



# Prevalence of lymphedema after mastectomy in women living with breast cancer: a systematic review of the influence of immediate reconstruction

*Prevalência de linfedema após mastectomia em portadoras de câncer de mama: uma revisão sistemática acerca da influência da reconstrução imediata*

RAFAEL VILELA EIRAS RIBEIRO<sup>1,2\*</sup>

### ■ ABSTRACT

This study aimed to analyze, through systematic review of literature, the influence of immediate reconstruction on the prevalence of lymphedema after mastectomy, in women living with breast cancer. The analysis considered the most relevant studies originally published, in any language, up to August 2018, indexed on the databases of the US National Library of Medicine, Cochrane Central Register of Controlled Trials, Web of Science, and Scientific Electronic Library Online. The sample comprised 10 publications that met the established criteria for inclusion and exclusion, including 2,425 patients who were subjected to mastectomy alone, and 2,772 patients who were subjected to mastectomy associated with immediate reconstruction of the breast. The prevalence of lymphedema was 20.95% in patients who had been subjected to mastectomy alone (n = 508), and 5.23% among those patients who were subjected to mastectomy associated with immediate reconstruction of the breast (n = 145), the difference being statistically significant ( $p < 0.001$ ). We concluded that mastectomy, when associated with immediate breast reconstruction, has a positive influence on the prognosis of patients living with breast cancer, thereby providing a much lower rate of lymphedema when compared with mastectomy alone.

**Keywords:** Mastectomy; Breast cancer-related lymphedema; Mammoplasty; Breast neoplasms; Excision of lymph nodes.

Institution: Santa Casa de Montes Claros,  
Montes Claros, MG, Brazil.

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<sup>1</sup> Santa Casa de Montes Claros, Montes Claros, MG, Brazil.

<sup>2</sup> Aspirante em Treinamento, Sociedade Brasileira de Cirurgia Plástica, São Paulo, SP, Brazil.

## ■ RESUMO

Este estudo objetivou analisar, por meio de uma revisão sistemática da literatura, a influência da reconstrução imediata na prevalência de linfedema após mastectomia em pacientes portadoras de câncer de mama. Foram analisados os mais relevantes estudos publicados originalmente em qualquer idioma até agosto de 2018, indexados às bases de dados US National Library of Medicine, Cochrane Central Register of Controlled Trials, Web of Science e Scientific Electronic Library Online. A amostra foi composta por 10 publicações que se adequaram aos critérios de inclusão e exclusão estabelecidos, incluindo 2.425 pacientes submetidas a apenas mastectomia e 2.772 pacientes submetidas à mastectomia associada à reconstrução imediata da mama. A prevalência de linfedema foi 20,95% nas pacientes submetidas a apenas mastectomia (n = 508) e de 5,23% nas pacientes submetidas à mastectomia associada à reconstrução imediata (n = 145), havendo diferença estatisticamente significativa ( $p < 0,001$ ). Concluiu-se que a mastectomia associada à reconstrução imediata influencia positivamente o prognóstico das pacientes portadoras de câncer de mama, proporcionando um índice significativamente menor de linfedema, quando comparada à realização de apenas mastectomia.

**Descritores:** Mastectomia; Linfedema relacionado a câncer de mama; Mamoplastia; Neoplasias da mama; Excisão de linfonodo.

## INTRODUCTION

In Brazil, it is estimated that breast cancer shall be the most common cancer among women in 2018 and 2019, accounting for 29.5% of all new cases of cancer in the country<sup>1</sup>. The treatment of patients with breast cancer, and therefore this cancer's aggressiveness, is set by the characteristics of the illness at the time of diagnosis. The main interventions that can be carried out, whether singly or in combination, are surgery (conservative surgery or mastectomy), radiotherapy, chemotherapy, and hormone therapy<sup>2</sup>.

Among the complications that occur after surgery for breast cancer, the most common one is lymphedema, a chronic condition that is brought about by the presence of a protein-rich fluid in the interstitial space<sup>3-6</sup>. The onset of lymphedema can happen immediately after surgery, in rare cases, or occur years after treatment<sup>6-10</sup>.

The etiology and risk factors for lymphedema seem to result from several different factors, which are not totally known. In general, it is well known that the main risk factors are: lymphadenectomy and/or axillary radiotherapy; obesity; and invasive procedures on limbs on the same side as the breast cancer<sup>11,12</sup>.

Whenever mastectomy is recommended, breast

reconstruction is also considered and can be performed either immediately or after the initial procedure (late breast reconstruction)<sup>13</sup>. However, considering the fall in morbidity provided by breast reconstruction carried out immediately after mastectomy, thereby reducing the surgical procedure and increasing patient satisfaction, it is important to identify the rate at which lymphedema occurs when this type of surgical procedure is performed.

## OBJECTIVE

This study aimed to analyze, through systematic review of literature, the influence of immediate breast reconstruction on the prevalence of lymphedema after mastectomy, among patients with breast cancer.

## METHODS

To comply with the proposed objective, we used a method based on the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA)<sup>14</sup> guideline for systematic reviews. We analyzed the most relevant studies that were originally brought out in any language, up to August 2018, but which were in some way indexed by the databases: US National Library

of Medicine (PubMed), Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and Scientific Electronic Library Online (SciELO), where the searches were carried out.

Seeking to choose high-quality studies of scientific evidence, we sought meta-analyses and randomized controlled clinical trials (RCCTs) on human subjects, without any restrictions as to the year of publication.

The following key words have been used, in different combinations: “lymphedema”, “lymphoedema”, “postmastectomy”, “mastectomy”, “breast cancer surgery”, “prevalence”, and “incidence”.

Criteria for inclusion and exclusion were applied, as set out in Chart 1.

The selection of the publications was first made based on an analysis of the title and of the abstract of the studies obtained resulting from the searches (Stage 1), then moving on to the elimination of duplicate results obtained in the different databases as researched (Stage 2). Afterwards, the complete versions of the publications were read, with the application of the criteria of inclusion and exclusion (Stage 3), seeking to select the publications to be included in the sample.

We must point out that the sample for this study

has included all the studies that have enabled the collection of data on the prevalence of lymphedema in female patients with breast cancer, specifically after mastectomy, or in cases of mastectomy associated with immediate breast reconstruction, or comparative studies considering these two surgical approaches. The exclusion criteria were the same as those used by Menezes et al<sup>15</sup>, that addressed late breast reconstructions, as also any studies in which lymphedema occurred only in a cumulative way, not allowing the collection of data regarding the total number of patients who developed this disease<sup>9,16</sup>.

In the publications included in the study sample, data were collected regarding the type and the number of surgical operations, the mean age of the patients, the method used for diagnosis, the period of monitoring, criteria for the identification of lymphedema, and the number of patients who exhibited this disorder. This data were then subjected to a meta-analysis for the establishment of the results of this study.

The statistical analysis of data, comparing the prevalence of lymphedema between mastectomized patients who had and had not been subjected to immediate breast reconstruction, was made using the software SPSS for Windows 15 (IBM SPSS Software,

**Chart 1.** Criteria for inclusion and exclusion of publications.

Criteria for Inclusion		
Delineation	•	RCCT
•	Meta-analysis	
•	Series of cases	
Sample	•	Humans
Intervention	•	Mastectomy only
•	Mastectomy associated with immediate reconstruction	
•	Comparison between the approaches as mentioned	
Period of publication	•	Unspecified
Language	•	Undefined
Criteria for Exclusion		
Delineation	•	Poorly explained and/or incomprehensible methodology
•	Case report	
•	Review of the literature	
Intervention	•	Mastectomy associated with late breast reconstruction
•	Non-surgical or unspecified treatment	
Method of publication	•	Abstract only

New York, USA), with use of the exact Fisher test with a significance level of  $p < 0.05$ .

## RESULTS

The searches carried out in different databases resulted in a sample of 248 different publications, which was reduced to 71 after the first stage of analysis (title and abstract), then further reduced to 33 after the second stage of analysis (removal of duplicates), and finally the group was further reduced, with only 10 publications remaining after the third and final stage of analysis (analysis of the full content of the articles); these met the criteria established for inclusion and exclusion.

Out of the 10 studies included in the sample of this meta-analysis, five addressed the prevalence of lymphedema in patients subjected to mastectomy alone<sup>10,17-20</sup>; two discussed the prevalence of lymphedema in patients subjected to mastectomy associated with immediate breast reconstruction<sup>6,21</sup>, while the final three studies compared both approaches<sup>22-24</sup>.

In all, the publications included in this sample included 2,425 patients who were submitted only to mastectomy, and 2,772 patients who had been subjected to mastectomy associated with immediate breast reconstruction; the mean ages of these two groups were 51.05 and 47.75 years respectively. The patients who were subjected only to mastectomy had a body mass index (BMI) of 25.97, while those patients who had mastectomy with immediate breast reconstruction had a mean BMI of 23.86 (Tables 1 and 2).

As we can see in Tables 3 and 4, lymphedema had a prevalence of 20.95% among patients who had mastectomy only (508/2,425), while in the case of those patients who had mastectomies associated with immediate breast reconstruction, the prevalence was 5.23% (145/2,772). The exact Fisher test showed a

statistically significant difference ( $p < 0.001$ ).

## DISCUSSION

Interest in the prognosis for patients undergoing treatment for breast cancer has increased considerably over the last few decades, both as a result of the increase in the number of new cases as also due to a search for better therapeutic options<sup>2,6,8-10</sup>. One of the factors that has triggered new studies is the occurrence of lymphedema in patients who have been subjected to mastectomy<sup>4-6,11,21,22</sup>, a topic that is still a cause for considerable controversy in the literature, especially with regard to factors related to etiology.

Here, we must point out that some factors of methodology could justify the controversy between the results obtained in different studies, such as the methods and the diagnostic criteria regarding lymphedema, as used by different authors. Most of the studies included in the sample used in this research used the method based on measurement of the circumference of the arm as a way to diagnose lymphedema<sup>10,17-19,22</sup>. There was a study that used a perometer together with arm measurement<sup>18</sup> or on an exclusive basis<sup>24</sup>; studies that used subjective evaluation by a specialist doctor (not using specific instruments, but just mentioning the appearance of clinical signs and symptoms)<sup>6,23</sup>; a study that made use of self-examination<sup>20</sup>; and another study that did not even mention the method used<sup>21</sup>.

As a criterion for diagnosis of lymphedema, most studies used an arm circumference of over 2 cm as the only criterion<sup>10,17,19,22</sup> or together with an increase of at least 10% in arm volume<sup>18</sup>. There was also one study that used the presence of hydroxy and a difference of at least 1.27 cm between arm circumferences<sup>20</sup>; four studies did not describe the diagnostic criterion in their methodologies<sup>6,21,23,24</sup>.

It is well known that lymphedema can appear

**Table 1.** General characteristics of the patients subjected to mastectomy only.

Study	Surgical operations (n)	Mean age (years)	Mean BMI (kg/m <sup>2</sup> )	Follow-up
Freitas Júnior et al. <sup>17</sup>	109	42.0	-	48 months
Petrek et al. <sup>20</sup>	263	52.3	-	20 years
Nesvold et al. <sup>18</sup>	263	55.0	26	Mean: 48 months
Park et al. <sup>19</sup>	450	50.0	-	24 months
Avraham et al. <sup>22</sup>	130	61	26	-
Card et al. <sup>23</sup>	549	-	28.6	Mean: 59 months
Lee et al. <sup>24</sup>	595	46.0	23.3	Mean: 53 months
Pandey & Shrestha <sup>10</sup>	66	-	-	12 months
TOTAL	2,425	-	-	-
MEAN	-	51.05	25.975	-

n: Number of cases; BMI: Body Mass Index; kg = kilos; m<sup>2</sup> =square meter; -: not specified in publication.

**Table 2.** General characteristics of the patients subjected to mastectomy and immediate breast reconstruction.

Study	Surgical operations (n)	Mean age (years)	Mean BMI (kg/m <sup>2</sup> )	Mean Follow-up
Avraham et al. <sup>22</sup>	186	45	24	-
Card et al. <sup>23</sup>	541	-	25.7	59 months
Crosby et al. <sup>21</sup>	1,499	50	25.7	56 months
Lee et al. <sup>24</sup>	117	45.0	21.9	53 months
Lee et al. <sup>6</sup>	429	43.0	22.0	45.3 months
TOTAL	2,772	-	-	-
MEAN	-	45.75	23.86	53.3 months

n: Number of cases; BMI: Body Mass Index; kg = kilos; m<sup>2</sup> =square meter; -: not specified in publication.

**Table 3.** Prevalence of lymphedema after mastectomy alone.

Study	Surgical operations (n)				Lymphedema			Total	
	Total	SM	SM+ALND	MRM	SM (n)	SM+ALND (n)	MRM (n)	n	%
Freitas Júnior et al. <sup>17</sup>	109	-	-	-	-	-	-	15	13.76
Petrek et al. <sup>20</sup>	263	-	-	-	-	-	-	128	48.67
Nesvold et al. <sup>18</sup>	263	77	-	186	6	-	37	43	16.35
Park et al. <sup>19</sup>	450	54	145	251	3	32	77	112	24.89
Avraham et al. <sup>22</sup>	130	59	71	-	8	28	-	36	27.69
Card et al. <sup>23</sup>	549	474	100	-	-	-	-	57	10.38
Lee et al. <sup>24</sup>	595	-	-	595	-	-	110	110	18.49
Pandey & Shrestha <sup>10</sup>	66	12	-	54	2	-	5	7	10.61
TOTAL	2,425	676	316	1,086	19	60	229	508	20.95

n: number of cases; -: data not supplied by the study; %: percentage; SM: simple mastectomy; SM+ALND: simple mastectomy associated with axillary lymph node dissection; MRM: modified radical mastectomy.

**Table 4.** Prevalence of lymphedema after mastectomy associated with immediate breast reconstruction.

Study	Surgical operations (n)				Lymphedema			Total	
	Total	SM	SM+ALND	MRM	SM (n)	SM+ALND (n)	MRM (n)	n	%
Avraham et al. <sup>22</sup>	186	93	93	-	6	23	-	29	15.59
Card et al. <sup>23</sup>	541	474	100	-	-	-	-	21	3.88
Crosby et al. <sup>21</sup>	1,499	1,067	432	-	7	43	-	50	3.34
Lee et al. <sup>24</sup>	117	-	-	117	-	-	11	11	9.40
Lee et al. <sup>6</sup>	429	280	149	-	-	-	-	34	7.93
TOTAL	2,772	1,914	774	114	13	66	11	145	5.23

n: number of cases; -: data not supplied by the study; %: percentage; SM: simple mastectomy; SM+ALND: simple mastectomy associated with axillary lymph node dissection; MRM: modified radical mastectomy.

immediately after mastectomy or even years after surgery<sup>6-10</sup>, and two of the studies here that were analyzed show that most patients showed some signs of lymphedema in the first year after surgery.<sup>17,18</sup>

Age is a controversial causative factor. While two studies included in this study did not find any statistically significant differences with regard to this variable<sup>19,21</sup>, another three studies did indeed show a rise in the occurrence of lymphedema related to

increased age of the patients who had mastectomies at the time of surgery<sup>6,17,24</sup>.

Moreover, some authors have associated the development of lymphedema in post-mastectomy patients with overweight and obesity<sup>11,12</sup>. In general, the studies included here confirm this association. Apart from the studies where overweight and obesity are statistically shown to be causative factors<sup>17,19</sup>, in the studies where obesity showed no statistical association

with lymphedema, there was a significant association of overweight as a causative factor<sup>20,22</sup>.

Furthermore, some studies have also confirmed that higher BMI levels (BMI > 25) were significantly associated with the occurrence of lymphedema<sup>6,21</sup>. According to Freitas Júnior et al.<sup>17</sup>, a possible cause for this positive association between higher BMI and the onset of lymphedema lies in the greater difficulty for the lymph to return in patients with a greater amount of fatty tissue.

We also point out that, in this study, the BMI of the patients who had mastectomy alone was higher (25.97 kg/m<sup>2</sup>) than that of patients who had mastectomies associated with immediate breast reconstruction (23.86 kg/m<sup>2</sup>). This shows that studies should standardize selection or division of the patients into groups according to their BMI to make it more feasible to confirm this factor as an element of proneness to the occurrence of lymphedema after mastectomy.

Some authors mention that dissection of the axillary lymph node is also a risk factor for the development of lymphedema after a mastectomy<sup>11,12</sup>. This was confirmed by this systematic review, as studies show that lymphadenectomy significantly increases the occurrence of lymphedema<sup>6,19</sup>, both when a simple mastectomy is performed along with dissection of the axillary lymph nodes, as also when the technique of modified radical mastectomy is used<sup>19</sup>.

It is well known that immediate breast reconstruction is a technique that confers many benefits to the patients, especially those whose breast cancers are in the early stages. These benefits include: prevention of disfiguration of the chest wall; reduction in costs; increased self-esteem; and general improvement in quality of life<sup>6,23,25</sup>. This technique has been prioritized in literature because it confers these benefits without affecting the biological behavior of the breast cancer or promoting any relapse or having any interference on auxiliary chemotherapy<sup>23,26</sup>.

In this study, we observed that apart from the benefits mentioned in the literature with regard to immediate breast reconstruction, this technique also has a potential to reduce the development of lymphedema among patients with mastectomies. Confirming the findings of some previous studies<sup>22-24</sup>, the results of this study show that the immediate breast reconstruction technique brought a significant reduction ( $p < 0.001$ ) in cases with lymphedema that was present in 5,23% of the patients subjected to mastectomy with immediate reconstruction, compared to the 20,95% observed among patients who received no breast reconstruction.

It is important to emphasize that literature states

that radiotherapy can be an important causative factor for the development of lymphedemas among patients who have had mastectomies for treatment of breast cancer<sup>11,12</sup>. However, out of the ten studies included in the sample used in this study, most of them<sup>10,17,18,20-23</sup> did not address the radiotherapeutic protocols to which the patients were subjected. This made it infeasible to establish a correlation between this factor and the development of lymphedema in both the treatment approaches addressed here.

In the three studies that considered this approach<sup>6,19,24</sup>, there was an influence of radiotherapy on the development of lymphedema, which increased according to the use of radiotherapy or the increase of the quantity used. In this regard, we mention the importance of standardization and division of groups of patients in further studies addressing this subject.

We also stress the importance of carrying out further studies on the occurrence of lymphedema in mastectomized patients, with methodologies duly standardized between them, and with greater monitoring time, especially when comparing mastectomy alone and the association of mastectomies with immediate or late breast reconstruction, which is still a gap in the literature. This would favor the acceptance and acknowledgment of surgical techniques that offer a better prognosis to patients with breast cancer.

## CONCLUSION

Based on our systematic review, we concluded that mastectomy associated with immediate breast reconstruction positively influenced the prognosis of patients with breast cancer, resulting in a significantly lower rate of occurrence of lymphedema, when compared to cases where mastectomy alone was performed. Provided there are no contraindications, we can use immediate breast reconstruction after mastectomies on patients undergoing treatment against breast cancer, in a safe and efficient way, with a view to reducing the risk of developing lymphedema.

## COLLABORATIONS

### RVER

Analysis and/or data interpretation, conception and design study, data curation, final manuscript approval, investigation, methodology, project administration, realization of operations and/or trials, writing - original draft preparation, writing - review & editing.



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## \*Corresponding author:

Rafael Vilela Eiras Ribeiro

Avenida Presidente Itamar Franco, nº 4001 - Dom Bosco, Juiz de Fora, MG, Brazil

Zip Code 36033-318

E-mail: vilelaeiras@hotmail.com