Original Article

Relationship of Body Mass Index and Secondary Lymphedema to Surgical Treatment of Breast Cancer: a retrospective study

Relação do Índice de Massa Corporal e Linfedema Secundário a tratamento cirúrgico do Câncer de Mama: estudo retrospectivo

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ABSTRACT | INTRODUCTION: Breast cancer is the most common neoplasm in the Brazilian female population, with lymphedema being one of its main surgical complications. **OBJECTIVE:** To verify the relationship between the body mass index and the development of lymphedema in the postoperative period of breast cancer, its relationship with the type of treatment received and the time elapsed from the surgery. **MATERIALS AND METHODS:** Medical records of 59 women were collected from May 2008 to February 2009 using data from anamnesis, physical exam; perimetry, estimated volume; reports, symptoms, and notes in medical records. The analysis was performed using means and standard deviations for the quantitative and qualitative variables (absolute and relative) and to verify the risk factors used, the Student's t-test and Pearson's chi-square test with a 5% significance level (0.05). **RESULTS:** The frequency of lymphedema was 47.5%, with 40.7% being obese. There was a significant difference between the groups of lymphedema and BMI (p=0.002). There is also a significant difference between lymphedema in the group without axillary radiotherapy (p=0.003) and an association between post-surgical time and lymphedema (p=0.006), being greater after six months of surgery. **CONCLUSION:** There is a correlation between obesity and the development of lymphedema. The types of treatment do not seem to have influenced their development, and the longer the surgery has elapsed, the greater the risk of their appearance.

KEYWORDS: Breast Neoplasms. Breast Cancer Lymphedema. Obesity. Elective Surgical Procedures.

RESUMO | INTRODUÇÃO: O câncer de mama é a neoplasia mais incidente na população feminina brasileira, sendo o linfedema uma de suas principais complicações cirúrgicas. **OBJETIVO:** Verificar a relação do índice de massa corpóreo e o desenvolvimento do linfedema no pós-operatório de câncer de mama, sua relação com o tipo de tratamento e ao tempo pós-cirúrgico. **MATERIAIS E MÉTODOS:** Foram levantados prontuários de 59 mulheres no período de maio de 2008 a fevereiro de 2009 utilizando dados da anamnese; exame físico; perimetria, volume estimado; relatos, sintomas e dados em prontuário. A análise foi feita por meio de médias e desvios padrões para as variáveis quantitativas e qualitativas (absoluta e relativa) e para verificação dos fatores de risco foi utilizado o Teste t de Student e Teste Qui-quadrado de Pearson com nível de significância de 5%. **RESULTADOS:** A frequência de linfedema foi de 47,5%, sendo que 40,7% eram obesas. Observou-se diferença significativa entre os grupos de linfedema e IMC (p=0,002). Nota-se ainda diferença significativa entre linfedema no grupo sem radioterapia de axila (p=0,003) e associação entre o tempo pós-cirúrgico e linfedema (p=0,006), sendo maior após 6 meses de cirurgia. **CONCLUSÃO:** Existe correlação entre obesidade e desenvolvimento do linfedema. Os tipos de tratamento parecem não ter influenciado o seu desenvolvimento e quanto mais tempo decorrido pós- cirurgia, maior o risco do seu aparecimento.

PALAVRAS-CHAVE: Neoplasias da mama. Linfedema Relacionado a Câncer de Mama. Obesidade. Procedimentos Cirúrgicos Eletivos.

Submitted 03/29/2021, Accepted 05/10/2021, Published 05/19/2021
J. Physiother. Res., Salvador, 2021 May;11(2):368-374
http://dx.doi.org/10.17267/2238-2704rpf.v11i2.3749 | ISSN: 2238-2704
Designated editors: Kátia Sá e Cristiane Dias

How to cite this article: Antonini M, Salerno GRF, Moro RS, Oliveira MVO, Ferraro O, Lopes RGC. Relationship of Body Mass Index and Secondary Lymphedema to Surgical Treatment of Breast Cancer: a retrospective study. J Physiother Res. 2021;11(2):368-374. http://dx.doi.org/10.17267/2238-2704rpf.v11i2.3749

Introduction

Malignant breast cancer is the second most common type of cancer in the world and the most common among women. Each year, 25% of new cancer cases in women are breast cancer. In Brazil, 66.280 new breast cancer cases were estimated for 2021, and the number of deaths was 16.724 in the year 2017. Statistics indicate an increase in the incidence in both developed and developing countries.[1]

Mammographic screening allows the detection of breast cancer earlier, favoring more effective and less aggressive behaviors, guaranteeing an increase in women's survival.[2] On the other hand, the increase in survival also leads to increased lymphedema, which is a chronic disease and difficult to treat, causing functional, psychological, and social disorders for breast cancer patients.[3]

Of the complications related to the surgical treatment of breast carcinoma, lymphedema has relevant implications because, in addition to its pathophysiology not yet been fully clarified, it has a prevalence of 12% to 30%, varying considerably according to the proposed treatment. The onset of lymphedema can be early, immediately after the operation, or late, appearing years after surgery.[4]

According to the Consensus of the International Lymphology Society (2016)[5], lymphedema is a clinical manifestation of insufficiency of the lymphatic system, with the consequent disorder in the transport of lymph. Lymphedema is a complication of high morbidity, directly affecting the patient's quality of life and psychological profile[6], extending to breast cancer. It is known that the main risk factors for the development of lymphedema are radiotherapy, infection, obesity and the number of lymph nodes removed. The size of the tumor and its location were not associated with a higher risk of lymphedema.[3,7]

However, its diagnosis can be obtained through clinical symptoms and signs presented by the patients. Among the reported symptoms, pain, paraesthesia, decreased function, and edema are the most frequent. Among the clinical signs are changes in perimetry, volumetry, and ultrasound; however, complementary exams are only indicated when there is doubt in the diagnosis.[3]

In addition, lymphedema can be classified as mild (less than 3cm), moderate (3 to 5cm), and severe (greater than 5cm), the greater the perimeter of the limb, the more adhesions, less functionality of the limb and greater treatment difficulties, therefore, requiring prevention as the best therapeutic strategy when risk factors are present.[7,8]

Among the modifiable risk factors for the control of lymphedema of the upper limbs is obesity; that is, weight control has become a recommendation in the current consensus and guidelines[9], being emphasized both in the pre-and post-surgical period.

Finally, lymphedema is one of the complications resulting from breast cancer treatment that brings with it physical-functional and psychological reactions that may directly interfere in the quality of life of this population. Measures to identify these risk factors for their onset may lead us to specific prevention protocols. Therefore, it became relevant to assess the relationship between body mass index and the development of lymphedema in the postoperative period of breast cancer, its relationship with the type of treatment received, and the time after surgery.

Material and methods

A retrospective study was carried out from May 2008 to February 2009 with 59 medical records of women who underwent surgical treatment for malignant breast cancer at a public hospital in São Paulo. For this investigation, medical records of women who underwent breast surgery for malignant neoplasia were included, excluding those who reported bilateral breast surgery, time of surgery less than three months, presence of axillary surgery, and previous chronic lymphedema.

All data tabulation was performed by the same researcher, considering the following variables; age, body mass index (BMI), pre-surgical clinical staging, type of surgery, the time elapsed until now, axillary approach considering the level of emptying in addition to the number of affected lymph nodes seen in the pathological, adjuvant with axonal and axillary radiotherapy, chemotherapy, hormone therapy, presence of complications such as seroma, hematoma, and infections of the surgical wound.

Moreover, to identify lymphedema, the values of the perimetry presented in the medical records in the physical examination part were transcribed, being identified as lymphedema the presentation of the difference of 2cm in the perimetry compared to the contralateral limb. Perimetric markings were performed at three specific points on the arm, three specific points on the forearm, wrist, and hands standardized by the hospital team. The same person always performed the evaluations to avoid mistakes in the appointments.

The data were analyzed and presented descriptively through means and standard deviations for the quantitative variables and the qualitative variables absolute (N) and relative frequencies (%). The quantitative variables, age, and BMI showed normality verified by the Kolmogorov-Smirnov test (KS); for that, we used Student's t-test and Pearson's chi-square test, with a significance level of 5% (α = 0,05), and all tests were concluded under a two-tailed hypothesis.

Results

Of the 59 medical records analyzed, the average age of 60±3.45 years was found, with an average BMI of 28.86±1.25 Kg/m2, and 40%, 23 women had a BMI above 30Kg/m2, i.e., obesity, the frequency of lymphedema was 47% (28 women).

Conservative surgery was performed on 54% (33) women, while radical surgery was performed on 45.8% (26) women. From the point of view of axillary treatment, 32.2% (19) women underwent sentinel lymph node biopsy (SLB), and 67.8% (40) patients underwent axillary lymphadenectomy. All patients who were referred for axillary lymphadenectomy had compromised lymph nodes. In addition, therapeutic complementation with breast radiotherapy (RT) occurred in 66.1% (39) women.

As for the existence of comorbidities, 66.1% (39) women had some chronic disease, the most prevalent in 56% (33) being systemic arterial hypertension (SAH) and 10% (6) women having diabetes mellitus (DM). Regarding the complications presented in the postoperative period, regardless of the type of surgery, 76.3% (45) women presented some symptoms, and 23.7% (14) did not present any complications. Among the complications mentioned, infection was identified in 95% (43) of them, 90% (40) had radiodermatitis, 95% (43) had erysipelas and seromas in 95% (43) of them (Table 1).

Table 1. Sociodemographic, anthropometric and clinical characteristics of 59 women who underwent surgical treatment for breast malignancy 2008-2009

Average Age	60±3.45 Years	
Average BMI	28.86±1.25 Kg/m^2	
	(N) %	**(N) %**
BMI	(23) 40% acima de 30 Kg/m^2	(36) 60% abaixo de 30 Kg/m^2
	(N)% done	**(N)% not done**
LS biopsy	(19) 32.2%	(40) 67.8%
Axillary lymphadenectomy	(40) 67.8%	(19) 32.2%
Breast RT	(39) 66.1%	(20) 43.9%
	(N)% present	**(N)% absent**
Lymphedema	(28) 47%	(31) 53%
Comorbidities	(39) 66.1%	(20) 43.9%
	(33) 56% SAH	
	(6) 10% DM	
Complications in the PO	(45) 76.3%	(14) 23.7%
Infection	(43) 95%	
Radiodermatitis	(40) 90%	
Erysipelas	(43) 95%	
Seromas	(43) 95%	

BMI: Body mass index, LS: Sentinel lymph node, RT: Radiotherapy, SAH: Systemic arterial hypertension, DM: Diabetes Mellitus, PO: postoperative.

Age, BMI, clinical and surgical characteristics concerning lymphedema, and the relationship to lymphedema are shown in Table 2. When verified as differences between the measurements of patients with and without lymphedema, significant data for BMI with greater measures for the group with lymphedema, mean/standard deviation of 31.3±5.8Kg/m2, while the group without lymphedema presents mean / standard deviation of 26.63 ± 6.2Kg/m2, with p=0.002.

Table 2. Association between age, BMI, clinical and surgical characteristics in relation to lymphedema in 59 women who underwent surgical treatment for breast malignancy 2008-2009

		Presence of lynphedema					Total	
		No		Yes				
		N	%	N	%	p value	N	%
Age	Not young	28	90.3	26	92.9	≥0.05	54	91.5
	Young	3	9.7	2	7.1	≥0.05	5	8.5
BMI	Normal	15	48.4	2	7.1	**=0.002**	17	28.8
	Overweight	7	22.6	11	39.3	**=0.002**	18	30.5
	Obese	9	29.0	15	53.6	**=0.002**	24	40.7
TNM	I	16	53.3	8	28.6	≥0.05	24	41.4
	II	8	26.7	15	53.6	≥0.05	23	39.7
	III	6	20.0	5	17.9	≥0.05	11	19.0
Surgery	Conservative	16	53.3	16	57.1	≥0.05	32	55.2
	Radical	14	46.7	12	42.9	≥0.05	26	44.8
Positive armpit	No	22	71.0	17	60.7	≥0.05	39	66.1
	Yes	9	29.0	11	39.3	≥0.05	20	33.9

BMI: Body Mass Index. TNM: Classification of the American Joint Committee on Cancer (AJCC) and International Union for Cancer Control (UICC). Where the letter T: Primary tumor, N: cancer has spread to nearby lymph nodes, M: Metastasis: cancer has spread to distant parts of the body. Varying its classification from I to IV. Inform the age cut-off point for the classification used in young and non-young people. (T-Student test).

Considering Table 3, which shows the description of treatments for the development of lymphedema, it is observed that 67.9% (19) women who received RT in the breast developed lymphedema, while 10.7% (3) of those who received RT in the armpit, developed lymphedema. Regarding CT, 28.6% (8) women who received chemotherapy presented lymphedema, compared to 35.5% (11) who did not develop such alteration. Regarding women who received HT, 29.5% (14) developed lymphedema compared to 32.5% (10) who did not. When associated with the type of treatment received and the development of lymphedema, there was a statistically significant difference only when comparing the non-execution of RT in the armpit and the development of lymphedema (p=0.003).

Table 3. Association between treatment frequencies in relation to lymphedema in 59 women who underwent surgical treatment for breast malignancy 2008-2009

		Presence of Lynphedema					Total	
		No		Yes				
		N	%	N	%	p value	N	%
Breast RT.	Não	11	35.5	9	32.1	≥0.05	20	33.9
	Sim	20	64.5	19	67.9	≥0.05	39	66.1
Armpit RT.	Não	29	93.5	25	89.3	**=0.003**	54	1.5
	Sim	2	6.5	3	10.7	≥0.05	5	8.5
CT	Não	20	64.5	20	71.4	≥0.05	40	7.8
	Sim	11	35.5	8	28.6	≥0.05	19	32.2
HT	Não	21	67.7	14	50	≥0.05	35	59.3
	Sim	10	32.3	14	50	≥0.05	24	40.7

* RT: Radiotherapy, CT: Chemotherapy, HT: hormonetherapy. (T-Student Test).

When analyzed, the association between post-surgery time and lymphedema, using Pearson's Chi-square test, can be observed that the association is significant (p=0.006) when analyzed from 6 to 24 months and above 24 months (Table 4).

Table 4. Association between post-surgical time and the appearance of lymphedema in 59 women who underwent surgical treatment for breast malignancy 2008-2009

Post-surgical time	Presence of Lymphedema					Total	
	No		Yes				
	N	%	N	%	p value	N	%
Less than 6 months	17	56.7	5	17.9	≥0.05	22	37.9
From 6 to 24 months	10	33.3	14	50	**=0.003**	24	41.4
More than 24 months	3	10	9	32.1	**=0.003**	12	20.7
Total	30	100	28	100	-	58	100

(Pearson's Chi-square test).

Discussion

The present study corroborates what is described in the literature of how prevalent is post-treatment secondary lymphedema of malignant breast cancer and the significant association with obesity.[9-12] Literature reviews show incidences from 6.7 to 62.5%, oscillating according to the variables evaluated[9,13] and the diagnostic criterion employed.[12]

Lymphedema has a multifactorial character, with factors related to surgery, the patient and the disease itself.[14,15] Among the factors related to surgery, the extension of axillary dissection seems to be the most important risk factor in the etiology of upper limb edema.[15]

In addition, when associated with axillary radiotherapy, the literature reports a significant increase in lymphedema.[2,13] However, in this study, we found no significant presence of lymphedema in women who underwent axillary radiotherapy, leading to a discussion that other variables may be more relevant in developing this morbidity, such as the presence of postoperative infections.

Axillary approach techniques such as sentinel lymph node (LS) seem to decrease the risk of this morbidity[16], provided it is performed carefully[10], as they present promising results in staging without the need for unnecessary ganglionic emptying as in the past.[17] In this study, most were submitted to axillary lymphadenectomy and a smaller percentage to the sentinel lymph node. However, the presence of lymphedema in this sample was not related to this variable but demonstrated an association of lymphedema with the extent of emptying and axillary involvement.

As for the factors related to the disease, it is known that the advanced stage of the disease is closely related to the risk of lymphedema due to the more invasive surgical approaches and lymph node involvement, and early diagnosis is essential for its prevention. In this study, we were able to observe that despite not showing statistical significance, there is an increase in the presence of lymphedema in more advanced staging, represented by 34 women who were in stage II and III, 20 presented the presence of lymphedema. In addition, they presented the presence of infections, such as erysipelas and radiodermatitis, one of the potentiators in the development of lymphedema.

However, among the various factors involved in the occurrence of lymphedema, age and obesity[19-21] need to be highlighted. Our results showed an incidence of 47.5% of lymphedema, with an average age of 60.41 years, and 71% were overweight or obese. It is known that the age over 45 years[19] was shown to be significant in the formation of lymphedema in modified radical mastectomies. Age is cited in several articles as a risk factor related to lymphedema[10,15,21], despite controversies.

Obesity has been the subject of studies related to post-surgical upper limb edema[22,23], patients undergoing quandrantectomy have obesity as the main predictive factor.[14] However, infection of the upper limbs and weight gain after surgery were the only risk factors with significant relationships for developing this complication.[11] In our research, we found an association between the risk of developing lymphedema and obesity; the higher the BMI, the greater the chance of its onset. Weight gain already brings with it several circulatory changes that end up decompensating a lymphatic system already compromised by surgery, leading to facilitation in the development of this condition.[5,7,10]

However, randomized clinical trials demonstrate that weight loss through diets is promising and that, regardless of the type of diet, weight loss seems to be an effective method in reducing arm volume during treatment.[20] As it is a chronic, multifactorial and incurable morbidity, there should be a greater focus on prevention. Currently, weight control is a preventive measure in most of the Guidelines[9], only a recommendation by societies in consensus.[1,5]

Despite the complications, surgery and radiotherapy are essential in the management and treatment of most patients with breast cancer, and the benefits outweigh the risk of lymphedema. Thus, we must act on preventable causal agents such as obesity without underestimating functional disability, the severity of symptoms, psychological afflictions, and patients' morbidity, and the nihilistic conduct is deplorable.[10]

In addition, lymphedema will become more prevalent as survival increases[13], with morbidity being more stressful.[9] Sometimes lymphedema has a much greater impact on worsening quality of life than the surgery itself, as the latter can be more easily disguised at the expense of edema.[10] Some subjective symptoms are also significantly associated with lymphedema, including paresthesia[18], but exclusively qualitative methods do not safely demonstrate the functional impact of lymphedema[12], but data such as these were not adequately identified in this study.

Likewise, prophylactic measures to reduce its occurrence, physical therapy interventions during the postoperative period, such as the recommendation to reduce weight, should be encouraged, especially when they directly affect patients' quality of life. However, some limitations of the study can be highlighted, such as the difficulty in establishing exact risk factors for the development of lymphedema and the investigation of the role of Physiotherapy in the prevention and/or treatment of this condition this group. The authors suggest prospective, longitudinal studies in centers specialized in breast cancer, with the proposal to investigate these variables in lymphedema.

Conclusion

There is a correlation between obesity and the development of lymphedema. The types of treatment do not seem to have influenced their development, and the longer post-surgery, the greater the risk of their appearance.

Authors' contributions

Antonini M participated in data collection, construction of results, and final review of the article. Salerno GRF participated in the construction of the results and in the final review of the article. Moro RS participated in the data collection and analysis of the results. Oliveira MVO and Ferraro O participated in data collection and writing reviews. Lopes RG participated in the analysis and construction of the results and final review of the scientific article.

Competing interests

No financial, legal, or political conflicts involving third parties (government, companies and private foundations, etc.) have been declared for any aspect of the submitted work (including, but not limited to grants and funding, participation in advisory council, study design, preparation manuscript, statistical analysis, etc.).

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