Visceral Adiposity Index in Breast Cancer Survivors: A Case-Control Study

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Received 28 August 2020; Revised 21 October 2020; Accepted 30 November 2020; Published 10 December 2020

1.Introduction

Breast cancer (BC) is the second most frequent neoplasm among the general population worldwide, only surpassed by lung cancer; however, it is the first cause of cancer morbidity and mortality in women [1, 2]. Smoking, fat-rich diet, high estrogen levels, obesity, alcohol consumption, hormone therapy, advanced maternal age, and late menopause are some of the known breast cancer risk factors [3–6]. Some of these risk factors are related to insulin resistance [7] and obesity [8].

Obesity is the excessive accumulation of fat in adipose tissue, with a positive energy imbalance and weight gain. Types of fat include visceral central and peripheral subcutaneous [9, 10]. The risk of developing cancer increases 1.6 times with a high body mass index (BMI) and the presence of visceral adiposity [11]. However, the relationship between BC and obesity is complex, as both are influenced by age,
menopause, and the expression of estrogen and progesterone receptors [9, 12]. Moreover, the conditions above are characterized by a chronic inflammatory state, and obesity can promote further inflammation in cancer by increasing the production of proinflammatory cytokines [13, 14].

In the majority of studies, obesity is ascertained resorting to BMI. This parameter cannot differentiate between visceral and peripheral fat. Interestingly, visceral adiposity index (VAI) is a marker of adipose tissue dysfunction, which comprises physical and biochemical parameters such as WC, BMI, triacylglycerols (TG), and high-density lipoprotein cholesterol (HDL-C) [15–17]. VAI has been associated with metabolic syndrome and cardiovascular and cerebrovascular diseases, particularly in men and advanced age; such an association is not reported for WC and BMI [18].

Breast cancer survivors with high fat mass have a higher risk of relapse and developing cancer in other parts of the body as well. Furthermore, these patients experience adverse effects induced by chemotherapy or radiation, including increased fat mass, adding to nausea, vomiting, energy loss, fatigue, and muscle mass loss [19, 20]. It is not clear, nevertheless, how visceral adiposity changes upon the development of BC and its therapeutic process. Therefore, our hypothesis was that VAI, a specific marker of central adiposity, as well as metabolic syndrome components are higher in BC survivors than in matched controls.

2. Materials and Methods

A case-control cross-sectional study was performed. Participants were recruited at the General Regional Hospital 251 of the Mexican Institute of Social Security (IMSS). The investigations included women between 40 and 65 years of age who were categorized in two groups. The first included women with breast cancer diagnostic at the follow-up, with at least one year without any BC-related chemotherapy with cytotoxic drugs, radiotherapy, or surgery, who attended regular oncology appointments; a review of their medical files was carried out in order to obtain general data and define all the inclusion and exclusion criteria. Patients with known type 2 diabetes, hypertension, kidney or hepatic failure, or any other chronic disease, which the research group considered could modify the variables under study, were excluded from participating in the study. The second group (control) comprised women who attended the hospital for annual mammography screening and were matched by age with the survivor group. The absence of BC was defined with the Martin–Hopkins equation, while glucose was evaluated with the hexokinase-UV/NAD test. HbA1c was measured by HPLC (high-performance liquid chromatography) utilizing a Variant II Turbo® system. All the tests were run by Quest Diagnostics®Clinical Analysis Laboratories (Mexico).

VAI was calculated with the following equation: $\frac{WC}{BMI} \times \frac{TG}{HDL-C}$.

2.2. Laboratory Procedures. Blood samples were taken with BD Vacutainer® Tubing SSTTM and EDTA K2 tubes. Once the sample was obtained, measurements were performed on an AU680 Beckman Coulter® device. HDL-C was determined with selective detergent methods; TG was determined with the glycerol phosphate oxidase test; low-density lipoprotein cholesterol (LDL-C) concentrations were calculated with the Martin–Hopkins equation, while glucose was measured with the hexokinase-UV/NAD test. HbA1c was measured by HPLC (high-performance liquid chromatography) utilizing a Variant II Turbo® system. All the tests were run by Quest Diagnostics®Clinical Analysis Laboratories (Mexico).

2.3. Statistical Analysis. A descriptive analysis was carried out for continuous variables through means and standard deviation. The normal distribution of the variables was found using the Kolmogorov–Smirnov test. The comparison of the means between the groups was by means of the t-test for variables that followed a normal data distribution, while Mann–Whitney U if they did not. A chi-squared test ($\chi^2$) was also run to find associations between qualitative variables. The statistical analysis was carried out with IBM® SPSS® Statistics, Mac version 25.

3. Results

A total of 56 women were enrolled in the BC survivor group and 54 women in the matched control group. However, 11 women (7 in the survivor group and 4 in the control) were excluded owing to the presence of diabetes mellitus diagnosed upon the study appointment. The final sample included 49 women in the BC survivor group and 50 controls. The most frequent histological subtype was ductal (83.7%), whereas the molecular subtype was luminal A (49.0%) (Table 1). 16 out of the 49 breast cancer patients were taking tamoxifen (32.7%), letrozole (18.4%), anastrozole (6.1%), and 21 no medication (42.9%). Control patients were free of any chronic medication.

Age, marital status, and personal BC history were not significantly different between groups (Table 2). Interestingly, WC was wider in the survivor group than in the control one ($p = 0.025$), though there were no differences in BMI and BW. With regards to body composition, there were
no differences in bioimpedance parameters nor in blood concentrations of glucose, HbA1c, HDL-C, LDL-C, and total cholesterol. However, TG concentrations were significantly higher in the survivor group as compared with controls (Table 3); in addition, VAI was also significantly higher in the group of survivors compared with controls (Figure 1).

4. Discussion

In this study, we found that BC survivors have a higher VAI than the control group, which is consistent with our hypothesis. These data suggest that BC survivors may have different early changes in their metabolic profile enhancing a predisposed condition for a future risk of diabetes or a cardiovascular disease [20].

Body composition has been associated with metabolic dysfunction, while increased body mass with changes in the physiological function of adipose tissue, inflammatory mediators, and chronic inflammation as well. Such factors have also been related to various cancers. Insulin resistance seems to be a possible link between obesity and cancer [21]. Even breast cancer has many well-described risk factors owing to which insulin resistance could play an important role in the disease [22].

Measuring insulin resistance in clinical daily practice is still a big challenge. Hyperglycemic hyperinsulinemic clamp is recognized as the gold standard method to measure insulin resistance, albeit it is a complex method that is only used in the sphere of research [23]. There exist various methods to assess insulin resistance with insulin measurements such as HOMA IR; yet, as in the case of insulin measurement, it is not readily available in most places. For this reason, surrogate indexes of insulin sensitivity have been proposed by means of affordable anthropometric and/or laboratory measures routinely gathered in clinical settings [24]. In the present study, we use VAI in the assessment of indirect insulin resistance measurement, as it has shown a good correlation with the gold standard method [25]. In clinical settings, it might be very useful, as it enables a better overview of metabolic health. Obesity and other related markers have been associated with the risk of BC recurrence [26–28]. However, this is the first study to show that VAI could be an important factor to assess in BC survivors.

Metabolic syndrome, with its various components, is a risk factor for BC recurrence; hence, it may be considered a recurrence predictor and be included as a part of diagnostic standards [29]. In this research, 59.2% of the survivors and 41.3% of the controls presented metabolic syndrome, which agrees with another study on Mexican women, in which the frequency was 57% in BC survivors and 36% in women without personal BC history [30].

Furthermore, other variables related to central obesity such as WC also increased in the BC survivor group, a result that concurs with VAI data. The advantage of using VAI is that it is a more complete index than WC, since it includes biochemical and physical variables to be computed, which produces a more accurate diagnosis of the nutritional status and metabolic syndrome presence or risk in this type of patients. This could be helpful to improve interventions or lifestyle modifications in BC survivors and prevent chronic diseases from developing in healthy women.

In the present study, the percentages of SMM, FFM, TBW, proteins, and minerals decreased, while BFM and SFT increased in the survivors when compared to controls, and they were not statistically significant though. Regardless of their statistical significance in this study, changes in these parameters have shown to contribute to decrease the patients’ quality of life [31, 32] and increase the risk of cancer [33]. We also found that BFM for BC survivors is 41.12%, concurring with data reported by Lee et al. (40.4%), using the same electrical bioimpedance technique [34].

These results bear similarities with those obtained in prospective studies performed with dual-energy X-ray absorptiometry (DEXA) for 12–15 months, which do not report differences between the body composition of surviving women and that of the general population nor between the types of therapy they received after the diagnosis of cancer [20, 26, 35]. By contrast, another report shows that electrical bioimpedance underestimates body fat percentage in comparison with DEXA [36]. This may be a limitation of this approach as we only used 2 frequencies to perform the electrical bioimpedance analysis.

The concentrations of blood lipids which have been associated with metabolic syndrome, cardiovascular disease, and atherosclerosis [37, 38] are elevated in survivor women. Our findings show that the survivors’ lipid profile differs from that of controls. While HDL-C and LDL-C are not significantly different between the groups, TG are significantly different between the groups, TG are significantly different between the groups, and metabolic syndrome presence or risk in this type of patients. This could be helpful to improve interventions or lifestyle modifications in BC survivors and prevent chronic diseases from developing in healthy women.

In Mexico, where our study was performed, there is a strong correlation between VAI and TG. Noticeably, elevated TG levels have been reported for Mexican population
Although there is no difference between the two groups, it needs to be corroborated by means of more specific studies.

Another limitation is the cross-sectional design of the study, which does not allow for a follow-up of BC survivors and establish whether there is a risk of either BC relapse or metabolic syndrome when VAI is elevated.

This research presents some limitations, for instance, a larger sample size of breast cancer survivors would be needed to identify strong associations between metabolic syndrome and breast cancer and establish thus a clearer relationship between VAI and its components with BC. Another limitation is the cross-sectional design of the study, which does not allow for a follow-up of BC survivors and establish whether there is a risk of either BC relapse or metabolic syndrome when VAI is elevated.

However, adhering to a healthy diet with high consumption of vegetables and fruits and reducing overweight and obesity will bring about additional beneficial effects in BC survivors by reducing the risk of relapse, comorbidities, and obesity will bring about additional beneficial effects in BC survivors and death [18]. In this sense, the inclusion of VAI in their follow-up becomes imperative.

The conclusion of this study is that VAI increases in BC survivors compared with controls, regardless of BMI. Early identifications of this marker may be useful as a tool in future studies to assess increments in the risk of metabolic syndrome and cardiovascular diseases among this population.

Data Availability

The data used to support the findings of this study are available from the corresponding authors upon request.

Ethical Approval

The authors certify that they complied with the ethical guidelines for authorship and publishing. The study was approved by the Local Health Research Committee 1503 of IMSS.

Consent

All the patients signed an informed consent form to participate.
Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

The authors would like to acknowledge the foundation IMSS founding provided by Research Stimulus Scholarship Program and Research and Advanced Studies Board of Universidad Autonoma del Estado de México for the financial support (4755-2019-CIB). They would also like to acknowledge to Master in Health Science Program, Universidad Autonoma del Estado de Mexico/PNPC CONACYT.

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