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EPIDEMIOLOGY

Preventing weight gain during adjuvant chemotherapy for breast cancer: a dietary intervention study

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Abstract Adjuvant chemotherapy significantly decreases recurrences and improves survival in women with early breast cancer (BC). However, the side effects of chemotherapy include weight gain, which is associated with poorer prognosis. We have previously demonstrated that by means of a comprehensive dietary modification which aims at lowering insulin levels it is possible to reduce body weight and decrease the bioavailability of insulin, sex hormones and the growth factors linked to BC risk and prognosis. We are now going to present a randomized controlled study of adjuvant diet in BC patients undergoing chemotherapy. The diet was designed to prevent weight gain during chemotherapy treatment. Women of any age, operated for invasive BC, scheduled for adjuvant chemotherapy and without evidence of distant metastases, were randomized into a dietary intervention group and a control group. The intervention implied changing their usual diet for the whole duration of chemotherapy, following cooking classes and having lunch or dinner at the study centre at least twice per week. 96 BC patients were included in the study. The women in the intervention group showed a significant reduction in their body weight (2.9 kg on average), compared with the controls. They also significantly reduced body fat mass, waist and hip circumferences, biceps, underscapular and suprailiac skinfolds, compared with the women in the control group. Our results support the hypothesis that dietary intervention during adjuvant chemotherapy for BC is feasible and may prevent weight gain.

Keywords Breast cancer · Chemotherapy · Weight control · Adjuvant diet · Intervention study

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Introduction

In high-income countries, the incidence of BC has increased steadily over the past decades, but BC survival is increasing too, suggesting a benefit from early detection and more effective adjuvant treatment [8, 46]. As a consequence, BC survivors are constantly increasing, and research investments for the identification of modifiable risk factors associated with BC recurrences have to be increased too [35].

Over 60 % of BC patients receive adjuvant chemotherapy [1], which decreases BC mortality by 30 % [16]. However, numerous studies have reported weight gain as a common side effect in women receiving adjuvant chemotherapy for BC [19]. Observational studies also reported that women gain more weight with chemotherapy than with other adjuvant treatments, such as tamoxifen or radiotherapy [15, 25, 39]. In the *Women's Healthy Eating and Living* study, the women treated with chemotherapy had a 65 % increased risk of gaining weight during treatment, compared to the women with no systemic treatment [39].

Body weight gain after chemotherapy usually ranges between 1 and 6 kg [4, 5, 9, 22, 25, 33, 37, 39, 44]. These data are clinically relevant, because BC patients who gain weight during chemotherapy are at increased risk for BC recurrences and mortality [10, 21, 27, 32, 34, 36, 42, 45], as

well as for several co-morbid conditions such as cardiovascular disease and diabetes [34, 45]. In addition, weight gain may negatively impact self-image and the quality of life [11, 14].

Camoriano and colleagues [10] first showed that the women who gained more than the median of the studied group had a higher risk of recurrence and death. Kroenke et al. [27] showed that increasing BMI from 0.5 to <2 kg/m^2 was associated with an increased risk of recurrence. The risk was even higher with an elevation of BMI >2 kg/m^2.

Among recently published papers on weight gain and BC prognosis, the 20-year follow-up study by Thivat et al. [42] showed a 2.28 increased risk of relapse in the group that experienced weight change compared to the group with stable weight. In another cohort study, every 5 kg weight gain after a BC diagnosis increased cardiovascular (19 %) and BC specific (13 %) mortality [34].

Research in this area has also suggested that weight gain mainly occurs in patients receiving cyclophosphamide, methotrexate and 5-fluorouracil (CMF) regimen [3, 13, 24, 31], while it occurs less in women treated with regimens containing anthracyclines [14, 18, 30]. However, other studies have demonstrated that weight gain during chemotherapy was higher among women treated with multiagent regimens over longer periods of time, irrespective of chemotherapy regimen [15, 22, 32, 45]. Longer follow-up data of the studies that did not report weight gain during treatments have shown a progressive weight gain after the completion of treatment [14, 18, 30].

Weight gain can be prevented by lifestyle. Our DIANA (DIet and ANdrogens) trials proved that a comprehensive dietary modification aiming at lowering insulin levels (by means of the low consumption of fats, refined carbohydrates and animal products, and the high consumption of whole grain cereals, legumes and vegetables) reduces body weight and waist circumference, improves insulin sensitivity and decreases the bioavailability of sex hormones and growth factors linked to BC risk and prognosis [5, 7]. Moreover, there is evidence that weight reduction may prevent BC recurrences [12]. The *Women's Intervention Nutrition Study* showed that a low-fat diet, which resulted in a 2.7 kg weight loss, was associated with a 24 % decrease in BC recurrences after a median follow up of 5 years [12]. Also our DIANA-2 trial suggested that moderate calorie restriction can decrease BC recurrences [6].

We hypothesized that the same dietary changes tested in our DIANA studies could be useful and acceptable for preventing weight gain during BC chemotherapy. Therefore, we conducted a randomized controlled study of adjuvant diet in BC patients. The primary goal of the study was to prevent weight gain, usually observed during chemotherapy, using an insulin lowering diet.

Another goal was to evaluate the feasibility of recruiting women early in their BC treatment and to evaluate whether or not women could comply with a weight control programme initiated during chemotherapy for BC.

Patients and methods

Patients

The women eligible for the study were: (a) of any age, (b) operated for invasive BC (any surgery, any loco-regional disease stage), (c) scheduled for adjuvant chemotherapy (d) without evidence of distant metastases, (e) with residence within the Milan area, (f) without family or working impediment which could prevent participation in the study activity twice a week in case of randomization into the intervention group, and, (g) agreeing to be randomized and participate in the assigned group.

The women were recruited at the National Cancer Institute of Milan before starting chemotherapy, between 2006 and 2008. They were fully informed about the study rationale and design and they signed the informed consent. We contacted 224 BC patients. 71 women were resident outside the Milan area, 51 either refused or could not guarantee participation in our activities because of family or work impediments, and 102 were eligible for the study.

The study was approved by the Institutional Review Board and the Ethical Committee of the National Cancer Institute of Milan.

Study design (Fig. 1)

The aim of our study was to test whether a diet aiming at lowering insulin levels, based on Mediterranean and macrobiotic recipes, may prevent the increase in body weight usually observed during adjuvant chemotherapy for BC. We expected: (a) an increase in weight gain and fat mass during chemotherapy in the control group, particularly in women treated with CMF, (b) no increase or a decrease of body weight in the intervention group, and, c) no differences between the intervention and the control groups for what concerns the effects of chemotherapy on haematological parameters.

We computed that, under the hypothesis of a clinically significant 2.5 kg increase in body weight in the control group (on average) and no change in the intervention group, the required number of subject was to be 36 per arm for a 90 % statistical power.

Among the 102 eligible women, 6 women changed the programmed adjuvant therapy and did not start chemotherapy. As a result, 96 BC patients were included in the study.

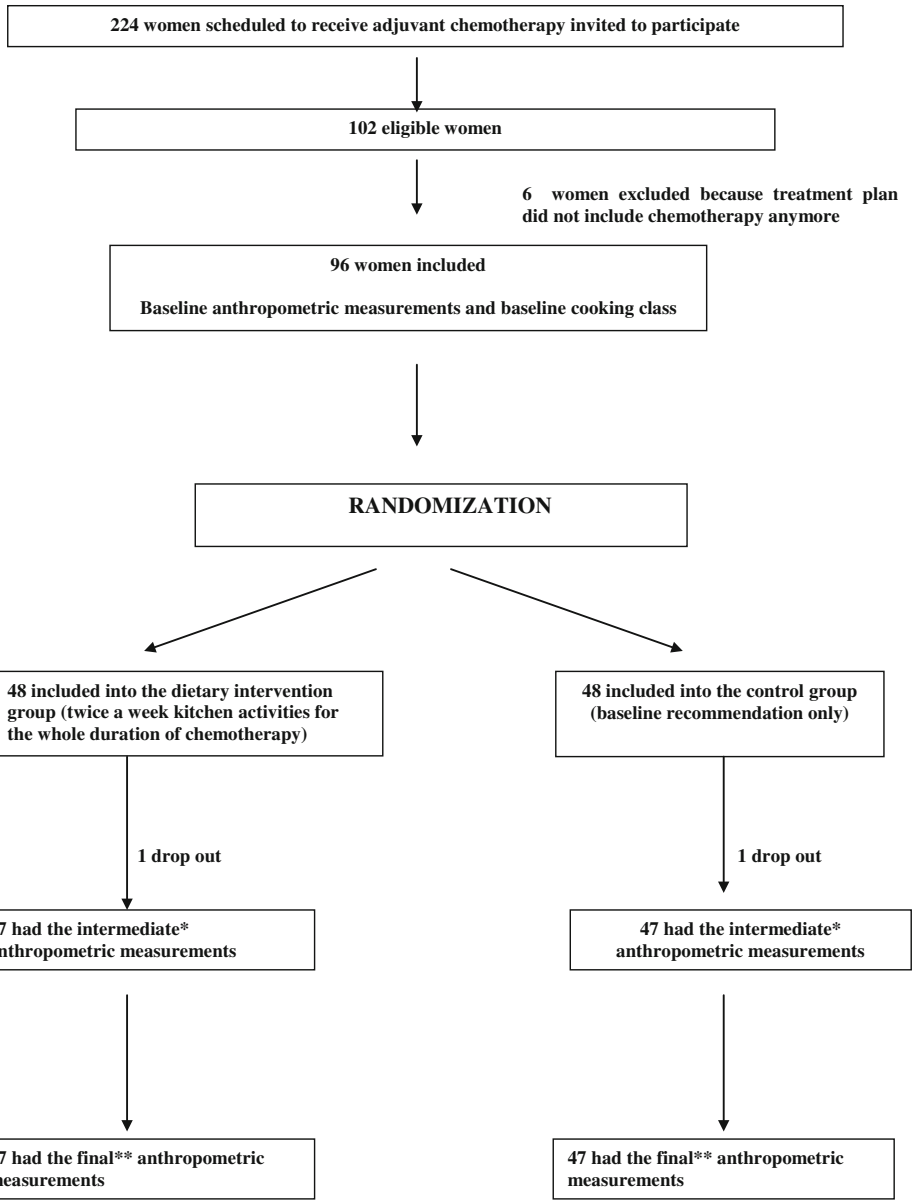

Fig. 1 Study design and activities. *Asterisks* After the end of the first cycle of chemotherapy (if scheduled as 2 subsequent cycles of different drugs) or after about 3 month of treatment. *Double asterisks* At the end of chemotherapy

All women received general recommendations for the prevention of cancer and a baseline brief kitchen course which included instructions on how to reduce the gastrointestinal side effects of chemotherapy.

The women were then randomized, after stratification by age (±50) and BMI (±25), into an active intervention group, which was required to participate in cooking classes and common meals at least twice per week for the whole duration of chemotherapy, and a control group, which only received baseline recommendations. Kitchen courses started either before any chemotherapy or after the first administration.

A single trained nurse obtained anthropometric measurements for all participants before starting adjuvant chemotherapy, at the end of the first cycle of treatment (usually after 3 months), and at the end of chemotherapy. Multiple measurements are informative because, usually, BC chemotherapy implies two cycles of treatment with different drugs, which may have different influence on weight change.

We weighed patients (dressed in light clothes), measured waist and hip circumferences, and also, using the Harpender Skinfold Caliper, underscapular, triceps, biceps and suprailiac skinfolds. Waist was measured at natural waist or, if not identifiable, at the midpoint between the iliac crest and the lower rib. Hip circumference was measured at the level of the throcanter. The underscapular skinfold was measured at the lower angle of the scapula; triceps and biceps skinfolds at the level of the mid-point between the acromiale and the radiale, on the mid-line of

the posterior and, respectively, anterior surface of the arm. The suprailiac skinfold was measured immediately above the iliac crest, on the most lateral side. Height measured at enrolment was used to compute body mass index (BMI). We also estimated lean and fat mass, both through skinfolds (using the Siri equation [41]) and impedance measurement (using the Dietosystem Human-Im Plus II segmental impedance device).

Reviewing patients' medical records, we collected data on cancer stage and treatment, and registered haematological exams before every chemotherapy administration, as well as any interruption or delay of chemotherapy administrations.

Dietary intervention

Our dietary recommendations were based on Mediterranean and macrobiotic recipes and on the avoidance of energy dense foods. We previously showed that adherence to such recommendations moderately decreases energy intake, by about 250 kcal/day [5].

The macrobiotic diet is mostly based on whole grain cereals (mainly rice, millet and occasionally spelt, barley and corn), pulses and selected vegetables, traditional soy products—such as miso (fermented soy paste), tamari (soy sauce) and occasionally tofu (soy cheese)–sesame oil, seaweeds and occasionally fish and desserts prepared without sugar and saturated fats [29]. Also the Mediterranean diet is based on daily consumption of cereal products (mainly wheat based pasta, bread, cous-cous) and various kinds of pulses, fruit and vegetables, olive oil, small amounts of wine, fish and occasionally cheese, yoghurt, eggs and meat [47].

The bases of the diet recommended to prevent gastrointestinal symptoms during chemotherapy were creams prepared with unrefined rice and other cereals, pulses, selected cooked vegetables, vegetable soups and miso soup (occasionally with wakame seaweed). Cereal creams were suggested in order to profit from all the nutritional advantages of whole grain cereals—including anti-inflammatory properties—while avoiding the irritating effect of a large amount of fibres on the gut mucosa. Miso is a highly nutrient condiment, rich in free amino acids (it contains all essential aminoacids, because it is prepared with both soy and barley or rice), and in proteolytic and lipolytic enzymes, and it is traditionally used to accompany every meal in order to improve digestion. Seaweeds are rich in minerals, and mucilages that protect the digestive tract. Meat and cheese consumption was discouraged to prevent colitis [2, 26, 43]. Patients who were used to regularly eating meat and cheese were offered alternatives based on vegetable proteins. In general, however, protein intake was reduced, in order to prevent acidosis and excessive intestinal putrefaction.

Dietary compliance assessments in both the intervention and the control group included repeated forms about the food consumed during the previous 24 h. The women were requested to write in these forms (39 food items plus a free line) all the foods they had eaten, or not eaten at all, at breakfast, lunch, dinner or between meals, whatever the portion size. Six forms were completed all along the study: three in the day of chemotherapy administration or in the following 2 days, and three in the intervals between administrations, avoiding the days in which the intervention women ate at the study centre.

Statistical methods

The anthropometric variables of the women included in the study were approximately normally distributed. Participants' BMI was calculated by dividing weight by squared height (kg/m^2).

At baseline, the means of continuous variables in the women included in the intervention group were compared with those of the control group using student's t test. χ^2 test was used to compare frequencies.

The statistical analysis focused on changes in weight and other relevant anthropometric variables, calculated as the difference between the end of the study (end of chemotherapy) and baseline values for each woman. The statistical significance of mean changes in the intervention group compared with controls was assessed by means of ANOVA. Multivariate ANOVA was used to control for potential confounding variables, such as age and body weight at baseline.

We also performed an analysis on changes in anthropometric variables, calculated as the difference between the end of the first cycle of chemotherapy and baseline, and between the end of the study (end of chemotherapy) and the end of the first cycle of chemotherapy.

All of the *P*s are two-tailed. All analyses were performed using the STATA 11 statistical package.

Results

Among the 96 randomized women, 94 completed the study. In fact, two women dropped out, one woman in the intervention group did not accept to change her diet, and one woman in the control group interrupted the treatment.

Overall, 63.8 % of the participants had conservative surgery and 36.2 % had radical mastectomy. 88.3 % of the tumours were infiltrating ductal BC. 53.2 % of the tumours were classified as oestrogen and progesterone receptor-positive and 17.0 % as oestrogen and progesterone receptor-negative.

Seventy-eight participants (81 %) received a chemotherapy regimen based on two subsequent cycles, scheduled as 4 + 4 administrations: anthracyclines with or without taxanes followed by CMF (71 women), or anthracyclines followed by taxanes (six women), or CMF alone (one woman).

Eighteen women (19 %) received 6, or less than 6, chemotherapy administrations. Out of them, a single woman was treated with CMF alone and two women with taxanes alone. The other 16 were treated with anthracyclines and cyclophosphamide, with (three women) or without taxanes (13 women).

Overall, 96 % of patients received anthracyclines, 56 % taxanes, and 77 % CMF (Table 1).

Table 1 describes the baseline major clinical and anthropometric characteristics of the 94 women who completed the trial. The women included in the intervention group were older (52.7 ± 10.8 vs 48.4 ± 9.4 years, $p = 0.05$). The two groups were comparable for anthropometric and clinical parameters, and for chemotherapy regimen and scheme of administration.

Table 2 shows the main results of the study. The table reports values of anthropometric parameters at baseline, at the end of the first cycle of chemotherapy (usually after 3 months), and at the end of chemotherapy. It also shows the p values of the comparisons between intervention and control groups for the anthropometric changes.

On average, between baseline and the end of chemotherapy body weight did not increase, neither among women within the intervention group nor among women within the control group. On average, it decreased by 2.9 kg in the intervention group and by 0.1 kg in the control group. The women included in the intervention group experienced larger and significant reduction in all the anthropometric parameters under study, except for triceps skinfold. We found significant differences not only for weight and BMI (primary end point of the study $p = 0.0001$), but also for waist and hip circumferences and underscapular, biceps and suprailiac skinfolds. The difference in weight change between the two groups remained significant after controlling for age and weight at baseline ($p = 0.0004$). Weight change was almost identical in lean and overweight women. The effect, however, was more pronounced in women above the age of 50 years (−3.7 kg in the intervention group and −0.48 in the control group, $p = 0.004$) than in younger women (−1.8 kg and respectively −0.04, $p = 0.038$).

We analysed lean and fat mass data through bioimpedance, and we found that the women in the intervention group had decreased fat mass by 2.29 kg and free-fat mass by 0.67 kg, with significant differences between the two groups; the women in the control group had decreased fat mass by 0.69 kg and increased free-fat mass by 0.06 kg; the difference in fat-free mass was largely due to total body water. These data do not suggest any differences in muscular mass between the intervention and control group. Basal metabolic rate decreased only slightly in the intervention group and increased slightly in the control group; the difference, however, was statistically significant.

Table 1 Baseline characteristics of the 94 women who completed the study

Variables (mean ± standard deviation)	Intervention group	Control group	p*
Age (years)	52.7 ± 10.8	48.4 ± 9.4	0.05
Height (m)	1.61 ± 0.07	1.63 ± 0.06	0.36
Weight (kg)	63.8 ± 11.8	64.7 ± 13.1	0.73
BMI (kg/m^2)	24.7 ± 4.5	24.7 ± 4.8	0.97
Systolic pressure (mm/Hg)	128.3 ± 17.7	131.1 ± 15.0	0.41
Diastolic pressure (mm/Hg)	82.4 ± 9.7	85.6 ± 8.4	0.09
Variables (%)			
G3 (poorly differentiated BC)	65.9 %	53.2 %	0.21
ER+	66.6 %	76.6 %	0.25
Her+	25.5 %	27.7 %	0.66
Sentinel node+	72.3 %	72.3 %	0.99
Patients received anthracyclines	94 %	98 %	0.49
Patients received taxanes	53.2 %	59.6 %	0.40
Patients received CMF	74.5 %	78.7 %	0.63
Patients received 6 or less chemotherapy administrations	17 %	21 %	0.33

* p value of differences using student's t test for continuous variables and χ^2 test for frequencies and percentages comparison

Table 2 Anthropometric changes in the randomized groups

Variables[a]	Intervention group			Control group			p^*	p^{**}	p^{***}
	Baseline	End of 1st cycle	End of chemotherapy	Baseline	End of 1st cycle	End of chemotherapy			
Weight (kg)	63.8(1.72)	61.1(1.75)	60.9(1.73)	64.7(1.91)	63.3(1.92)	64.6(1.98)	0.00	0.06	0.00
BMI (kg/m^2)	24.7(0.66)	23.6(0.68)	23.6(0.67)	24.7(0.70)	24.1(0.70)	24.6(0.73)	0.00	0.06	0.00
Waist (cm)	81.4(1.52)	78.7(1.52)	78.4(1.43)	80.5(1.56)	79.0(1.54)	80.4(1.58)	0.00	0.05	0.00
Hip (cm)	101.3(1.38)	98.9(1.41)	98.6(1.38)	102.2(1.41)	100.7(1.34)	102.3(1.46)	0.00	0.23	0.00
Triceps skinfold (mm)	19.9(1.06)	18.5(1.10)	17.8(1.05)	22.4(1.00)	21.2(1.01)	21.6(1.09)	0.07	0.91	0.03
Biceps skinfold (mm)	12.2(0.94)	11.2(0.98)	11.2(0.98)	12.2(0.92)	12.4(0.99)	12.6(0.90)	0.02	0.02	0.53
Underscapular skinfold (mm)	17.6(1.14)	16.4(1.18)	16.0(1.19)	18.3(1.15)	17.2(1.18)	18.6(1.19)	0.01	0.78	0.00
Suprailac skinfold (mm)	13.6(1.05)	12.2(1.07)	12.4(1.07)	13.3(1.04)	12.6(1.04)	13.8(1.03)	0.01	0.12	0.08
Fat mass (kg)	20.0(1.47)	17.4(1.42)	17.7(1.48)	21.0(1.77)	19.6(1.71)	20.3(1.82)	0.03	0.32	0.03
Free fat mass (kg)	43.4(0.62)	42.6(0.66)	42.7(0.64)	44.2(0.76)	43.9(0.65)	44.3(0.74)	0.01	0.45	0.44
Basal metabolism (kcal)	1307(13.5)	1289(14.3)	1292(13.8)	1325(16.4)	1318(14.0)	1326(16.0)	0.01	0.45	0.44
Total water (Lt)	32.9(0.67)	32.4 (0.77)	32.8(0.81)	34.0(0.90)	34.0(0.75)	34.3(0.86)	0.62	0.52	0.99

[a] Variables are presented as mean (standard error)

* ANOVA between baseline and end of chemotherapy comparing intervention versus control group

** ANOVA between baseline and end of first cycle of chemotherapy comparing intervention versus control group

*** ANOVA between end of first cycle and end of chemotherapy comparing intervention versus control group

We also estimated body lean and fat mass through skinfolds measurements. The correlation between fat mass estimated through bioimpedance and fat mass estimated through skinfolds was 0.96. However, bioimpedence slightly overestimated body fat change relative to skinfold measurements (−2.29 versus −1.88 kg).

When comparing data at baseline and at the end of the first cycle of chemotherapy treatment, in which 96 % of women used anthracyclines, we observed that both the intervention and the control group experienced a reduction in weight, BMI, waist and hip circumferences and underscapular, triceps and suprailiac skinfolds (Table 2). All the reductions were higher in the intervention group. Biceps skinfold was reduced in the intervention group and did not change in the control group. Comparing the two groups, we found significant differences only for biceps skinfold ($p = 0.02$) and borderline significant differences for waist circumference ($p = 0.05$), weight and BMI ($p = 0.06$).

Table 2 also shows the anthropometric change between the end of the first cycle and at the end of chemotherapy treatment, in which the vast majority of women used CMF. The intervention group continued to moderately lose weight (−0.2 kg) and fat mass, estimated by bioimpedence (−0.4 kg), and reduced all circumferences and skinfolds. On the contrary, the control group significantly increased body weight (+1.3 kg), fat mass (+2 kg, $p = 0.0001$), and all the other anthropometric parameters, with the exception of biceps and triceps skinfolds. Body weight increased particularly in the women of the control group treated with CMF (1.7 kg). Comparing the two randomized groups, we found significant differences for weight, BMI, waist and hip circumferences, triceps and underscapular skinfolds and fat mass.

We also evaluated the compliance with the proposed diet by analysing the dietary data from six 24-h recalls. We analysed separately the three 24-h recalls collected far form the chemotherapy administration, and the three collected in the day of the administration or in the two following days. The latter showed very low consumption frequencies (only vegetables were consumed slightly more than once per day). The women included in the intervention group consumed significantly less frequently white bread, sugar and processed meat. As for the 24-h recalls collected in the interval between chemotherapy administration the women included in the intervention group showed a significantly higher frequency of the consumption of whole grain cereals (2.2 vs 0.8 times per day) and legumes (0.5 vs 0.3 times per day), and a significantly lower frequency of the consumption of sugar (0.4 vs 0.9 times per day), refined cereal products (1.1 vs 2.1 times per day), dairy products (0.5 vs 0.9 times per day) compared with the women of the control group ($p < 0.01$ for all comparisons). There were no significant differences for the consumption of meat (0.4 vs 0.5 times per day), vegetables (2.1 vs 1.8 times per day), and fruits (1.4 vs 1.4 times per day).

We also analysed haematological changes along the whole chemotherapy treatment. Red blood cells, white blood cells, platelets and haemoglobin significantly decreased

between baseline and the end of chemotherapy in both groups of women. The comparison between the two groups did not show any significant differences (data not shown).

On several occasions patients had to postpone chemotherapy administrations because of toxicity. This occurred 27 times among the intervention women and 28 times among control women. Clinical notes registered mucositis in 18 controls and 11 intervention women.

Discussion

The main results of our study were the significant reduction of weight and fat mass in the women included in the dietary intervention group compared with the women belonging to the control group. Previous studies on BC survivors treated with moderate calorie restriction after the end of chemotherapy suggested that a weight reduction of the same order of magnitude is associated with a reduction in BC recurrences [6, 12]. The women in the intervention group also significantly reduced waist and hip circumferences, biceps, underscapular and suprailiac skinfolds compared with the women in the control group, who showed only minor changes in these variables. These results suggest that fat mass reduction is distributed in both visceral and subcutaneous body compartments.

Contrary to our expectations, we observed a slight weight decrease also in the control group. The lack of weight gain in the control group may have two explanations: (a) adjuvant chemotherapy is not related with an increase in weight; (b) general information about healthy diet, provided to both groups before randomization, was sufficient to avoid an increase in weight also in the control group. Such contamination of the control group is interesting and suggests that general recommendations may be sufficient to obtain the desired effect.

There is evidence that post-diagnosis weight gain among BC survivors is highly correlated with type and duration of treatment [45]. Researches in this area have suggested that systemic treatment (adjuvant chemotherapy) produced significantly more weight gain than localized treatment (surgery and/or radiation only) and that weight gain was higher among women treated with multi-agent regimens over longer periods of time [45]. Harvie et al. [24] reported a mean weight gain of 3.3 kg among women treated with 6 months of CMF adjuvant therapy, a finding that is consistent with studies in which patients were treated with similar protocols [3, 13, 31]. Others have reported that, when only four administrations of adriamycin and cyclophosphamide were the dominant therapy, weight gain during treatment was minimal, and in most cases not significant [14, 17, 18, 30]. In our study, almost all women received chemotherapy regimens containing anthracyclines (with or without taxanes) during the first cycle of chemotherapy, which may explain why they did not gain weight neither in the dietary arm nor in control arm. On the other hand, weight gain with CMF adjuvant chemotherapy is well known [3, 13, 31], and in our study, CMF was usually administered as the second drug. Between the end of first cycle of treatment and the end of chemotherapy, only the women included in the dietary arm experienced weight reduction, while the women included in the control group gained weight, particularly if treated with CMF.

We would also like to remind that some ‘contamination’ of the control group was unavoidable, and was actually incorporated in the study design, because for ethical reasons, we provided the whole study population with general dietary recommendations for the prevention of cancer and offered them a baseline cooking course giving instructions to reduce the side effects of chemotherapy. Furthermore, the BC patients who accepted to participate in the study were highly motivated to change their diet. This improved compliance in the intervention group, but also the comparison group was likely to modify their behaviour. All these factors might have influenced the weight reduction observed in the control group.

Weight gain is expected when energy intake exceeds energy expenditure. It has been suggested that, in BC patients receiving chemotherapy, weight gain may occur because of reduced physical activity [14, 17, 20, 40], and of the reduction of resting metabolic rate due to the loss of lean body mass while adipose tissue increases [15, 28, 38]. Increase of food intake has been also suggested to play a role in weight variation [15, 24, 37]. Chemotherapy treatment is often linked with sleep restriction that impairs glucose metabolism and alters the cross-talk between the periphery and the brain, favoring excessive food intake and thus weight gain [23]. Furthermore, chemotherapy induces premature menopause, and women generally gain weight in menopause.

In our study, only the women included in the intervention group significantly reduced their fat-free mass. They also slightly, but significantly, reduced their basal metabolism. Nevertheless, such minimal change in the metabolic rate does not support a major role of this factor in explaining weight gain during chemotherapy. Physical activity may be important, but would not explain why weight gain occurs with CMF and not with anthracycline chemotherapy. We do not have, however, information on women’s physical activity. The induction of iatrogenic menopause, on the contrary, could be an important mechanism, consistent with our observation of a somewhat smaller weight decrease in women under 50 years of age.

Our study adds to the evidence that the energy density of food is a major factor. Furthermore, our results support the hypothesis that a dietary intervention during adjuvant

chemotherapy for BC is feasible. Actually, only one woman dropped out of the intervention because of difficulties in changing her diet.

The intervention aimed at teaching BC patients changes that they can incorporate into their daily lifestyle and at encouraging long-term changes. This area is worthy of future study, in order to reduce a well-known negative prognostic factor for BC survivors.

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Conflicts of interest None.

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