

POST-MASTECTOMY BREAST CANCER RECURRENCE: AN ASSESSMENT OF THE SCIENTIFIC LITERATURE

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Abstract: Goal: To carry out the analysis and review of available articles on the recurrence of breast cancer (breast CA; BC), highlighting the main findings of the scientific literature on the topic. **Methodology:** The study consists of a literature review carried out between June and August 2022, with a bibliographic survey in the databases: PubMed, Analysis and Retrieval System Online (MedLine); Scientific Electronic Library Online (SciELO), Google Scholar and LILASCS. **Results:** A total of 10 articles met the eligibility criteria for the topic and were used to compose the review. Studies have shown the possibility of an association between the type of surgery used to treat breast CA and greater recurrence, but other findings suggest greater importance of factors such as molecular characteristics and histological type. **Conclusion:** Although there is evidence that points to the possibility of the influence of surgical variables on BC recurrence rates, the fact that there are few conclusive studies on the subject does not allow for a categorical statement.

Keywords: Breast cancer; Surgery; Relapses.

INTRODUCTION

The Breast cancer (BC) is a neoplasm with a high incidence worldwide, being considered the most common malignancy among women. It is a heterogeneous disease at the molecular level, a fact that greatly affects both the degree of involvement of the breast region and the prognosis and treatment of the disease itself. It is estimated that in 2018, 2.1 million women were diagnosed with the disease, which is approximately one woman every 18 seconds. In addition, 626,670 women died from complications or due to BC (HARBECK et al., 2019).

However, although it is a disease with a multiplicity of presentations and with several factors associated with its presentation, the evolution, locoregional impact of breast CA

and metastatic burden are shared between the various types of presentation and influence therapy. Breast CA, when diagnosed in its initial phase - that is, when there is no involvement of lymph nodes or distant metastases - is usually treatable and has a high recurrence rate among affected patients. This is increased when associated with integrative and multidisciplinary practices, increasing the cure rate by 70-80% (BRAY et al., 2015; HARBECK et al., 2019).

On the other hand, metastatic BC is not considered a curable disease with currently known treatment methods. Assistance, then, is focused on reducing symptoms and palliative measures for greater patient survival. Therefore, advancing BC is considered a treatable disease, although with lower survival when compared to the disease in the initial phase. The treatment of the disease is associated with an improvement in patient survival and a reduction in symptoms both associated with the disease and chemotherapy treatment (HARBECK et al., 2019).

CM is neatly classified into 5 subtypes, taking into consideration, histological and molecular characteristics. One of the factors that lead to its classification is the expression of specific receptors, which are: Estrogen receptor, progesterone receptor and the receptor for epidermal growth factor 2 (HER2). Neoplasms that do not express any of the above receptors are called "triple negative", which has a poor prognosis when compared to other types (CARDOSO et al., 2017).

CM treatment has two pillars: locoregional treatment and systemic therapy. Locoregional treatment is carried out by removing the tumor lesion and lymph nodes, when these are affected, in the case of already disseminated diseases, through mastectomy, together with the use of radiotherapy. Systemic treatment is carried out with chemotherapy drugs, chosen according to the type of BC (WAKS; WINER,

2019).

One of the biggest issues with CM is its relatively high recidivism rate, which greatly impacts its treatment (WU et al., 2019). Therefore, this article seeks to clarify the factors associated with BC recurrence, searching for the main factors associated with it within the scientific literature.

METHODOLOGY

This is a literature review, which is a method that favors analysis and research results without judicious or prospecting purposes. The sequence of steps for the construction of this study was defined. Starting with the elaboration of the guiding question of the research, followed by the search in the literature of primary studies, then the relevant information contained in the studies that were included in the previous stage is extracted, as well as their evaluation and finally, the analysis and synthesis of the review results and presentation of the literature review.

In this sense, the inclusion and exclusion criteria were defined. To enter the scope of the study, the selected articles needed to be original, in addition to being available in full text form, published in Portuguese, English and Spanish, they needed to be indexed in databases defined during the period from January 2007 to June 2007, 2022 and that presented topics related to post-mastectomy BC recurrence.

It is also noteworthy that theses, literature reviews and dissertations were excluded, in addition to other works that did not belong to the scope of the study. Furthermore, articles that appeared duplicates in searches were only considered once. The literature search was carried out in August 2022, in the following databases: PubMed, Analysis and Retrieval System Online (MedLine); Scientific Electronic Library Online (SciELO), Google Scholar and LILASCS.

RESULTS AND DISCUSSION

A search was carried out in the databases using the descriptors established for the research. 299 studies were found using the descriptors highlighted by this study. Of these, 152 were articles and had the full text for evaluation. After applying inclusion and exclusion criteria, 10 articles were selected.

To better elucidate the topic, a table (Table 01) was organized with the main literary findings.

Mastectomy remains an essential pillar in the treatment of breast CA. The rate of surgeries of this type has been increasing and reflects the importance of breast cancer therapy. Within mastectomy, the option for the type or surgical approach intrinsically depends on the tumor subtype and the patient's staging (WAKS; WINER, 2019). In less advanced BCs, the option for breast-conserving surgery is a viable option and is accompanied by equal or even higher success rates than more invasive approaches. The use of Haslsted's radical mastectomy has been falling into disuse due to the great morbidity caused post-surgery and the sequelae associated with the procedure. However, its use is still seen in cases of advanced disease and stage T3-T4 (TOSELLO et al., 2018).

It is known that around 30% of breast cancers may have local or distant recurrence. The pathophysiological mechanism is complex and several hypotheses have been postulated to explain this recurrence rate. Some authors point to the possibility of cells remaining in a dormant state that can be reactivated by multiple processes. Other authors point to the possibility of factors associated with both the molecular and histological characteristics of the tumor and the patient's immunocomplexity (RIGGIO; VARLEY; WELM, 2021).

Among the articles analyzed, the main theme was the search for the association of some surgical modality with the predisposition

Author and Year	Main findings
(WANG et al., 2011)	This study sought to identify the association between BC prognosis and recurrence in triple-negative and HER2+ patients. It was found that these patients have a lower survival rate and a higher recurrence rate of breast CA when compared to other patients with more favorable molecular profiles.
(ABI-RAAD et al., 2011)	This study sought to verify the degree of implication of the use of post-mastectomy radiotherapy in reducing the recurrence of breast CA without lymph node invasion. It was found that the use of radiotherapy does not generate benefit in these patients and does not contribute to greater survival.
(PORUK et al., 2015)	In this 6-year retrospective study, nipple-sparing surgery and skin-sparing mastectomy were compared regarding the incidence of recurrence. In this cohort, no significant difference was found between both surgical modalities in terms of recurrence and overall mortality from BC.
(ISERN et al., 2011)	In the comparison between patients who underwent breast reconstruction late with large flaps and those who underwent only mastectomy, those who underwent only mastectomy had lower recurrence when compared to the first.
(CHENG et al., 2009)	This study demonstrated that patients undergoing breast-conserving surgery have a lower rate of BC recurrence when compared to patients undergoing conventional mastectomy.
(WU et al., 2019)	Patients undergoing nipple-sparing mastectomy had a low incidence. The intermodal comparison showed that patients with negative hormone receptor and/or HER2+ have a higher recurrence rate when compared to patients without these characteristics.
(REDDY et al., 2011)	In this study, the incidence of recurrence was compared in patients undergoing isolated mastectomy and mastectomy associated with breast reconstruction. No significant difference was found between the two modalities regarding the recurrence of breast CA, nor was there any difference found between the recurrence time between the modalities.
(DILLEKÅS et al., 2016)	The BC recurrence rate was evaluated in two groups: those who had immediate post-mastectomy breast reconstruction and those with delayed breast reconstruction. In the intergroup comparison, it was found that there is no significant difference between the recurrence rate between the groups analyzed.
(ZHANG et al., 2017)	This study sought to verify the correlation between mastectomy and breast reconstruction simultaneously and a lower incidence of BC recurrence. In comparison with the use of mastectomy alone, no significant difference was found between the option for one or another treatment modality for breast CA.
(NEDUMPARA; JONKER; WILLIAMS, 2011)	A prospective study was carried out seeking to verify the impact of performing breast reconstruction surgery after mastectomy. It was found that the use of breast reconstruction immediately after mastectomy did not increase or reduce the risk of local recurrences. Furthermore, no results were found that indicated an impact on the prognosis of the patients studied.

Table 1: Main findings of the articles selected for the literature review

Source: Own authorship, 2022.

for BC recurrence. It was also analyzed whether the molecular profile of the neoplasm had an impact on this fact and, in some studies, a prospective analysis was carried out in relation to the patient's mortality.

In one of the studies, tumor surface markers were analyzed and an attempt was made to evaluate the possibility of them serving as predictors of tumor recurrence. In a retrospective analysis, Wang et al. (2011) analyzed several cases of diagnosed BC and sought to correlate their molecular profile with the rate of tumor recurrence. It was found that tumors that are classically considered to have a worse prognosis (HER2+ and triple negative) have a higher incidence of recurrence when

compared to other types of tumors.

In another study, comparing recurrence among patients undergoing breast-conserving surgery, similar results were found. However, triple-negative patients did not show a significant difference in the incidence of tumor recurrence, with higher recurrence rates being seen in hormone receptor-negative patients and in HER2+ patients (WU et al., 2019).

In another approach, the influence of adjuvant treatment on reducing post-mastectomy tumor recurrence in patients with less advanced disease was sought. In this work, the application of radiotherapy was prospectively evaluated regarding the incidence of disease reactivation. The

results indicated that there was no benefit for these patients, however, the author emphasizes that in cases of locally advanced diseases, radiotherapy continues to be highly recommended for controlling the neoplasia (ABI-RAAD et al., 2011).

Other authors sought to compare total mastectomy surgery with the conservative approach. In two studies it was shown that in both cases the recurrence rates do not differ from each other, stating that it must not be an impacting factor in the choice of surgical modality (CHENG et al., 2009). Regarding the evaluation of conservative approaches, in the comparison between skin-sparing mastectomy and nipple-sparing mastectomy, neither of them showed a greater association with the recurrence of breast CA in the patients evaluated (PORUK et al., 2015).

Reddy et al. (2011), sought to verify that performing isolated mastectomy is associated with a higher incidence rate of BC recurrence in women. However, no difference in recurrence rate was found when comparing the isolated use of mastectomy and reconstruction simultaneously with surgery. Similar findings were made by Zhang et al. (2017), which also found no statistically significant difference between the times of onset of tumor recurrences.

In another study, similar variables were evaluated. The results were convergent regarding little or no influence of the time of breast reconstruction and the appearance of tumor recurrences, which were also considered

to have little impact on the patients' prognosis (NEDUMPARA; JONKER; WILLIAMS, 2011).

However, other studies obtained different correlations. In one of the studies it was found that patients who underwent reconstruction surgery together with mastectomy have a better prognosis when breast CA recurs (ISERN et al., 2011). On the other hand, in the evaluation of patients undergoing skin-sparing surgery, it was found that when reconstruction was performed early, these patients had fewer recurrences compared to those in whom it was performed late. However, the authors emphasize that the ethical and logistical difficulties of double-blind randomized studies make it difficult to affirm these findings (PORUK et al., 2015).

CONCLUSION

The recurrence of breast CA is a topic of debate within the scientific literature. The studies seem to differ regarding the greater or lesser impact of certain variables. The presence of molecular characteristics with a worse prognosis may be more influential in the recurrence of the neoplasm. The surgical modality has findings that are often divergent from each other. The use of a more invasive or conservative modality does not seem to influence this parameter, while performing an earlier or later reconstruction has greater nuances that must be analyzed in subsequent studies. The low number of randomized studies appears to be an obstacle to categorical statements on the topic.

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