

Weight gain after adjuvant chemotherapy in patients with early breast cancer in Istanbul Turkey

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Abstract Weight gain is a well-known and unwanted complication of adjuvant chemotherapy in breast cancer. We observed that the female Turkish cancer patients frequently gain weight with adjuvant treatment of breast cancer and planned to examine the magnitude of this problem in early breast cancer patients treated at our hospital. A total of 176 early breast cancer patients who received their adjuvant systemic therapy in Marmara University Hospital between 2003 and 2007 are included in the study. We recorded their weight before and after chemotherapy and also a year after chemotherapy to find out whether the change with weight is transitory. We have also recorded demographic information, including the educational level, menopausal status, the type of chemotherapy or hormonal treatment administered stage of disease, marital status, occupation and the underlying diseases to analyze the relationship between change in weight and these parameters. Median age of patients was 53 and 72% of patients were postmenopausal. Educational level was equally distributed for primary education (27%), high school (40%), and university (33%). The majority of the patients (76%) was married, had two children (69%) and was housewife (60%). Family history of any cancer was high (32%). Most of the patients had stage II cancer (56%), received anthracyclines+/- taxane based chemotherapy (98%) and had no underlying disease (68%). The majority also did not smoke (73%) or drink alcohol (93%). A total of

67% and 72% patients gained weight upon completion and one year after completion of chemotherapy. Mean weight before the chemotherapy, upon completion of chemotherapy and one year after completion of chemotherapy were 68.9 kg, 70.6 kg ($P = 0.000$) and 71.9 kg ($P = 0.000$) respectively. Mean body mass index was 27.1 at baseline, 27.8 upon completion of chemotherapy ($P = 0.000$) and 28.3 one year after completion of chemotherapy ($P = 0.000$). Age, menopausal status, multiparity and presence of comorbid diseases had statistically significant impact on weight gain following adjuvant therapy in breast cancer patients ($P = 0.000$, $P = 0.008$, $P = 0.015$ and $P = 0.017$ respectively). This study shows that Turkish women with early breast cancer gain weight after adjuvant systemic therapy, in line with European and American counterparts. This increase in weight is maintained at least one year after adjuvant therapy. Given the adverse consequences of weight gain in terms of both breast cancer prognosis and general health, it is necessary to inform patients about this change and to develop strategies for weight maintenance during and after systemic therapy.

Keywords Chemotherapy · Breast cancer · Adjuvant treatment · Weight gain

Introduction

Obesity is a global health problem associated with increased risk of chronic diseases including breast cancer (BC) [1, 2]. There is considerable evidence that obesity at the time of BC diagnosis confers poorer prognosis [3–6]. Moreover, it has been shown that patients with BC frequently gain weight during or after adjuvant systemic therapy in multiple studies for more than two decades [7–13]. Importantly,

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postdiagnosis weight gain has shown to be associated with worse prognosis in many studies [8, 9, 11, 12, 14], but not all [15, 16]. A review of the literature suggests patients with BC gain 2.5–6.2 kg during the first year after diagnosis [17]. Weight gain and obesity contribute to either development of chronic diseases including diabetes, hypertension or deterioration of attendant comorbidities during adjuvant systemic therapy. In addition, weight gain together with the breast surgery and alopecia further damages self image and has a negative impact on the quality of life [18]. While some retrospective studies identified a number of potential patient and therapy-related factors associated with weight gain over time, the reasons for postdiagnosis weight gain have not been clearly identified. Chemotherapy (CT), being or becoming postmenopausal after diagnosis, decreased physical activity, dietary factors such as increased caloric intake, psychosocial factors have all been implicated for postdiagnosis weight gain in patients with early BC [8, 9, 17, 19–23]. It is important to know that all studies showing evidence of significant weight gain following adjuvant treatment were reported from the United States and Western European countries. Such evidence has not been observed in Korean women with early BC suggesting that some other ethnic, biologic or genetic factors which might play a role [24].

Turkish women can be considered obese compared to many western European countries with a mean body mass index (BMI) of 29.2 for women >30 years old. [25]. Additional weight gain after diagnosis is a common complaint of our patients receiving adjuvant therapy in Istanbul. We planned to investigate the frequency and magnitude of weight gain and its relation with various social, clinical, pathological, patient and therapy-related factors upon completion of and 1 year after adjuvant therapy.

Patients and methods

Study population

We made a retrospective chart review of women with operable stage I–III, histologically confirmed early BC who have received adjuvant systemic therapy at Marmara University Hospital between 2003 and 2007. The body weight (BW), pathological factors such as tumor size, nodal status, hormone receptor status, clinical factors (menopausal status, age) and treatment characteristics (type of adjuvant therapy) are noted. Patients were excluded when their records did not include baseline BW measured ± 1 week of diagnosis, before systemic therapy is commenced. Post-treatment weight measured within 1 month of completion of CT and at the end of first year (± 1 month) after

completion of adjuvant CT. Patients with distant metastases and history of other malignancies were excluded. Additional information such as social characteristics including marital status, number of children, cigarette/alcohol use, family history of cancer, occupation and presence of other comorbid diseases was noted.

Statistical analysis

The main objective of the study was to find out the frequency and magnitude of weight gain immediately after and 1 year after completion of adjuvant CT. Descriptive analyses were performed to examine distributions, means and standard deviations of all continuous variables using SPSS version 13.0, SPSS, Chicago. A two-way repeated-measures ANOVA test is used to compare means of repeated BW measurements and body mass indices when there are two and more categories. A two-sided *P* value of 0.05 was considered statistically significant. The difference

Table 1 Baseline characteristics of the study population

	<i>n</i>	%
Menopausal status		
Premenopausal	50	28.4
Postmenopausal	126	71.6
Tumor stage		
T1	30	17.0
T2	101	57.4
T3	45	25.6
Nodal status		
Node negative	67	38.0
Node positive	109	62.0
Estrogen/progesterone receptor status		
Positive	143	81.3
Negative	33	18.7
Her-2 status (immunohistochemistry)		
0/1+	88	50.0
2/3+	33	18.8
Unknown	55	31.2
Adjuvant treatment		
Chemotherapy	49	27.8
Endocrine therapy	5	2.8
Chemotherapy + endocrine therapy	122	69.4
Type of surgery		
Mastectomy	121	68.8
Breast-conserving surgery	55	31.2
Weight* (mean)	69	
Height* (mean)	1.58	
BMI* (mean)	27.1	
Age (median)	53	

* Before chemotherapy, at the time of diagnosis

Table 2 Demographic/social characteristics of the study population

	<i>n</i>	%
Education		
Primary school	68	39
High school	51	29
University & Higher	57	32
Current smokers	128	73
Alcohol intake*	12	7
Family history of cancer**	57	32
Marital status		
Single	20	11
Married	134	76
Divorced	22	13
Number of children		
0	31	17
1	47	27
2	74	42
3	15	9
>3	9	5
Patients receiving vitamin supplements	35	20
Comorbid endocrinologic diseases		
Hypertension	26	15
Diabetes	9	5
Hypo/hyperthyroidism	7	4
Hyperlipidemia	16	9
Occupation		
Working or retired	87	49.4
Housewife (never worked)	89	50.6

* >1 drink/week

** First- and/or second-degree relatives with cancer

between the baseline and postchemotherapy (immediately after and 1 year after completion of chemotherapy) weights was calculated as the change in BW. Friedman (non-parametric *K*-related samples test) test is used to determine the change over time. BMI was calculated as weight (kg) divided by height (meter squared).

Results

A total of 176 patients who had received their adjuvant systemic therapy at Marmara University Hospital between 2003 and 2007 are included. Median age was 53 (30–100). Seventy-two percent of patients were postmenopausal. Fifty-six percent of patients had stage II disease, and 81% tumors were positive for both or either of estrogen and progesterone receptors by immunohistochemistry. Almost all patients (97%) received adjuvant CT; 65% received anthracycline based, and 32% received anthracycline/taxane-based treatment, 3% of patients received only

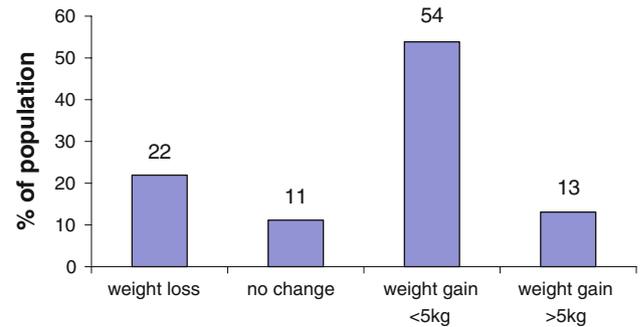


Fig. 1 Weight change upon completion of chemotherapy

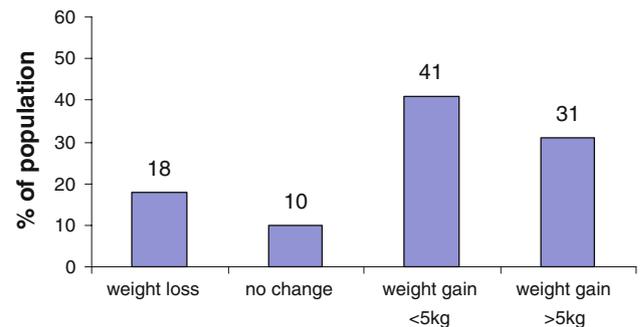


Fig. 2 Weight change 1 year after completion of chemotherapy

endocrine therapy (ET) (Table 1). Social and demographic characteristics of study population were shown in Table 2. Educational level was as follows: 27% had primary education, 40% graduated from high school and 33% had finished a university. Majority of patients (76%) were married and had two children (69%) and housewife (60%). Family history of any cancer was high (32%).

A total of 67 and 72% patients gained weight upon completion of and 1 year after CT (Figs. 1, 2). Seven percent of 119 patients who gained weight immediately after completion of CT returned to their baseline weight in 1 year, and only 4% of them lost weight compared to their baseline. Thirty-eight percent of patients who lost weight ($n = 38$) upon completion of chemotherapy gained weight in following year.

There was an overall 2.4% increment in the mean BW after completion of CT and 1.8% 1 year after diagnosis. Mean weight before the CT was 68.9 and increased to 70.6 upon completion of CT ($P = 0.000$) and to 71.9 kg one year after completion of CT ($P = 0.000$) (Table 3; Fig. 3). Mean BMI was 27.1 at baseline, 27.8 immediately after CT ($P = 0.000$) and 28.3 1 year after CT ($P = 0.000$). There has been a 2.58% increment in the mean BMI immediately after CT ($P = 0.000$) and 1.7% increment 1 year after CT ($P = 0.000$).

The relationship between weight gain and patient characteristics (clinical, demographic and tumoral

Table 3 Changes in body weight and body mass index immediately after and 1 year after adjuvant chemotherapy

Mean baseline BW	Mean BW after CT (kg)	Mean BW 1 year after CT (kg)	Change in baseline BW/BW after CT/1 year after diagnosis (%)
68.9±12.5	70.6±12.2 * <i>P</i> = 0.000	71.9±12.6 * <i>P</i> = 0.000	2.40/1.84
Mean baseline BMI	Mean BMI after CT (kg/m ²)	Mean BMI 1 year after CT (kg/m ²)	Change in baseline BMI/BMI After CT/1 year after diagnosis (%)
27.1±4.9	27.8±4.7 * <i>P</i> = 0.000	28.3±4.8 * <i>P</i> = 0.000	2.58/1.79

BW body weight, BMI Body mass index, CT chemotherapy

* *P* values for comparisons with baseline values

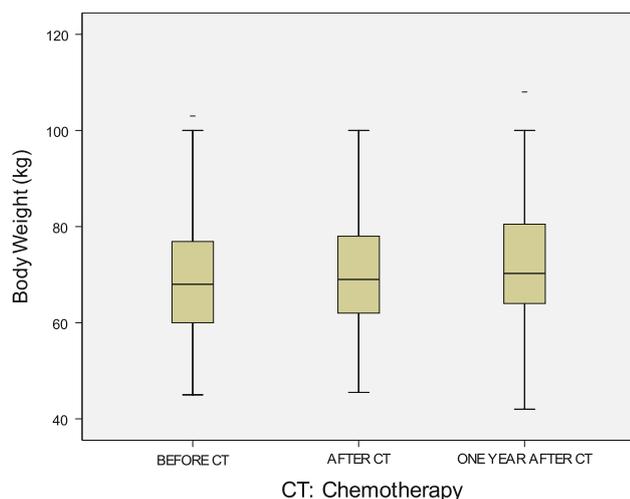


Fig. 3 Changes in body weight and body mass index immediately after and 1 year after adjuvant chemotherapy

characteristics) was shown in Tables 4 and 5. Age, menopausal status, multiparity and presence of comorbid diseases have statistically significant impact on weight gain following adjuvant therapy in patients with BC (*P* = 0.000, 0.008, 0.015 and 0.017, respectively).

Discussion

Our study has shown that Turkish patients with early BC who had been treated in Marmara University Hospital gained weight after adjuvant CT and this unwanted effect had been maintained at least 1 year after diagnosis. We have found our patients have gained 2.4% weight immediately after and gained additional 1.8% weight 1 year after completion of CT. This weight gain is in the range of what was reported in western literature [17]. It is important to note that 28% of the patients received only adjuvant CT, 3% received only ET and 69% patients received both CT and ET. Most of previous studies have shown that CT has been significantly associated with weight gain following BC diagnosis [7, 8, 10, 17, 20, 26–32]. The causal effect

between tamoxifen and weight gain is less supported by randomized trials [33–35] (Table 5).

Age, menopausal status, multiparity and presence of comorbid diseases emerged as statistically significant predictors of weight in our study. Patients <50 years of age, premenopausal patients, patients with more children and patients who have comorbid diseases other than BC gained weight significantly right after completion of and 1 year after CT compared to patients >50 years of age, postmenopausal patients, patients with fewer children and patients with no comorbid disease, respectively. Patients with premenopausal BC are at higher risk for weight gain since CT frequently induces premature menopause. Most previous studies have reported that patients with premenopausal BC are more likely to gain weight after diagnosis [8, 9, 18, 20, 26, 31, 32, 36].

Modified dietary habits and physical activity less than usual have been investigated as reasons for weight gain in patients with BC for a long time [19, 37, 38]. However, it is important to know that interpretation of data on caloric intake and physical activity is often difficult due to methodological differences among trials. It is noteworthy to remind that cultural and social characteristics of Turkey have been influenced both from western and middle eastern countries due to its geographical location. Dietary habits of Turkish people may be partially responsible for weight gain during and after CT. Turkish patients with cancer believe that they could recover from myelosuppression by consuming high amounts of “pekmez”, a dense and sweet syrup made from condensed juices of grape, fig or mulberry. In addition, both the patients and caregivers think that patients could cope with side effects of the treatments better by eating more. Almost all patients pursue a sedentary life with limited or no physical activity during and after chemotherapy. This study did not make assessments to examine the potential factors underlying weight gain; therefore, the above-mentioned comments on dietary characteristics and physical activity should be interpreted with caution.

Forty-four percent of our study population were overweight (BMI > 25), and 22% of patients were obese

Table 4 The relationship between weight gain and clinical/pathological characteristics

Characteristics	Before chemotherapy	After chemotherapy	1 year after chemotherapy	<i>P</i> value
Age				
<50	63.6	66.1	68.1	0.000*
>50	72.7	73.7	74.6	
Menopausal status				
Premenopausal	64.1	66.5	67.9	0.008*
Postmenopausal	70.8	72.2	73.5	
Tumor stage				
1	66.7	69.1	69.3	0.080
2	68.6	70.1	71.6	
3	71.4	72.9	74.6	
Nodal status				
Node negative	68.5	70.6	71.5	0.404
Node positive	69.3	70.7	72.3	
Receptor status				
Positive	68.7	70.7	71.9	0.596
Negative	69.7	70.1	71.9	
Her-2 status (IHC)				
0/1+	68.4	69.6	71.2	0.522
2/3+	71.3	73.6	74.9	
Adjuvant treatment				
Chemotherapy (CT)	68.4	69.6	71.0	0.458
Endocrine therapy (ET)	64.0	67.0	66.6	
CT + ET	69.3	71.1	72.5	
Type of surgery				
Mastectomy	69.4	71.1	72.5	0.241
BSC	68.1	69.4	70.7	

* *P* < 0.05

(BMI > 30) at the time of BC diagnosis. The mean baseline BMI was 27.1 ± 4.9 in our study population, and 72% of the study population was postmenopausal at the time of diagnosis. This is consistent with the information that obesity is a risk factor for development of BC [39–41]. As in many developing countries, educational level and economical status are the major determinants of reaching healthcare facilities and preventive interventions. Although we did not observe an association between educational level and weight gain in our study, it may be the major reason of being overweight or obese at the time of BC diagnosis. It is important to note that our study population is a well-educated group with intermediate economic status.

The other two factors that had significant impact on weight gain in our study were multiparity and presence of comorbid diseases other than breast cancer. Obesity is associated with an increased risk of chronic diseases such as diabetes, hypertension, osteoarthritis, and these comorbid diseases themselves might induce weight gain and cause metabolic disturbances in patients with BC. It has been

shown that multiparity is associated with increased risk of obesity compared to nulliparity in white women [42].

Turkish women are more obese than other European counterparts and slightly less obese than the women in the United States. The prevalence of a BMI of >30 in Turkish women who are between 50 and 54 years of age is reported as 39% and of a BMI of >25 kg/m² is noted as 78% in the WHO Global Infobase [43]. Given most of the Turkish patients with early BC were overweight or obese at baseline, weight gain during and after adjuvant systemic therapy leads to an important health problem for cancer survivors and a considerable economic burden for the social security systems. Many other studies have shown that a return to prediagnosis weight is unlikely even more than a year after diagnosis in patients with early BC [23, 27, 32]. One year after completion of CT, only 10% of our population maintained their prediagnosis baseline BW. Factors associated with weight gain after diagnosis of BC have been investigated in a subgroup of participants who completed their baseline dietary assessment and subsequently enrolled in the Women's Healthy Eating and

Table 5 The relationship between weight gain and patient demographic characteristics

	<i>n</i> (%)	Before CT	After CT	1 year after CT	<i>P</i> value
Education					
Primary school	68 (38.6)	70.7	72.2	73.3	0.319
High school	51 (29.0)	69.3	70.5	72.3	
University	57 (32.4)	66.5	68.7	70.1	
Smoking Status					
Smokers	48 (27.3)	67.8	69.5	70.4	0.655
Never smokers	128 (72.7)	69.4	71.0	72.5	
Alcohol intake*					
Yes	12 (6.8)	68.1	69.5	71.4	0.823
No	164 (93.2)	68.9	70.6	71.9	
Family history of cancer**					
Yes	57 (32.4)	68.2	70.1	71.6	0.788
No	119 (67.6)	69.2	70.1	72.1	
Marital status					
Single	20 (11.4)	66.6	68.9	70.1	0.456
Married	134 (76.1)	67.9	69.6	71.1	
Divorced or widow	22 (12.5)	76.8	77.6	78.3	
Number of children					
0	31 (17.6)	64.5	67.1	68.2	0.019*
1	47 (26.7)	66.9	68.9	69.8	
2	74 (42.0)	70.6	72.3	74.1	
3	15 (8.5)	68.4	68.8	70.3	
>3	9 (5.1)	81.3	80.2	80.5	
Patients receiving vitamin supplements					
Yes	35 (80.1)	67.2	68.9	70.4	0.964
No	141 (19.9)	69.3	71.0	72.3	
Comorbid disease					
Absent	119 (67.6)	65.8	67.9	69.4	0.017*
Present	57 (32.4)	75.4	76.1	77.2	
Occupation					
Housewife (never worked)	89 (50.6)	70.7	72.3	73.3	0.372
Working or retired	87 (49.4)	67.0	68.8	70.5	

CT chemotherapy

* $P < 0.05$

Living (WHEL) study [23]. The results indicated that only 10% of participants returned to their prediagnosis BW over the course of the study [23].

Our study has limitations due to its retrospective nature and small sample size. Therefore, the timing and the method of the weight measurements may vary. In addition, we did not examine the potential indicators of weight gain including energy expenditure, dietary factors, change in menopausal status during chemotherapy and psychological factors. Of note, this is a single center retrospective study; a multicenter prospective study would be more representative. Our study population is relatively well educated, predominantly employed or retired; hence, our results may not be generalizable to the population of all BC survivors in Turkey. Nevertheless, this study is the first study to report adjuvant chemotherapy-related weight change from

Turkey. It is important to know that the Turkish patients gain weight after adjuvant therapy. Moreover, this gain lasts at least a year after completion of therapy, meaning the adverse impact of this change is not a short-term event. Our findings underscored the fact that all Turkish patients with early BC should be informed about the magnitude of weight gain during and after CT at the time of treatment planning so that they could take personal precautions for weight management including dietary intervention, physical activity and behavior modification. We think that efforts to elucidate the mechanisms of weight gain are of paramount importance not only for the prognosis of the BC itself but also for the maintenance of general health. This is not an issue only for developed western countries but also for developing countries like Turkey.

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