Article published online: 2022-10-06

BJO
Brazilian Journal of Oncology

ORIGINAL ARTICLES CLINICAL ONCOLOGY

Assessment of body mass index and its relationship with breast cancer survival in a clinical oncology service in the Federal District

Avaliação do índice de massa corporal e sua relação com a sobrevida ao câncer de mama em um serviço de oncologia clínica do Distrito Federal

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ABSTRACT

Objective: The purpose of this study was to analyze the relationship between obesity and clinical outcomes in breast cancer patients by evaluating the mean body mass index (BMI) and overall survival. **Material and Methods:** The research's method consisted of a retrospective observational and descriptive study without intervention, carried out in a public oncology service in Brazils Federal District. We selected breast cancer patients with hormonal expression positivity in follow-up from January 2016 to December 2020. **Results:** 305 female patients were evaluated, aged between 33 and 92 years old (average age of 59). Most patients were over 55 years old (63.3%). The mean weight of the patients was 71.70±9.10 kilograms. Regarding BMI, 38.7% of patients were classified as obese. As for the immunohistochemical classification (IHC), 72.9% of the patients were luminal B. Among the patients in which the initial treatment was registered, 56.1% received hormone therapy, while 43.9% received chemotherapy. The intention to treat in most patients was curative. Most patients had disease staging between II and III. As for the outcome, most patients were still undergoing treatment (83.0%) at the time of data collection. Correlating the IHC classification with patient survival, there was no significant difference between patient's classified as luminal A and those classified as luminal B (*p*: 0.342). There was also no significant difference between non-obese and obese patients in the assessment of overall survival and weight (*p*: 0.917). **Conclusion:** Despite the high prevalence of obesity in the studied population, the overall survival of this group did not differ from the non-obese group, even in the analyzes by IHC profile.

Keywords: Body mass index; Survival; Breast neoplasms.

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Financial support: none to declare.
Conflicts of interest: The authors declare no conflict of interest relevant to this manuscript.
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Received on: April 25, 2022 | **Accepted on:** August 19, 2022 | **Published on:** October 6, 2022
DOI: https://doi.org/10.5935/2526-8732.20220348

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RESUMO

Objetivo: O objetivo deste estudo foi analisar a relação entre obesidade e desfechos clínicos em pacientes com câncer de mama, avaliando o índice de massa corporal (IMC) médio e a sobrevida global. **Material e Métodos:** O método da pesquisa consistiu em um estudo observacional retrospectivo e descritivo sem intervenção, realizado em um serviço público de oncologia do Distrito Federal. Selecionamos pacientes com câncer de mama com positividade de expressão hormonal em acompanhamento de janeiro de 2016 a dezembro de 2020. **Resultados:** Foram avaliadas 305 pacientes do sexo feminino, com idade entre 33 e 92 anos (idade média de 59). A maioria dos pacientes tinha mais de 55 anos (63,3%). O peso médio dos pacientes foi de 71,70±9,10kg. Em relação ao IMC, 38,7% dos pacientes foram classificados como obesos. Quanto à classificação imuno-histoquímica (IHQ), 72,9% dos pacientes eram luminal B. Entre os pacientes em que o tratamento inicial foi registrado, 56,1% receberam terapia hormonal, enquanto 43,9% receberam quimioterapia. A intenção de tratar na maioria dos pacientes foi curativa. A maioria dos pacientes apresentou estadiamento da doença entre II e III. Quanto ao desfecho, a maioria dos pacientes ainda estava em tratamento (83,0%) no momento da coleta de dados. Correlacionando a classificação do IHQ com a sobrevida do paciente, não houve diferença significativa entre os pacientes classificados como luminal tipo A e os classificados como luminal tipo B (*p*: 0,342). Também não houve diferença significativa entre pacientes não obesos e obesos na avaliação da sobrevida global e peso (*p*: 0,917). **Conclusão:** Apesar da alta prevalência de obesidade na população estudada, a sobrevida global deste grupo não diferiu do grupo não obeso, mesmo nas análises por perfil IHC.

Descritores: Índice de massa corporal; Sobrevida; Neoplasias mamárias.

INTRODUCTION

Nowadays, breast cancer is the second most frequent tumor in the world, and the first among females, affecting about 2.1 million women.[1] Some of the main risk factors for breast cancer are advanced age, early menarche, late menopause, first pregnancy after 30 years, nulliparity, family history of breast cancer and lifestyle habits such as obesity, alcohol consumption, and smoking.[2]

Obesity is a disease characterized by excessive accumulation of body fat that compromises the proper functioning of the body.[3] The body mass index (BMI) is the most used calculation as a diagnostic parameter for overweight and obesity.[4-6] Excess weight significantly increases serum insulin concentrations and the release of inflammatory cytokines, in addition to increased peripheral estrogen conversion.[8]

Literature data shows that patients with breast cancer who are overweight or obese at diagnosis have a significantly higher risk of disease recurrence and are less likely to be alive in ten years, when compared to patients with adequate weight, especially in post-menopause.[7,11]

In view of the worse outcome related to obesity in patients with breast cancer, it is important to assess how this factor interferes in our population of women.

OBJECTIVES

The purpose of this study was to analyze the relationship between obesity and clinical outcomes in breast cancer patients by evaluating the mean body mass index (BMI) and overall survival. The primary endpoints were to assess the mean body mass index (BMI) of patients with hormone receptor-expressing breast cancer and to assess the relationship between BMI and overall survival after primary treatment (neoadjuvant, adjuvant, and palliative). The secondary endpoints were to compare the average weight among patients with breast cancer with hormone receptor expression, to analyze the overall survival of patients with breast cancer with hormone receptors according to the IHC profile (luminal A x luminal B) and the classification of BMI.

MATERIAL AND METHODS

This research consists of a retrospective, observational and descriptive study, without intervention, carried out in a tertiary public hospital in the Federal District. The collection of clinical and demographic data was performed from January 2016 to December 2020. Patients were selected from a database fed by completing the High-Cost Procedure Authorization (*Autorização de Procedimento de Alto Custo - APAC*) forms. The inclusion of 285 patients was estimated. There was no direct contact with the selected patients, and the free and informed consent term was waived.

To calculate the BMI, the weight and height data of the patients, collected during their first appointment, were used. The result of this calculation informs that a BMI inferior to 18.5 indicates malnutrition, between 18.5 and 24.9 indicates adequate weight, between 25 and 29.9 indicates overweight and equal to or above 30 indicates obesity.

Tumors were classified as luminal A – like and luminal B – like. Luminal A – like tumors were defined as those with ER and/or PR expression ³20%, Ki-67 index less than 14% and negative for HER-2 amplification and/or overexpression. Tumors defined as luminal B – like had positive hormone receptors, but at lower levels and/or proliferative index >15%.[12,13,15,16]

The overall survival, which is defined as the time between the diagnosis of breast cancer (localized or metastatic) until death from any cause, was considered as an outcome of the study.

Were included in this study female patients aged over 18 years old, diagnosed with ductal or lobular breast malignancy (regardless of staging), with ER and/or PR expression ≥1% and negative for amplification and/or overexpression of HER-2, after the first treatment, whether neoadjuvant, adjuvant or palliative. As exclusion criteria, we adopted: male patients; patients with neoplasms whose primary site is not the breast or breast neoplasms with special histologies (non-ductal and non- lobular); patients who started treatment at another institution.

The comparison between patients of different age groups, in relation to their BMI, was performed using the One-Way ANOVA test. The same test was used to compare patients with different stages of the disease, in relation to their weight. The assessment of the association between the patients' age group and their BMI classification was performed using the chi-square test.

The evaluation of the relationship between the variables: a) immunohistochemical classification (IHC); b) initial treatment; c) intention of treatment; d) BMI classification; and e) age group; with patients' survival was performed using the Kaplan-Meier test, using the log-rank method (Mantel-Cox), with presentation of the respective Kaplan-Meier survival curve.

The analysis of the relationship between patients' weight or obesity, in each age group evaluated in this study, in relation to patient survival, was performed using the Cox regression test. The same test was used to assess the relationship between different treatment intentions, considering the weight of patients in relation to survival as a covariate. The other results of the variables evaluated in this study were presented in the form of descriptive statistics or in the form of tables. Statistical analysis was performed using the SPSS statistical program, version 24.0, considering a significance level of 5%.[17]

This study was not funded by any institution, did not present conflicts of interest and was approved by the ethics and research committee of the health department of the Federal District through *Plataforma Brazil* under the number CAAE: 48817621.1.0000.5553.

RESULTS

Between January 2016 and December 2020 total of 305 female patients were evaluated, aged between 33 and 92 years, with a mean age of 60.33 ± 7.3 years old (mean ± standard deviation of the mean) and a median age of 59 and an interquartile range of 17. The mean weight of the patients was 71.70 ± 9.10 kilograms. The median follow-up period was 850 days (mean deviation of 580 days).

Table 1 presents the clinical and demographic characteristics of the patients evaluated in this study. Most patients were over 55 years old (63.3% - n=193), and they were classified in terms of BMI as adequate in 60.7% (n=185), obese in 38.7% (n=118) and undernourished in 0.7% (n=2). The most frequent histological subtype was luminal B – like (72.9 % - n=196).

Table 1. Clinical and demographic characteristics of the patients evaluated in this study.

Variable	% (n)
Age group	
Less than 45 years	10,2 (31)
Between 45 and 55 years old	26,6 (81)
Over 55 years	63,3 (193)
BMI classification	
Undernourished	0,7 (2)
Adequate	60,7 (185)
Obese	38,7 (118)
Immunohistochemical classification	
Luminal A – like	27,1 (73)
Luminal B – like	72,9 (196)
No information	36
Initial treatment	
Hormone therapy	56,1 (165)
Chemotherapy	43,9 (129)
No information	11
Treatment intention	
Curative	84,4 (243)
Palliative	15,6 (45)
No information	17
Treatment	
Hormone therapy curative	46,9 (135)
Hormone therapy Palliative	8,3 (24)
Chemotherapy curative	37,5 (108)
Chemotherapy Palliative	7,3 (21)
No information	17
Staging	
I	17,9 (52)
II	32,4 (94)
III	34,5 (100)
IV	14,5 (42)
No information	17
Outcome	
In treatment	83,0 (253)
Medical release	2,0 (6)
Death	12,8 (39)
Segment loss	2,3 (7)

A histogram of the BMI of the patients evaluated in this study is shown in Figure 1. Among the patients in which the initial treatment was registered, 56.1% (n=165) received hormone therapy, while 43.9% (n=129) received chemotherapy, whether neoadjuvant, adjuvant or palliative. The treatment intention of most patients was curative (84.4% - n=243), and for 46.9% (n=135) the treatment was curative hormone therapy, for 8.3% (n=24) it was palliative hormone therapy, for 37.5% (n=108) it was curative chemotherapy and for 7.3% (n=21) it was palliative chemotherapy. Most patients had disease staging between II and III (66.9% - n=194). As for the outcome, most patients were still undergoing treatment (83.0% - n=253), 2.0% (n=6) of them had been discharged, 12.8% (n=39) of them passed away and 2.3% (n=7) of them lost the treatment follow-up.

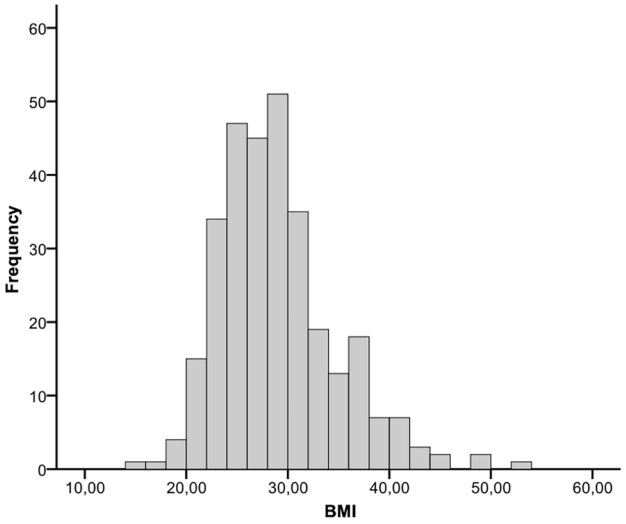

Figure 1. Histogram of the BMI of the patients evaluated in this study. Mean ± standard deviation of the mean: 28.99 ± 0.33.

Most patients younger than 45 years old had an adequate BMI (77%). In patients between 45 and 55 years old, there was also a predominance of adequate BMI (64.2%), but to a lesser extent when compared to patients younger than 45 years old. In patients over 55 years of age, the proportion of obese women was the highest (41.5%). There was no significant difference between patients of different age groups, in relation to their BMI (One-Way ANOVA test, *p*=0.207). There was also no association between the patients' age group and their BMI classification (chi-square test, *p*=0.480). The result of the evaluation of the relationship between age group and BMI of the patients evaluated in this study is shown in Table 2.

The result of the comparison between different staging of the disease, in relation to the body weight of the patients, is presented in Table 3. The survival curve, in the Kaplan-Meier assessment, relating the IHC classification with the survival of patients, is shown in Figure 2. There was no difference between patients classified as luminal A – like and those classified as luminal B – like (luminal A – like: mean of 84.00 weeks; luminal B – like: mean of 128.55 weeks) (Kaplan-Meier test – log-rank/Mantel-Cox: *p*=0.342).

Table 3. Result of the comparison between different staging of the disease, in relation to the body weight of the patients.

Staging	Body weight (kg)
I	68,52±1,90
II	72,79±1,59
III	72,89±1,64
IV	71,02±1,85
In Situ	64,50±4,50
P value	0,481

Results are presented as mean ± standard error of the mean. p-value in the one-way ANOVA test

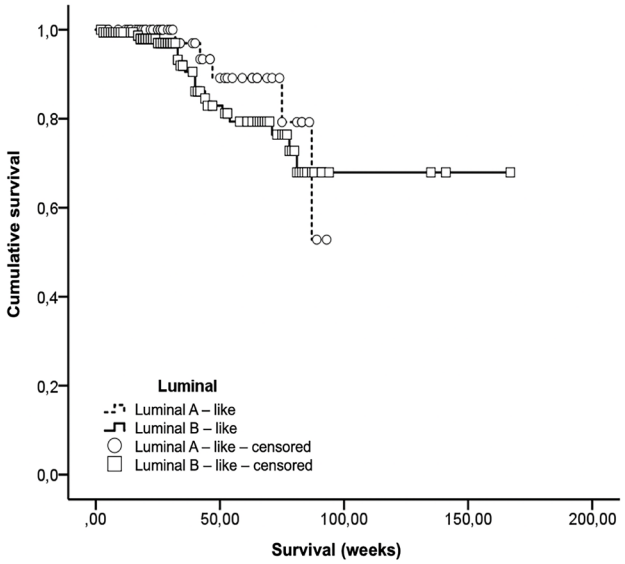

Image 2. Survival curve, in the Kaplan-Meier assessment, relating the IHC classification with patient survival

There was also no relevant statistical difference between patients with different staging, in relation to body weight (One-way ANOVA test, *p*=0.481).

Table 2. Assessment of the relationship between age group and BMI of the patients evaluated in this study.

Variable	Less than 45	Age Group Between 45 and 55 years old	Over 55 years	P value
BMI	27,26±0,91	29,07±0,59	29,24±0,43	0,207
BMI classification				
Undernourished	0,0 (0)	0,0 (0)	1,0 (2)	
Adequate	71,0 (22)	64,2 (52)	57,5 (111)	0,480
Obese	29,0 (9)	35,8 (29)	41,5 (80)	

In contrast, patients who received initial chemotherapy treatment (mean 183.89 weeks) survived longer than those whose initial treatment was hormone therapy (mean 119.56 weeks) (Kaplan-Meier test – log-rank/Mantel-Cox: *p*=0.001) – Figure 3.

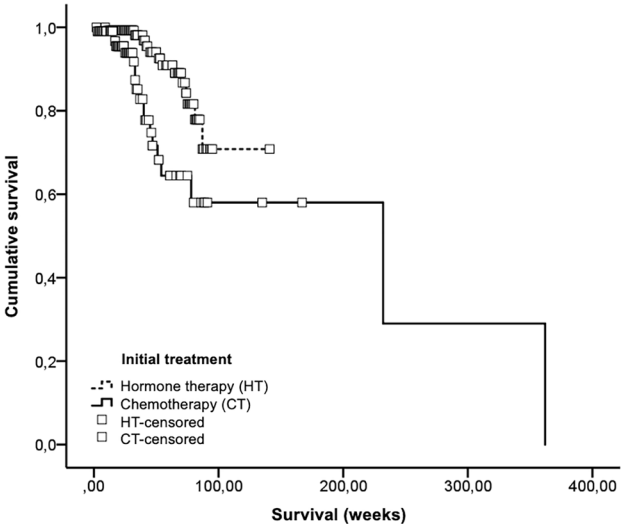

Image 3. Survival curve, in the Kaplan-Meier assessment, relating initial treatment with patient survival
Chemotherapy: mean of 190.68 weeks; Hormone therapy: mean of 119.9 weeks (Kaplan-Meier test - Log rank/Mantel-Cox: p=0.002)

The overall survival curve, in the Kaplan-Meier assessment, relating obesity to patient survival is shown in Figure 4. There was no difference between non-obese and obese patients (non- obese: mean 206.49 weeks; obese: mean of 112.34 weeks) (Kaplan-Meier test – log-rank/Mantel-Cox: *p*=0.917).

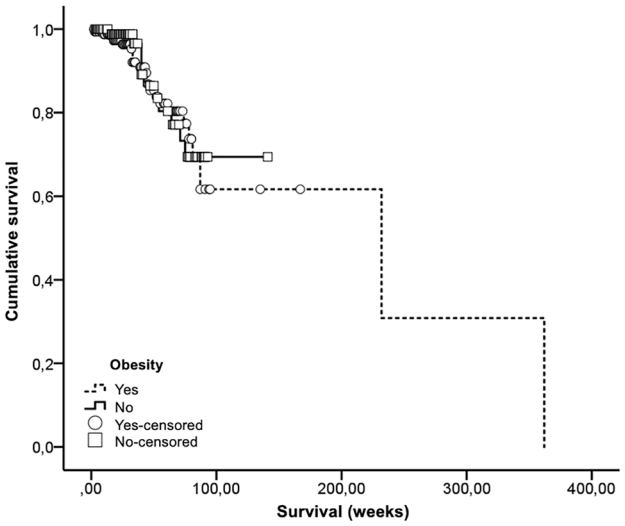

Image 4. Survival curve, in the Kaplan-Meier assessment, relating obesity to patient survival
Non-obese: mean of 206.12 weeks; Obese: mean of 113.83 weeks (Kaplan-Meier test - Log rank/Mantel-Cox: p=0.802)

The analysis of the relationship between weight and age groups demonstrates that there was no association with patient survival (Cox regression test, weight: *p*=0.653; age group: *p*=0.771). Considering only obese patients, there was no relationship with patient survival, both among those who received hormone therapy (Cox regression test, obesity: *p*=0.863; age group: *p*=0.433) and among those who received chemotherapy (obesity: *p*=0.563; age group: *p*=0.390). These results are shown in Figures 5 and 6, respectively.

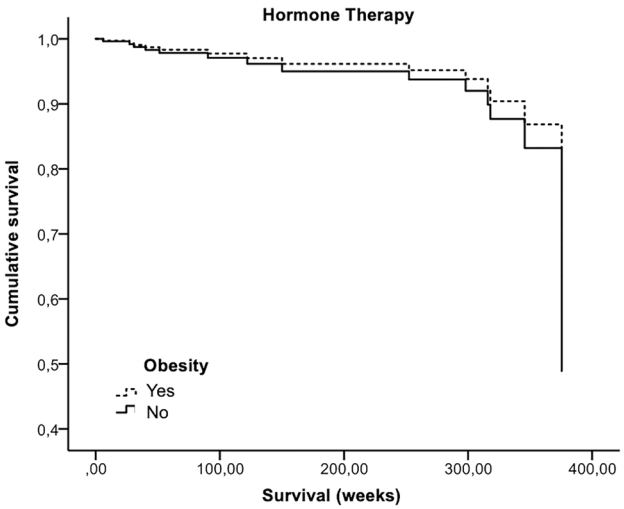

Image 5. Survival curve, in the Kaplan-Meier assessment, relating obesity, according to patient age groups, among patients undergoing hormone therapy
Cox regression test, obesity: p=0.863; age group: p= 0.433

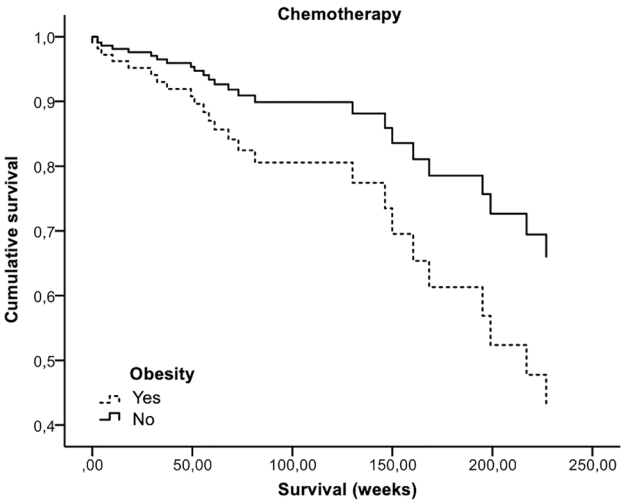

Image 6. Survival curve, in the Kaplan-Meier evaluation, relating obesity, according to the age groups of the patients, among patients undergoing chemotherapy
Cox regression test, obesity: p=0.863; age group: p= 0.433

In general, patients who received treatment with curative intent had a greater survival rate than those who received treatment with palliative intent, considering their weight as a covariate (Cox regression test, weight: *p*=0.828; intent to treat: *p*<0.001). The survival rate of those who received curative treatment was 4.26 times greater than that of those who received palliative treatment (95% confidence interval ranging from 1.97 to 9.21 times). These results are illustrated in Figure 7.

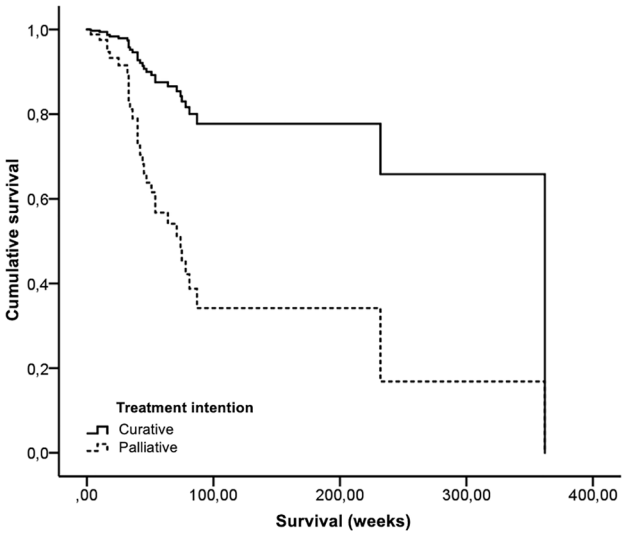

Image 7. Survival curve, in the Kaplan-Meier evaluation, relating the intention to treat with the survival of the patients, according to their weight
Cox regression test, weight: p=0.828; intention to treat: p <0.001; 95% confidence interval ranging from 1.97 to 9.21 times

Among patients undergoing hormone therapy, both with curative and palliative treatment intentions, there was no difference between non-obese and obese patients in terms of survival (Kaplan-Meier test – log-rank/Mantel-Cox - curative hormone therapy: *p*=0.175; palliative hormone therapy: *p*=0.077). These results are shown in Figures 8 and 9, respectively.

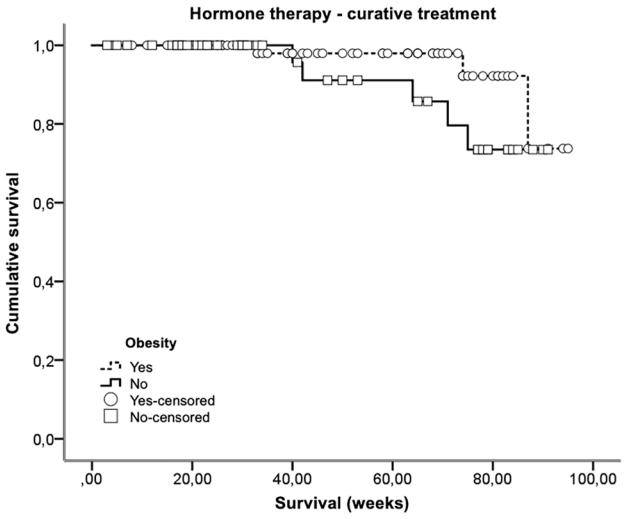

Image 8. Survival curve, in the Kaplan-Meier assessment, relating obesity to survival, among patients undergoing hormone therapy with curative treatment intent
Non-obese: mean of 91.05 weeks; Obese: mean 82.90 weeks (Kaplan-Meier test - Log rank/Mantel-Cox: p=0.175)

As between patients undergoing chemotherapy, both with curative and palliative treatment intent, there was no difference between non-obese and obese patients in terms of survival (Kaplan- Meier test – log-rank/Mantel-Cox - curative chemotherapy: *p*=0.806; palliative chemotherapy: *p*=0.610). These results are shown in Figures 10 and 11, respectively.

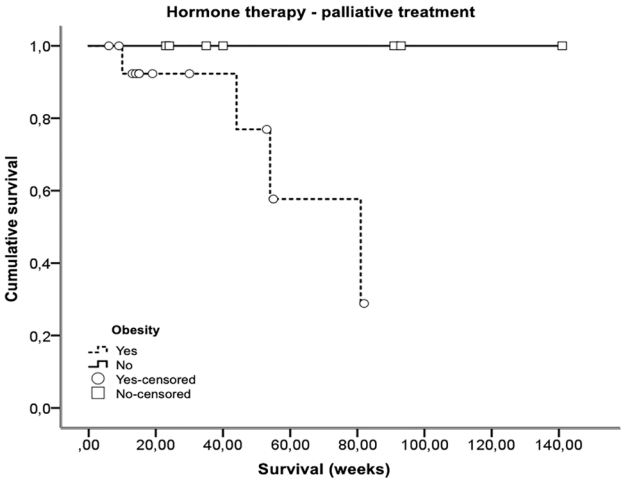

Image 9. Survival curve, in the Kaplan-Meier assessment, relating obesity to survival, among patients undergoing hormone therapy, with palliative treatment intent
There was no difference in survival between non-obese and obese patients (Kaplan-Meier test - Log rank/Mantel-Cox: p=0.077)

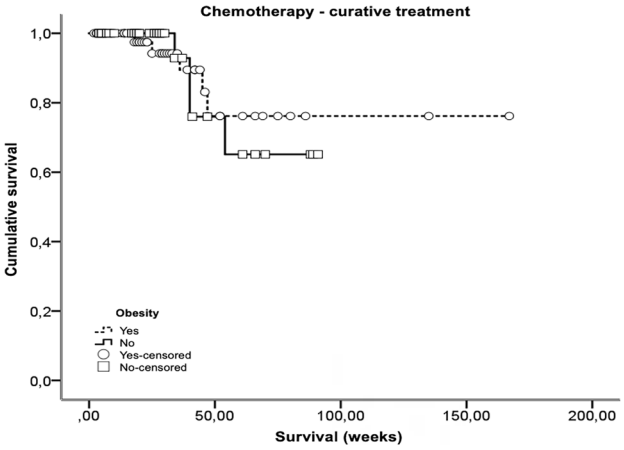

Image 10. Survival curve, in the Kaplan-Meier assessment, relating obesity to survival, among patients undergoing chemotherapy, with curative treatment intent
Non-obese: mean of 136.29 weeks; Obese: mean of 4.30 weeks (Kaplan-Meier test - Log rank/Mantel-Cox: p=0.806)

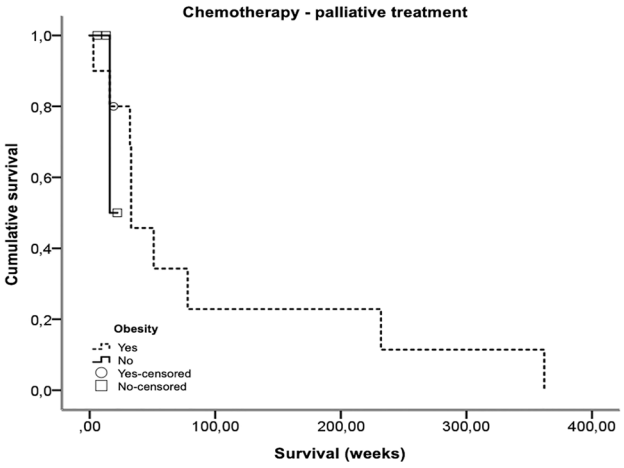

Figure 11. Survival curve, in the Kaplan-Meier assessment, relating obesity to survival, among patients undergoing chemotherapy, with palliative treatment intent.
Non-obese: mean of 95.73 weeks; Obese: mean of 19.00 weeks (Kaplan-Meier test – log-rank/Mantel-Cox: p=0.610).

DISCUSSION

Breast neoplasms are classified according to histological and molecular characteristics into tumors that express ER and/or RP, considered hormone receptor-positive breast cancers, tumors that express HER-2, and tumors that do not express ER, PR, or HER-2.[16] In the present study, we evaluated patients with hormone receptor expression, with a predominance of patients classified as luminal B (72.9%).

The mean age observed in this cohort was 60.33 years old, like the analysis obtained in the studies by Carmo et al. (2016)[14] and García Fernández et al. (2014),[15] but different from the Brazilian AMAZONA cohort in which the mean age was 54.[14,15,22] Regarding menopausal status, most patients were postmenopausal.

Analyzing the survival of patients in relation to the immunohistochemical subtype, there was no difference between patients classified as luminal A – like (mean of 84.00 weeks) and those classified as luminal B (mean of 130.04 weeks). It is known that breast tumors with luminal classification are more frequent and have a better prognosis.[2,12,14] Brazilian studies with patients with luminal breast tumors showed 5-year survival ranging from 79.5% to 93.38%.[14] This difference observed between the studies may be the result of methodological differences.

The present study showed that patients whose initial treatment was chemotherapy survived longer than those whose initial treatment was hormone therapy. This result can be attributed to the retrospective factor of the study and the fact that we did not separate the analysis by chemotherapy versus curative and palliative hormone therapy.

Most of our patients were early stage II and III. Correlating the staging with breast cancer survival, a survival rate of 80.0% is shown in stage IIa, 70.0% in stage IIb, 50.0% in stage IIIa, 32% in stage IIIb and in stage IV of 5.0%.[19] In the AMAZON cohort, overall survival was significantly different between molecular subtypes and was independent of pathological stage for patients in stages II and III.[22]

When analyzing the relationship between obesity and the survival of patients with breast cancer with the presence of hormone receptors, we did not observe any difference between non-obese and obese patients. This result is contrary to data in the literature, which shows that a higher BMI is associated with a lower breast cancer-specific survival.[21] A study published by Iwase et al. (2021)[11] showed that after neoadjuvant chemotherapy, a higher BMI was significantly related to a lower rate of pathological complete response and lower disease-free survival when compared with normal BMI. In addition, postmenopausal Asian women who had an increase in BMI ≥5.0 were observed to be significantly more likely to develop breast cancer than those with a stable BMI (defined as a change in BMI of ± 2.5).[19]

In our series, there was no relationship between the weight of patients and survival in each age group. This differs from data in the literature, in which weight gain >10% of body weight was suggestively associated with increased risk of breast cancer-specific mortality.[21] Postmenopausal women with waist circumference ≥90cm were significantly more likely to develop breast cancer than those with waist circumference <70cm.[19]

Perhaps the reason there is no statistically significant difference between non-obese and obese patients is the difficulty in obtaining adequate data, since this is a retrospective study, through analysis of medical records.

As expected, patients who received treatment with curative intent had a longer survival than those who received treatment with palliative intent. The survival rate of those who received curative treatment was 4.26 times greater than that of those who received palliative treatment. A literature review published in 2010 showed that the median survival of metastatic patients is around 24 months, but it can range from a few months to several years.[20]

This work has some limitations. This is a retrospective study, with analysis of data retrieved from medical records. In addition, the analysis of overweight and obesity was performed by calculating the BMI, in a single moment, and overweight or obesity could not be evaluated through other methods, such as the measurement of waist circumference (WC), circumference abdominal/hip (WHR), calculation of body fat mass or bioimpedance. In addition, the non-differentiation, in most analysis, between patients with curative and palliative treatment may have contributed to some of the results observed.

CONCLUSION

Obesity is a modifiable risk factor for cancer. The relationship between obesity and breast cancer risk is complex and differs by tumor characteristics, menopausal status, and exogenous hormone use. It is described in the literature that a higher BMI is associated with a lower breast cancer-specific survival. Despite the high prevalence of obesity in the population studied, the overall survival of this group did not differ from the non-obese group, even in the analysis by IHC profile.

Studies that assess body fat distribution and not just BMI may, perhaps, be more adequate to assess this relationship.

AUTHORS' CONTRIBUTIONS

K.F.F: Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Manuscript writing, Provision of study materials or patient; L.N.W: Conception and design, Data analysis and interpretation, Final approval of manuscript, Manuscript writing; L.A.A: Conception and design, Final approval of manuscript, Manuscript writing; E.S.C.O: Final approval of manuscript, Manuscript writing; R.A.C: Conception and design, Data analysis and interpretation, Manuscript writing, Provision of study materials or patient

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ABBREVIATION LIST

APAC - Autorização de procedimento de alto custo
BMI - Body mass index

ER - Estrogen receptor

HER-2 - Human epidermal growth factor receptor-type 2 IHC - Immunohistochemical classification

PR - Progesterone receptor WC - Waist circumference

WHR - Circumference abdominal/hip