Weight change in women with breast cancer (IIIB) after treatment

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DOI: https://doi.org/10.36104/amc.2020.1563

Abstract

Introduction: the effect of overweight and obesity in patients with breast cancer has been widely described. Despite the recognition of ethnic differences in these associations, information is still lacking for the Latin American population.

Methods: a retrospective, longitudinal cohort study with non-probabilistic sampling. The main objective was to describe how weight behaved after multimodal cancer treatment in women with locally advanced luminal A subtype breast cancer.

Results: the average age at cancer diagnosis was 52 years. The average follow-up time was 2.3 years, during which there was a 12.1% rate of recurrence. Most patients were overweight/obese (67.56%), with an average variation of -0.17 kg at the end of follow up. Patients with metastasis had a greater weight loss than those without recurrence (-5.06 kg, $p<0.05$).

Conclusions: overweight and obesity are a prevalent characteristic of locally advanced luminal A breast cancer patients. There was no conclusive evidence of increased risk of metastasis or death related to excess weight in this population. To the contrary, weight loss was a statistically significant characteristic of patients with distal recurrence during follow up, although it was not established as a causal factor. (Acta Med Colomb 2020; 45. DOI: https://doi.org/10.36104/amc.2020.1563).

Key words: *weight, overweight, obesity, breast cancer, metastasis, neoplasia*.

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Received: 07/XI/2019 Accepted: 15/IV/2020

Introduction

Overweight is recognized as one of the main preventable risk factors for cancer. Up to 30% of mortality due to this disease could be avoided if excessive weight gain were addressed. Regrettably, this phenomenon shows epidemic behavior with a rising prevalence, especially in developing countries.

One of the prototypes of the impact of overweight on malignancies is breast cancer. This association may be due to mechanisms such as increased oxidative stress, peripheral conversion of sex hormones (1), adipokines and inflammatory cytokines involved in the inhibition of cellular apoptosis, migration and increased proliferation of malignant cells (2).

From a clinical perspective, several cohort studies have researched the association between overweight/obesity and breast cancer prognosis. Most have reported a concerning association between overweight and decreased survival and increased distant recurrence (3-5). Strikingly, a low BMI (< 18.5 kg/m^2) also showed decreased overall and breast cancer-specific survival (6).

Considering that weight behavior (increasing or decreasing) and cancer are health phenomena which are determined by genetic and environmental factors, it is pertinent and justifiable to research their relationship in different populations and territories. Especially when most of the body of evidence is derived from white and Asian women, and the results in Latin American women are still scant.

Methods

This was a retrospective, longitudinal cohort study with descriptive objectives which was approved by the ethics committees of the participating institutions. Convenience non-probability sampling was used with data obtained from the records of two oncology reference centers in northeastern Colombia. The medical records inclusion period was from 2005-2015 (10 years) and the following selection criteria were considered: a) women over the age of 18, b) having a diagnosis of invasive breast cancer, c) being classified as stage IIIB, d) luminal A subtype (hormone receptor-positive and HER2/neu-negative), e) having received multimodal

treatment (mastectomy, chemotherapy, radiation and hormone therapy with tamoxifen), f) no clinical suspicion of residual (local) disease postoperatively or recurrence at the beginning of follow-up (first year), and g) having at least two recorded weights at least six months apart, after beginning cancer treatment.

The main objective was to describe the weight behavior in selected patients during a 24 month follow up period after finishing multimodal cancer treatment. In addition, the relationship with the outcomes of distant recurrence (metastasis) and mortality would be explored, recognizing the scope of the available sample.

The results analysis was carried out using the STATA 14.0® software package and Microsoft Excel®, applying measures of central tendency, dispersion, comparison of proportions (χ^2) and analysis of variance. Statistical significance was established as $p < 0.05$.

Results

A total of 1,662 breast cancer records were reviewed; of these, 74 patients fulfilled the strict selection criteria. The sociodemographic characteristics are described in Table 1.

The average follow up after finishing cancer treatment was 2.33 years. There were nine tumor recurrence events, five with bone metastasis, three pulmonary and one brain, which, in turn, was associated with the only recorded death.

No patients had a BMI <18 kg/m^2; on the contrary, 67.56% were classified from the first recorded weight as overweight/obese. At the end of follow up, the overweight subgroup increased, mainly due to migration of obese patients who lost weight. However, no patient had enough weight loss to be reclassified in the WHO underweight group (Table 2).

In general, weight remained steady, comparing the first and the last recorded weight, with an absolute difference of means of -0.17 kg. However, in the patients with metastasis, there was a difference adjusted for

The patients' follow up appointments were every four to six months. Therefore, a comparative analysis of periods was proposed using ANOVA, without achieving statistical significance in the comparison of means between patients with or without distant recurrence. However, a clinical tendency towards weight loss was identified in patients with recurrence during the third follow up period (18-24 months), compared to their counterparts without metastasis (Table 4).

Clinical weight variation was established if at least one of three criteria was met: 1) a weight gain or loss of at least 5% of the initial weight, 2) a change of plus or minus two BMI points from the initial score, or 3) a change in WHO weight group at any time during follow up (Table 5).

Discussion

This is the first longitudinal study to date in a Colombian population which seeks to describe the behavior of weight in women with breast cancer. The reason for only choosing luminal A type patients was that tumors with hormone receptors are known to be more susceptible to extra-ovarian estrogen production (7, 8) and part of the heterogeneity in the results of many studies is due to not recognizing this differential susceptibility between intrinsic subtypes.

Population data in Colombia (ENSIN 2010), similar to what is recorded in developed countries, show an alarming prevalence of overweight/obesity, mainly in women, with more than 60% of women over the age of 40 being overweight/obese (9).

This study found a prevalence of overweight/obesity of 67.56% from the beginning of follow up, and it remained practically unchanged despite multimodal treatment (68.92%). Interestingly, no woman was underweight at the beginning or end of the study. This suggests that, in this population, overweight may be a common characteristic among women diagnosed with breast cancer, as has been described in other studies (10).

The evidence suggests that the relationship between overweight and the risk of breast cancer is different in pre and postmenopausal women. There are data which suggest an inverse or protective relationship of overweight in young women, before menopause (11). However, these conflicting

Table 1. *Sociodemographic characteristics.*

Characteristic (n)	General percentage %
Age at diagnosis (74)	52.01 years (SD 10.76, 26-78)
Residence (72)	%
Rural	12.50 (9)
Urban	87.50 (63)
Socioeconomic level (48)	%
One	4.17 (2)
Two	20.83 (10)
Three	37.50 (18)
Four	33.33 (16)
Five	2.08 (1)
Six	2.08 (1)
Marital status (57)	%
Single	33.33 (19)
Married	8.77 (5)
Common law	57.89 (33)
Age at menarche (42)	13.54 years (SD 1.64, 10-18)
Age at menopause (9)	48.55 years (SD 4.69, 41-55)
Term pregnancies (70)	2.97 (SD 2.28, 0-14)
Breastfeeding (30)	%
No	16.67
Yes	83.33
Birth control (44)	%
No	52.27
Yes	47.73
Smoking (33)	%
No	72.3 (24)
Yes	27.27 (9)

results may be explained by a greater presentation of basal tumors in young women, whose biological susceptibility to the effects of fat mass are not well understood. Once again, this study overcame this difficulty by homogenizing the patients by molecular subtype, and this could explain why, despite 51% of the women in this cohort being under 50 years old, and most being premenopausal, there were no statistical differences in the variables of interest compared with patients who reported being menopausal. Perhaps the effect of weight in women with luminal A breast cancer is independent of the patients' fertility status.

It is important to compare the results reported by Cuello-López et al. who, in 2017, presented a cross-sectional study analyzing weight as a prognostic variable in Colombian women (12), which showed that postmenopausal patients at an oncology center in Medellín had a positive association between BMI and the luminal A subtype. This same study found a low prevalence (1.53%) of women with breast cancer who were underweight, while there was a high frequency (65.4%) of overweight/obesity, similar to what was described in our study. Furthermore, Gutiérrez et al. described a group of 45 patients in Mexico (13), all at a locally advanced stage (III) with a high prevalence (86.6%)

Table 2. *Patient distribution by weight subgroups according to the WHO classification.*

WHO Group	Beginning of follow up %	End of follow up %	Group tendency
Underweight	0 (0)	0 (0)	Stable
Normal weight	32.43 (24)	31.08 (23)	Decrease
Overweight	44.59 (33)	51.35 (38)	Increasse
Obesity	22.97% (17)	17.57 (13)	Decrease

Table 3. *Anthropometric measurements during follow up.*

Anthropometric measurements (74)	Initial average	Final average	Nonrecurrence group (65)	Recurrence group (9)	p
Height (mt)	1.57	1.57	1.57	1.57	0.84
Weight (kg)	67.02	66.85	67.10	61.80	0.87
BMI (kg/m^2)	26.93	26.88	27.95	26.77	0.90

Table 4. *Difference in weight averages at the various measurement times every four to six months.*

Time of follow up	General group average	Average of subgroup without recurrence	Average of subgroup with recurrence	ANOVA
Beginning of follow up Initial weight Initial BMI	 67.02 (74) 26.93	 67.10 (65) 26.95	 66.45 (9) 26.77	 0.87 0.90
Period 1 Weight BMI	 67.11 (74) 26.96	 67.15 (65) 26.95	 66.83 (9) 26.77	 0.93 0.97
Period 2 Weight BMI	 67.91 (73) 27.33	 68.15 (64) 27.43	 66.17 (9) 26.65	 0.64 0.61
Period 3 Weight BMI	 67.57 (70) 27.10	 68.23 (61) 27.36	 *63.08 (9) 25.37	 0.21 0.15
Period 4 Weight 4 BMI 4	 67.03 (62) 26.85	 67.72 (53) 27.11	 62.95 (9) 25.36	 0.28 0.23
Period 5 Weight BMI	 68.24 (40) 27.12	 68.58 (34) 27.25	 66.3 (6) 26.43	 0.70 0.68
Period 6 Weight BMI	 68.12 (34) 26.95	 68.46 (28) 27.05	 66.55 (6) 26.53	 0.75 0.81
Period 7 Weight BMI	 69.52 (27) 27.20	 71.38 (22) 27.78	 61.34 (5) 24.68	 0.10 0.18
Period 8 Weight BMI	 72.85 (18) 28.22	 73.07 (16) 28.42	 71.05 (2) 26.63	 0.81 0.60
End of follow up Final weight Final BMI	 66.85 (74) 26.88	 67.54 (65) 27.05	 61.88 (9) 25.71	 0.18 0.40

Table 5. *Frequency of weight variability according to the various definitions accepted in the study.*

Variability criterion	General (74) %	Without recurrence (65) %	With recurrence (9) %	p value
5% of the initial weight				0.32
Absent	40.54 (30)	33.78	6.75	
Present	59.45 (44)	54.05	5.40	
2 BMI points				0.46
Absent	55.41 (41)	47.29	8.10	
Present	44.59 (33)	40.54	4.05	
WHO group				0.13
Absent	75.68 (56)	68.91	6.75	
Present	24.34 (18)	18.91	5.40	
At least one criterion				0.97
Absent	33.78 (25)	29.72	4.05	
Present	66.22 (49)	58.10	8.10	
Absolute weight difference	-0.17 kg	+ 0.50 kg	-5.06 kg	0.01

of overweight/obesity, which coincides with our findings and those of other studies in the hemisphere, with a high prevalence of overweight consistently reported over 50% in populations with similar characteristics to those of the patients presented in the current study.

One of the strengths of this study was the analysis of the temporal behavior of weight, evaluating its tendency at various patient observation times. Therefore, one of the main data of interest was weight variability defined by several criteria (BMI, weight in kg, and WHO group). Weight behavior patterns have been identified in the literature according to body mass index prior to treatment. Thus, women with BMIs closer to normal had a greater tendency to gain weight, compared with obese women, who even tended to lose weight (14). In this cohort, the stability of weight between the first and last record is remarkable; however, it must be noted that there was weight variability between these periods, but the tendency was to stabilize, returning to the initial weight.

There are studies with significant population samples, such as the study by Chen et al. in China, which report a general tendency to gain close to two kg in the first 18 months after chemotherapy (15). The current study found a subtle but generalized tendency to lose weight (-0.17 kg) which differs from the described behavior as well as from Western studies such as the *Women's Healthy Eating and Living Study* (WHEL). Once again, this could be due to ethnic differences, which justifies the performance of this type of studies to record the populational differences.

The rate of recurrence was 12.1%, which is significantly greater than that reported in other studies, with a risk of metastasis less than 9% during the longest observation periods (60 months) (16, 17). The design of this study does not identify possible causes associated with the relative increase in the number of metastatic events. However, patients with overweight/obesity, like most of the participants in this cohort, are known to have worse outcomes (8, 18, 19). For example, neoplasms in overweight women are larger, have a worse proliferation index and more lymphatic metastases (20).

It should be noted that there was a statistical difference in the degree of weight loss between patients with and without distant recurrence, a phenomenon which occurred even before the clinical diagnosis of metastasis. In most cases, weight loss was clinically significant after the first 18 months of follow up. This gives validity to the longitudinal assessment of weight in cancer patients as a classic indicator of active cancer.

To conclude, it should be recognized that this is a study limited by its small sample size, short follow up period, lack of other more specific anthropometric measurements and lack of randomization. It is hoped that this paper will lay the groundwork for prospective and analytical studies interested in continuing to analyze the relationship between weight and cancer in the Latin American population, with a more robust methodology which will improve the power and scope of the results.

Conclusions

Overweight and obesity are a very prevalent characteristic in patients with locally advanced luminal A breast cancer. There was no conclusive evidence of increased risk of metastasis or death associated with excess weight in this population. On the contrary, weight loss was a statistically significant characteristic of patients with distant recurrence during follow up, although it was not able to be defined as a causal factor.

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