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## Percent Body Fat Change in Chinese Women After Adjuvant Chemotherapy for Breast Cancer

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**Background:** Weight gain is a common side effect observed in breast cancer (BC) patients undergoing adjuvant chemotherapy, although the characteristics and mechanism are not been fully understood. This study aimed to investigate percent body fat (%BF) change, and identify the associated risk factors among Chinese women receiving chemotherapy for BC.

**Material/Methods:** A prospective longitudinal study was conducted on a cohort of 140 Chinese female patients with BC between June 2016 and October 2017. Data on demographic and clinical features were collected using a standard protocol. Anthropometric parameters including body weight and %BF were measured before and after chemotherapy. Multiple logistic analysis was performed to identify the risk factors for %BF change.

**Results:** A total of 52.9% and 58.6% of the 140 patients experienced gains in weight and %BF after chemotherapy, respectively, with mean increases of  $2.1 \pm 1.9$  kg and  $1.3 \pm 2.2\%$ , respectively. Fifty-eight patients gained %BF over 2.5% of the baseline value. Moreover, premenopausal women had a greater mean %BF gain than postmenopausal women ( $P=0.018$ ). Logistic analysis showed that premenopausal status, younger age, multi-agent chemotherapy regimen, high-calorie diet, and decreased physical activity were independent variables that induced %BF gain.

**Conclusions:** %BF gain occurred frequently in Chinese women after adjuvant chemotherapy for BC, especially in premenopausal women. An effort should be made to the management of %BF.

**MeSH Keywords:** **Adipose Tissue • Breast Neoplasms • Chemotherapy, Adjuvant • Premenopause**

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## Background

Breast cancer (BC) is the most frequently diagnosed cancer and ranks the sixth leading cause of cancer-related death in Chinese women [1]. Weight gain and obesity are common occurrences in women receiving adjuvant chemotherapy for BC, with the 50–96% prevalence commonly reported [2–4]. Many studies have indicated that weight gain during chemotherapy not only adversely affect patients' cardiovascular health and life quality [5,6], but also increases the risk of BC recurrence and death [7,8]. Multiple reasons for weight gain have also been suggested, including premenopausal status, high-calorie diet, decreased physical activity, and multi-agent chemotherapy regimen, although the underlying mechanism has not been clearly elucidated [3,9–11].

Studies indicated that weight gain during chemotherapy was associated with an increase in fat mass and decrease in lean body mass [12]. However, most previous researches focused on changes in body weight or body mass index (BMI) [2,13,14], which might not accurately depict changes in adipose or lean tissue [15]. It is increasingly recognized that percent body fat (%BF), which can accurately measure the amount of whole body fat mass, is a better and more practical measure of obesity, especially for Asian populations [16,17]. As a result, a study of change in %BF during BC chemotherapy might not only provide important information about the mechanism by which weight gain influences prognosis, but might also contribute to development of a better weight management program.

The objective of this study was to investigate %BF change and identify the associated risk factors among Chinese women receiving chemotherapy for BC. Our initial hypothesis was that women were more likely to experience changes in %BF than body weight during BC chemotherapy.

## Material and Methods

### Study population

This was a prospective longitudinal study carried out in Comprehensive Breast Health Center, Ruijin Hospital affiliated to Shanghai Jiaotong University School of Medicine from June 2016 to October 2017. Patients who met the following criteria were enrolled in the study: 1) histologically diagnosed with stage I-III invasive BC and had received radical surgery; 2) within 1 month of starting adjuvant chemotherapy; 3) adult Chinese women ( $\geq 18$  years of age), able to speak and read Chinese. Patients would be excluded from the study if they had health conditions that contraindicated exercise participation, previous treatment for another cancer, or mental illness that prevented survey comprehension. This study was conducted

according to the principles of Declaration of Helsinki and was approved by the Ethics Committees of our hospital (R-2016-39). All participants provided written informed consent.

### Data collection

Demographic and clinical data were recorded by interviews and reviews of patients' medical records, including age, menopausal status, tumor stage, histological type, presence of receptors [estrogen receptor, progesterone receptor, and human epidermal growth factor 2 (HER2) receptor], chemotherapy regimens, daily caloric intake, and physical activity during chemotherapy sessions. Of these, menopausal status was established when at least 12 months elapsed from the last menstrual period. Tumor was staged according to the American Joint Committee on Cancer (AJCC) TNM classification (Version 7.0). According to tumor receptor characteristics (BC molecular type), patients were classified as luminal A/B (positive estrogen and/or progesterone receptors), HER2 (HER2 positive, positive and negative hormone receptors) or basal type (triple-negative BC). Chemotherapy regimens were divided into 4 groups: carboplatin-, anthracycline-, taxane-, or anthracycline plus taxane-based chemotherapy.

At the end of chemotherapy, each participant completed a food frequency questionnaire (FFQ) [18] and an International Physical Activity Questionnaire (IPAQ) [19] to assess the daily caloric intake and moderate physical activity level over the previous 3 months, respectively. A total of 100 food items and food groups were included in the FFQ and that covers about 90% of commonly consumed foods in Shanghai. The quantity, frequency of consumption (daily, weekly, monthly, or never) for each item or food group was recorded with the aid of photographs to illustrate portion sizes. Dietary intake data were converted into nutrient intake data using the continuously updated in-house nutrient database based on the nutritional software of traditional Chinese medicine combining with western medicine (NCCW) (Version 11.0, Qingdao University Medical College, China), which reflected the China Food Composition. The American Cancer Society recommends 30 minutes or more of moderate physical activity at least 5 days per week for BC patients, so this study focused on the level of moderate physical activity. According to IPAQ guidelines, moderate physical activity was defined as activities causing little to moderate rise in breathing and heart rate [3.0–6.0 metabolic equivalents (METs)]. The physical activity energy expenditure was calculated by multiplying weekly frequency, usual duration, and metabolic equivalent of the respective activity category (METs-minutes/week) [19].

A series of anthropometric parameters were also collected by the study's registered nurse on the first day before and after chemotherapy, including weight, height, waist circumference (WC), hip circumference, and %BF. All the tests were performed

in the morning. Participants were asked to fast overnight, to avoid any vigorous physical activity for at least 48 hours before the procedure, and to urinate or defecate before the measurements were taken. For all participants, weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm, without shoes and in light clothing. WC was measured in cm at the level of the umbilicus with the participant standing. Hip circumference was measured in cm at the greatest protrusion of the buttocks. BMI and waist-to-hip ratio (WHR) were calculated as weight/height<sup>2</sup> (kg/m<sup>2</sup>) and waist/hip (both in cm), respectively. %BF was measured by bioelectrical impedance assessment (BIA) device (InBody 770, Biospace, Korea), in accordance with the manufacturer's guidelines. Patients were allowed to rest in the supine position for 10 minutes before performing this test.

### Statistical analysis

Statistical analyses were performed with SPSS software (Version 19.0, IBM, Chicago, IL, USA). Chi-square and Student's *t*-test were utilized to analyze the differences in patient characteristics and outcomes. To identify the risk factors for %BF change, multiple logistic regression analysis was conducted. The odds ratio (OR) and 95% confidence interval (95% CI) were estimated for each factor. For all tests, a *P* value of <0.05 was considered significant.

## Results

### Patient characteristics

There were 140 BC patients included in this study, and the general characteristics of the study population are summarized in Table 1. Among them, 56 women were premenopausal and 84 were postmenopausal, with a median age of 53 years (range, 20–81 years). Fifty patients were diagnosed with stage I BC, 74 patients had stage II BC, and 16 patients had stage III BC. According to tumor receptor characteristics, 73 cases were classified as luminal A/B, 40 cases as HER2 and 27 cases as basal type. All the patients received 4–8 cycles of adjuvant chemotherapy, with a median duration of 18 weeks (range, 12–24 weeks). The chemotherapy regimens included carboplatin- (n=14), anthracycline- (n=14), taxane- (n=48), and anthracycline plus taxane-based (n=64). During chemotherapy sessions, the median daily caloric intake and moderate physical activity level of the total cohort were 1554 calories and 310 METs-minutes/week, respectively.

### Changes in anthropometric characteristics

A series of anthropometric parameters were measured before and after chemotherapy, and a significant gain was observed in

**Table 1.** General characteristics of study population.

Variable	Total (n=140)
Age, years	53 (20–81)
Menopausal status	
Premenopausal	56 (40.0%)
Postmenopausal	84 (60.0%)
Tumor stage	
I	50 (35.7%)
II	74 (52.9%)
III	16 (11.4%)
Histological type	
Infiltrating ductal carcinoma	105 (75.0%)
Ductal carcinoma <i>in situ</i>	25 (17.8%)
Infiltrating lobular carcinoma	2 (1.4%)
Colloid carcinoma	4 (2.9%)
Other types	4 (2.9%)
Molecular type	
Luminal A/B	73 (52.1%)
HER2	40 (28.6%)
Basal	27 (19.3%)
Chemotherapy regimen	
Carboplatin-based	14 (10.0%)
Anthracycline-based	14 (10.0%)
Taxane-based	48 (34.3%)
Anthracycline plus taxane-based	64 (45.7%)
Chemotherapy length, weeks	18 (12–24)
Daily caloric intake, cals	1554 (1012–2307)
Moderate physical activity, METs-minutes/week	310 (0–1260)

HER2 – human epidermal growth factor 2; MET – metabolic equivalents of the task.

weight ( $P<0.001$ ), BMI ( $P=0.006$ ), and %BF ( $P<0.001$ ) (Table 2). The mean weight and %BF changes for all participations were  $1.4\pm 2.3$  kg and  $0.9\pm 2.5\%$ , respectively, with 74 patients gaining weight (mean weight gain= $2.1\pm 1.9$  kg) and 82 gaining %BF (mean %BF gain= $1.3\pm 2.2\%$ ). Among the patients with %BF gain, 24 gained less than 2.5% of the baseline %BF, 36 gained between 2.5% and 5.0%, and 22 gained more than 5%. We also observed that 61 patients and 55 patients experienced a loss in body weight ( $0.7\pm 1.6$  kg) and %BF ( $0.4\pm 2.0\%$ ), respectively. We

**Table 2.** Changes in anthropometric characteristics after chemotherapy.

Variable	Before chemotherapy	After chemotherapy	P value
Weight, kg	59.7±8.1	61.1±8.5	<0.001
BMI, kg/m <sup>2</sup>	23.4±3.2	23.7±3.4	0.006
WC, cm	84.0±3.6	84.0±4.6	0.694
WHR	0.90±0.05	0.90±0.09	0.371
%BF	32.9±5.9%	33.8±6.7%	<0.001

BMI – body mass index; WC – waist circumference; WHR – waist-to-hip ratio; %BF – percent body fat.

**Table 3.** Changes in %BF after chemotherapy.

Variable	Total (n=140)	Premenopausal (n=56)	Postmenopausal (n=84)
Same %BF	3 (2.1%)	1 (1.8%)	2 (2.4%)
%BF loss	55 (39.3%)	12 (21.4%)	43 (51.2%)
%BF gain	82 (58.6%)	43 (76.8%)	39 (46.4%)
<2.5%	24	12	12
2.5–5%	36	19	17
>5%	22	12	10
%BF before chemotherapy	/	31.4±4.9%	33.8±6.4%
%BF after chemotherapy	/	32.5±6.2%	34.6±7.9%
P value, intra-group	/	<0.001	0.004

%BF – percent body fat.

further examined the %BF change stratified by menopausal status and found that both groups showed a significant %BF gain after chemotherapy ( $P<0.001$  and  $P=0.004$ , respectively). Notably, premenopausal women had a greater mean %BF gain than postmenopausal women ( $1.1\pm 2.0\%$  vs.  $0.8\pm 2.2\%$ ,  $P=0.018$ ) (Table 3).

### Risk factors associated with %BF gain

Multivariate logistic analysis was performed to identify risk factors associated with %BF gain of more than 2.5% of the baseline value after chemotherapy (Table 4). The results indicated that age <50 years (OR=1.27, 95% CI: 1.11–2.34), anthracycline plus taxane-based chemotherapy (OR=1.18, 95% CI: 1.07–1.94), daily caloric intake  $\geq 1600$  calories (OR=1.46, 95% CI: 1.20–3.03) and physical activity  $\leq 450$  METs-minutes/week (OR=1.37, 95% CI: 1.13–2.68) were independent variables that inducted %BF gain. In addition, compared with postmenopausal women, premenopausal women showed a 1.33-fold (95% CI: 1.10–2.62) increased risk to develop %BF gain during chemotherapy sessions. No significant association was detected for other variables, including baseline weight, tumor stage, histological type, molecular type, chemotherapy length, etc.

### Discussion

Weight gain is a common side effect observed in female patients undergoing chemotherapy for BC [2,3]. Evidence exists that obesity not only significantly increases the risk of developing BC, but also is a major risk factor for recurrent disease and decreased survival [7,8,20]. Camoriano et al. [21] reported that premenopausal patients who gained over 5.9 kg had a risk of relapse 1.5 times greater and a risk of death 1.6 times greater than women gaining less weight. Several mechanisms have been proposed to explain the adverse effect of obesity and weight gain on BC prognosis. The major mechanism is the elevated estrogen synthesis by adipose tissue which stimulated tumor growth and metastasis, especially in postmenopausal women [22,23]. Insulin and some adipokines also may influence BC progression and outcome by enhancing angiogenesis [24]. Hence, it is important to recognize that weight management is indispensable for improving BC patients' long-term health.

Body weight and BMI are the most commonly used measures of overweight and obesity. However, recent studies have demonstrated that %BF is a more important predictor of weight

**Table 4.** Multivariate logistic analysis of risk factors associated with %BF gain.

Variable	%BF gain $\geq 2.5\%$ (n=58)	Other %BF change (n=82)	Multivariate	
			OR (95% CI)	P value
Age, years				
$\geq 50$	26	54	1 (reference)	
$< 50$	32	28	1.27 (1.11–2.34)	0.019
Menopausal status				
Postmenopausal	27	57	1 (reference)	
Premenopausal	31	25	1.33 (1.10–2.62)	0.021
Baseline weight, kg				
$< 60$	32	47	1 (reference)	
$\geq 60$	26	35	1.09 (0.48–1.92)	0.074
Baseline BMI, kg/m <sup>2</sup>				
$< 24$	27	51	1 (reference)	
$\geq 24$	31	31	0.96 (0.34–1.65)	0.350
Baseline WC, cm				
$< 85$	30	45	1 (reference)	
$\geq 85$	28	37	1.13 (0.36–1.83)	0.692
Baseline WHR				
$< 0.85$	28	48	1 (reference)	
$\geq 0.85$	30	34	1.20 (0.28–2.01)	0.471
Baseline %BF				
$< 30.0\%$	25	38	1 (reference)	
$\geq 30.0\%$	33	44	1.17 (0.53–2.78)	0.518
Tumor stage				
I	21	29	1 (reference)	
II–III	37	53	0.92 (0.42–1.76)	0.273
Histological type				
Infiltrating ductal carcinoma	40	65	1 (reference)	
Others	18	17	1.90 (0.75–4.79)	0.174
Molecular type				
Luminal A/B				
Present	32	41	1 (reference)	
Absent	26	41	0.73 (0.14–3.17)	0.205
HER2				
Present	20	20	1 (reference)	
Absent	38	62	1.04 (0.53–3.80)	0.142

**Table 4 continued.** Multivariate logistic analysis of risk factors associated with %BF gain.

Variable	%BF gain $\geq 2.5\%$ (n=58)	Other %BF change (n=82)	Multivariate	
			OR (95% CI)	P value
Basal				
Present	10	17	1 (reference)	
Absent	48	65	1.98 (0.29–5.51)	0.493
Chemotherapy regimen				
Others	25	51	1 (reference)	
Anthracycline plus taxane-based	33	31	1.18 (1.07–1.94)	0.043
Chemotherapy length, weeks				
<18	21	34	1 (reference)	
$\geq 18$	37	48	0.80 (0.20–2.89)	0.762
Daily caloric intake, cals				
<1600	19	47	1 (reference)	
$\geq 1600$	39	35	1.46 (1.20–3.03)	0.012
Moderate physical activity, METs-minutes/week				
>450	14	40	1 (reference)	
$\leq 450$	44	42	1.37 (1.13–2.68)	0.010

%BF – percent body fat; OR – odds ratio; CI – confidence interval; BMI – body mass index; WC – waist circumference; WHR – waist-to-hip ratio; HER2 – human epidermal growth factor 2; MET – metabolic equivalents of the task.

management decision-making than body weight or BMI, particularly in Chinese female population [25,26]. Freedman et al. [27] suggested some women with BC might not experience significant changes in weight or BMI after chemotherapy, but they appeared to undergo unfavorable changes in body composition. A comparable result was observed in our study, where 52.9% and 58.6% of the 140 female BC patients experienced gains in weight and %BF after chemotherapy, respectively, with mean increases of 2.1 kg and 1.3%, respectively. Moreover, 58 patients gained %BF over 2.5% of the baseline value. This suggested that women were more likely to experience changes in body composition than body weight during chemotherapy for BC. In addition, our study found that premenopausal women exhibited a greater %BF gain than postmenopausal women during chemotherapy ( $P=0.018$ ), as has been indicated by a number of investigators [27,28]. From the aforementioned results, we conclude that patients should pay more attention to the management of %BF rather than body weight during BC treatment.

WC and WHR are also widely used to evaluate obesity. Compared with BMI, they can better reflect the accumulation of intra-abdominal fat [26]. Recent studies have revealed that the circulating sex hormone concentrations could influence

body fat content and distribution [23]. Instead, different adipose tissue distribution may reflect an altered hormonal profile of BC patients and thus possibly affect prognosis and response to therapy [29,30]. Studies have also showed that WC and WHR are positively correlated with the risk and prognosis of BC [31–33]. A study by Harvie found that WC increased during chemotherapy and continued to increase in the post-chemotherapy period so that at 1 year, BC patients had increased 5.1 cm from baseline [34]. In our study, there appeared to be an increase in WC and WHR after chemotherapy, but these changes were not statistically significant. As our median observation time was only 18 weeks, an extension of follow-up would help draw definitive conclusion. This is an issue which we intend to address in further work.

In the present study, we also evaluated the potential risk factors for %BF gain after BC chemotherapy. The results showed that, compared with postmenopausal women, premenopausal women displayed significantly higher risk for %BF gain. This was consistent with the finding from other studies [28]. Research suggested that premature amenorrhea caused by adjuvant chemotherapy might trigger increased fat accumulation and alterations in fat distribution [21]. We also found that the younger group of women were more likely to have %BF gain than

the older group, and this might be because the cutoff age of 50 years in this study was close to the average age of menopause in our local population. In addition, our study showed that the risk of %BF gain appeared to be greater in women receiving multi-agent than single agent chemotherapy regime. A similar finding was reported by Demark-Wahnefried et al. [11] and Jatoi et al. [35]. But the reason for this phenomenon has not been thoroughly clarified. Furthermore, a variety of studies have highlighted that lifestyle has an important impact on body composition changes [9,10,36]. It was obvious in this study that increased dietary intake and reduced energy expenditure were found to contribute significantly to %BF gain during BC chemotherapy. In addition to these factors, baseline weight, tumor stage, and treatment length have also been reported to be associated with %BF gain [22,37,38], but no significant association was detected in our study. The explanations for these differences remain to be elucidated and might well give insights into the mechanisms involved.

To our knowledge, this is the first study specifically designed to investigate %BF change in Chinese women after adjuvant chemotherapy for BC, but some limitations should also be noted. First, the sample size of this study was relatively small,

which might place a limitation on the assessment of creativity. Second, bioelectrical impedance-derived body composition might be affected by hydration status, ambient temperature, and recent exercise. Last but not least, other risk factors not included in this study cannot be examined for confounding effects. Hence, further validation of our findings is warranted.

## Conclusions

Our study results suggested that %BF gain occurred frequently in Chinese women after adjuvant chemotherapy for BC, especially in premenopausal women. Moreover, premenopausal status, younger age, multi-agent chemotherapy regimen, high-calorie diet, and decreased physical activity were the potential risk factors for %BF gain. %BF management should be an integral part of the entire course of BC treatment, and our findings provide valuable information for the development of interventions to curb deleterious changes in %BF.

## Conflicts of interest

The authors declare no potential conflicts of interest.

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