Obesity Facts

Research Article

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DOI: 10.1159/000529834

Received: August 9, 2022
Accepted: February 17, 2023
Published online: March 7, 2023

Association of Body Fat Distribution and Risk of Breast Cancer in Pre- and Postmenopausal Women

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Keywords
Breast cancer · Body fat mass · Obesity · UK Biobank · Prospective study

Abstract

Introduction: Obesity is a risk factor for both the development of and mortality from breast cancer in postmenopausal but not in premenopausal women. However, which part of the fat mass is associated with risk remains unclear, and whether the difference in the risk for breast cancer is associated with discrepancy in the distribution of fat with menstrual status requires further study. ***Methods:*** A dataset from the UK Biobank, which included 245,009 female participants and 5,402 females who developed breast cancer during a mean follow-up of 6.6 years, was analyzed. Body fat mass was measured according to bioelectrical impedance at baseline by trained technicians. Age- and multivariable-adjusted hazard ratios and corresponding 95% confidence intervals for associations between body fat distribution and the risk for breast cancer were estimated using Cox proportional-hazards regression. Height, age, education level, ethnicity, index of multiple deprivation, alcohol intake, smoking, physical activity, fruit consumption, age at menarche, age at first birth, number of births, hormone replacement therapy, family history of breast cancer, hysterectomy, and ovariotomy were adjusted for potential confounders. ***Results:*** Fat distribution differed between pre- and postmenopausal women. After menopause, there was an increase in fat mass in different body segments (arms, legs, and trunk). After age- and multivariable adjustment, fat mass in different segments, BMI, and waist circumference were significantly associated with the risk for breast cancer among postmenopausal but not premenopausal women. ***Conclusion:*** Postmenopausal women exhibited more fat in different body segments, which are associated with increased risk for breast cancer, compared to premenopausal women. Fat mass control throughout the body may be beneficial in mitigating the risk for breast cancer and was not limited to abdominal fat alone among postmenopausal women.

Introduction

With an incidence of 11.6%, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer-related death among women according to Global Cancer Statistics [1]. Many factors (hereditary, genetic, and nonhereditary) are involved in the occurrence of breast

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cancer; however, hereditary and genetic factors account for only 5–10% of cases, which implies that the major causes of breast cancer are nonhereditary. Alcohol consumption, early menarche [2, 3], late menopause [4], obesity in postmenopausal women [5], and high concentrations of endogenous estradiol [6] as nonhereditary factors are all associated with breast cancer. Obesity, one of the few modifiable risk factors, has received special attention. There is substantial evidence that obesity is a risk factor for both the development of and mortality from breast cancer [7–9]. However, this risk factor is not identical in different menstrual states, and an explanation for this remains unclear. Many studies have reported that body mass index (BMI) is positively associated with an increased risk for breast cancer among postmenopausal women [9–13]. However, before menopause it is inversely [14–16] or not related to the risk [17]. Besides, postmenopausal women with increased levels of body fat are at elevated risk of breast cancer despite having a normal BMI [18].

Previous studies have used BMI to evaluate the risk for breast cancer; however, this metric has limitations because it cannot reflect body fat distribution and overall body fat level. Although some researchers have found that there is no difference between bioelectrical impedance data and anthropometric indices (e.g., waist circumference [WC] and BMI) [9] in predicting the risk for postmenopausal breast cancer, there remains a lack of data regarding differences in fat mass distribution between pre- and postmenopausal women and the risk for breast cancer. Fat mass distribution is quite different with changes in menstrual status [19, 20]. It remains unknown whether premenopausal women have a different risk for breast cancer than postmenopausal women due to differences in body fat distribution (arms, legs, and trunk). It is also debatable whether postmenopausal women require targeted control of body fat to reduce the risk for breast cancer. Further exploration of fat mass distribution in pre- and postmenopausal women and how it affects the risk for breast cancer may be helpful in the prevention of breast cancer.

Based on the UK Biobank dataset, we aimed to further analyze the differences in fat mass distribution among pre- and postmenopausal women and its association with the risk for breast cancer.

Methods

Data Source and Participants

Our data were obtained from UK Biobank (application number 51671, August 2019) which is a large population-based prospective cohort study of over 500,000 individuals aged between 37 and 73 years recruited throughout England, Wales, and Scotland between 2006 and 2010. UK Biobank study was approved by the North West Multi-center Research Ethics Committee, Scottish Community Health Index Advisory Group, and the England and Wales Patient Information Advisory Group. Details on study design and survey methods of UK Biobank cohort have been well described elsewhere [21, 22]. All participants provided written informed consent before data collection.

263,520 female participants from UK Biobank who had complete data for body composition were included. Participants were excluded if they had any cancer diagnosis prior to baseline (except for nonmelanoma skin cancer ICD-10 C44) (n = 17,120), were pregnant (n = 149), or subsequently withdrew (n = 1,242) from the UK Biobank. Finally, this study included a total of 245,009 female participants, of which 75,284 were premenopausal and 169,725 were postmenopausal (online suppl. Fig. S1; for online suppl. material, see https://doi.org/10.1159/000529834). Menstruation status is defined as follows: women who reported that their periods had stopped at recruitment were defined as postmenopausal. Women with unknown menopausal status were defined as postmenopausal if they reached 53 years or over at recruitment based on the criteria established previously [23] and the remaining women were defined as premenopausal.

Data Collection

Participants were invited to complete a touch-screen questionnaire during the baseline to collect the information on demographics (i.e., age, education, ethics, index of multiple deprivations, etc.), menstrual history, reproductive history, family history, lifestyle factors, and hormone replacement therapy. Physical measurements including weight, height, WC, hip circumference, waist-to-hip ratio, and BMI were also collected at the baseline. A repeat assessment of all baseline measures was conducted to minimize measurement error. Standing height was measured by the Seca 202 device (Seca, Hamburg, Germany). The Wessex nonstretchable sprung tape measure (Wessex, UK) was used to measure WC and hip circumference. BMI was calculated by dividing weight (kg) by the square of standing height (m^2). The Tanita BC-418MA body composition analyzer (Tanita, Tokyo, Japan) was used to measure fat mass of whole body, arms, trunk, and legs by bio-impedance. Body fat/body weight was represented as body fat percentage (BFP).

Ascertainment of Breast Cancer Cases

Breast cancer cases were identified by cancer and death registries from the Health and Social Care Information Centre (in England and Wales) and the National Health Service Central Register (in Scotland). Eligible participants contributed person-years from recruitment date until the date of last follow-up (October 30, 2015), date of death, or the first breast cancer diagnosis (ICD-10 codes C50), whichever came first.

Statistical Analyses

Statistical analyses were performed using the R software version 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria). Data are expressed as mean (standard deviation) or number (percentage). For covariates with selections of "do not know" and "prefer not to answer," or with missing covariate data, an "unknown/missing" response category was created.

Comparisons of continuous body composition measures, including BMI, body fat mass, BFP, WC, trunk fat mass, and limb fat mass, between premenopausal and postmenopausal women were performed using a two-sample Student's *t* test. The risk for breast cancer was calculated according to quartiles and as a continuous per unit increase in baseline body size/composition. We tested the proportional-hazards assumption by Schoenfeld tests in the UK Biobank. No violation of this assumption was found. Cox regression models, with age as the underlying timescale, were used to estimate hazard ratio (HR) and corresponding 95% confidence interval (CI).

Age was adjusted for using a basic Cox regression model. In the multivariable-adjusted model, height, age, educational level, ethnicity, index of multiple deprivation, alcohol intake, smoking, physical activity measured according to metabolic equivalent task, fruit consumption, age at menarche, age at first birth, number of births, hormone replacement therapy, family history of breast cancer, hysterectomy, and ovariotomy were adjusted. All statistical tests were two tailed and differences with $p < 0.05$ were considered to be statistically significant.

Results

245,009 female participants were involved in the analysis. A total of 1,351 women developed breast cancer before menopause and 4,051 after menopause during a mean follow-up of 6.6 years.

Table 1 summarizes baseline characteristics of the participants according to whole-body fat mass by quartiles [24]. For premenopausal and postmenopausal participants, index of multiple deprivation and WC were likely to increase with whole-body fat mass. Participants with lower whole-body fat mass tended to never smoke and engaged in higher levels of physical activity, had higher fruit and vegetable intake, and lower rates of hypertension and diabetes.

Differences in fat mass levels among pre- and postmenopausal women are summarized in Table 2. In general, body fat levels were higher among postmenopausal women than premenopausal women ($p < 0.001$). Trunk-leg fat mass ratio was also higher in postmenopausal women. Comparatively, fat free mass of the whole body, trunk, arms, and legs were lower after menopause.

Data reported in Table 3 demonstrate the association between fat mass in different body segments and the risk for breast cancer among pre- and postmenopausal women. There was insufficient evidence to support associations between body fat, either distributed in trunk, arms, or legs which measured by quartile or 1-unit increase and breast cancer risk in premenopausal women.

Age- and multivariable-adjusted HRs and 95% CIs for the association of the body fat measures according to quartile with the risk for breast cancer in postmenopausal women demonstrated that, compared with female participants in the lowest quartile of whole-body fat mass, those in the second (multivariable-adjusted HR 1.19 [95% CI: 1.04–1.35]), third (multivariable-adjusted HR 1.26 [95% CI: 1.10–1.44]), and highest (multivariable-adjusted HR 1.54 [95% CI: 1.35–1.76]) quartiles were all associated with an increased risk for breast cancer. An increase of 1 unit (multivariable-adjusted HR 1.02 [95% CI: 1.01–1.02]) was also associated with risk. The risk for breast cancer was further evaluated in participants according to fat mass in different body segments. Divided by quartile or an increase of 1 unit all demonstrated a significant association with an increased risk for breast cancer. Women in the top quartile of the trunk (multivariable-adjusted HR 1.57 [95% CI: 1.37–1.79]), arms (multivariable-adjusted HR 1.57 [95% CI: 1.37–1.80]), and legs (multivariable-adjusted HR 1.53 [95% CI: 1.34–1.75]) had the greatest increase in breast cancer risk compared to those in the lowest quartile. The risk for breast cancer increased by a factor of 1.03, 1.10, 1.04 separately for the trunk, arms, and legs, respectively, per unit increase. After adjustments for age and multiple variables, BMI and WC were associated with the risk of breast cancer in postmenopausal women according to quartile.

Discussion

In this large prospective study, we found that whole-body fat mass, BFP, and body fat in the trunk, arms, and legs were higher in postmenopausal than in premenopausal women. Statistically, these body fat measures had significantly positive associations with the risk for breast cancer after menopause, which is highly consistent with BMI and WC. However, before menopause, body fat measurements had no statistically significant association with breast cancer risk.

Fat mass distribution differed between pre- and postmenopausal women. Douchi et al. [20] reported that the amounts of trunk, total body fat mass measured using dual-energy X-ray absorptiometry, and the trunk-leg fat mass ratio were significantly higher in postmenopausal women which is in accordance with our findings. Palmera and Clegg [19] also reported that females have different adipose distributions in different menstrual status: they tend to have more subcutaneous fat mainly on hips and thighs before menopause, which protects against the negative consequences associated with obesity and the metabolic syndrome [19]. However, in our analysis, we did not observe similar results. The fact that we could not distinguish between visceral and subcutaneous fat mass may be an explanation.

Comparatively, the fat-free mass of postmenopausal women was lower than that of premenopausal women, which is consistent with physiological changes. After menopause, decreases in estrogen and vitamin D levels and

Table 1. Characteristics of study participants

Characteristics	Whole-body fat mass (premenopausal)				Whole-body fat mass (postmenopausal)			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
N	23,523	18,229	16,083	17,449	38,001	43,078	44,961	43,685
Age, mean (SD), years	46.2 (3.9)	46.6 (4.2)	46.9 (4.3)	46.9 (4.3)	59.6 (5.5)	60.3 (5.3)	60.6 (5.3)	60.2 (5.3)
Menarche age, mean (SD), years	13.3 (1.6)	13.1 (1.6)	13.0 (1.6)	12.7 (1.7)	13.1 (1.6)	13.0 (1.6)	12.9 (1.6)	12.7 (1.7)
Menopause age, mean (SD), years	–	–	–	–	49.8 (4.7)	50.0 (4.8)	49.9 (5.1)	49.8 (5.3)
Age at first live birth, mean (SD), years	27.6 (5.0)	26.8 (4.9)	26.2 (4.9)	25.2 (5.0)	25.7 (4.5)	25.2 (4.3)	24.7 (4.3)	24.2 (4.4)
Null birth number, *N* (%)	6,150 (26.1)	4,351 (23.9)	3,761 (23.4)	4,726 (27.1)	7,242 (19.1)	6,485 (15.1)	6,385 (14.2)	6,620 (15.2)
White, *N* (%)	21,706 (92.3)	16,792 (92.1)	14,614 (90.9)	15,597 (89.4)	36,319 (95.6)	41,296 (95.9)	43,078 (95.8)	41,332 (94.6)
IDM, mean (SD)	16.5 (13.1)	17.5 (13.6)	18.7 (14.3)	21.9 (15.8)	15.4 (12.4)	15.8 (12.6)	16.8 (13.3)	19.3 (14.7)
BMI, mean (SD), kg/m^2	22.0 (1.8)	24.8 (1.7)	27.6 (2.0)	34.2 (4.9)	22.0 (1.8)	24.9 (1.7)	27.7 (2.0)	33.6 (4.4)
WC, mean (SD), cm	71.7 (5.4)	78.8 (5.5)	85.6 (6.3)	99.5 (10.8)	72.6 (5.7)	80.0 (5.9)	87.0 (6.5)	99.9 (10.2)
Never smoking, *N* (%)	15,229 (64.7)	11,630 (63.8)	10,155 (63.1)	10,930 (62.6)	22,992 (60.5)	25,441 (59.1)	25,643 (57.0)	24,203 (55.4)
Never drinking, *N* (%)	1,638 (7.0)	1,231 (6.8)	1,287 (8.0)	1,846 (10.6)	3,515 (9.2)	3,593 (8.3)	4,101 (9.1)	5,522 (12.6)
MET, mean (SD), minutes/week	2,750 (2,560)	2,450 (2,340)	2,280 (2,320)	1,970 (2,200)	2,970 (2,690)	2,720 (2,540)	2,490 (2,440)	2,110 (2,270)
Fruit and vegetable intake, mean (SD), portions/day	3.0 (2.5)	2.8 (2.3)	2.8 (2.4)	2.7 (2.4)	3.7 (2.9)	3.6 (2.6)	3.4 (2.6)	3.2 (2.5)
Family history of cancer, *N* (%)	6,546 (27.8)	5,231 (28.7)	4,839 (30.1)	5,270 (30.2)	13,976 (36.8)	16,298 (37.8)	17,338 (38.6)	16,869 (38.6)
HRT, *N* (%)	836 (3.6)	826 (4.5)	833 (5.2)	882 (5.1)	3,892 (10.2)	3,837 (8.9)	3,590 (8.0)	2,723 (6.2)
Hypertension, *N* (%)	8,017 (34.1)	7,794 (42.8)	8,267 (51.4)	11,789 (67.6)	23,569 (62.0)	30,162 (70.0)	34,683 (77.1)	37,248 (85.3)
Diabetes, *N* (%)	1,449 (6.2)	1,241 (6.8)	1,414 (8.8)	2,489 (14.3)	4,012 (10.6)	5,315 (12.3)	6,503 (14.5)	9,550 (21.9)

IDM, index of multiple deprivation; BMI, body mass index; WC, waist circumference; MET, metabolic equivalent task; HRT, hormone replacement therapy; SD, standard deviation.

athletic ability may accelerate reduction in muscle and bone mineral levels, which mainly consists of fat-free mass.

BMI cannot reflect the distribution of fat. However, in our study, we used bioimpedance to separate fat in the trunk, arms, and legs and further analyze its association with the risk for breast cancer in both pre- and postmenopausal women. However, we did not find any association between BMI, WC, and whole-body fat mass, or different segments and breast cancer risk in premenopausal women. This is consistent with the results of previous investigations [15, 17, 25]. Another study found that BMI had an inverse linear association with breast cancer in premenopausal women, especially for those between 18 and 24 years of age (HR per 5 kg/m^2

Table 2. Comparison of segmental body composition between premenopausal and postmenopausal women

	Premenopausal women	Postmenopausal women
Whole-body fat mass, mean (SD), kg	26.10 (10.70)	27.30 (9.76)*
Fat mass of arms, mean (SD), kg	2.80 (1.65)	2.86 (1.48)*
Fat mass of trunk, mean (SD), kg	13.10 (5.62)	13.80 (5.11)*
Fat mass of legs, mean (SD), kg	10.20 (3.71)	10.60 (3.45)*
BFP, mean (SD)	35.10 (7.28)	37.20 (6.65)*
Trunk-leg fat mass ratio, mean (SD)	1.27 (0.23)	1.29 (0.21)*
Whole-body fat-free mass, mean (SD), kg	45.60 (5.19)	44.10 (4.90)*
Fat-free mass of arms, mean (SD), kg	4.62 (0.68)	4.54 (0.64)*
Fat-free mass of trunk, mean (SD), kg	25.60 (2.68)	24.80 (2.54)*
Fat-free mass of legs, mean (SD), kg	15.40 (1.99)	14.70 (1.91)*
Trunk-leg fat-free mass ratio, mean (SD)	1.67 (0.09)	1.69 (0.11)*

SD, standard deviation; BFP, body fat percentage. *p value <0.001.

difference, 0.77 [95% CI: 0.73–0.80]) [16]. The difference may, in part, be explained by the fact that the women we involved were 37–73 years of age and no much younger participants. Other factors such as irregular menstrual cycle and abnormal follicular cycle, which have less exposure to estrogens and progesterone, may also reduce the risk [26, 27]. Despite the neutral effects of body fat distribution on the risk for breast cancer among premenopausal women, we still advocate for appropriate weight control because high BMI contributes to 4.0 million deaths globally and is associated with other chronic diseases, including cardiovascular disease [28, 29], diabetes mellitus, chronic kidney disease [28], and many other cancers [30] according to research from the Global Burden of Disease (GBD) 2015 Obesity Collaborators [31].

In our study, body fat mass was measured using bioelectrical impedance to further analyze the associations between body fat distribution in different parts and the risk for breast cancer in both pre- and postmenopausal women. We concluded that body fat mass or fat mass in different body segments, BMI, and WC demonstrated a significant positive association with breast cancer among menopausal women. WC, BMI, overall fat, and body fat distribution were highly consistent with the risk for breast cancer among postmenopausal women. The potential mechanisms have been analyzed in nine prospective studies, which suggested that postmenopausal women with breast cancer had higher levels of estradiol and estrogen than breast cancer-free postmenopausal women [32]. In addition, elevated estrogen levels may promote cell proliferation and proangiogenic activity, which may lead to the development of breast cancer [33]. Our results also suggest that not only fat mass in the trunk or abdominal adiposity but entire fat mass and fat mass in different body segments were associated with the increased risk for breast cancer among postmenopausal women. This implies that a decrease in total body fat or BMI levels, resulting from a decrease in fat mass of any body segment, may be beneficial in mitigating cancer risk among postmenopausal women and is not limited to abdominal fat.

Strengths and Limitations

Strengths of this study include its nationwide, prospective cohort and large sample sizes, with a follow-up of approximately 6.6 years, and detailed measurements that analyzed fat mass distribution and its association with the risk for breast cancer in both pre- and postmenopausal women. In our analysis, we used bioimpedance to measure fat mass, which has been regarded to be the gold standard, and is more accurate than anthropometric measures [34–36]. Multivariable adjustments were used to control for multiple potential confounders.

However, this study also had limitations, the first of which was the definition of pre- and postmenopausal women. Women who did not know their menopausal status were defined as postmenopausal if they were ≥53 years of age at recruitment, and the remaining women were defined as premenopausal. In general, there may be a misclassification bias in the number of pre- and postmenopausal women. Second, due to the lack of histological information, we did not further analyze the effects of fat mass on each subtype of breast cancer. Third, body fat mass was measured only at baseline, and we could not analyze the association between body fat changes and the risk for breast cancer. Finally, this cohort consisted mainly of Europeans; therefore, characteristics of other ethnicities remain unclear.

Table 3. Association of different segmental fat mass and breast cancer risk in pre- and postmenopausal women

Bio-impedance measurement	Premenopausal women				Postmenopausal women			
	quartile	cases, *n*	age adjusted	multivariable adjusted	quartile	cases, *n*	age adjusted	multivariable adjusted
			HR (95% CI)	HR (95% CI)			HR (95% CI)	HR (95% CI)
Whole-body fat mass, kg	Q1 (5.0–18.5)	303	1 [reference]	1 [reference]	Q1 (5.0, 20.5)	773	1 [reference]	1 [reference]
	Q2 (18.5–23.9)	353	1.09 (0.94–1.25)	1.14 (0.94–1.38)	Q2 (20.5, 25.7)	975	1.25 (1.14–1.38)	1.19 (1.04–1.35)
	Q3 (23.9–31.4)	366	1.05 (0.91–1.23)	1.12 (0.91–1.37)	Q3 (25.7, 32.4)	1,045	1.29 (1.18–1.42)	1.26 (1.10–1.44)
	Q4 (31.4–110.0)	306	0.96 (0.83–1.12)	1.00 (0.80–1.25)	Q4 (32.4, 108.0)	1,182	1.51 (1.38–1.66)	1.54 (1.35–1.76)
Continuous per 1-unit increase			1.00 (0.99–1.00)	1.00 (0.99–1.01)			1.01 (1.01–1.02)	1.02 (1.01–1.02)
BFP, %	Q1 (8.8–30.0)	315	1 [reference]	1 [reference]	Q1 (9.4, 32.8)	815	1 [reference]	1 [reference]
	Q2 (30.0–35.0)	347	1.12 (0.98–1.29)	1.07 (0.88–1.29)	Q2 (32.8, 37.4)	952	1.16 (1.05–1.28)	1.09 (0.95–1.25)
	Q3 (35.0–40.1)	370	1.04 (0.89–1.21)	1.11 (0.90–1.35)	Q3 (37.4, 41.7)	1,065	1.25 (1.14–1.38)	1.26 (1.10–1.43)
	Q4 (40.1–69.3)	296	0.91 (0.78–1.06)	0.93 (0.74–1.17)	Q4 (41.7, 69.8)	1,143	1.38 (1.25–1.51)	1.46 (1.28–1.67)
Continuous per 1-unit increase			1.00 (0.99–1.00)	1.01 (0.99–1.01)			1.02 (1.01–1.02)	1.02 (1.02–1.03)
Fat mass of trunk, kg	Q1 (0.6–9.1)	297	1 [reference]	1 [reference]	Q1 (0.6, 10.2)	772	1 [reference]	1 [reference]
	Q2 (9.1–12.2)	352	1.12 (0.97–1.29)	1.10 (0.90–1.34)	Q2 (10.2, 13.2)	980	1.22 (1.10–1.34)	1.16 (1.02–1.33)
	Q3 (12.2–16.3)	372	1.12 (0.97–1.31)	1.17 (0.96–1.44)	Q3 (13.2, 16.8)	989	1.26 (1.14–1.38)	1.20 (1.05–1.37)
	Q4 (16.3–59.9)	306	0.97 (0.84–1.13)	0.97 (0.77–1.21)	Q4 (16.8, 48.3)	1,230	1.55 (1.41–1.70)	1.57 (1.37–1.79)
Continuous per 1-unit increase			1.00 (0.99–1.01)	1.00 (0.99–1.02)			1.03 (1.02–1.03)	1.03 (1.02–1.04)
Fat mass of arms, kg	Q1 (0.2–1.7)	287	1 [reference]	1 [reference]	Q1 (0.2, 1.9)	762	1 [reference]	1 [reference]
	Q2 (1.7–2.4)	371	1.09 (0.94–1.26)	1.02 (0.83–1.24)	Q2 (1.9, 2.5)	868	1.20 (1.09–1.33)	1.17 (1.02–1.34)
	Q3 (2.4–3.4)	351	1.05 (0.90–1.23)	1.12 (0.91–1.37)	Q3 (2.5, 3.5)	1,162	1.33 (1.20–1.46)	1.35 (1.18–1.54)
	Q4 (3.4–24.0)	318	0.98 (0.84–1.14)	1.03 (0.82–1.29)	Q4 (3.5, 25.0)	1,181	1.46 (1.33–1.61)	1.57 (1.37–1.80)
Continuous per 1-unit increase			0.98 (0.95–1.02)	1.01 (0.96–1.06)			1.07 (1.05–1.09)	1.10 (1.07–1.13)
Fat mass of legs, kg	Q1 (1.6–7.7)	321	1 [reference]	1 [reference]	Q1 (2.1, 8.3)	774	1 [reference]	1 [reference]
	Q2 (7.7–9.3)	334	1.05 (0.91–1.22)	1.07 (0.88–1.30)	Q2 (8.3, 10.0)	979	1.19 (1.08–1.31)	1.11 (0.97–1.27)
	Q3 (9.3–11.8)	360	1.04 (0.89–1.20)	1.11 (0.91–1.36)	Q3 (10.0, 12.2)	1,033	1.29 (1.18–1.42)	1.30 (1.14–1.49)
	Q4 (11.8–52.8)	312	0.94 (0.81–1.10)	1.01 (0.81–1.26)	Q4 (12.2, 54.1)	1,188	1.47 (1.34–1.61)	1.53 (1.34–1.75)
Continuous per 1-unit increase			0.99 (0.98–1.01)	1.00 (0.98–1.02)			1.03 (1.02–1.04)	1.04 (1.03–1.05)
BMI, kg/m^2	Q1 (14.5–22.9)	338	1 [reference]	1 [reference]	Q1 (14.6, 23.7)	828	1 [reference]	1 [reference]
	Q2 (22.9–25.5)	355	1.09 (0.94–1.26)	1.12 (0.92–1.36)	Q2 (23.7, 26.3)	1,002	1.18 (1.07–1.30)	1.24 (1.09–1.41)
	Q3 (25.5–29.3)	326	0.97 (0.83–1.13)	1.07 (0.87–1.32)	Q3 (26.3, 29.8)	1,069	1.25 (1.14–1.37)	1.41 (1.24–1.60)
	Q4 (29.3–67.3)	322	0.93 (0.80–1.08)	1.06 (0.85–1.32)	Q4 (29.8, 68.1)	1,134	1.35 (1.23–1.48)	1.58 (1.38–1.80)
Continuous per 1-unit increase			0.99 (0.98–1.00)	1.00 (0.99–1.02)			1.02 (1.01–1.02)	1.03 (1.02–1.04)

Table 3 (continued)

Bio-impedance measurement	Premenopausal women quartile	cases, *n*	age adjusted HR (95% CI)	multivariable adjusted HR (95% CI)	Postmenopausal women quartile	cases, *n*	age adjusted HR (95% CI)	multivariable adjusted HR (95% CI)
WC, cm	Q1 (41.4–74.0)	305	1 [reference]	1 [reference]	Q1 (46.0, 76.0)	728	1 [reference]	1 [reference]
	Q2 (74.0–81.0)	386	1.15 (1.00–1.32)	1.26 (1.04–1.53)	Q2 (76.0, 84.0)	1,046	1.20 (1.09–1.32)	1.16 (1.01–1.33)
	Q3 (81.0–90.0)	323	1.00 (0.85–1.16)	1.07 (0.86–1.33)	Q3 (84.0,93.0)	1,058	1.25 (1.14–1.38)	1.26 (1.10–1.44)
	Q4 (90.0–163.0)	330	0.94 (0.80–1.10)	1.07 (0.85–1.35)	Q4 (93.0, 171.0)	1,210	1.42 (1.29–1.56)	1.47 (1.28–1.69)
Continuous per 1-unit increase			1.00 (0.99–1.00)	1.00 (0.99–1.01)			1.01 (1.01–1.02)	1.01 (1.01–1.02)

BFP, body fat percentage; BMI, body mass index; WC, waist circumference.

Conclusion

In our study, we found that postmenopausal women have higher levels of whole-body fat and fat mass in different body segments compared to premenopausal women. Among postmenopausal women, the fat mass in different body segments was strongly associated with the increased risk for breast cancer. This indicates that the management of whole-body weight and fat in any part of the body will contribute to reduce the risk for breast cancer but is not limited to the abdomen.

Acknowledgments

This work was conducted using the UK Biobank Resource (application number 51671). We thank the participants and staff of the UK Biobank cohort for their valuable contributions.

Statement of Ethics

Subjects have given their written informed consent. This study protocol was reviewed and approved by the North West Multi-center Research Ethics Committee, Scottish Community Health Index Advisory Group, and the England and Wales Patient Information Advisory Group, approval number 51671.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This work was supported by the Startup Fund for the 100 Top Talents Program, Sun Yat-sen University, under Grant No. 392012; Sanming Project of Medicine in Shenzhen under Grant No. SZSM202011007; and the Hospital Research Fund of SAH-SYSU under Grant No. ZSQYLCKYJJ202028.

Author Contributions

Yang Cao wrote original draft. Zhen Zhang, Dan Hu, and Xinwei Huang contributed to the methods and discussion parts. Bin Xia had the data analysis. Fangping Li and Jinqiu Yuan had revised the manuscript and finally approved the version to be published.

Data Availability Statement

Data were obtained from UK Biobank (application number 51671, approved August 2019). Information on data availability and access procedures are described on the study Website (http://www.ukbiobank.ac.uk/). Further inquiries can be directed to the corresponding authors.

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