Evaluation of metabolic syndrome and obesity in breast cancer survivors undergoing interdisciplinary approach: a prospective cohort study

Vanildo Prado, Daniel Buttros*, Eduardo Carvalho Pessoa, Luciana de Araújo Brito Buttros, Heloisa Maria de Lucca Vespoli, Jorge Nahás Neto, Eliana Aguiar Petri Nahas

ABSTRACT

Objective: The purpose of this study was to evaluate the occurrence of the metabolic syndrome and obesity during the first year after the diagnosis of breast cancer in women undergoing interdisciplinary approach. Methods: In this prospective study, 81 women (age ≥45 years) with recent histological diagnosis of breast cancer, no established cardiovascular disease, who attended at a single specialized center with an interdisciplinary approach (medical, nutritionist, and psychological) were included. Results: Women with metabolic syndrome were considered to have three or more diagnostic criteria: waist circumference >88 cm, triglycerides ≥150 mg/dL, high-density lipoprotein <50 mg/dL, blood pressure ≥130/85 mmHg, and glucose ≥100 mg/dL. Obesity was considered when body mass index >30 kg/m² and abdominal obesity with waist circumference >88 cm. The evaluations were carried out at three time points: first cancer visit (T0m), 6 months (T6m), and 12 months (T12m). For statistical analysis, the McNemar test was used to compare these time points and the chi-square test was used for trends. The mean age of the patients was 58.4±10.7 years, and 83.3% of them were in the postmenopausal stage. There were no differences in the metabolic syndrome, body mass index, and waist circumference assessments at the indicated time points. When comparing the individual quantitative criteria for metabolic syndrome, there was a statistically significant difference in the values of triglycerides and blood glucose. At times T0m, T6m, and T12m, an increase in the mean triglyceride values was observed, 121, 139.4, and 148.46 mg/dL (p=0.003) and a reduction in the mean glucose values, 106.6, 100.46, and 98.96 mg/dL (p=0.004), respectively. Conclusion: Women with breast cancer subjected to interdisciplinary evaluation did not show an increase in the occurrence of metabolic syndrome and obesity during the first year following their cancer diagnosis.

KEYWORDS: breast cancer; metabolic syndrome; obesity; interdisciplinary approach.

INTRODUCTION

The concept of longevity in patients treated for breast cancer is well established, requiring strategies to improve the quality of life, control complications, and prevent death from general and oncological causes. Women with luminal tumors treated using endocrine therapy in the early stages of the disease have an excellent 20-year prognosis. With increased survival, death from other causes becomes a reality, and cardiovascular disease (CVD) is relevant in this scenario. A recent observational study evaluating cardiovascular outcomes in about half a million postmenopausal women with or without breast cancer found an increased risk of heart failure, pericarditis, and deep vein thrombosis, which persisted for up to 5 years after the diagnosis. The authors concluded that women with a history of breast cancer were at increased risk for CVD compared to women without cancer.

Metabolic syndrome (MetS) is defined by a set of metabolic risk factors that include abdominal obesity, dyslipidemia, systemic hypertension, and hyperglycemia and significantly increase the risk of acute myocardial infarction, stroke, and breast cancer. Buttros et al., evaluating postmenopausal women treated for breast cancer compared to women without cancer, observed a significant increase in the risk of MetS, abdominal obesity, atherosclerotic disease, diabetes, and hypertriglyceridemia. Women treated for breast cancer, who have MetS, have poorer overall and disease-free survival. An observational study, evaluating approximately 9,000 women in the early stages of breast cancer, showed a higher risk of CVD among those with MetS.

https://doi.org/10.29289/2594539420220007
cancer, demonstrated that all components of MetS were statistically correlated with deaths from CVD and that abdominal obesity was correlated with breast cancer-specific mortality\(^4\).

In this context, it is important to understand the importance of controlling body weight and improving metabolic health in women treated for breast cancer. A Cochrane Library meta-analysis evaluated body weight management in overweight and obese women treated for breast cancer. The authors concluded that interdisciplinary interventions (including physical, nutritional, and psychological support) had a significant impact on reducing body weight, with a consequent decrease in body mass index (BMI) and waist circumference (WC) and an improved quality of life\(^6\). The 2021 National Comprehensive Cancer Network (NCCN) suggests that all cancer patients should be encouraged to achieve and maintain an adequate BMI\(^10\). A study that evaluated the actions of the interdisciplinary team with respect to 13,722 women with breast cancer concluded that the introduction of team care was associated with improved patient survival\(^11\). Thus, interdisciplinary teamwork is essential for the success of cancer treatment.

The purpose of this study was to evaluate the occurrence of the MetS and obesity during the first year after the diagnosis of breast cancer in women undergoing interdisciplinary approach.

**METHODS**

**Study Design and Sample Selection**

This is a prospective clinical study carried out between August 2019 and December 2020 at the Center for Specialties and Diagnostic Support (CEAD) of the Municipal Health Foundation in the city of Rio Claro/SP/Brazil. Nonprobabilistic voluntary sampling was used. All patients treated during the study period were enrolled if the following criteria were met:

- age >245 years;
- recent histological diagnosis of breast cancer;
- stage I, II, or III;
- no established CVD;
- treated in the Unified Health System; and
- patient’s agreement to participate in the study.

The women were evaluated at three time points: at diagnosis/first visit (T0m), after 6 months (T6m), and after 12 months (T12m). All evaluations were performed by the same researcher (Prado V).

**Interdisciplinary Approach**

All women diagnosed with breast cancer were treated by the CEAD interdisciplinary team throughout the study follow-up, as per the service routine, without a specific intervention in this study. The team consisted of a mastologist (Prado V.), responsible for visits at the time of diagnosis and during cancer treatment; a nutritionist, who conducted a nutritional evaluation and provided dietary guidelines; and a psychologist, who helped the patient absorb the impact of the diagnosis and understand the disease discovery process.

**Clinical Data**

The following data were collected through individual interviews: age, age at and time since menopause, parity, smoking, previous use of menopausal hormone therapy (MHT), family history of CVD, personal history of systemic hypertension, diabetes, dyslipidemia, frequency of physical activity, and blood pressure. Patients with a daily smoking habit were defined as smokers, regardless of the number of cigarettes smoked. Women who performed aerobic physical exercise of moderate intensity, for at least 30 min, 3–5 times a week (90–150 min/week), or resistance exercises 3 days a week, were considered active. Women who met three or more of the diagnostic criteria proposed by the U.S. National Cholesterol Education Program/Adult Treatment Panel III (NCEP-ATPIII)\(^12\) were considered positive for MetS: WC >88 cm, triglycerides (TG) ≥150 mg/dL, high-density lipoprotein (HDL) cholesterol <50 mg/dL, systemic blood pressure ≥130/85 mmHg, and blood glucose ≥100 mg/dL or under treatment. The following data were obtained for anthropometric evaluation: weight, height, BMI (=weight/height\(^2\)), and WC. The 2002 World Health Organization criteria were used to classify patients, according to BMI: normal (≤24.9 kg/m\(^2\)), overweight (25–29.9 kg/m\(^2\)), and obese (≥30 kg/m\(^2\)). For the measurement of WC, the midpoint between the last rib and the iliac crest was used, with the patient in a standing position; values over 88 cm were considered elevated (abdominal obesity)\(^12\). All clinical evaluations were performed at the time of diagnosis (T0m) and repeated after 6 months (T6m) and 12 months (T12m).

**Biochemical Analysis**

The lipid and glucose profiles were evaluated by measuring total cholesterol (TC), HDL, low-density lipoprotein (LDL), TG, and glucose. Blood samples were collected from each participant after a 12-h fast. TC, HDL, TG, and glucose measurements were processed by the RAXT automatic biochemical analyzer (Technicon\(^®\), USA) and quantified by the colorimetric method, using specific commercially available reagents (Sera-Pak\(^®\), Bayer, USA). The method is linear up to 800 mg/dL for TG and up to 900 mg/dL for TC. LDL was calculated from the Friedewald formula, whose use has limitations when TG values exceed 400 mg/dL. LDL was obtained by subtracting the TC value from the sum of HDL plus TG divided by 5. The values considered optimal were TC <200 mg/dL, LDL >50 mg/dL, LDL <100 mg/dL, TG <15 mg/dL, and blood glucose <100 mg/dL\(^12\). All measurements were performed on the first visit and repeated after 6 and 12 months.

**Pathology and Immunohistochemistry**

From the analysis of medical records, the following data were obtained: histopathological diagnosis of breast cancer, histological
grade, hormone receptor (estrogen receptor [ER] and progesterone receptor [PR]), human epidermal growth factor receptor-2 (HER-2), epithelial proliferative activity (Ki67), tumor stage, and treatments performed (i.e., surgery, radiotherapy, chemotherapy, and endocrine therapy). The tumor diameter was obtained from histopathological reports, and the tumor was graded as grade I (well-differentiated), II (moderately differentiated), or III (undifferentiated). The pathological staging of the tumor was defined according to the Sixth edition of the American Joint Committee on Cancer (AJCC). TNM system (tumor size, lymph node status, metastasis)13.

Statistical Analysis
The variables were analyzed using the Shapiro-Wilk test for normality and the Levene’s test for homogeneity. Quantitative variables were tested for normality using the Kolmogorov-Smirnov test, and as they did not conform to a normal distribution, the nonparametric Friedman test was applied. When the variable showed a statistically significant difference, Dunn’s post-hoc test was used. For data analysis, the mean and standard deviation were calculated for quantitative variables and frequency and percentage for qualitative variables. For qualitative variables, analysis of variance in relation to the time point (diagnosis/T0, 6 months/T6m, and 1 year/T12m) was performed using the McNemar test. Regarding the association between frequencies of categorical characteristics, the chi-square test of trends was employed. In all tests, a significance level of 5% or the corresponding p-value was adopted. Statistical analyses were performed using the Statistical Analysis System (SAS), version 9.4.

Ethical Approval
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki. Ethical approval was awarded by the Research Ethics Committee of the Botucatu Medical School, Universidade Estadual Paulista "Júlio de Mesquita Filho" (UNESP). Informed consent was obtained from all individual participants included in this study.

RESULTS
During the study period, a total of 81 women with breast cancer were enrolled. Among these, 72 patients underwent sample collection at 6 and 12 months (Figure 1). The clinical and oncological characteristics of the women with a recent breast cancer diagnosis (n=72) are shown in Tables 1 and 2. The average age of the patients was 58.4±10.7 years, of which 83.3% were postmenopausal. The patients on average were overweight (BMI 25.0–29.9 kg/m²), with an elevated WC (>88 cm) and baseline values of TC, LDL, and glucose above optimal levels (Table 1). Only 23.6% of the patients reported prior use of menopausal hormone therapy, 87.5% reported not performing regular physical activity, and 18% were smokers (data not shown).

There was a higher proportion of women with good oncological prognosis factors for breast cancer. The most prevalent profile was early-stage disease (94.4% in stages I and II), tumors

Table 1. Initial descriptive clinical characteristics of the 72 women with breast cancer.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>58.4</td>
<td>10.7</td>
</tr>
<tr>
<td>Menopause age, years</td>
<td>48.6</td>
<td>3.8</td>
</tr>
<tr>
<td>Time since menopause, years</td>
<td>13.1</td>
<td>8.8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>72.9</td>
<td>15.4</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.6</td>
<td>0.1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.9</td>
<td>6.1</td>
</tr>
<tr>
<td>WC, cm</td>
<td>97.2</td>
<td>13.2</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>132.7</td>
<td>15.4</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>82.2</td>
<td>10.9</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>203.1</td>
<td>36.1</td>
</tr>
<tr>
<td>HDL, mg/dL</td>
<td>56.2</td>
<td>13.2</td>
</tr>
<tr>
<td>LDL, mg/dL</td>
<td>124.7</td>
<td>30.0</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>121.0</td>
<td>50.7</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>106.6</td>
<td>28.0</td>
</tr>
</tbody>
</table>

BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein; LDL: low-density lipoprotein.
≤2 cm (56.94%), axillary node negative (72.2%), hormone receptor positive (79.1% ER and 72.2% PR), and HER2 negative (86.1%). Regarding the treatments performed, 73.6% of the patients underwent conservative surgery, 58.3% underwent chemotherapy, and 78% received radiotherapy (Table 2). Also, 64% were undergoing endocrine therapy during the final evaluation (T12m).

Table 2. Descriptive oncological characteristics of the 72 women with breast cancer.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency (n)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>33</td>
<td>45.83</td>
</tr>
<tr>
<td>Stage II</td>
<td>35</td>
<td>48.61</td>
</tr>
<tr>
<td>Stage III</td>
<td>4</td>
<td>5.56</td>
</tr>
<tr>
<td>Tumor size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 2 cm</td>
<td>45</td>
<td>56.94</td>
</tr>
<tr>
<td>&gt;2 cm and ≤5 cm</td>
<td>26</td>
<td>36.11</td>
</tr>
<tr>
<td>&gt;5 cm</td>
<td>5</td>
<td>6.94</td>
</tr>
<tr>
<td>Axillary lymph node negative</td>
<td>52</td>
<td>72.22</td>
</tr>
<tr>
<td>ER+</td>
<td>57</td>
<td>79.17</td>
</tr>
<tr>
<td>PR+</td>
<td>52</td>
<td>72.22</td>
</tr>
<tr>
<td>HER2-</td>
<td>62</td>
<td>86.11</td>
</tr>
<tr>
<td>Ki67 &lt;14%</td>
<td>50</td>
<td>69.44</td>
</tr>
<tr>
<td>Conservative surgery</td>
<td>53</td>
<td>73.61</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>19</td>
<td>26.39</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>42</td>
<td>58.33</td>
</tr>
<tr>
<td>Endocrine therapy</td>
<td>50</td>
<td>69.44</td>
</tr>
<tr>
<td>Radiation</td>
<td>56</td>
<td>77.78</td>
</tr>
</tbody>
</table>

ER+: estrogen receptor positive; PR+: progesterone receptor positive; HER2-: human epidermal growth factor receptor-2 expression negative; Ki67: epithelial proliferative activity.

Table 3. Comparison of the incidence of metabolic syndrome and its components at the three evaluation time points for the 72 women with breast cancer.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>T0m</th>
<th>T6m</th>
<th>T12m</th>
<th>Time points compared</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic syndrome</td>
<td>Yes</td>
<td>27</td>
<td>31</td>
<td>32</td>
<td>0.332</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>45</td>
<td>41</td>
<td>40</td>
<td>0.55</td>
</tr>
<tr>
<td>WC&gt;88 cm</td>
<td>Yes</td>
<td>53</td>
<td>58</td>
<td>57</td>
<td>0.125</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>19</td>
<td>14</td>
<td>15</td>
<td>0.209</td>
</tr>
<tr>
<td>BP≥130×85 mmHg</td>
<td>Yes</td>
<td>47</td>
<td>40</td>
<td>47</td>
<td>0.167</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>25</td>
<td>32</td>
<td>25</td>
<td>0.249</td>
</tr>
<tr>
<td>TG≥150 mg/dL</td>
<td>Yes</td>
<td>18</td>
<td>26</td>
<td>32</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>54</td>
<td>48</td>
<td>40</td>
<td>0.55</td>
</tr>
<tr>
<td>Glucose≥100 mg/dL</td>
<td>Yes</td>
<td>33</td>
<td>29</td>
<td>28</td>
<td>0.302</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>39</td>
<td>43</td>
<td>44</td>
<td>0.61</td>
</tr>
<tr>
<td>HDL&lt;50 mg/dL</td>
<td>Yes</td>
<td>29</td>
<td>29</td>
<td>26</td>
<td>0.648</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>43</td>
<td>43</td>
<td>46</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Data are expressed as absolute numbers (%). T0m: time of diagnosis; T6m: 6 months; T12m: 12 months; WC: waist circumference; BP: blood pressure; TG: triglycerides; HDL: high-density lipoprotein cholesterol. Significant difference at p<0.05 (bold) (chi-square test for trends).

In the evaluation of MetS, no differences were observed at the three time points: 37.5, 43, and 44.4% of the patients had MetS at the time of diagnosis, at 6 months, and at 12 months, respectively (p=0.332). Likewise, four of the components of MetS (i.e., WC, HDL, blood pressure, and glucose) did not differ at the three time points, with the exception of hypertriglyceridemia (≥150 mg/dL), which increased from 25% at T0 to 44.4% at T12m (p<0.05) (Table 3).

In the quantitative comparison of the clinical and laboratory criteria for MetS at the three time points evaluated, a statistical difference was observed in the TG and glucose (Table 4). In relation to TGs, there was a progressive increase in the mean values (121, 139.4, and 148.4 mg/dL) at the three time points (T0m, T6m, and T12m) (p=0.001) (Figure 2). Blood glucose analysis showed a progressive decrease in the mean values (106.6, 100.4, and 98.9 mg/dL) at the three time points (T0m, T6m, and T12) (p=0.005) (Figure 3). The other clinical and laboratory criteria were not statistically different (Table 4).

There was no significant association between oncological treatment (surgery, chemotherapy, endocrine therapy, and radiotherapy) and the metabolic outcomes (MetS and its components) evaluated (data not shown).

DISCUSSION

From our analysis, women with a recent diagnosis of breast cancer, who received medical, nutritional, and psychological care during the first year of cancer treatment, showed major benefits in terms of metabolic health. In addition to the significant decrease in serum glucose levels, there was no increase in the...
incidence of MetS, weight gain, and abdominal obesity. On the
other hand, increases in TG concentration and hypertriglyceri-
demia were observed during the first year.

MetS is considered a risk factor for a poor prognosis in
women treated for breast cancer, with lower overall and spe-
cific survival2. In our study, 37.5% of the women had MetS
at the time of breast cancer diagnosis, and after 12 months,
the incidence of MS was 44.4%, no significant difference.
Abdominal obesity and hypertension were the most preva-
ent components of MetS throughout the study period, hav-
ing been observed at the initial and final time points in 73.6% and
65.2% of the subjects and 79.1% and 65.2% of the patients,
respectively (p>0.05 in both cases). Our findings are in agree-
manship with those presented by Simon et al.2, who, after evalu-
ating 8641 women with breast cancer, found that abdominal
obesity and arterial hypertension were the most prevalent
criteria among participating women2.

Women treated for breast cancer did not experience
weight gain or increased WC during the first year of follow-
up. Obesity is correlated with a poorer prognosis in women
with breast cancer. Chan et al.14 evaluated the risk of mortal-
ity in 213,000 women with breast cancer, considering the BMI
at the time of diagnosis. They demonstrated that women with
a BMI >30 kg/m² (obese) have a higher risk of mortality when
compared to women with a BMI between 20 and 25 kg/m²
(nonobese) (OR 1.41, 95%CI 1.29–1.53). Regarding the meno-
pausal status, when obesity was present at the time of breast
cancer diagnosis, premenopausal women had a higher long-
term risk of mortality than postmenopausal women (OR 1.75,
95%CI 1.26–2.41 vs. OR 1.34, 95%CI 1.18–1.53). The authors
noted that the risk of death from any cause in obese women
is cumulative over time14.

Among our patients, 83.3% of which were postmenopausal,
the mean BMI during the period evaluated falls into the over-
weight classification, namely, 28.9 kg/m² at T0m and 28.8 kg/
m² after 1 year. Our data are in harmony with the report by
Simon et al.2, who also observed that most women studied had
a BMI between 25 and 30 kg/m². Abdominal obesity, defined as
a WC >88 cm, is also considered a risk factor for a poor prog-
nosis in women with breast cancer. In a recent publication,
Buono et al.8 followed 717 women with early-stage breast can-
cer for 10 years and demonstrated poorer overall survival (OR
2.34, 95%CI 1.32–4.14) and specific survival (OR 3.24, 95%CI
1.64–6.41) in women with breast cancer and abdominal obe-
sity4. Our data demonstrate that the women did not show a
significant increase in WC during follow-up, even though
the majority had abdominal obesity at the time of diagnosis
(73.6%) and at the end of the study (79.1%).

Another important factor related to metabolic health is dia-
abetes. A meta-analysis evaluating the impact of diabetes on the
prognosis of 49,000 women treated for breast cancer found that

Table 4. Comparison of clinical and laboratory characteristics
at the three evaluation time points for the 72 women with
breast cancer.

<table>
<thead>
<tr>
<th>Features</th>
<th>T0m</th>
<th>T6m</th>
<th>T12m</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>72.9 (15)</td>
<td>72.6 (14.7)</td>
<td>73.0 (15.3)</td>
<td>0.728</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.9 (6.1)</td>
<td>28.8 (5.7)</td>
<td>28.8 (5.9)</td>
<td>0.842</td>
</tr>
<tr>
<td>WC, cm</td>
<td>97.2 (13.2)</td>
<td>97.1 (12.1)</td>
<td>96.6 (12.6)</td>
<td>0.683</td>
</tr>
<tr>
<td>TC, mg/dL</td>
<td>203.1 (36.1)</td>
<td>207.3 (39.9)</td>
<td>201.3 (40.4)</td>
<td>0.348</td>
</tr>
<tr>
<td>HDL, mg/dL</td>
<td>56.2 (13.1)</td>
<td>55.9 (18.1)</td>
<td>56.8 (14.5)</td>
<td>0.894</td>
</tr>
<tr>
<td>TRIG, mg/dL</td>
<td>121.0 (139.4)</td>
<td>139.4 (61.3)</td>
<td>148.4 (68.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>GLUC, mg/dL</td>
<td>106.6 (28)</td>
<td>100.4 (22.8)</td>
<td>98.9 (18.6)</td>
<td>0.005</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>132.7 (15.4)</td>
<td>130.6 (17.6)</td>
<td>132.2 (15.5)</td>
<td>0.432</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>82.2 (10.8)</td>
<td>81.4 (9.9)</td>
<td>83.6 (9.54)</td>
<td>0.156</td>
</tr>
</tbody>
</table>

Data are expressed as mean (standard deviation). T0m: time of diagno-
sis; T6m: 6 months; T12m: 12 months; BMI: body mass index; WC: waist
circumference; TC: total cholesterol; HDL: high-density lipoprotein; TRIG:
triglycerides; GLUC: blood glucose; SBP: systolic blood pressure; DBP:
diastolic blood pressure.

Significant difference at p<0.05 (bold) (McNemar test).

Figure 2. Comparison at the three evaluation time points of the
72 women with breast cancer, according to triglyceride variable.

Figure 3. Comparison at the three evaluation time points of the
72 women with breast cancer, according to blood glucose variable.
a diagnosis of diabetes prior to breast cancer was a risk factor for lower overall survival and disease-free survival (OR 1.51, 95%CI 1.34–1.70 and OR 1.28, 95%CI 1.09–1.50, respectively)15. These results are similar to those presented by Spalutto et al.16 at the San Antonio Breast Cancer Symposium 2020 (SABCS/2020). This population study of more than 86,000 participants, with 1347 treated for breast cancer, concluded that diabetes reduced the survival of women with breast cancer, who were primarily black and had a low income16.

Hyperglycemia is also correlated with a poorer oncological prognosis. Buono et al.8 demonstrated lower overall survival and disease-free survival in women with breast cancer with blood glucose ≥110 mg/dL. Our data showed significant results regarding serum glucose concentration, which decreased over the course of 1 year of follow-up. At the initial time point, mean blood glucose was 106.6 mg/dL and at the end of 12 months, it was 98.9 mg/dL (p=0.005). With respect to the baseline value of ≥100 mg/dL, there was no statistical significance in the comparison at different time points. Although the present study did not perform a specific nutritional intervention, we believe that nutritional guidelines had an impact on the reduction in blood glucose, since the women also did not increase their body weight and WC during the same period.

Dyslipidemia is a feature of MetS found in obese and diabetic patients. Elevated TC, hypertriglyceridemia, and decreased HDL cholesterol were associated with an increased cancer risk of 18, 15, and 20%, respectively17. In women treated for breast cancer, dyslipidemia is also associated with a poorer prognosis. In breast cancer mortality studies, the use of statins for the treatment of dyslipidemia has shown survival benefits, suggesting that cholesterol may promote tumor progression18. The Women’s Health Initiative study indicated that the administration of statins independently contributed to the reduction of advanced stage breast cancer, especially in patients with tumors that were positive for ER expression19. In our study, we assessed HDL cholesterol and TGs. HDL cholesterol averaged 56.2 mg/dL at the time of breast cancer diagnosis, with no differences during the follow-up period. Regarding HDL of <50 mg/dL (component of MetS), the incidence was 40.2% at baseline and 36.1% at 12 months, but the differences did not reach statistical significance. On the other hand, TGs showed significant changes in this study. Both the mean concentration and the values considered abnormal (≥150 mg/dL) increased significantly during follow-up. There was an increase in the occurrence of hypertriglyceridemia among the patients, from 25% at diagnosis to 44.4% at the end of 1 year.

A possible explanation for this increase in TGs is the oncological treatments performed, specifically endocrine therapy with tamoxifen or an aromatase inhibitor. Tamoxifen, which is a selective estrogen receptor modulator (SERM), has a favorable effect on the lipid profile, with reduction from 10 to 15% in total serum cholesterol and from 15 to 22% in LDL cholesterol20-23. In contrast, some studies have reported increases in TG values in patients treated with tamoxifen, a risk factor for hypertriglyceridemia20,22. Aromatase inhibitors (AIs), in turn, by bringing the patient into a state of excessive hypoestrogenism, have a direct correlation with increased cholesterol. The ATAC24 and BIG I-9827 studies reported a higher incidence of hypercholesterolemia in patients treated with anastrozole and letrozole, respectively, when compared to women treated with tamoxifen. Approximately 70% of the women in our study were treated with endocrine therapy, the majority (83.3%) with AI because they were postmenopausal. Anastrozole is the AI of choice to initiate endocrine therapy in postmenopausal women in our service, and tamoxifen, in premenopausal women. Although we did not find a significant relationship between endocrine therapy and the increase in TGs, we believe that our small sample size and the short evaluation period (1 year) influenced our results.

Another relevant piece of data in the present study are the factors that enter into a good oncological prognosis of the recruited women. Approximately 95% of the participants were in stage I or II at the time of diagnosis of breast cancer. Regarding predictive and prognostic factors, most of them were positive for ER and PR (79% and 72%, respectively) and 86% were HER-2 negative. The AMAZONA study was a retrospective cohort that evaluated approximately 2300 women with breast cancer from all regions of Brazil24. The proportion of women with early-stage (I and II) breast cancer was 76.8%, lower than that found in our study. Immunohistochemical factors were also discrepant, with 63.8% positivity for ER, 54.9% for PR, and 62.6% negativity for HER-2. Data such as BMI and MetS were not reported in the AMAZONA study28.

This study has some limitations, mainly due to the small number of patients, the fact that they were recruited from only one center and the short follow-up period of 1 year. However, all the women underwent interdisciplinary evaluation, including medical, nutritional, and psychological assessments. This approach was not interpreted as an intervention, as it is the routine at the service in question. Perhaps, this interdisciplinary routine is responsible for the good results obtained, such as a significant improvement in blood glucose and maintenance of MetS and BMI status. Although we do not have it in our service, we believe that the team would be more effective with the inclusion of physical education in the patients’ routine. The interdisciplinary approach is essential for improvement in the survival and quality of life of women under treatment for breast cancer29,31.
CONCLUSION

Women with breast cancer undergoing interdisciplinary approach did not show an increase in the incidence of MetS and obesity during the first year following cancer diagnosis. Among the components of MetS, there was a reduction in blood glucose values and an increase in TG values.

REFERENCES


AUTHORS’ CONTRIBUTIONS

VP, DB, EPN: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. ECP, LB, HV, JNN: Project administration.


