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Original Articles

Correlation between the body mass index of patients with breast cancer before and after chemotherapy

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Summary

The objective of this work was to show how the influence of the microenvironment in tumor cells and consequently the onset and tumor progression is becoming increasingly more evident. Cancer is the second leading cause of death in the developed world, surpassed only by heart disease and obesity, and is increasingly recognised as an oncogenic factor in the genesis of this tumor. Inflammatory mediators related to obesity are suspected to play a role in oncogenic modification of substrates metabolism of nutrients, most patients diagnosed with breast cancer underwent chemotherapy treatment, and this may be an aggravating factor of obesity. The authors selected 49 patients with previous diagnosis of breast cancer who had undergone chemotherapy and evaluated data regarding body mass index (BMI) before and after chemotherapy. They observed that there was statistical difference of BMI of patients before and after chemotherapy with $p = 0.03$. Comparing the groups, a statistical difference was found between overweight and obesity grade II and overweight and obesity grade III. Patients with a diagnosis of breast cancer usually showed on average a BMI 27.84, worsening after chemotherapy to 28.64. These findings can help to accelerate the division and cell reproduction, because obesity is a risk factor for breast cancer, and weight gain seems to be a major factor after treatment and may influence the prognosis of these women.

Key words: Breast cancer; Body mass index; Chemotherapy; Body weight.

Introduction

Overweight and obesity are very important factors associated with breast cancer [1]. In the United States, obesity incidence has reached a plateau, however its prevalence (body mass index [BMI] is higher than 30) is around 30%. People who are overweight (BMI > 25 and < 30) accounts for 65 % of the population. In regards to breast cancer, the relationship between obesity and risk is complex, however, it does not show any increased effect in pre-menopausal women, however, it is associated with increased risk in post-menopausal women.

With the ability to stratify breast cancer according to the subtype, epidemiological studies have shown that obesity is strongly associated with an increased risk of triple negative breast cancer in premenopausal and postmenopausal women, while the luminal types are associated with obesity only during the post-menopausal period [2].

Determining the risk factors can help reduce the risk of breast cancer as well as the health differences observed. Studies in preclinical models show that the type of diet intake induced obesity is associated with breast tumors [3].

Adipose tissue is found near many invasive cancers. In breast cancer, the first local tumor invasion results show interactions with fully differentiated adipocytes. In addition to its energy storage function, mature adipocytes are also active endocrine cells that are likely to affect tumor behavior through a signaling processes [4].

In 2003, the results of a large US and UK cohort study reported a surprising association between obesity and cancer [5, 6]. Studies show survival linking obesity and breast cancer were summarized in two meta-analyzes: one of the meta- analysis included 43 studies involving women diagnosed with breast cancer between 1963 and 2005, and the sample size ranged from 100 to 42,4168 cases (median 1,192). The meta-analysis showed worse survival among obese compared with non-obese women with breast cancer. Survival varied little and depended on some parameters used such as the body mass index or waist-hip ratio (WHR) as a measure of obesity [6-8]. Since then, it is estimated that being overweight or obese contributes to 20% of cancer deaths in the United States [5, 6]. In the case of obesity, which is one of the few modifiable risk factors that disturbs homeostasis tissue and influences breast cancer, the development of more effective therapeutic strategies to combat breast cancer is essential in order to control the disease [6].

We also have chemotherapy, which is one of the treat-

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ments for breast cancer. Chemotherapy is reported to also have changes in weight during and after treatment of patients [9].

In a meta-analysis of 141 articles, BMI was positively associated with an increased incidence of breast cancer in postmenopausal women, along with the colon, endometrial, esophageal, gallbladder, pancreas, kidney cancer, thyroid, leukemia, multiple myeloma, and non-Hodgkin's lymphoma in women [10]. The results were less significant for breast cancer in pre-menopausal women [11]. There is also the idea that BMI is not a perfect measure of adiposity. Other measures such as WHR and waist circumference, which are specific measures of abdominal or central adiposity, may be better to assess the risk of cancer [12]. Two meta-analyses that examined correlation between WHR and risk of breast cancer in premenopausal women reported positive associations [13, 14].

All the therapies used to treat breast cancer (surgery, radiotherapy, hormone therapy, and chemotherapy) may be adversely affected by obesity. Usually we associate chemotherapy treatment for breast cancer. With chemotherapy, it is common to gain weight during treatment, which can be explained by decreased physical activity, increased food intake, and effects of corticosteroids [14]. It is worth noting firstly that in obesity, there are some physiological changes that can alter the distribution and elimination of drugs [15, 16]. The obesity effects on hepatic metabolism have not been well characterized, however, it is known that many anticancer drugs (such as cyclophosphamide) are extensively metabolized by CYP enzymes of the complex, especially the CYP3A4e CYP2C817, these being present in small amounts in obese individuals. Studies show that several drugs passing through the phase I metabolism (oxidation, reduction, hydrolysis, hydration, and isomerization) may have clearance unchanged or increased in obese patients, and that drugs that pass the Phase II metabolism (glucuronidation, glycosylation, sulfation, methylation, acetylation, condensation and conjugation with glutathione, amino acids or fatty acids) have shown increasing its elimination [15]. Changes in liver pathophysiology associated with obesity and fatty liver and fibrosis can result in reduced drug oxidation. On the other hand, the combination of drugs is often increased in obese individuals, and the presence of cardiac dysfunction in obesity can change the duration of the hepatic blood flow that, in turn, can affect the elimination of drugs [15, 16]. From the previously outstanding data, it is clear that obesity can cause changes in the pharmacokinetics of some drugs although only few studies have documented the influence of body fat on the pharmacokinetics of antineoplastic drugs [17]. A better understanding of this interference occurs with the understanding that the overweight in obese patients is usually arising from adipose tissue rather than smallest muscular increment [17].

Further epidemiological studies with various measurement parameters could bring greater benefits. In addition, studies suggest a positive association between the metabolic syndrome as a whole, with many of its individual components and the risk of breast cancer. The many confounding variables that may mediate this effect should be considered [18, 19]. Studies should evaluate geographically diverse populations, and changes in the metabolic syndrome, such as weight, which can affect the incidence of the disease and treatment outcomes after initial diagnosis of breast cancer.

The combination of chemotherapy associated with obesity and breast cancer were analyzed in this study. The authors' objective was to evaluate the patients diagnosed with breast cancer belonging to all molecular groups and that were undergoing chemotherapy while assessing BMI, waist circumference, waist and hip size, and tumor before and after chemotherapy. The combination of chemotherapy associated with obesity and breast cancer were analyzed in this study.

Materials and Methods

The selection of patients was carried out in the mastology clinic of the Department of Obstetrics and Gynecology of the Brotherhood of Santa Casa de São Paulo (ISCMSP) from August 2013 to July 2014. The authors selected 26 patients diagnosed with breast cancer, which had tumors larger than two cm and was indicated to undergo neoadjuvant chemotherapy treatment.

The work is the prospective longitudinal type and was approved by the Research Ethics Committee recognized by the CONEP number 401 029 (20.09.2013). The 49 patients selected in the mastology clinic signed a free and informed consent form and were evaluated through an entry form at work. The card contained height, staging, histological type, BMI, waist circumference, and hip data before chemotherapy. At the end of the sessions of chemotherapy, these patients were evaluated again comparing data weight, height, BMI, waist circumference, and hip and tumor size.

Exclusion criteria were patients with breast tumor ineligible to neoadjuvant chemotherapy, patients who did not have a BMI and waist and hip measurement before and after chemotherapy, and patients who were pregnant or who became pregnant during chemotherapy.

Results

The average age of the patients referred to in this study was 52.15 years, with a standard deviation of 9.649. The highest frequency was related to patients 51-55 years old, with 23.08%.

Figure 1 shows the distribution of patients regarding BMI before chemotherapy. The mean BMI before chemotherapy was 27.849 (overweight). Figure 2 shows the distribution of patients in relation to BMI after chemotherapy. The mean BMI after chemotherapy was 28.64 (overweight).

When comparing the variable weight before and after chemotherapy, a weight average before chemotherapy was 71.03 kg and 71.91 kg after treatment, with standard deviation of 13.03 and 12.48, respectively. Student's *t*-test analysis used for parametric data found differences between groups with $p = 0.0378$, confidence interval (CI) (-1.705 to

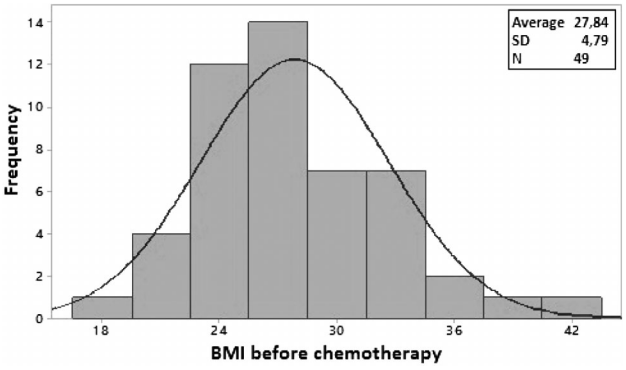

Figure 1. — Histogram (normal curve) of BMI before chemotherapy.

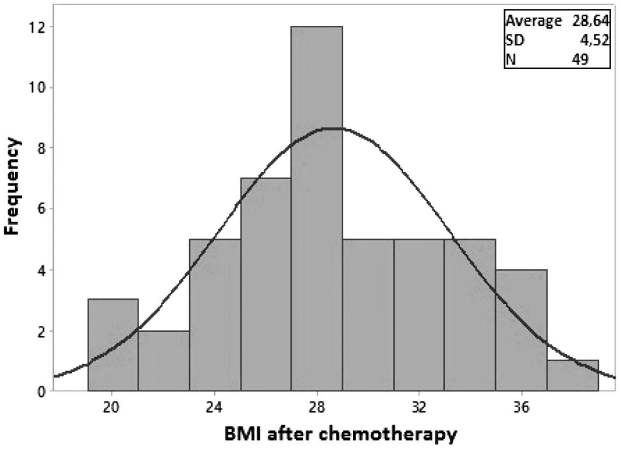

Figure 2. — Histogram (normal curve) of BMI after chemotherapy.

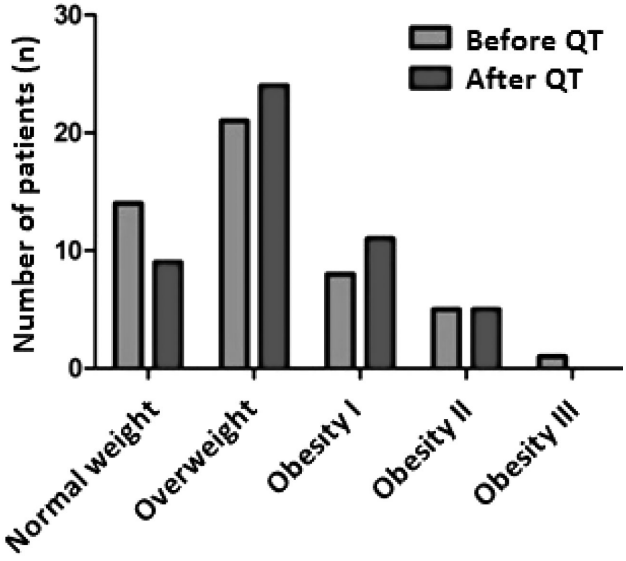

Figure 3. — Comparison of the degree of obesity among groups.

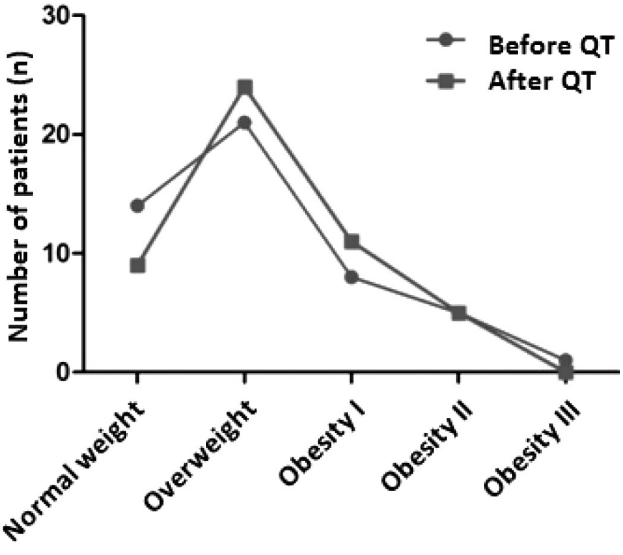

Figure 4. — Comparison among all groups: normal, overweight and obesities compared to chemotherapy.

-0.05322). Figure 3 shows the weight of the histogram comparison before and after chemotherapy and there was an increase in the average weight of patients, the difference being 0.8793 kg after chemotherapy.

According to WHO, the patients BMI results were classified into categories and their absolute and relative frequency calculated. The present authors noted that there was a higher prevalence of overweight patients in the group before and after chemotherapy. However, after chemotherapy, there was an increased number of patients in the obesity group grade I. There was significant difference with p = 0.0323, to run the t-test comparing the results of BMI before and after treatment, CI (-0.7243 to -0.03441).

When the paired t-test was performed to check for statistical differences in BMI of patients before and after chemotherapy, it was noticed that there was a statistical difference with p = 0:03, with CI of 90% (-1.5144; -010,417), and mean paired difference of -0.81 (BMI before QT - BMI Post QT).

The present authors also noted that of the 49 patients, 69.39% (n = 34) of them gained weight after chemotherapy and 30.61% (n = 15) lost weight and according to the χ^2 test, p = 0.007 it was observed that there was a significant difference between those who had increased BMI and those who had a decreased BMI with p = 0.007.

The measurements of BMI after diagnosis and chemotherapy treatment occurred on average 3.8 years after chemotherapy (Figure 3).

When performing the one-way analysis of variance with statistical significance of p = 0.0044 with Bonferroni post-test

showed statistical difference between Overweight group and obesity grades II and III overweight and obesity (Figure 4).

When performing two-way analysis of variance comparing the results of the groups before and after chemotherapy, no statistical significance ($p > 0.05$) resulted for all groups, Normal, overweight, grades I, II and III obesity showed no significant change in these groups before and after chemotherapy.

Discussion

The present study goes against the literature that demonstrates that breast cancer is less prevalent in women younger than 40 years [20], and that the peak incidence is between 50 to 60 years, coinciding with the present data that found casuistry more often in the age groups between 51 and 55 years in 23.08% of cases and in 7.7% of cases of women below 40 years.

The authors also noticed that there was an increase in weight of patients after chemotherapy ($p = 0.0378$). In agreement with literature, there was a progressive tendency of weight gain in women with breast cancer in adjuvant therapy [21], although it is not yet clear, the cause of weight gain can be explained with the decrease in physical activity, food intake, use of corticosteroids during treatment, changes in basal metabolic activity, and menopause [22].

It was also found that the average tumor size was higher in obesity group with grade 1, which is the group that showed better response to chemotherapy, with tumor shrinkage averaged 41.91 %, followed by the group with normal weight who had tumor response average of 30% after chemotherapy. The group with the worst response was the group with obesity grade 3, probably related to the change of metabolic degradation or lack of dose adjustment taking into consideration the peripheral resistance to drugs.

In relation to tumor size, when this parameter was compared with BMI or WHR before and after chemotherapy, there was no statistically significant difference.

Conclusion

Avoiding weight gain before and after diagnosis of breast cancer can be very tricky. Obese patients may show a great deal of breast tumor and often with worse prognosis. In contrast, grade 3 obesity patients may exhibit decreased response to chemotherapy, which can reflect problems in metabolizing drugs. Preventing weight gain improves quality of life and the prognosis of the disease. Many studies are needed to explain obesity and impact on survival. Currently, the indications of a healthy lifestyle, regular activity, and normal weight appear to assist in controlling the disease.

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