

# Therapeutic Approaches to Post-Mastectomy Pain Syndrome

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## Abstract

**Background:** Breast cancer is increasingly common in society and post-mastectomy pain is a striking condition associated with surgery, both intra and postoperatively. The post-mastectomy syndrome is characterized by the persistence of pain for more than 3 months after the procedure. It is mostly of neuropathic origin and is highly refractory to treatments, which vary from clinical to surgical measures and alternative techniques. In this context, it is essential to understand the possible approaches to these patients. **Objective:** Understand alternatives for pain management in patients undergoing mastectomy, especially in those in whom pain persists for more than 3 months. **Methods:** Systematic literature review, conducted in the Virtual Health Library databases includes: Lilacs, SciELO, Medline, PubMed and Cochrane between 2018 and 2023, restricted to articles in English with the descriptors: Mastectomy, chronic Pain, Nerve Blocks and Breast Cancer. 317 articles were found involving the descriptors presented, all in English. After reading the abstracts, 28 articles were selected. **Results:** This review analyzed 28 scientific studies that rigorously met the previously established characteristics in the sample selection. The synthesis included the following aspects: author/year of publication, article title, objective, type of study and database. **Conclusion:** It was concluded that, according to the analyzed studies, post-mastectomy pain is a problem that has increased its incidence and that needs the attention of health professionals. The use of antineuropathic medications, nerve blocks, fat grafting, lymph node transplantation, therapy, physical activity and acupuncture are some examples of therapeutic approaches for these women. Therefore, the team must assist the patients, seeking to provide a better prognosis, quality of life and comfort.

## Keywords

Mastectomy, Chronic Pain, Nerve Blocks, Breast Cancer

## 1. Introduction

Cancer is among the diseases that kill the most in the world and, in most cases, its treatment is aggressive, leading most people to fear the disease. Among women, the most common type is breast [1] [2]. It is generally necessary to combine several therapeutic approaches, including radiotherapy, chemotherapy, surgery and/or medication [3] [4].

Fortunately, a great advance has already been observed in these therapies, significantly increasing the survival rate of patients [3] [5] [6]. However, depending on the type of therapeutic resource adopted, there may be impacts on the woman's life for months or years after the end of treatment.

Mastectomy is still indicated in many cases and is associated with persistent pain, which greatly impacts patients' quality of life [7]. Chronic pain, usually accompanied by lymphedema, reduced mobility of the upper limb, asthenia and fatigue reduce productivity at work, in addition to generating high costs with medical consultations, difficulty in taking care of the house and children, and become a constant reminder of the disease [5] [8] [9].

In this context, it is notable that this patient starts to have substantial psychophysical changes, leading to anxiety, depression, and sleep disturbance in the survivors [9] [10] [11].

That said, it is clear the importance of understanding post-mastectomy pain syndrome, its main risk factors, pathophysiology, diagnosis and, mainly, possible conducts to not only treat, but also prevent the onset of the condition. This mission must be carried out by a multidisciplinary team [12] understanding that the focus should not only be on fighting cancer, but also enabling the patient, after treatment, to return to her activities and recover her functionality and quality of life.

In this context, this study is justified, as it seeks information on pain management in post-mastectomy women, aiming to provide better care for this population, since a large proportion of these women are susceptible to experiencing chronic pain.

## 2. Objective

The objective of the study is to understand alternatives for pain management in patients undergoing mastectomy, especially in those in whom pain persists for more than 3 months.

## 3. Material and Methods

### 3.1. Data Sources and Search Strategy

This systematic literature review adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) recommendations and assesses the managing pain in patients with post-mastectomy syndrome. A broad electronic search was performed using the Virtual Health Library (VHL), which

includes: Lilacs, SciELO, Medline, PubMed, and Cochrane, using the descriptors: Mastectomy, Chronic Pain, Nerve blocks and Breast Cancer. These search terms were used individually and in varying permutations, such as chronic pain after mastectomy, nerve blocks in mastectomy, and chronic pain in breast cancer. After searching the databases, it was observed that these terms, both separately and together, were mentioned in the majority of research involving the subject. Therefore, the most cited were chosen to compose this systematic review.

To ensure the contemporary relevance of the data, the search was limited to articles written in English, published in peer-reviewed journals, between the years 2018 and 2023. This time frame was chosen to ensure that the information contained is the most up-to-date possible.

### 3.2. Eligibility Criteria

Initially, 317 articles were found, which underwent a relevance test consisting of the inclusion criteria: 1) reference to the terms pain and mastectomy; 2) analysis of pain-related events in post-mastectomy patients; 3) description of results associated with pain control in post-mastectomy patients; and 4) publication in selected language and periods.

After a detailed analysis, 172 articles were excluded due to duplication and failure to present the proposed theme. After reading the abstracts, 73 articles were excluded for not presenting the full text and the proposed theme. Finally, after reading the articles in full, 44 articles were excluded for not presenting the proposed criteria mentioned above, which include therapeutic approaches to post-mastectomy syndrome, without conflicts of interest or bias. For this evaluation, all studies were carefully read and those that received any type of benefit or those that obtained results substantially different from the others were disregarded.

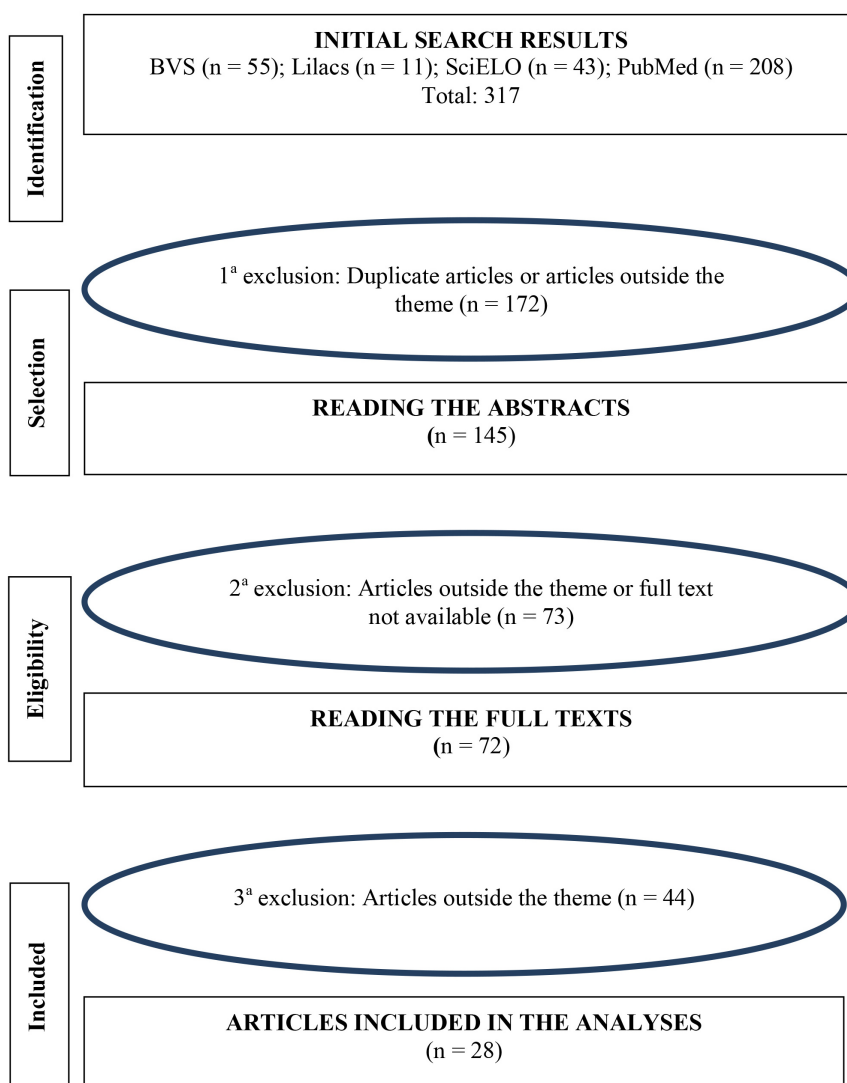
Thus, this review is based on the remaining 28 articles that met the pre-established eligibility criteria for the analysis, as shown in (Figure 1).

### 3.3. Data Extraction and Statistical Analysis

Studies that met the inclusion criteria were divided among the authors and data were independently extracted into a standardized spreadsheet. The articles were evaluated by the researchers and any discrepancies were resolved by consensus. The following information was collected: author/year of publication, article title, objective, type of study and data base.

In summary, a narrative synthesis was applied to approach the data found, and a descriptive statistical analysis was performed using the Office 2021 Excel program for Mac.

In this way, it was possible to gather the main results of each study and carry out a qualitative assessment of the information obtained. From this, a comparative analysis was carried out, taking into account the frequency of the results and the credibility of the study, and this review was systematized.



**Figure 1.** PRISMA flow diagram: representation of eligibility and inclusion of articles.

## 4. Results

After eliminating duplicates and selecting publications, the articles were read in full, from which the parameters proposed in the analytical matrix of the present study were analyzed.

This systematic literature review analyzed 28 scientific studies that rigorously met the previously established characteristics in the sample selection. Of this total of articles, 6 were quantitative/qualitative studies, 9 were a quantitative study and 13 were qualitative.

The synthesis of these selected scientific articles is presented below, covering the following aspects: author/year of publication, article title, objective, type of study and database (**Table 1**).

## 5. Discussion

Breast cancer is the most common malignancy among women [1] [2] [13] and

**Table 1.** Description of the articles selected for analysis.

Author Date	Article Title	Study Purpose	Type of Study	Data Base
[1] Tait, R. C. <i>et al.</i> , 2018	Persistent Post-Mastectomy Pain: Risk Factors and Current Approaches to Treatment	Describe mechanisms, risks, and treatments related to persistent post-mastectomy pain	Qualitative	PubMed
[2] Liukas, T. <i>et al.</i> , 2023	Towards automated risk prediction of persistent pain: Exploring psychosocial factors from electronic health records after breast cancer surgery	Describe psychosocial factors associated with postoperative persistent pain of breast cancer	Qualitative	PubMed
[3] Chappell, A. G. <i>et al.</i> , 2021	Post-Mastectomy Pain Syndrome: An Up-to-Date Review of Treatment Outcomes	Synthesize the existing evidence on Post-Mastectomy Pain Syndrome treatment	Qualitative	PubMed
[4] Yuksel, S. S. <i>et al.</i> , 2021	Post Mastectomy Pain Syndrome: A Systematic Review of Prevention Modalities	Synthesize the interventions for neuropathic pain after breast surgery	Qualitative	PubMed
[5] Chang, P. J. <i>et al.</i> , 2021	A Targeted Approach to Post-Mastectomy Pain and Persistent Pain following Breast Cancer Treatment	Clearly different pain occurs following treatment for breast cancer	Qualitative	PubMed
[6] Chappell, A. G. <i>et al.</i> , 2020	Post-Mastectomy Pain Syndrome: Defining Perioperative Etiologies to Guide New Methods of Prevention for Plastic Surgeons	Address surgeons behaviors to reduce post-mastectomy pain risks	Qualitative	PubMed
[7] Wang, K. <i>et al.</i> , 2018	Prevalence of pain in patients with breast cancer post-treatment: A systematic review	Evaluate the prevalence and severity of persistent pain after breast cancer treatment	Quantitative	PubMed
[8] Calapai, M. <i>et al.</i> , 2021	Post-Mastectomy Pain: An Updated Overview on Risk Factors, Predictors, and Markers	Describe risk factors, predictors, and potential biomarkers associated with chronic pain after breast surgery	Qualitative and Quantitative	PubMed
[9] Kannan, P. <i>et al.</i> , 2022	Efficacy of physical therapy interventions on quality of life and upper quadrant pain severity in women with post-mastectomy pain syndrome: a systematic review and meta-analysis	Determine the efficacy of physical therapy interventions on quality of life and pain severity in post-mastectomy pain syndrome	Quantitative	PubMed
[10] Chen, V. E. <i>et al.</i> , 2020	Post-mastectomy and post-breast conservation surgery pain syndrome: a review of etiologies, risk prediction, and trends in management	Summarized the literature to elucidate the etiology, risk factors and management for post-mastectomy pain syndrome	Qualitative	PubMed
[11] Pak, L. M. <i>et al.</i> , 2022	How Much Pain Will I Have After Surgery? A Preoperative Nomogram to Predict Acute Pain Following Mastectomy	Identify patients at high risk of moderate-severe pain following mastectomy	Quantitative and Qualitative	PubMed
[12] Beederman, M. <i>et al.</i> , 2021	Post-Breast Surgery Pain Syndrome: Shifting a Surgical Paradigm	Create a focused outline that gear the plastic surgeon to the care of patients with post-mastectomy pain syndrome	Qualitative	PubMed

## Continued

[13] Flores, E. M. <i>et al.</i> , 2023	One year follow-up on a randomized study investigating serratus anterior muscle and pectoral nerves type I block to reduced neuropathic pain descriptors after mastectomy	Demonstrated the differences between nerve block to reduced acute perioperative pain	Quantitative and Qualitative	MedLine
[14] Mendonça, F. T. <i>et al.</i> , 2023	Long-term Efficacy of Pectoserratus Plane Block (PSPB) for Prevention of Post-mastectomy Pain Syndrome: Extended Follow-up From a Randomized Controlled Trial	Examined whether nerve block could reduce incidence of post-mastectomy pain syndrome	Quantitative	PubMed
[15] Cheng, Y. <i>et al.</i> , 2023	Effects of Different Doses of Esketamine on Postoperative Quality of Recovery in Patients Undergoing Modified Radical Mastectomy: A Randomized, Double-Blind, Controlled Trial	Compared the effects of intraoperative different dose esketamine infusion on the quality of early postoperative recovery	Quantitative	PubMed
[16] Khoury, A. L. <i>et al.</i> , 2021	Trigger point injection for post-mastectomy pain: a simple intervention with high rate of long-term relief	Identify the rate of long-term resolution of post-mastectomy pain after trigger point injections	Quantitative and Qualitative	PubMed
[17] Lu, Z. <i>et al.</i> , 2021	Transcutaneous electrical acupoint stimulation before surgery reduces chronic pain after mastectomy: A randomized clinical trial	Determine the efficacy of transcutaneous electrical acupoint stimulation (TEAS) before anesthesia induction in reducing chronic pain	Quantitative	PubMed
[18] Urits, I. <i>et al.</i> , 2020	Chronic Pain Following Cosmetic Breast Surgery: A Comprehensive Review	Address the pathophysiology, clinical presentation, and treatment of patients with chronic postoperative pain following cosmetic breast surgery	Qualitative	PubMed
[19] Fujii, T. <i>et al.</i> , 2019	A randomized controlled trial of pectoral nerve-2 (PECS2) block vs. serratus plane block for chronic pain after mastectomy	Identify the efficacy of nerve block for post-mastectomy pain syndrome	Quantitative and Qualitative	PubMed
[20] Abbas, D. N. <i>et al.</i> , 2018	Thermal Versus Super Voltage Pulsed Radiofrequency of Stellate Ganglion in Post-Mastectomy Neuropathic Pain Syndrome: A Prospective Randomized Trial	Compare the efficacy and safety of thermal versus super voltage pulsed radiofrequency application in neuropathic post-mastectomy pain	Quantitative	PubMed
[21] Grasso, A. <i>et al.</i> , 2020	Ultrasound-Guided Interfascial Plane Blocks for Non-Anesthesiologists in Breast Cancer Surgery: Functional Outcomes and Benefits	Investigate the feasibility of performance of axillary lymphadenectomy using anterior serratus muscle plane block associated with intravenous sedation	Quantitative	SciELO
[22] Dinh, K. H. <i>et al.</i> , 2020	Post-operative Nausea and Analgesia Following Total Mastectomy is Improved After Implementation of an Enhanced Recovery Protocol	Identify the association between better control of nausea and vomiting and less use of opioids and postoperative pain	Quantitative and Qualitative	PubMed

## Continued

[23] McGugin, C. J. <i>et al.</i> , 2019	Enhanced Recovery Minimizes Opioid Use and Hospital Stay for Patients Undergoing Mastectomy with Reconstruction	Examined the effects of an enhanced recovery program on inpatient opioid and hospital length of stay for mastectomy patients	Quantitative	PubMed
[24] Azizoddin, D. R. <i>et al.</i> , 2023	Perioperative Sleep Disturbance Following Mastectomy: A Longitudinal Investigation of the Relationship to Pain, Opioid Use, Treatment, and Psychosocial Symptoms	Evaluate the relationship between the individual patient an surgical factors with greater sleep disturbance following breast surgery	Quantitative and Qualitative	PubMed
[25] Steinhorsdottir, K. J. <i>et al.</i> , 2020	Dexamethasone Dose and Early Postoperative Recovery after Mastectomy: A Double-blind, Randomised Trial	Compare the use of 24 and 8 mg of dexamethasone on early recovery after mastectomy	Quantitative	PubMed
[26] Calapai, M. <i>et al.</i> , 2023	Effects of Physical Exercise and Motor Activity on Oxidative Stress and Inflammation in Post-Mastectomy Pain Syndrome	Evaluate the effects of physical activity on the intensity and interference of chronic pain in the quality of life of women underwent mastectomy	Qualitative	PubMed
[27] Deng, C. <i>et al.</i> , 2022	Aromatherapy Plus Music Therapy Improve Pain Intensity and Anxiety Scores in Patients With Breast Cancer During Perioperative Periods: A Randomized Controlled Trial	Investigate the effect of perioperative aromatherapy or/plus music therapy on pain and anxiety level in women experiencing breast cancer surgery	Qualitative	PubMed
[28] Hasoon, J. <i>et al.</i> , 2021	Erector Spinae Plane Block for the Treatment of Post Mastectomy Pain Syndrome	Describe the utilization of erector spinae plane block for neuropathic breast pain after mastectomy	Qualitative	PubMed

its treatment usually involves the association of radiotherapy and/or chemotherapy with surgical approaches. Thanks to the great advances in science, with genetic mapping and sequencing [5], more diagnoses have been made and, over the years, there are more and more survivors of the disease [3] [6].

However, the treatment can leave marks on patients, reducing their quality of life, with high levels of anxiety and depression [7] [13]. Among these sequelae, one of the most reported and that greatly impacts women's functionality is persistent pain, especially in those undergoing mastectomy [4] [5] [8]. In this sense, the term Post-Mastectomy Pain Syndrome (PMPS) was established, defined by the International Association for the Study of Pain (IASP) as "chronic pain in the anterior wall of the chest, axilla and/or upper half of the arm, beginning after mastectomy or quadrantectomy and persisting for more than three months after surgery" [3] [4] [6] [14] [15]. Studies indicate that this pain after breast surgery occurs in more than 50% of women, being classified as moderate to severe [2] [8] [13] [16] [17].

The details of pathophysiology of this pain condition has not yet been elucidated, but it is known that it is multifactorial, with different etiologies [7] [8] [12]. Chief among these is neuropathic injury, where there is damage to the

nerves during surgery and/or radiation, with the intercostobrachial nerve being the most frequently affected [3] [5] [6] [18].

Injury to the nerve can occur intraoperatively, with retraction and malpositioning of the arm, leading to nerve compression, or postoperatively, with stretching and pressure from bruising and scarring [6]. However, neuromas formed by traction and/or laceration also justify neuropathy, as they function as a pacemaker, resulting in continuous firing.

Other causes of pain are musculoskeletal (such as scapulothoracic bursitis, shoulder impingement syndrome, and glenohumeral adhesive capsulitis), myofascial [3], lymphedema (usually due to associated radiotherapy or lymphadenectomy), and nociplastic [5].

Post-Mastectomy Pain Syndrome can occur in any patient undergoing breast surgery. However, some responsible factors are already known by increasing the risk of developing the condition, such as young people, pre-existing depression and anxiety [13], sleep disorders, high body mass index (BMI), bilateral mastectomy and surgical technique (manipulation of nerves and axillary lymph node resection have greater chances of compromise) [1] [2] [7] [8] [11] [17] [19]. In addition, several studies point out that inadequate control of acute pain after surgery is strongly related to the persistence and chronicity of pain [1] [10] [11] [13], since prolonged stimulation of nociceptive neurons contributes to the core awareness [11].

The diagnosis is clinical, with a physical examination being mandatory [20]. Thus, by excluding non-neuropathic causes of pain such as infection, musculoskeletal or oncological recurrence, neuropathy is defined [12]. Complementary tests can be used, such as magnetic resonance imaging or positron emission tomography to check for brachial plexus infiltration or fibrosis, and electromyography to assess sensory and motor delay in the brachial plexus [20].

Patients often describe the pain as continuous or intermittent, burning and/or pinpoint, associated with palpable allodynia and hyperalgesia [8] [16] [18]. Furthermore, it is influenced by temperature variations, with periods of worsening and improvement [15]. It may also be associated with lymphedema, numbness, stiffness, and limited range of motion of the shoulder [9].

Therefore, it is clear that post-mastectomy pain has a negative impact on quality of life, with significant impairment of functionality and psychosocial distress [1] [9]. Research indicates that this impairment has a greater influence on the routine of young women, with greater loss of work days and difficulties in caring for children. Furthermore, the occurrence of pain in cancer survivors represents an ongoing memory of the disease and treatment and is seen by some as a sign of residual disease, leading to fears of worsening or recurrence [9].

That said, it is extremely important to treat the various approaches to Post-Mastectomy Pain Syndrome, ranging from clinical and minimally invasive measures to surgeries and complementary methods [3] [4].

Initially, it is interesting to address measures aimed at preventing the condition, which mainly involves the reduction of immediate postoperative pain.



With less acute pain, the chances of chronic pain are also reduced. Among these measures, the association of intraoperative fentanyl with ultrasound-guided peripheral block stands out, since high doses of opioids activate N-methyl-D-aspartate (NMDA), which has a pro-nociceptive effect and consequently causes hypersensitivity [8] [13] [21]. The most commonly performed blocks are PEC 2, with blockade of the lateral and medial pectoral, intercostal, and intercosto-brachial nerves [4] [14] [19]. With this association, patients feel less post-surgical pain, have fewer adverse effects (especially nausea and vomiting), and have shorter hospital stays [11] [21] [22] [23].

This practice is included in the enhanced post-surgical recovery protocol (*ERAS—Enhanced Recovery After Surgery*), which also indicates the use of intra-operative antiemetics, warns about the use of volatile anesthetics and the importance of a good doctor-patient relationship, with pre-operative counseling, in which the patient feels safe with the procedure and the team [10] [11] [22] [23] [24].

Studies also indicate that the administration of 8 mg of dexamethasone concomitantly with analgesics contributes to reducing the inflammatory process, resulting in less intense pain [25]. The main objective of these behaviors is to promote a better quality of recovery [22].

Continued use of opioids for more than two weeks after surgery is associated with sleep disturbances, which negatively affects recovery, increasing the risk of pain persisting [13].

However, even with all these precautions, the pain can become chronic, determining the post-mastectomy pain syndrome. In these cases, treatment is complex, involving a pain specialist, plastic surgeon (if reconstruction is necessary) [6], physiotherapist, among others [12]. Treatment refractoriness is mainly associated with multiple facets of pain. Neuroinflammation leads to the release of inflammatory markers. The values of interleukin (IL)- $1\beta$ , IL-6 and IL-10 and C-reactive protein (CRP) can be used as prognostic predictors of long-term pain, being higher in more chronic pain [8] [13] [26] [27]. In addition, there is an increase in cortisol and a decrease in prolactin and CD4, CD8 and CD56 lymphocytes [8].

In these cases, first-line treatment is anti-neuropathic drugs such as tricyclic antidepressants, amitriptyline, serotonin-norepinephrine reuptake inhibitors, duloxetine, and gabapentinoids [3] [15]. If adequate analgesia is not available, tramadol and peripheral nerve blocks are considered second-line. Opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) do not usually work well [8].

In addition, corticosteroids may be useful when neuroma is present, in which the medication contributes to stimulus inhibition, generating rapid or delayed pain relief [16] and topical capsaicin at 0.075% improves burning sensation [3].

Associated with conventional treatments, complementary techniques have been proposed, with good analgesic results. Cognitive behavioral therapy (CBT), physical exercise, acupuncture, aromatherapy and music therapy are some examples.

The great influence of depression, anxiety and sleep disorders makes clear the need for a psychosocial approach, with CBT having a primordial role. [3] [10] [11]. Physical activity is essential for providing better recovery of functional capacities, strength and flexibility, as well as improvement of pain, asthenia and reduction of hematological alterations such as neutropenia, anemia and thrombocytopenia, and stretching and exercises should aerobic and resistance exercises should be integrated into treatment as soon as possible after surgery [9] [26].

Studies indicate that patients who underwent acupuncture sessions for four weeks improved physical health problems and perceived general health [10]. In addition, transcutaneous electrical stimulation at acupuncture points before anesthetic induction in patients undergoing mastectomy is related to a decrease in opioid consumption and the incidence of chronic pain six months after surgery, and should be a considerable conduct [17].

Aromatherapy and music therapy, which have already been used for other clinical conditions, are associated with reduced anxiety, pain and IL-6 levels, with enhanced results when both techniques are combined [27].

However, in some cases, the pain remains refractory to such procedures, requiring more invasive approaches, such as autologous fat grafting in an area of cicatricial retraction with pain and nerve entrapment [12], blockade of the erector spinae plane (ESP) [28], excision of neuroma, transplantation of lymph nodes from the inguinal region to the axillary region (in cases of lymphedema) and pulsed radiofrequency [3]. Studies show that thoracic nerve blocks lead to immediate improvement in pain, but for a short period of time, less than one month [3] [4].

One study aimed to validate a scale to determine a woman's risk of having moderate or severe post-mastectomy pain so that, in these cases, more intense analgesia could be performed. In this scale, eight points would be assessed: age at the time of surgery, BMI, depression, stress, previous use of pain medication, neoadjuvant chemotherapy, extent of surgery (single or bilateral) and reconstruction (yes or no) [11]. This measure has not yet been adopted as a protocol, but it is a possibility for physicians to adopt a more active posture, avoiding the onset of post-mastectomy pain syndrome and its consequences for women.

## 6. Conclusions

With the advancement of treatments for breast cancer, more and more women are surviving the disease. Therefore, it is essential that efforts are made to understand the marks that therapies leave on patients, so that they can be minimized and women can return to their activities and functionality, with quality.

Currently, there are several measures that aim to reduce the chances of the patient developing post-mastectomy pain syndrome, most of which are described in ERAS, including the use of antiemetics and the association of peripheral blockade with intraoperative anesthesia, aiming to reduce the consumption of opioids and, as a consequence, less nausea and vomiting, shorter hospital stay

and lower risk of postoperative hyperalgesia. This is because the better the acute pain control, the lower the chances of pain chronification.

When it comes to treating post-mastectomy pain, several drugs are available; tricyclic antidepressants (amitriptyline, duloxetine) and gabapentinoids are included in the first line of treatment. In the absence of satisfactory analgesia, tramadol and peripheral blocks are options. For some patients, it may also be necessary to use more invasive measures, such as autologous fat grafting, excision of neuromas or lymph node transplantation.

Concomitant to these measures, complementary behaviors that are extremely valuable include cognitive behavioral therapy, which will help with the patient's psychological aspect, reducing anxiety and assisting in the way they view the painful condition, and the practice of physical activities, which will provide improved mobility and asthenia.

It is notable that there are several viable approaches, and the healthcare team must be attentive to the patient's needs and provide assistance not only during the presence of the disease, but also after the end of treatment.

Thus, the need for a better understanding of post-mastectomy pain syndrome and its approach is evident, as well as the adoption of new measures and/or multidisciplinary approaches, which will certainly bring greater comfort and a better prognosis for the population addressed.

Furthermore, it is also important to highlight the need for more research, especially with regard to the combination of drugs with alternative therapies, aiming to expand the evidence of the benefits related to these associations.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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