



## Precautions against lymphedema in women with breast cancer after axillary dissection: scoping review

*Precauções para linfedema em mulheres acometidas por câncer de mama pós esvaziamento axilar: revisão de escopo*

*Precauciones para el linfedema en mujeres con cáncer de mama después del vaciamento axilar: revision de alcance*

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### ABSTRACT

**Objective:** to identify and map strategies recommended for prevention of lymphedema in patients after axillary dissection during breast cancer treatment. **Method:** this scoping review was conducted in August 2019 across eight databases and eight gray literature data sources. The final sample comprised 13 journal articles that met eligibility criteria. **Results:** the studies, most of which were randomized, conducted in North America, and offered Level 1a evidence. None of the studies reviewed found traditionally employed preventive measures, such as limiting weight training or avoiding venipuncture and blood pressure measurements, to be effective. Evidence indicated that controlling modifiable lymphedema-related risk factors – namely high BMI (> 25 kg/m<sup>2</sup>) and chemotherapy administration in the ipsilateral arm – was a preventive measure. **Conclusion:** no significant evidence was reported for traditionally recommended preventive measures against lymphedema, and modifiable factors figured prominently among risk factors for lymphedema.

**Descriptors:** Breast Neoplasms; Lymphedema; Risk Factors; Precaution.

### RESUMO

**Objetivo:** identificar e mapear estratégias preconizadas para prevenção de linfedema em pacientes submetidas a esvaziamento axilar em tratamento do câncer de mama. **Método:** revisão de escopo realizada em agosto de 2019 considerando oito bases de dados e oito bases da literatura cinzenta. A amostra final foi composta por 13 artigos, selecionados de acordo com critérios de elegibilidade. **Resultados:** os estudos foram predominantemente randomizados, com nível de evidência 1a, e realizados na América do Norte. Medidas preventivas tradicionalmente utilizadas, como limitar exercícios com carga ou evitar punção venosa e aferição de pressão arterial, não se demonstraram efetivas em nenhum dos estudos encontrados. Foi evidenciado como medida preventiva o controle dos fatores de risco modificáveis associados ao linfedema: IMC elevado (> 25 kg/m<sup>2</sup>) e quimioterapia administrada no braço ipsilateral. **Conclusões:** não foram apresentadas evidências significativas para medidas cotidianamente preconizadas na prevenção do linfedema, e fatores de risco modificáveis se destacaram entre os riscos para seu desenvolvimento.

**Descritores:** Neoplasias da Mama; Linfedema; Fatores de Risco; Precaução.

### RESUMEN

**Objetivo:** identificar y mapear las estrategias recomendadas para la prevención del linfedema en pacientes después de una disección axilar durante el tratamiento del cáncer de mama. **Método:** esta revisión de alcance se realizó en agosto de 2019 en ocho bases de datos y ocho fuentes de datos de literatura gris. La muestra final comprendió 13 artículos de revistas que cumplieron con los criterios de elegibilidad. **Resultados:** los estudios, la mayoría de los cuales fueron aleatorios, se realizaron en Norteamérica y ofrecieron evidencia de Nivel 1a. Ninguno de los estudios revisados encontró que las medidas preventivas empleadas tradicionalmente, como limitar el entrenamiento con pesas o evitar la punción venosa y las mediciones de la presión arterial, sean efectivas. La evidencia indicó que el control de los factores de riesgo relacionados con el linfedema modificables, a saber, un IMC alto (> 25 kg / m<sup>2</sup>) y la administración de quimioterapia en el brazo ipsilateral, era una medida preventiva. **Conclusión:** no se informó evidencia significativa de las medidas preventivas recomendadas tradicionalmente contra el linfedema, y los factores modificables figuraron de manera prominente entre los factores de riesgo para el linfedema.

**Descriptores:** Neoplasias de la Mama; Linfedema; Factores de Riesgo; Precaución.

## INTRODUCTION

Breast cancer is a generic term used to designate a complex group of malignant neoplasms that originate in the mammary glands, with potential for invasion of tissues and organs. It corresponds to the most common cancer in women in the world, thus constituting an important public health problem responsible for the death of thousands of people annually<sup>1,2</sup>.

In 2017, the National Cancer Institute (*Instituto Nacional de Câncer*, INCA) recorded 16,927 deaths due to cancer in Brazil and, in 2018, it estimated the incidence of 59,700 breast cancer cases, with significant prevalence in females<sup>3</sup>.

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A number of studies<sup>2,4,5</sup> demonstrate an increase in the mean survival rate, around 80% - 90% for these patients, and highlight progress in survival over five years due to the increase in the cure rate and the evolution in the forms of treatment.

The treatment of malignant breast neoplasms commonly includes isolated or concomitant use of chemotherapy, hormone therapy, radiation therapy and/or surgery. Conservative surgery is the most widely used therapeutic option, especially in the early stages of the disease, with high rates of partial and/or complete resolution<sup>6,7</sup>. It can be classified as partial mastectomy, segmental mastectomy, tumorectomy or quadrantectomy.

Some cases, however, are indicated for radical surgery, depending on clinical factors suggestive of poor prognosis (tumor size, presence of metastatic lymph nodes, among others). The types of surgical treatment mentioned above may or may not be associated with axillary emptying or sentinel lymph node biopsy, a method traditionally used even in cases of negative armpit and very relevant for staging in defining the type of adjuvant treatment to be performed<sup>7-9</sup>.

Nevertheless, important complications related to "axillary emptying" are evidenced, including paresthesia, joint dysfunction and edema, conditions that are directly associated with greater morbidity and that can contribute to the development of emotional problems, as well as interfering in the life activities of these patients<sup>9,1</sup>.

In addition, it is shown that patients are prone to the risk of lymphedema related to axillary lymphadenectomy, a potentially serious and disabling condition caused by the leakage of lymph into the interstitial space. This causes a chronic inflammatory process that can affect the upper limb, the trunk and/or the breast, with psychosocial and functional implications, and a direct interface with the patients' quality of life<sup>8,11</sup>.

In this sense, it is pertinent to determine methods to prevent lymphedema. However, there are still important gaps regarding preventive measures and management guidelines for these patients. Thus, it is necessary to clarify and determine strategies to prevent this disease, considering its severity and risks to patients who are subjected to axillary emptying<sup>12-14</sup>.

In view of the above, the present study aims to identify and map recommended strategies for the prevention of lymphedema in patients undergoing axillary dissection associated with the treatment of breast cancer.

## METHOD

This is a scoping review built according to the model of the Joanna Briggs Institute, Reviewer's Manual, with the theoretical guidelines of Arksey and O'Malley. This method seeks to map and evidence a collection of studies in the scientific literature on a given subject matter<sup>15</sup>.

To elaborate the research question, the PCC strategy was followed: P- Population, C- Concept and C- Context<sup>15</sup>. In the present study, Population: Patients with breast cancer, Concept: Standard precautions for lymphedema, and Context: Axillary emptying. In view of this, the following research question was created: What precautions are recommended for cancer patients after axillary emptying?

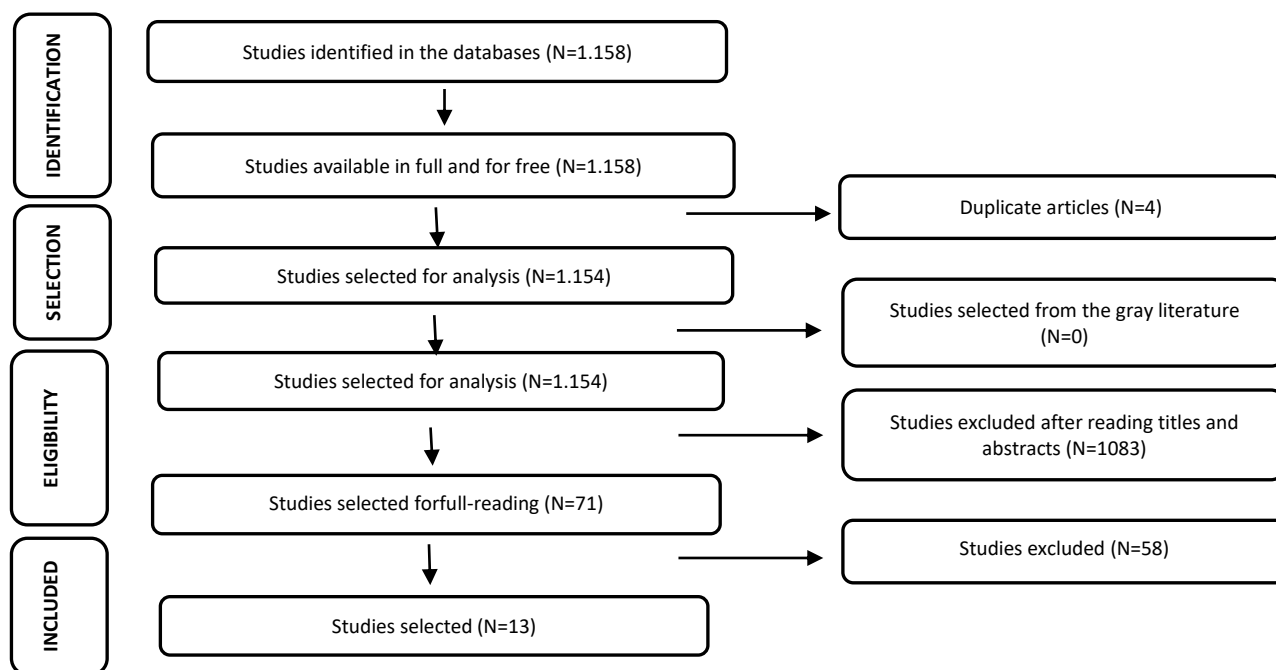
For the initial stage of data collection, it was necessary to identify the relevant terms in the Health Sciences Descriptors (*Descritores em Ciências da Saúde*, DECS) and Medical Subject Headings (MeSH), as well as the main keywords used in studies on the content of interest cataloged in the National Library of Medicine (PubMed) and in the Cumulative Index of Nursing and Allied Health Literature (CINAHL)<sup>15</sup>.

To develop the search strategy, only the indexed keywords Lymphedema risk (#1), Breast cancer (#2), Axillary dissection (#3), and the Boolean operator "AND" were applied. With the execution of the #1 AND #2 AND #3 combination, it was possible to find numerous studies.

The search for the materials was carried out in the PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), SCOPUS, COCHRANE, WEB OF SCIENCE, PSYCHINFO, Latin American and Caribbean Literature in Health Sciences (*Literatura Latino-Americana e do Caribe em Ciências da Saúde*, LILACS) and Education Resources Information Center (ERIC) databases. With regard to searches in the gray literature, the following were consulted: CAPES Thesis and Dissertation Portal, The National Library of Australia's Trove (Trove), Academic Archive Online (DIVA), DART-Europe E-Theses Portal, Electronic Theses Online Service (ETOS), Open Access Scientific Repository of Portugal (*Repositório Científico de Acesso Aberto de Portugal*, RCAAP), National ETD Portal and Theses Canada. All searches took place in August 2019.

The inclusion criteria were correspondence with the objective of the present study and availability of publications in full through the Portal of Journals of the Federal University of Rio Grande do Norte (*Universidade Federal do Rio Grande do Norte*, UFRN), in electronic media in Portuguese, Spanish, English or French. Studies in the form of reviews, editorials, case reports, letters to the editor and opinion articles were excluded, as well as duplicate documents.

The articles found were pre-selected from reading their titles and abstracts. Materials that belonged to the theme and that presented content in agreement with the objective were read in full for the final selection of the studies, as shown in Figure 1.



**FIGURE 1:** Flow diagram of the selection of publications Natal, RN, Brazil, 2019

As extraction strategy, all articles selected for the final sample were inserted into a spreadsheet in Microsoft Excel 2010, divided into: type of study, year of publication, country of origin, objective, population and results. For the present study, ethical contemplation was not necessary, as the articles are publicly available.

After applying the aforementioned inclusion and exclusion criteria, 13 articles were selected, and the data were compiled in a spreadsheet for general analysis of the information. The levels of evidence listed according to the JBI<sup>(15)</sup> demonstrate the reliability strength of the studies, of which 46.2% were level 1.a, 15.3% 2.c, 30.8% 3.c and 7.7% 3.d.

## RESULTS

Figure 2 lists the final number of files used in the research, as well as their titles, years of publication and respective countries. No materials were found in the gray literature, so those selected in the databases were exclusively articles, which make up a total of 13 studies.

ARTICLE	TITLE	YEAR	COUNTRY
Article 1	<i>Heavy-Load Lifting: Acute Response in Breast Cancer Survivors at Risk for Lymphedema</i>	2018	Denmark
Article 2	<i>Association Between Precautionary Behaviors and Breast Cancer–Related Lymphedema in Patients Undergoing Bilateral Surgery</i>	2017	USA
Article 3	<i>Risk factors for lymphoedema in women with breast cancer: A large prospective cohort</i>	2016	Australia
Article 4	<i>Impact of Ipsilateral Blood Draws, Injections, Blood Pressure Measurements, and Air Travel on the Risk of Lymphedema for Patients Treated for Breast Cancer</i>	2016	USA
Article 5	<i>Physical activity for the affected limb and arm lymphedema after breast cancer surgery</i>	2009	Norway
Article 6	<i>Randomized Controlled Trial of Weight Training and Lymphedema in Breast Cancer Survivors</i>	2006	USA
Article 7	<i>Fatores associados ao linfedema em pacientes com câncer de mama</i>	2011	Brazil
Article 8	<i>A randomized cross-over trial to detect differences in arm volume after low- and heavy-load resistance exercise among patients receiving adjuvant chemotherapy for breast cancer at risk for arm lymphedema: study protocol</i>	2016	Denmark
Article 9	<i>Effect of air travel on lymphedema risk in women with history of breast cancer</i>	2010	Canada
Article 10	<i>Lifestyle Risk Factors Associated with Arm Swelling Among Women with Breast Cancer</i>	2012	USA
Article 11	<i>Prevalence of Lymphedema in Women With Breast Cancer 5 Years After Sentinel Lymph Node Biopsy or Axillary Dissection: Patient Perceptions and Precautionary Behaviors</i>	2008	USA
Article 12	<i>Progressive Resistance Training to Prevent Arm Lymphedema in the First Year After Breast Cancer Surgery: Results of a Randomized Controlled Trial</i>	2019	Denmark
Article 13	<i>Case-Control Study to Evaluate Predictors of Lymphedema After Breast Cancer Surgery</i>	2009	USA

**FIGURE 2:** Characterization of the publications regarding year of publication and country Natal, RN, Brazil, 2019.

The articles that made up the final sample were published between 2006 and 2019. Seven (53.8%) are from North America, four (30.8%) from Europe, one (7.7%) from South America and one (7.7%) from Oceania.

The main methods found were Randomized Clinical Trials (46.2%), Cohort (46.2%) and Case-control (7.7%). With reference to the databases, five were selected in PubMed (38.4%), five in SCOPUS (38.4%), two in LILACS (15.5%) and one in Web of Science (7.7%).

With regard to the objectives of the studies analyzed, the majority (38.46%) sought to assess the incidence of lymphedema after axillary lymphadenectomy (uni- or bi-lateral/partial or total) in women affected by breast cancer. Other studies (61.54%) evaluated the influence of factors associated with lifestyle and alternative methods on the occurrence and severity of lymphedema in upper limbs after breast cancer-related lymphadenectomy.

In addition, the results that refer to the main factors associated and not associated with the development of lymphedema related to breast cancer were also evaluated. The findings are compiled and presented in Figure 3.

Articles	Factors not associated with Lymphedema	Factors associated with the development and worsening of Lymphedema
Article 1	Exercises with load and those of daily life.	High BMI (above 25).
Article 2	Blood pressure measurement, blood collection, air travel (regardless of quantity and duration), injections and infusions.	High BMI (greater than 25) and taxane-based chemotherapy administered to the ipsilateral limb.
Article 3	Blood pressure measurement, blood collection, air travel, injections and daily life activity.	High BMI (greater than 25) and taxane-based adjuvant chemotherapy in the homolateral limb arm.
Article 4	Blood pressure measurement, blood collection, air travel, and injections.	High BMI (greater than 25), cellulite on the upper limb.
Article 5	Exercises with load and activities of daily living.	High BMI (above 25).
Article 6	Variable resistance exercises with free load.	High BMI (above 25).
Article 7	Reduced movement of the homolateral limb, schooling, number of children.	Chemotherapy and radiotherapy on the homolateral side, radical mastectomy, extension of the axillary dissection, thrombosis and high BMI (greater than 25).
Article 8	Air travel, exercises with load.	Chemotherapy administered to the limb, radiotherapy to the armpit in which emptying was performed.
Article 9	Venipuncture, construction of arteriovenous fistula in patients undergoing hemodialysis.	High BMI (greater than 25), infection in the limb (cellulitis).
Article 10	Weightlifting, venipuncture, blood pressure check.	Sauna use, Hypertension, Obesity.
Article 11	Arm where surgery was performed, tight clothing.	High BMI (greater than 25), infection (cellulitis), injury to the homolateral arm and type of surgery performed.
Article 12	Leg press, elbow flexion and shoulder abduction exercises.	Armpit radiation, number of positive lymph nodes, high BMI (greater than 25).
Article 13	Resistance exercises, air travel.	Axillary radiation therapy, high BMI (greater than 25), active cancer status.

**FIGURE 3:** Synthesis of the main results of the articles selected for the final sample (N=13). Natal, RN, Brazil, 2019.

The main guidelines observed in the studies with regard to the prevention of lymphedema were as follows: avoid exposure to heat; do not cut a cuticle or bite a nail; restrict use of limb overload; avoid blood collection, application of vaccines, infusions; do not check blood pressure in the ipsilateral arm; and wear compressive clothing during air travel.

## DISCUSSION

In view of the results found in the present scoping review, it is possible to verify that most of the studies were carried out from the year 2006. This can be related to the increasing incidence of breast cancer cases worldwide and to the introduction of personalized therapies that had long-term complications, with extensive surgery and removal of lymphatic chains<sup>2</sup>.

North America had the largest number of studies developed, given that it may be associated with the high investment in health and in research that enables early diagnoses, since the rapid diagnosis for lymphedema is a key to an effective treatment<sup>16</sup>.

Thus, to identify the preventive measures that are related to the development of lymphedema, studies with robust methodologies and high levels of evidence are necessary so that precautions are assertively given, with well-defined risk factors<sup>17</sup>.



Recent evidence composed a guideline<sup>18</sup> that demonstrated the prevalence of risk reduction actions based only on the pathophysiology of lymphedema in a non-personalized way. However, in view of the advances in cancer treatment, these conducts go through questions about their effectiveness and the need for excessive care, since there is not enough evidence to support these actions that generate anxiety and change lifestyle unnecessarily<sup>8</sup>.

Thus, lymphedema has been associated with numerous variables (number of lymph nodes removed during surgery, high BMI, among others), and the risk factors that demonstrate significant impacts are not yet clearly and objectively compiled.

Based on the results of each selected study, listed in Figure 3, it is possible to identify the main current recommendations and the factors that can be linked to the pathogenesis and prevention of lymphedema. In the next paragraphs, individual discussions on measuring blood pressure, performing venipuncture, wearing compressive clothing during air travel, as well as performing daily activities and exercises with load<sup>11</sup> are presented.

#### **Measurement of blood pressure in the ipsilateral limb**

For many years, it was believed that women who underwent breast surgery with axillary emptying should avoid measuring the pressure on the ipsilateral limb due to the compression exerted on the arm to favor the leakage of the lymph. In these situations, the reading could be done on the lower limbs, although at risk of inaccuracies<sup>19</sup>.

On the other hand, this data is in agreement with the findings of the present scope review, so that clinical trials and meta-analysis studies<sup>9,20,22,23</sup> demonstrate the non-relationship of measurement in the homolateral arm with the increase in arm edema or effects to long-term and increasing risk for lymphedema. This and other unsubstantiated precautions generate distress in women who survive breast cancer for fear of developing complications.

#### **Venipuncture in the homolateral limb**

Venipuncture is considered an invasive procedure with risk of infection, and for long periods it was avoided by women who underwent axillary lymphadenectomy due to the risk of lymphedema, information that is contrary to the findings of the present study.

The risk factors that are closely linked to this complication, including cellulite and infections, as shown in the studies<sup>20,24,25</sup>, are adversities that can be associated with inadequate care with the limb or complications of the inappropriate technique.

However, high-evidence studies<sup>19,20,22,23</sup> demonstrate that the isolated puncture procedure performed correctly does not predispose these patients to risk, making collection impossible because it is the homolateral limb, since the recommendations have minimal relation to development lymphedema. In addition, a randomized study<sup>24</sup> did not find a relationship of increased risk for lymphedema, after lymphadenectomy, in procedures for the construction of arteriovenous fistula and periodic puncture.

#### **Use of compressive clothing during air travel**

The relationship between air travel and the development or worsening of lymphedema in women undergoing axillary emptying was explained for a long time by the sudden pressure difference, kept lower in the cabin. These data are not in line with the information found in the present scope review<sup>6,14</sup>.

The recommendation for this scenario was the use of compressive clothing during flights<sup>6,14</sup>. However, cohort studies<sup>19,20,22,26,27</sup> do not demonstrate an association between air travel and lymphedema, and do not show significance in the number of hours elapsed and the number of flights.

#### **Carrying out activities of daily living and physical exercises with load**

Countless women subjected to axillary lymph node dissection as part of the treatment for breast cancer report feeling of heaviness and limited range of motion, which leads to avoid limb movement. Linked to this, poorly supported recommendations that have been suggested for years denote restrictions on the use of loads and activities of daily living with greater overload<sup>28</sup>.

However, several studies<sup>22,29-33</sup> show that exercise helps lymphatic flow, as well as increasing tissue flexibility, muscle strength gain and muscle functions, without increased risk for lymphedema. Thus, the maintenance of activities of daily living, sports and controlled exercises with load is indispensable for reducing anxiety and feelings of anguish, with an improvement in the quality of life of these patients.





In view of the data presented, the studies highlight the risk factors of greatest clinical relevance in the development of lymphedema: high BMI, axillary radiotherapy in the limb of lymph node dissection, taxane-based chemotherapy administered to the homolateral limb, use of sauna, infections of the arm and presence of cellulite.

## CONCLUSION

Given the findings, it is noted that the main precautions for patients who underwent axillary emptying related to breast cancer refer to the control of BMI and blood pressure, decreased risk of infection and not applying chemotherapy and radiotherapy to the homolateral limb to the surgery.

In addition, the results of the study promote innovation, dissemination and dissemination of a theme that is of great relevance to Nursing, since it lists and maps the main precautions recommended for patients undergoing axillary emptying. In addition, it summarizes risk factors that are concatenated with the procedure and demand care from the multidisciplinary team, from Nursing and from the patient.

That said, it is emphasized that the study constitutes a scoping review and, therefore, only lists findings from the scientific literature, without having the reliability to prove such results. Thus, there is a demand for experimental research studies in order to prove precautions and risk factors that can influence the quality of life and safety of patients undergoing axillary emptying related to breast cancer.

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