect effect ($a_2 \times b_2$). Indirect effects were tested based on 5000 bootstrap samples using the percentile bootstrapping method. BMI, body mass index; BFP, body fat percentage; CI, confidence intervals.

TABLE 2. Generalized linear mixed models evaluating the effect of obesity on the changes in sexual functioning between pre- and post-radiotherapy.

	Obesity measures							
	Body mass index				Body fat percentage			
Predictors	B	SE	*t*	*p*	B	SE	*t*	*p*
Fixed effects								
Intercept	1.99	0.20	10.00	<0.001	1.91	0.22	8.77	<0.001
RT	0.30	0.16	1.88	0.064	0.60	0.21	2.87	0.005
Obesity	0.18	0.23	0.80	0.424	0.16	0.25	0.63	0.532
RT × obesity	−0.27	0.20	−1.35	0.183	−0.59	0.23	−2.54	0.013
Endometrial cancer	0.72	0.28	2.56	0.013	0.80	0.29	2.76	0.008
Prior treatment	−0.20	0.26	−0.78	0.438	−0.22	0.26	−0.84	0.405
	Variance	SE	*z*	*p*	Variance	SE	*z*	*p*
Random effects								
Intercept	0.32	0.10	3.16	0.002	0.35	0.1	3.21	0.001
Model summary	AIC = 169.00, $F = 2.73$ ($p = 0.026$)				AIC = 167.92, $F = 3.58$ ($p = 0.006$)			

Generalized linear mixed models with a total of 74 observations (data from 54 patients pre-radiotherapy and 20 patients post-radiotherapy) were estimated based on a normal distribution with random intercepts using a log-link function. To interpret the coefficients (B), exponentiate the coefficients (exp(B)) of the predictors. Sexual functioning was measured by Female Sexual Function Index total scores (the higher, the better). AIC, Akaike's information criteria (the smaller, the better); RT, radiotherapy; SE, standard errors; B, unstandardized coefficients.

to post-radiotherapy (slope = −0.59, $p = 0.013$). Fig. 3 depicts the changes in sexual functioning by obesity and its measure, based on the mean estimates of FSFI total scores obtained from the generalized linear mixed models. Only patients without BFP-based obesity showed a significant increase in FSFI total scores post-radiotherapy, compared to pre-radiotherapy (B = 0.60, $p = 0.005$) although their scores were still far below the cut off score for sexual dysfunction (*i.e.*, FSFI total scores ≤26.55). BMI-based obesity had no effect on the changes in sexual functioning.

Because BFP-based obesity significantly influenced the changes in sexual functioning from pre- to post-radiotherapy, we performed *post-hoc* tests using two separate generalized linear mixed models: one for patients with BFP-based obesity and the other for patients without BFP-based obesity. Among patients with BFP-based obesity, FSFI total scores post-radiotherapy were almost the same (*i.e.*, 1.01 times as high) as their pre-radiotherapy scores (B = 0.01, $p = 0.949$). Among patients without BFP-based obesity, FSFI total scores post-radiotherapy were on average 1.76 times higher than their pre-radiotherapy scores (B = 0.56, $p = 0.019$).

4. Discussion

We examined the effect of obesity on sexual functioning in racially diverse women with gynecologic cancer pre- and post-radiotherapy. Most patients, regardless of obesity, had extremely poor sexual functioning pre-radiotherapy, but patients with obesity reported slightly better sexual functioning pre-radiotherapy than those without obesity. This difference in sexual functioning pre-radiotherapy by obesity, however, disappeared after adjusting for cancer type and prior treatment. Interestingly, only when obesity was measured by BFP, there was a negative effect of obesity on the changes in sexual functioning from pre- to post-radiotherapy. Sexual functioning remained poor even 6 months after the completion of radiotherapy, and obesity may have further delayed the recovery of sexual functioning among gynecologic cancer patients treated with radiotherapy.

Although our study suggests that obesity may negatively affect the changes in sexual functioning among gynecologic cancer patients after radiotherapy, the effect was only identified when obesity was measured and defined based on BFP, not BMI. The use of BMI as an indicator of obesity (≥30 kg/m^2), particularly for post-menopausal women, has been criticized because it may not accurately represent excessive body adiposity among individuals with varying body composition and shape [19]. Given that gynecologic cancer patients are all female, primarily over 50 years, and likely to be natural or treatment-induced menopausal [19], they are likely to have more body fat and less muscle and bone mass, compared to males, younger individuals, and premenopausal women with the same BMI [5, 19]. While BMI can be a useful indicator for "body size", it may be insufficient to accurately estimate "excessive adipose tissues" among gynecologic cancer patients, leading to a misunderstanding of the association between obesity and sexual functioning.

The difference in the results by obesity measures suggests that the size of the body may have a minimal influence on sexual functioning, but the composition of the body (*e.g.*, excessive adipose tissues) may play a more important role in sexual functioning among gynecologic cancer patients treated with radiotherapy. Both radiation and excessive adipose tissues can induce inflammatory responses, leading to various symptoms,

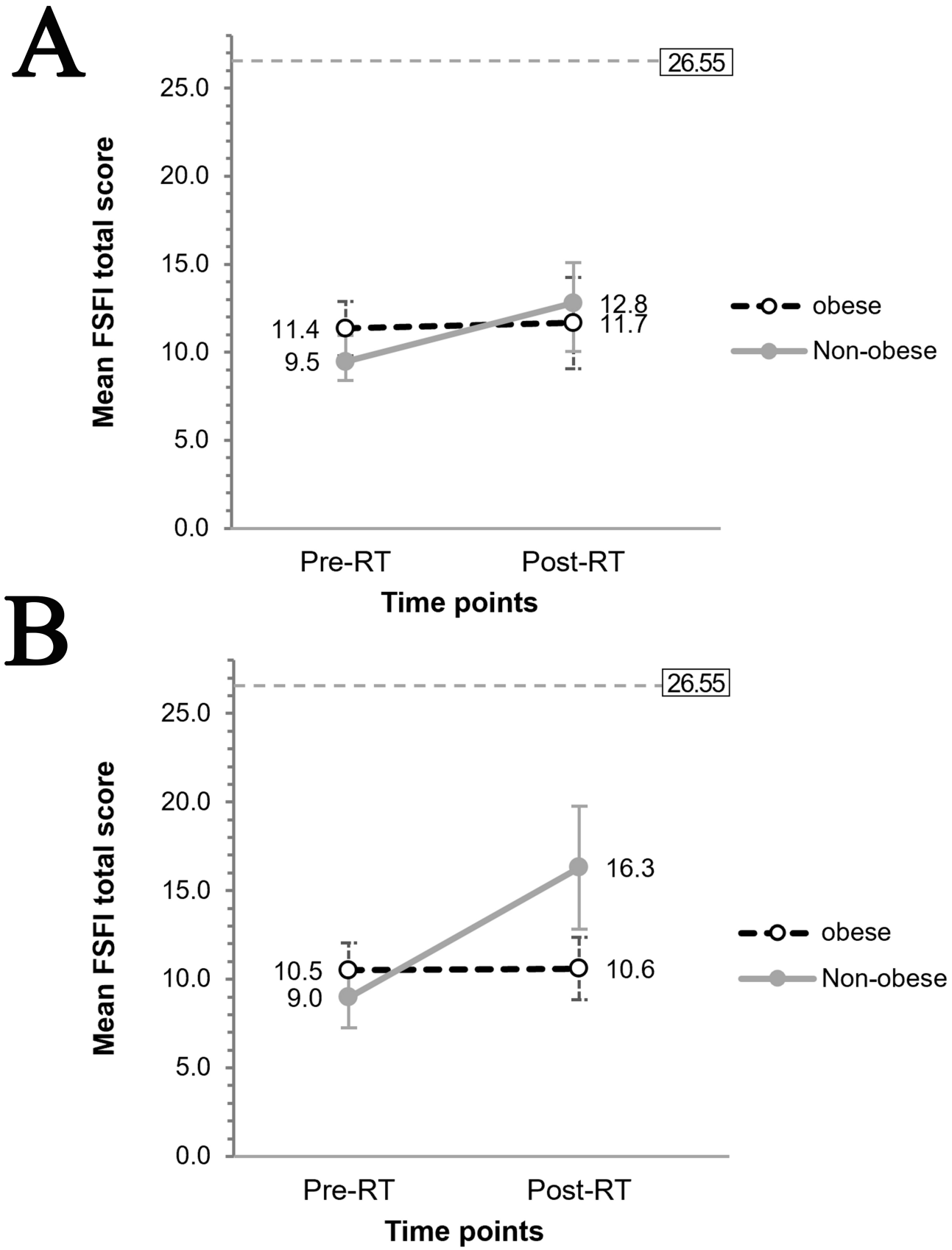

FIGURE 3. Estimated changes in sexual functioning between pre- and post-radiotherapy by obesity. (A) BMI-based obesity. (B) BFP-based obesity. Mean estimates of FSFI total scores were obtained from normal generalized linear mixed models with random intercepts using a log-link, adjusting for interpatient variability, cancer type and prior treatment. The dotted grey horizontal line indicates the cutoff score for sexual dysfunction (*i.e.*, FSFI total scores $\leq$26.55). Error bars indicate $\pm$ one standard errors of mean. BFP, body fat percentage; BMI, body mass index; FSFI, Female Sexual Function Index (the higher, the better); RT, radiotherapy.

such as fatigue, diarrhea, lymphedema, and vaginitis [8, 9, 30]. These inflammation-related symptoms can negatively affect sexual functioning [10, 31]. Radiotherapy can impair sexual functioning among gynecologic cancer patients, regardless of obesity [10]. However, patients with obesity may require more time to recover from the impairment due to the combination of the inflammatory effects of irradiation and excessive adipose issues. Future research with more accurate or supplementary measures of obesity could enhance understanding of the relationship between obesity and sexual functioning among gynecologic cancer survivors.

While we found a positive association between physical well-being and sexual functioning among gynecologic cancer patients, regardless of obesity and its measure, there was no statistical evidence that obesity affects sexual functioning through physical or emotional well-being pre-radiotherapy. However, our results showed that the difference in physical well-being between patients with and without obesity was clinically meaningful ($\geq$2–3 points) [32]. Patients with obesity reported worse physical well-being than those without obesity. Given that physical well-being was measured by assessing the level of symptoms, such as pain, fatigue, and nausea, these non-sexual physical symptoms should be addressed as part of interventions to improve sexual functioning among gynecologic cancer patients, especially for those with obesity.

Regardless of obesity, patients reported an extremely low level of sexual functioning pre-radiotherapy, which continued post-radiotherapy. The median FSFI total scores of our patients were far below the FSFI cutoff score of 26.55 for sexual dysfunction both pre- and post-radiotherapy [24]. Based on the same cutoff score, the global prevalence of female sexual dysfunction is 66% among those with cancer [7] and 50% among those with obesity [11]. However, more than 80% of our patients had sexual dysfunction both pre- and post-radiotherapy. If patients have not yet completed cancer treatment, they may experience decreased sexual desire or distractions from sexual activities merely due to anxiety over diagnosis and treatment outcomes or other priorities, leading to decreased sexual functioning. Similar to our findings, this decreased sexual functioning may continue for a long time even after the completion of treatment, which may be more frustrating to patients. More in-depth investigations to identify multidimensional reasons for the extremely poor sexual functioning and early sexual health interventions, including before and during cancer treatment may benefit gynecologic cancer patients.

One limitation of this study was the small sample size. We employed robust statistical methods, such as imputation and mixed models, to mitigate the effects of missing data. Due to sample size constraints, we adjusted for two covariates, selected based on statistical significance in association with both obesity and sexual functioning. Although we found no significant differences in sexual functioning by age, treatment modalities, and cancer stage in our sample, larger studies or cohort studies are needed to additionally control for these variables. The FSFI, while useful, has known limitations [26, 33], including its focus on heterosexual women with partners and its potential to underestimate sexual functioning. Future researchers could incorporate supplementary or alternative measures of sexual functioning, such as PROMIS Sexual Function and Satisfaction and the Female Sexual Distress Scale, to provide a better understanding of how obesity affects sexual functioning. Sexual functioning is a multifactorial process, influenced by biological factors, such as menopausal status at diagnosis, sex hormones (*e.g.*, androgens, estrogens, and progesterone) [34], and psychosocial factors, such as relationship with a partner, body image concerns, and fear of recurrence, in addition to obesity [10, 34]. Because data on these factors were unavailable, interpretation of the results should be cautious. Studies using more direct measurement of adiposity, such as dual x-ray absorptiometry, may better inform the association between obesity and sexual functioning among gynecologic cancer patients. However, it would be essential to have clinical interventions available to make such investments in diagnostics cost-effective.

5. Conclusions

The findings from this study suggest that obesity, specifically when measured by BFP is associated with delayed recovery of sexual functioning in gynecologic cancer patients receiving radiotherapy. However, further research with larger sample sizes and more precise measures of obesity is needed to better understand the relationship between obesity and sexual functioning. Given that sexual functioning remained significantly impaired both pre- and 6 months post-radiotherapy, regardless of obesity, increasing clinical attention and developing and implementing effective interventions to improve sexual functioning are critical priorities for this population.

ABBREVIATIONS

BMI, body mass index; BFP, body fat percentage; FSFI, Female Sexual Function Index; FACT-G, Functional Assessment of Cancer Therapy-General; CUN-BAE, Clinica Universidad de Navarra-Body Adiposity Estimator; IQR, interquartile range; FIGO, International Federation of Gynecology and Obstetrics; RT, radiotherapy; CI, confidence intervals; AIC, Akaike's information criteria; SE, standard errors; B, unstandardized coefficients.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

HL—Conceptualization, Methodology, Formal analysis, Investigation, Data Curation, Writing-Original draft preparation, Writing-Review and editing, Visualization. DWB—Conceptualization, Methodology, Writing-Review and editing, Funding acquisition. JBB—Conceptualization, Methodology, Writing-Review and editing. YJH—Methodology, Writing-Review and editing. TYE—Resources, Writing-Review and editing. JWS—Resources, Writing-Review and editing. NK—Resources, Writing-Review and

editing. KAY—Conceptualization, Methodology, Writing-Review and editing, Supervision. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Because this study is a secondary analysis of non-identifiable data from a prospective observational study, the Emory University Institutional Review Board (IRB) determined that this study did not need to be reviewed by the IRB. The parent study was approved by the Emory University IRB Committee (#IRB000858823) and obtained all subjects' consent to participate.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.ejgo.net/files/article/191203510506427187 2/attachment/Supplementary%20material.docx.

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