

# AXILLARY SURGERY IN BREAST CANCER: ACUTE POSTOPERATIVE COMPLICATIONS IN A HOSPITAL COHORT OF WOMEN OF RIO DE JANEIRO, BRAZIL

Abordagem cirúrgica axilar no câncer de mama: complicações pós-operatórias agudas em uma coorte hospitalar de mulheres do Rio de Janeiro

Flávia Oliveira Macedo<sup>1\*</sup>, Anke Bergmann<sup>1</sup>, Rosalina Jorge Koifman<sup>2</sup>,  
Daniele Medeiros Torres<sup>1</sup>, Rejane Medeiros Costa<sup>1</sup>, Ilce Ferreira da Silva<sup>3</sup>

## ABSTRACT

**Objective:** To analyze the incidence of early postoperative complications in women with breast cancer according to the axillary surgery. **Methods:** An observational study of a cohort of women diagnosed with T1-T2N0M0 clinical stage breast cancer attended at the Brazilian National Cancer Institute from January 2007 to December 2009. The outcome was defined as post-surgical complications in the affected upper limb, such as: axillary web syndrome, winged scapula, paraesthesia and surgical wound, seroma and wound infection. The incidence of simple complications was estimated. The crude and adjusted Odds Ratios, with their respective 95% confidence intervals, were estimated by Multiple Logistic Regression analysis. **Results:** The incidence of postoperative complications was significantly lower in sentinel lymph node biopsy (axillary web syndrome: 6.0%; paraesthesia: 45.2%; winged scapula: 9.1%; seroma: 28.5%; wound infection: 3.8%) than in axillary lymphadenectomy (axillary web syndrome: 22.5%; paraesthesia: 89.8%; winged scapula: 50.0%; seroma: 69.4%; wound infection: 12.9%). Compared to those who underwent axillary lymphadenectomy, the risk of postoperative complications in those in whom sentinel lymph node biopsy was performed was significantly lower. **Conclusion:** The sentinel lymph node biopsy technique was an independent protective factor for acute postoperative complications when compared to axillary lymphadenectomy.

**KEYWORDS:** Breast neoplasms; lymphadenectomy; postoperative complications; sentinel lymph node biopsy.

## RESUMO

**Objetivo:** Analisar a incidência de complicações pós-operatórias precoces em mulheres com câncer de mama de acordo com a cirurgia axilar. **Métodos:** Estudo observacional de uma coorte de mulheres diagnosticadas com câncer de mama em estágio clínico T1-T2N0M0 atendidas no Instituto Nacional de Câncer do Brasil de janeiro de 2007 a dezembro de 2009. O desfecho foi definido como complicações pós-cirúrgicas no membro superior afetado, tais como: síndrome da rede axilar, escápula alada, parestesia e ferida cirúrgica, seroma e infecção da ferida. A incidência de complicações simples foi estimada. Os Odds Ratios bruto e ajustado, com seus respectivos intervalos de confiança de 95%, foram estimados por análise de Regressão Logística Múltipla. **Resultados:** A incidência de complicações pós-operatórias foi significativamente menor na biópsia de linfonodo sentinela (síndrome da rede axilar: 6,0%; parestesia: 45,2%; escápula alada: 9,1%; seroma: 28,5%; infecção da ferida: 3,8%) do que na linfadenectomia axilar (síndrome da rede axilar: 22,5%; parestesia: 89,8%; escápula alada: 50,0%; seroma: 69,4%; infecção da ferida: 12,9%). Em comparação com aqueles que foram submetidos a linfadenectomia axilar, o risco de complicações pós-operatórias naqueles nos quais a biópsia de linfonodo sentinela foi realizada foi significativamente menor. **Conclusão:** A técnica de biópsia de linfonodo sentinela foi um fator de proteção independente para complicações pós-operatórias quando comparadas à linfadenectomia axilar.

**PALAVRAS-CHAVE:** Neoplasias da mama; excisão de linfonodo; complicações pós-operatórias; biópsia de linfonodo sentinela.

<sup>1</sup>Instituto Nacional do Câncer – Rio de Janeiro (RJ), Brazil.

<sup>2</sup>Escola Nacional de Saúde Pública Sérgio Arouca – Rio de Janeiro (RJ), Brazil.

<sup>3</sup>Fernandes Figueira Institute, Fundação Oswaldo Cruz – Rio de Janeiro (RJ), Brazil.

\*Corresponding author: flaomacedo@gmail.com

Conflict of interests: nothing to declare.

Received on: 03/30/2018. Accepted on: 07/14/2018.

## INTRODUCTION

Breast cancer is the most frequent tumor site and the leading cause of cancer death among women worldwide, with an incidence ranging from 31.3 per 100.000 women in developing countries, such as Brazil, to 73.4 per 100.000 women in developed countries in 2012<sup>1</sup>. There is evidence that the actions for the early detection of breast cancer are still ineffective in Brazil, leading to diagnoses in advanced stages. A study carried out in the country<sup>2</sup> used the Database of Hospital Cancer Registries in Brazil between 2000 and 2009, and included 59.317 women with breast cancer. This study showed that only 19.1% of women were diagnosed in stage I and 53.4% in advanced stages, in which aggressive treatments are necessary and several adverse effects can result from them, such as early and late postoperative complications in the upper limb homolateral to the surgery<sup>2</sup>.

Among the early postoperative complications, the axillary web syndrome, paraesthesia, winged scapula, seroma and surgical wound infection are recognized<sup>3</sup>. In women with early-stage breast cancer, the surgical approach may be more conservative, depending on the presence or absence of axillary involvement. Thus, for adequate axillary staging, the surgical treatment of breast cancer involves an approach through axillary lymphadenectomy (AL) and/or sentinel lymph node biopsy (SLNB). AL is associated with an increase in early postoperative morbidities, and to minimize such complications, SLNB was incorporated, marking the advancement of breast surgical treatment. It is considered the preferred method of staging breast cancer in patients with clinically negative axilla with T1 or T2 classification<sup>4,5</sup>. Although some studies report the presence of early morbidities in women submitted to SLNB, the frequency is lower than in AL<sup>6-8</sup>.

In Brazil, few studies have addressed the comparison of early complications according to the axillary approach, focusing mostly on AL<sup>9-11</sup>, while those describing the incidence in both axillary approach evaluated only a few complications<sup>12-16</sup>. Therefore, the aim of the present study is to estimate the risk of early postoperative complications according to the axillary surgical approach.

## METHODS

An observational study was performed in a cohort of women with breast cancer and clinical stage T1 and T2N0M0 enrolled and attended at the Hospital of Cancer III (HCIII/INCA), from Jan/2007 to Dec/2009. The patients were identified by the Hospital Cancer Registry of HCIII/INCA (HCR/HCIII), using electronic and physical records. Data collection was performed based on the physiotherapy and nursing service reports, using a standardized form. This study was approved by the Ethics and Research Committees of the National Cancer Institute (INCA) and Sérgio Arouca National School of Public Health (ENSP).

Among the 1.417 women (clinical stage T1-T2N0M0) identified at the database, 210 (14.8%) presented different clinical

stages from T1-T2N0M0 on medical reports; 108 (7.6%) had in situ histological type; 28 (2.0%) did not undergo surgery or did not undergo an axillary approach; 11 (0.8%) had previous cancer; 40 (2.8%) had previous contralateral and/or homolateral breast cancer; 42 (3.0%) had bilateral synchronous breast cancer; and 18 (1.3%) had undergone treatment (completely or partially) outside the INCA. Twenty-seven patients (1.9%) were lost due to the non-identification of physical records. Thus, 933 women with tumors with up to 5 cm, clinically negative axilla and absence of distant metastasis, were included in the present study.

Sociodemographic, clinical and lifestyle information were collected. The exposure was the axillary surgical approach, defined as SLNB or AL, and then categorized into: SLNB only, SLNB followed by AL or AL only. The outcome was defined as postoperative complications in the affected upper limb and surgical wound. Information on upper limb complications (axillary web syndrome, winged scapula, paraesthesia and surgical wound, seroma and wound infection) were collected in the 1st evaluation of the physiotherapy sector that may have occurred within 3 months after the surgery. Information about the complications that occurred in the operative wound (seroma and wound infection) were collected from the nursing reports.

Axillary web syndrome (AWS) was defined as the presence of palpable and/or visible fibrous cords in the axilla or along the upper limb homolateral to the surgery, being more frequently observed with elevation and abduction of the upper limb. The winged scapula (WS) was considered the condition in which the medial border and lower angle of the scapula become more prominent in the thorax. It was assessed by visual observation during active elevation of the upper limbs or by the Hoppenfeld test, which consists of the patient standing in orthostatic posture, flexing shoulders at 90 degrees, joining hands, laying flat on the wall and extending the elbows, and pushing hands against the wall. The paraesthesia of the region innervated by the intercostobrachial nerve was defined by the presence of burning pain, shooting pain, pressure sensation and numbness in the lateral region of the thorax, medial region of arm and/or axilla, being assessed by touch and/or referenced by the patient. Seroma was defined by the nursing report as a collection of fluids formed after removal of the suction drain and located in the breast, and/or axilla requiring aspiration. The surgical wound infection (WI) was identified through nursing reports of infection associated with the use of antibiotic therapy.

Mean, median and standard deviation of continuous variables was estimated, while categorical variables were evaluated by frequencies. Differences between the means were evaluated using the Mann-Whitney test for continuous variables. Differences between proportions were assessed using the chi-square test. A significant level of 5% was considered for both tests.

The incidence for each acute complication was estimated, and the crude and adjusted odds ratios (OR) and their respective

95% confidence intervals were performed using the Logistic Regression analysis. A multivariate analysis was carried out to estimate the effect of the axillary approach on each acute complication, adjusted by confounding variables. The inclusion criteria in the multivariate analysis was the biological relevance or a  $p < 0.20$  in the crude analysis. The exclusion criteria of the model was a  $p > 0.05$  in the model. Statistical significance was calculated using the Wald statistic. The model adjustment was verified by residue analysis. All analyses were performed using the Statistical Package for Social Science (20.0 version).

## RESULTS

The mean age of the study population was 57.9 years ( $\pm 12.6$ ), with an average of 2 lymph nodes removed ( $\pm 1.19$ ) in patients submitted to SLNB alone, 17.8 ( $\pm 5.35$ ) in those submitted to

SLNB  $\pm$  AL, and 18.1 ( $\pm 6.30$ ) in those who underwent AL directly. Regarding nutritional status, the mean Body Mass Index (BMI) was  $29.2 \text{ kg/m}^2$  ( $\pm 32.2$ ), with 68.8% of the women being classified as overweight or obese. Around 53% reported being housewives, 11.7% of the women were smokers and 24.7% had a habit of consuming alcoholic drinks. In the comparison between groups, it was observed that those submitted to AL at the diagnosis of breast cancer were significantly older ( $>60$  years: 67.9%) when compared to women who had SLNB (43.8%) and SLNB followed by AL (33.3%), and had house activities as their main occupation (AL: 72.1%, SLNB $\pm$ AL: 47.9%, SLNB: 51.4%) (Table 1).

Clinical and treatment variables distribution according to the axillary approach (Table 1) revealed that the majority of women had clinical stage I (61.6%), underwent conservative surgery (52.8%), and were not submitted to breast reconstruction (83.7%). Regarding the axillary approach, 73.2% of the women

**Table 1.** Distribution of socio-demographic characteristics, nutritional status, clinical status and treatment according to the axillary approach of the cohort of women with breast cancer (T1-2N0M0).

Variables	N total (%) or mean (SD)	Axillary Surgery (%)			$\chi^2$ p-value
		SLNB	SLNB+AL	AL	
Age (mean $\pm$ SD)	57.9 (12.6)	57.3 (DP=12.2)	55.0 (DP=12.2)	59.9 (DP=13.9)	
Age					
<40	55 (5.9)	41 (6.0)	13 (9.0)	1 (0.9)	<0.001
40–59	459 (49.2)	343 (50.2)	83 (57.6)	33 (31.1)	
$\geq 60$	419 (44.9)	299 (43.8)	48 (33.3)	72 (67.9)	
Occupation					
Unemployed	35 (3.8)	28 (4.1)	4 (2.8)	3 (2.9)	0.001
External job	398 (43.0)	301 (44.5)	71 (49.3)	26 (25.0)	
At home	492 (53.2)	348 (51.4)	69 (47.9)	75 (72.1)	
BMI					
Underweight	36 (3.9)	30 (4.4)	5 (3.5)	1 (1.0)	0.471
Suitable	254 (27.3)	193 (28.3)	34 (23.6)	27 (25.7)	
Overweight	334 (35.8)	244 (35.7)	53 (36.8)	37 (35.2)	
Obesity	308 (33.0)	216 (31.6)	52 (36.1)	40 (38.1)	
Clinical Stage					
T1N0M0 (I)	575 (61.6)	478 (70.0)	65 (45.1)	32 (30.2)	<0.001
T2N0M0 (IIA)	358 (38.4)	205 (30.0)	79 (54.9)	74 (69.8)	
Type of Breast Surgery					
Conservative	493 (52.8)	423 (61.9)	61 (42.4)	9 (8.5)	<0.001
Mastectomy	440 (47.2)	260 (38.1)	83 (57.6)	97 (91.5)	
Breast Reconstruction					
No	781 (83.7)	557 (81.6)	124 (86.1)	100 (94.3)	<0.001
Immediate	124 (13.3)	109 (16.0)	14 (9.7)	1 (0.9)	
Late	28 (3.0)	17 (2.5)	6 (4.2)	5 (4.7)	

\*The difference in sample size corresponds to the absence of information; SD: standard deviation; SLNB: sentinel lymph node biopsy; AL: axillary lymphadenectomy; BMI: body mass index.

underwent SLNB, 15.4% SLNB followed by AL, and 11.4% underwent firstly AL. Most women (66.4%) removed 1 to 3 lymph nodes, and 24.7% removed more than 10. Compared to women with SLNB, women submitted to AL presented statistically more advanced clinical stage (SLNB: 30%; SLNB+AL: 54.9%; AL: 69.8%), a greater frequency of mastectomy (SLNB: 38.1; SLNB+AL: 57.6%; AL: 91.5%) and removed more than 10 lymph nodes (SLNB: 0%; SLNB+AL: 94.4%; AL: 89.5%).

The incidence of surgical WI (3.8%) and seroma (28.5%) was statistically lower in women submitted to SLNB than in those submitted to AL (69.4% for seroma, and 12.9% for infection) (p=0,000). Compared to women submitted to AL, those who underwent SLNB presented a statistically lower incidence of the AWS (AL: 22.5% vs. SLNB: 6.0%), paraesthesia (AL: 89.8% vs. SLNB: 45.2%), and WS (AL: 50% vs. SLNB: 9.1%) (p: 0,000) (Table 2).

A multivariate analysis showed that compared to the women submitted to AL, those submitted to SLNB had a lower risk of seroma (OR=0.32; 95%CI 0.22–0.47), after adjusting for age, type of breast surgery, immediate breast reconstruction and BMI. Also, SLNB provided a protection for WI (OR=0.38; 95%CI 0.22–0.70), after adjusting for seroma and BMI (Table 3). Compared to AL, SLNB conferred a statistically significant protection against AWS, after adjusting for age, winged scapula and paraesthesia (OR=0.37; 95%CI 0.21–0.63). Similarly, it was observed a significant protection against paraesthesia,

**Table 2.** Incidence of the early postoperative complications of the cohort of women with breast cancer (T1-2N0M0) according to the axillary approach.

Variables	N total (%)	Axillary Surgery N (%)		χ <sup>2</sup> p-value
		SLNB	AL	
<b>Wound Infection</b>				
No	870 (93.8)	654 (96.2)	216 (87.1)	0.000
Yes	58 (6.2)	26 (3.8)	32 (12.9)	
<b>Seroma</b>				
No	562 (60.6)	486 (71.5)	76 (30.6)	0.000
Yes	366 (39.4)	194 (28.5)	172 (69.4)	
<b>Axillary Web Syndrome</b>				
No	764 (89.3)	575 (94.0)	189 (77.5)	0.000
Yes	92 (10.7)	37 (6.0)	55 (22.5)	
<b>Paraesthesia</b>				
No	356 (42.3)	332 (54.8)	24 (10.2)	0.000
Yes	486 (57.7)	274 (45.2)	212 (89.8)	
<b>Winged Scapula</b>				
No	672 (79.3)	552 (90.9)	120 (50.0)	0.000
Yes	175 (20.7)	55 (9.1)	120 (50.0)	

\*The difference in sample size corresponds to the absence of information; SLNB: sentinel lymph node biopsy; AL: axillary lymphadenectomy.

regardless of age and type of breast surgery (OR=0.10; 95%CI 0.06–0.16). Likewise, the SLNB conferred a statistically significant protection for the WS (OR=0.12; 95%CI 0.08–0.18), regardless of the type of breast surgery and the presence of AWS (Table 3). Crude analyses are presented in supplementary material.

## DISCUSSION

Considering the 933 women diagnosed with early staging breast cancer, treated at HCIII/INCA from 2007 to 2009, the incidence of wound complication was statistically lower among women submitted to SLNB compared to those who underwent AL. Such findings corroborate with the literature, suggesting an incidence of surgical WI in SLNB from 0.9 to 10.0%, and in women with AL this incidence varies from 3.0 to 17.0<sup>17-21</sup>. Although the incidence of seroma in women submitted to SLNB (28.5%) was significantly lower compared to AL (69.4%), it was higher than those observed in European, American and Brazilian studies. In these cases, the incidence of seroma ranged from 1.8 to 14.0% in women submitted to SLNB, whereas in those submitted to AL, it ranged from 7.6 to 32.0%<sup>14,17-21</sup>. Compared to the estimates observed in the literature, the high seroma incidence in the women of the

**Table 3.** Crude and adjusted odds ratios of early postoperative complications in women with breast cancer (T1-2N0M0) according to the axillary approach.

Variables	Crude Analysis		Adjusted Analysis*	
	OR	95%CI	OR	95%CI
<b>Seroma</b>				
AL (SLNB+AL and AL)	1		1	
SLNB	0.18	0.13–0.24	0.32	0.22–0.47
<b>Wound Infection</b>				
AL (SLNB+AL and AL)	1		1	
SLNB	0.27	0.16–0.46	0.38	0.22–0.70
<b>Axillary Web Syndrome</b>				
AL (SLNB+AL and AL)	1		1	
SLNB	0.22	0.14–0.35	0.37	0.21–0.63
<b>Paraesthesia</b>				
AL (SLNB+AL and AL)	1		1	
SLNB	0.09	0.06–0.15	0.10	0.06–0.16
<b>Winged Scapula</b>				
AL (SLNB+AL and AL)	1		1	
SLNB	0.10	0.07–0.14	0.12	0.08–0.18

SLNB: sentinel lymph node biopsy; AL: axillary lymphadenectomy; OR: odds ratio; CI: confidence interval; \*seroma: adjusted for age, wound infection, type of breast surgery, immediate breast reconstruction and BMI; \*wound infection: seroma and BMI; \*axillary web syndrome: age, winged scapula and paraesthesia; \*paraesthesia: age and type of breast surgery; \*winged scapula: type of breast surgery and axillary web syndrome.

present study could be due to differences on the seroma definition over the studies. The criteria for seroma diagnosis adopted by such studies included only seroma observed in the axilla, while in the present study it included seroma as the axilla only, as those observed in breast or plastron<sup>17-21</sup>.

Reduced risk of seroma and surgical wound infection observed for SLNB were found in a meta-analysis conducted in China<sup>8</sup>, USA<sup>3</sup> and Austria<sup>7</sup>, as compared to AL. Kell et al.<sup>3</sup> suggest a lower risk of surgical wound infection (OR=0.58; 95%CI 0.42–0.80) and seroma (OR 0.40; 95%CI 0.31–0.51) in women treated with SLNB alone, compared to those submitted to AL. A smaller incision and less extension in the dissection and rupture of lymphatic tissue related<sup>3</sup> to SLNB approach could explain the lower risk of infection and seroma.

Also, this study showed that women submitted to SLNB presented a significantly lower frequency of postoperative complications in the upper limb and scapular region homolateral to the surgery when compared to women submitted to AL. Although the physiopathology of AWS is still not well established, studies have suggested a lymphovenous damage, hypercoagulation, superficial venous and lymphatic stasis as well as disorders and lesions of tissues as result of rupture of superficial lymphatic and blood vessels during axillary surgery. It is likely that SLNB promotes a lower risk because it removes a small number of lymph nodes, reducing the injury of the collectors and axillary lymph capillaries<sup>22</sup>.

In a study conducted in Rio de Janeiro, 193 women diagnosed with breast cancer from September 2008 to June 2009 were included. A lower incidence of AWS was observed among women submitted to SLNB (11.7%) when compared to those who performed AL (36%) at 45 days after surgery. The authors observed a 68% reduction in the risk of AWS among those who underwent SLNB as compared to AL<sup>15</sup>. A similar result was observed in another study conducted at the same institution with a population of 203 women also evaluated at 45 days (SLNB=4%, AL=24%,  $p<0.001$ ) and 6 months (SLNB=2%, AL=16%,  $p<0.002$ )<sup>14</sup>.

In all published studies so far, the frequency of AWS was statistically lower among women who underwent SLNB (ranging from 0.9% to 20%), compared to those who were treated with AL (ranging from 5.2 to 72%)<sup>18,23,24</sup>. Comparing to the literature, the low incidence of AWS observed in the present study points out to the quality of the physiotherapy service of HCIII/INCA, which performs evaluations and produces guidelines for the prevention of postoperative complications before surgical treatment and postoperative follow-up<sup>25</sup>.

A great divergence still exists concerning the incidence of sensorial disorders in patients submitted to the surgical treatment of breast cancer. Cohort studies and some randomized studies found an estimated incidence of altered sensitivity ranging from 2 to 23% for SLNB and 23.3 to 85% for AL<sup>17,26,27</sup>.

Fabro et al.<sup>13</sup> developed a cohort study to evaluate pain syndrome after surgical treatment for breast cancer with patients who underwent SLNB or AL. The authors found that in the first evaluation 61.3% patients had altered touch sensitivity in the internal region of the arm. In addition, young women (<40 years) and those submitted to AL (more than 15 lymph nodes removed) showed a significant increased risk of painful syndromes, defined by the presence of the perception of hyperesthesia in the internal region of the arm or axilla. The great variability in the incidence could be explained by the variation in the method of measurement and classification of this complication (subjective and/or objective assessment), and the time length between surgery and first evaluation.

Two meta-analysis performed by Kell et al.<sup>3</sup> and Li et al.<sup>8</sup> observed a 75 and 74% reduction in the risk of sensory disorders, respectively, for patients submitted to SLNB only compared to women who received AL. Similarly, in our study, SLNB conferred a 90% reduction in the risk of sensitivity change, even after adjusting by age and type of breast surgery. Although the risk reduction is 15% different between the present study and two meta-analysis<sup>3,8</sup>, we observed an effective protection for sensorial disorders promoted by the SLNB approach.

There are few studies in Brazil and worldwide comparing the incidence of WS in women submitted to SLNB and AL. However, in all of them the WS was more frequent in women submitted to AL. Paim et al.<sup>12</sup> conducted in Brazil a study with 96 patients, and observed a higher WS incidence (8.4%) in patients who underwent AL than in women submitted to SLNB (0%). At a randomized clinical trial conducted by Adriaenssens et al.<sup>28</sup>, greater WS incidence was seen on AL (21.3%), as compared to SLNB only (4.2%). Also, AL was strongly associated with the WS conferring a 10.6-fold risk of WS, regardless of age and BMI, when compared to SLNB. A prospective cohort study conducted in Brazil<sup>16</sup> found a higher incidence in women submitted to AL (22.6%) when compared to those receiving SLNB only (2.9%) after 15 days postoperative ( $p<0.01$ ).

Studies that included only women submitted to AL found incidences ranging from 27<sup>9</sup> to 73.3%<sup>10</sup>. Divergence between results may be due to a small sample size of those studies, as well as a time length after surgery ranging from the immediate postoperative period up to 12 months<sup>9-11,29</sup>. In addition, WS is a condition diagnosed by clinical observation and there are different clinical tests for assessment<sup>10</sup>. Thus, different WS incidence estimates may arise depending on the clinical tests and criteria used to assessment. Compared to patients submitted to AL, we found an 88% reduction in the risk of WS for patients who underwent SLNB, adjusted by type of breast surgery and AWS. This protection conferred by the SLNB could be explained by the fact that this surgery allows the resection of a smaller number of lymph nodes and preserve the long thoracic nerve, avoiding the anterior serratus muscle deficiency<sup>30</sup>.

The present study was the first Brazilian study to evaluate the effect of the axillary approach on the incidence of all major early postoperative complications in women with breast cancer, controlling for the effect of complications of each other. Plus, it has the advantage of including the largest number of patients among all Brazilian studies related to early postoperative complications, reducing type-II error. However, there are also limitations that should be considered, such as those inherent in retrospective studies. Collecting data based on medical, physiotherapy, and nursing records could introduce limitations related to the data quality obtained in the routine appointments. However, in the HCIII/INCA those health care services have standardized

protocols and a team specialized aiming to promote interventions for prevention of such complications.

## CONCLUSION

The present study suggests that the SLNB significantly reduced the risk of early surgical complications such as infection, seroma, AWS, paraesthesia and WS, even after adjusted by age, BMI, type of breast surgery and other related complications. However, although the SLNB technique promotes a protective effect, it still presents some risk complications, which should be a focus of prevention, management and follow-up.

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