Sentinel Lymph Node Biopsy in T3 and T4b Breast Cancer Patients: Analysis in a Tertiary Cancer Hospital and Systematic Literature Review

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Keywords

Breast neoplasms · Sentinel lymph node biopsy ·
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staging

Abstract

Introduction: Breast cancer represents the most common type of cancer among women in the world. The presence and extent of axillary lymph node involvement represent an important prognostic factor. Sentinel lymph node biopsy (SLNB) is currently accepted for T1 and T2 with negative axillae (N0); however, many patients with T3–T4b tumors with N0 are often submitted to unnecessarily axillary lymph node dissection. **Materials and Methods:** This is a retrospective, observational study of patients treated for breast cancer between 2008 and 2015, with T3/T4b tumors and N0, who underwent SLNB. A systematic review of the literature was also carried out in 5 bases. **Results:** We analyzed 73 patients, and SLNB was negative for macrometastasis in 60.3% of the cases. With a mean follow-up of 45 months, no ipsilateral axillary local recurrence was observed. In the systematic review, only 7 articles presented data for analysis. Grouping these studies with the present series, the rate of N0 was 32.1% for T3 and

61.0% for T4b; grouping all studies (T3 and T4b $n = 431$) the rate was 32.5%. **Conclusions:** SLNB in T3/T4b tumors is a feasible and safe procedure from the oncological point of view, as it has not been associated with ipsilateral axillary relapse.

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Introduction

Breast cancer is a worldwide public health problem, with 2.1 million new cases annually [1, 2]. In the USA, an estimated 226,860 new cases are diagnosed each year, with decreasing mortality [3], unlike in Brazil, where 59,700 new cases are expected each year, with increasing mortality [4, 5]. Annually, 520,000 deaths are attributed to breast cancer globally, with approximately 60% of these deaths occurring in developing countries, making breast cancer the most frequent cause of cancer death in women in those regions [1].

Breast cancer behaves heterogeneously; however, the prognosis is directly associated with the disease stage at diagnosis. Thus, the presence and extension of axillary lymph node involvement represent an important prognostic factor that greatly impacts therapeutic decisions

since the presence of axillary lymph node metastases decreases the 5-year survival [6].

For many years, based on Halsted's principle of centrifugal spreading of breast cancer, all patients with breast cancer systematically underwent axillary lymph node dissection (ALND), even when no suspicious axillary lymph nodes were present upon clinical examination [7]. ALND, however, is associated with higher rates of seroma, infection, axillary pain, upper limb paresthesia, limited shoulder mobility, and lymphedema [8–10].

Previously, many patients have undergone ALND, even in the absence of metastatic disease. Thus, the concept of sentinel lymph node biopsy (SLNB) [11] for breast cancer [12, 13] emerged and is characterized as a high-accuracy method for determining the axillary state, with a low axillary recurrence even with a considerable false-negative rate of up to 10% [14–19]. Thus, SLNB was established as the standard method for determining axillary status in breast cancer in clinically N0 patients. This method was initially proposed for tumors smaller than 3 cm and later for tumors of up to 5 centimeters despite limited studies evaluating the oncological safety of applying the method in tumors larger than 3 cm [7, 20–23].

As per the American Cancer Society (ACS), SLNB is acceptable for T1 and T2 tumors with N0 axillae. However, in T3 and T4b stage patients, the method is controversial even when clinically N0 axillae are present [6, 24, 25]. Generally, T3 and T4b tumors are candidates for neoadjuvant treatment, and SN identification rates are significantly better when mapping is performed prior to neoadjuvant chemotherapy. In patients with clinically negative axillae, this rate can reach 100%, and it reached 81% after neoadjuvant chemotherapy in a group of patients who were clinically N0 or N1 at presentation. Among patients with successful mapping, the false-negative rate is high (11%). The reasons for this rate are unclear and may be related to lymphatic obstruction with tumor emboli or lymphatic scars caused by chemotherapy, consequently creating new drainage patterns [26].

Studies evaluating SLNB in T3 and T4b cancer patients have demonstrated high false-negative rates (8–18%); however, other researchers have shown that SLNB efficacy in large tumors correlates more with the surgeon's experience than with tumor size [27, 28]. We found isolated reports in the literature on SLNB use for T3 and T4b tumors without neoadjuvant chemotherapy, generally using case series with limited numbers of patients [7, 20–23, 29], with no reviews being performed. SLNB use in clinically N0, T3, and T4b cancer patients, with or without neoadjuvant chemotherapy, seems acceptable for patients, considering the prevalence of breast cancer, since small changes in the therapeutic approach allow preservation of many axillae.

Materials and Methods

This is a retrospective observational study of breast cancer patients treated at the Barretos Cancer Hospital who were diagnosed with clinicopathological stage T3 or T4b cancer and who underwent SLNB between 2008 and 2015. This study was approved by the Research Ethics Committee (No. 1244/2016).

Patients with T3 or T4b stage tumors and clinical N0 axillae who did not undergo neoadjuvant treatment were included. Fine-needle aspiration biopsy (FNAB) was performed in patients with ultrasonographic suspicion determined by cortical lymph node thickening >3 mm. In the absence of cancer, all patients underwent SLNB. Patients with metastatic disease or primary inflammatory carcinoma (T4d) or who underwent neoadjuvant treatment prior to SLNB were excluded.

Patients underwent SLNB using different methodologies (patent blue dye and nuclear medicine). In the intraoperative period, all of the patients underwent intraoperative frozen sectioning, and in the presence of lymph node metastasis these patients underwent ALND. Upon examination of the SLNB paraffin-embedded sections, only patients with macrometastasis underwent ALND (Fig. 1).

Immunohistochemical (IHC) profiling of the SN and tumor was performed in all cases to define the hormone receptors (estrogen and progesterone), Ki67, and human epidermal growth factor receptor-2 (HER2). In cases where HER2 was uncertain based on IHC, fluorescence in situ hybridization (FISH) was performed. Isolated tumor cells (ITC) were considered to indicate cancer-free SN.

The main points evaluated were the identification rate of the sentinel lymph node and its positivity. The axillary recurrence rate homolateral to the treatment was also evaluated. The follow-up time was calculated from the date of surgery to the date of the last outpatient return visit. Patients with no follow-up for a period twice the length of the estimated time for a return visit were considered lost to follow-up. Cancer-specific overall survival was evaluated.

In the statistical analyses, frequencies and percentages were calculated for categorical variables, and mean and minimum and maximum values were calculated for numeric variables. The Kaplan-Meier method was used to evaluate recurrence and survival. IBM® SPSS software for Mac22® was used.

Systematic Literature Review

Using the patient/intervention/comparison/outcome (PICO) methodology, the following were considered: P = breast cancer, I = sentinel lymph node, C = T3 and T4 tumors, and O = axillary preservation. An electronic search was performed with a specific strategy for each database as follows:

PubMed/Web of Science/Cochrane: (Breast Neoplasms or Tumors, Breast or Breast Tumors or Breast Tumor or Tumor, Breast or Neoplasms, Breast or Breast Neoplasm or Neoplasm, Breast or Breast Cancer or Cancer, Breast or Cancer of the Breast or Mammary Cancer or Cancer, Mammary or Cancers, Mammary or Mammary Cancers or Malignant Neoplasm of Breast or Breast Malignant Neoplasm or Breast Malignant Neoplasms or Malignant Tumor of Breast or Breast Malignant Tumor or Breast Malignant Tumors or Cancer of Breast or Breast Carcinoma or Breast Carcinomas or Carcinoma, Breast or Carcinomas, Breast or Mammary Carcinoma, Human or Carcinoma, Human Mammary or Carcinomas, Human Mammary or Human Mammary Carcinomas or Mammary Carcinomas, Human or Human Mammary Carcinoma or Mammary Neoplasms, Human or Human Mammary Neoplasm or Human Mammary Neoplasms or Neoplasm, Human Mammary or Neoplasms, Human Mammary or Mammary Neoplasm, Human) and (Sentinel Lymph Node Biopsy or Lymph Node Biopsy, Sentinel or Biopsy, Sentinel Lymph Node) and (T3

Fig. 1. Diagnostic flowchart for axillary evaluation. IFE, intraoperative freezing evaluation.

Fig. 2. PRISMA flowchart (2009 standard).

breast cancers or T4 breast cancers or large breast cancer or large advanced breast cancer or locally advanced breast cancer) and (avoid axillary dissection or Axilla or Underarm or Armpit or preservation the axillary lymph node dissection).

Lilacs: (Breast Neoplasms or Neoplasias da Mama or Neoplasias da Mama or Câncer de Mama or Câncer da Mama or Câncer de Seio or Câncer do Seio or Câncer Mamário or Neoplasias or mamarias or Tumores da Mama or Tumores de Mama or Tumor

Table 1. Summary of pathological features

Variable	Category	Cases, <i>n</i> (%)
Histological type	IDC (NOS)	56 (76.7)
	ILC	9 (12.3)
	Papillary	4 (5.5)
	Mucinous	3 (4.1)
	Colloid	1 (1.4)
Nottingham histologic grade	1	6 (8.2)
	2	35 (47.9)
	3	32 (43.8)
Molecular subtype (IHC)	Luminal A	14 (19.2)
	Luminal B-HER2 –	39 (53.4)
	Luminal B-HER2 +	4 (5.5)
	HER 2	6 (8.2)
	Triple negative	10 (13.7)
Clinical stage T (TNM)	T2	18 (24.7)
	T3	38 (52.0)
	T4b	17 (23.3)

IDC (NOS), invasive ductal carcinoma (not otherwise specified); ILC, invasive lobular carcinoma.

de Seio or Tumores de Seio or Tumores Mamários) and (Sentinel Lymph Node Biopsy or Biopsia del Ganglio Linfático Centinela or Biópsia de Linfonodo Sentinela or Biópsia de Gânglio Linfático Sentinela) and (tumor T3 or tumores T3 or tumor T4 or tumores T4 or cancer localmente avançado or tumor localmente avançado and tumors localmente avançado or large breast cancer or large advanced breast cancer or locally advanced breast cancer) and (Axilla or Axila or avoid axillary dissection or preservation the axillary lymph node dissection).

Embase: ([Breast Neoplasms] or [Tumors, Breast] or [Breast Tumors] or [Breast Tumor] or [Tumor, Breast] or [Neoplasms, Breast] or [Breast Neoplasm] or [Neoplasm, Breast] or [Cancer, Breast] or [Cancer of the Breast] or [Mammary Cancer] or [Cancer, Mammary] or [Cancers, Mammary] or [Mammary Cancers] or [Malignant Neoplasm of Breast] or [Breast Malignant Neoplasm] or [Breast Malignant Neoplasms] or [Malignant Tumor of Breast] or [Breast Malignant Tumor] or [Breast Malignant Tumors] or [Cancer of Breast] or [Breast Carcinoma] or [Breast Carcinomas] or [Carcinoma, Breast] or [Carcinomas, Breast] or [Mammary Carcinoma, Human] or [Carcinoma, Human Mammary] or [Carcinomas, Human Mammary] or [Human Mammary Carcinomas] or [Mammary Carcinomas, Human] or [Human Mammary Carcinoma] or [Mammary Neoplasms, Human] or [Human Mammary Neoplasm] or [Human Mammary Neoplasms] or [Neoplasm, Human Mammary] or [Neoplasms, Human Mammary] or [Mammary Neoplasm, Human]) and ([Sentinel Lymph Node Biopsy] or [Lymph Node Biopsy, Sentinel] or [Biopsy, Sentinel Lymph Node]) and ([T3 breast cancers] or [T4 breast cancers] or [large breast cancer] or [large advanced breast cancer] or [locally advanced breast cancer]) and ([avoid axillary dissection] or [preservation the axillary lymph node dissection] or [Axilla or Underarm or Armpit]).

The titles and abstracts were evaluated, and articles of interest were selected and evaluated in full. Only articles associated with the present study's objectives were included. Figure 2 summarizes the article selection process.

Table 2. Correlation between tumor size and presence of lymph node metastasis

	Cancer free	Presence of micrometastasis	Presence of macrometastasis	Cancer free	N+ ^a , %
cT3 pT2	6	0	3	9	33.3
pT3	22	4	21	47	44.7
T4b	9	3	5	17	29.4
Total	37	7	29	73	39.7

Values are presented as numbers unless otherwise stated. ^a Considering only patients with macrometastasis.

Results

Seventy-three women with breast cancer with a mean age of 53.9 years (range 20–87, SD 12.5) were analyzed. Upon clinical examination, the largest tumor axis averaged 5.19 cm (range 2.1–9.5). At mammography this axis averaged 3.55 cm (range 1.5–8.1), and at breast ultrasound it averaged 6.95 cm (range 1.3–8.4). The axillae were evaluated via ultrasound in 71 patients, 87.3% of whom had axillae free of cancer suspicion and 12.7% of whom exhibited lymph nodes with cortical thickening (>3 mm) and underwent FNAB, which revealed no cancer suspicion.

The SN were identified in all cases. In 64.4% of the cases, technetium-99 m was used as the SN tracer; in 4.1%, patent blue dye was used; and in 31.5%, double staining was performed. On average, 2 SN (1–7) were identified, and all were evaluated intraoperatively via frozen sectioning. SN involvement was observed in 37% of patients, while 63% showed no evidence of malignancy. All cases presenting SN involvement in the intraoperative period underwent level I, II, and III ALND.

All of the patients underwent histopathological evaluation of the mammary lesion via thick-needle biopsy, and their tumor characteristics are shown in Table 1. The main histological type was invasive ductal carcinoma (76.7%), followed by invasive lobular carcinoma (12.3%). Most tumors were Nottingham histologic grade G2 or G3 (91.7%) and luminal Her-2 negative (72.6%).

The definitive histopathological analysis showed an average tumor size of 5.68 cm (range 3.1–14.0), and pathological skin involvement was confirmed in 15 patients (20.5%). In this analysis (Table 2), 18 cases (24.7%) were cT2, with pT3 confirmed after surgery. Nine patients (12.3%) were originally cT3 but were classified as pT2 based on the histopathological analysis after surgery; however, all of the tumors were larger than 3 cm. Finally, 29 cT3 patients (39.7%) remained pT3. The initial clinical evaluations were considered cases of skin involvement regardless of whether skin involvement was confirmed on

the histopathology. Of these cases, 17 (23.3%) were considered T4b. Table 3 shows the association between stage and lymph node involvement.

Most patients underwent mastectomy (58.9%) and SLNB (60.3%) as the final surgical treatment (Table 3). In 2 cases, the SN was negative on the frozen section but positive on the paraffin-embedded section, and these cases subsequently underwent ALND. Therefore, 29 patients (39.7%) who were clinically and radiologically N0 became N-positive by macrometastasis after surgical treatment and thus underwent ALND. Upon analyzing the paraffin-embedded sections, 7 cases presented micrometastasis, while 37 showed no lymph node involvement. Of these 37 cases, 30 were evaluated IHC. Of these, micrometastasis was observed in 1 patient, and ITC were found in 3 patients. The occurrence of micrometastasis and ITC in the SN did not implicate ALND performance. Figure 1 shows the diagnosis and treatment flowchart based on SN results.

All of the patients underwent adjuvant treatment (Table 3), with chemotherapy being performed in 84.9% of cases, radiotherapy in 91.8% of cases, and hormone therapy in all patients with positive hormone receptors. Of the 10 Her2-positive patients, only 7 received adjuvant Herceptin.

The mean follow-up was 45 months (range 17.5–98.8), with no patients lost to follow-up. During this period, no ipsilateral axillary recurrence was observed; local recurrence (breast/resection site) occurred in 3 patients (4.1%), and locoregional recurrence occurred in 3 patients (4.1%): 1 in the contralateral axilla, 1 in the internal mammary chain, and 1 in the contralateral breast without ipsilateral axillary recurrence. Three patients showed distant metastasis. During this period, 86.3% of the patients remained alive without disease, 5.5% were alive with disease, 5.5% died of associated comorbidities, and 2.7% died from malignant cancer progression. Evaluating the overall actuarial survival, 91.1% of the patients were alive at 60 months and 75.9% were alive at 72 months (Fig. 3a). Evaluating the specific actuarial survival, 96.8% of the patients were alive at 60 months and 80.6% were alive at 72 months (Fig. 3b).

Systematic Review

A total of 504 articles were found, i.e., 245 on PubMed, 110 on Embase, 15 on Cochrane Trials, 1 on Cochrane Review, and 133 on the Web of Science. Eight duplicate articles were excluded, 463 articles were excluded after analyzing the title and abstract, and 2 were unavailable in English. Thus, 31 articles were analyzed in full, 24 of which were excluded because they presented no data to analyze. The remaining 7 articles were included in the present analysis (Fig. 2).

Greer et al. [30] evaluated 2,983 women, but only 30 had tumors >5 cm (T3), with 47% being negative for

Table 3. Treatment performed

Variable	Category	Patients, n (%)
<i>Surgical treatment</i>		
Breast surgery	Simple mastectomy	21 (28.8)
	Skin-sparing mastectomy	17 (23.3)
	Nipple-sparing mastectomy	5 (6.8)
	Oncoplastic quadrantectomy	13 (17.8)
	Classic quadrantectomy	5 (6.8)
Axillary surgery	Axillary lymph node dissection	29 (39.7)
	Sentinel lymph node biopsy	44 (60.3)
<i>Adjuvant treatment</i>		
Adjuvant chemotherapy	12T/4AC	20 (27.4)
	4AC/12T	14 (19.2)
	6FAC	8 (10.9)
	4AC	7 (9.6)
	6CMF	4 (5.5)
	4AC/4T	3 (4.1)
	Other regimens	6 (8.2)
	Not used	11 (15)
Adjuvant trastuzumab ^a	Used	7 (70)
	Not used	3 (30)
RXT adjuvant breast	Mama + boost	18 (24.7)
	Resection site	49 (67.1)
	Not used	6 (8.2)
RXT adjuvant axilla/SCF	Used	40 (54.8)
	Not used	33 (45.2)
Adjuvant HT	Anastrozole	32 (54.2)
	Tamoxifen	22 (37.3)
	SWITCH (TMX-ANZ)	3 (5.0)
	Letrozole	1 (1.7)
	Exemestane	1 (1.7)

^a n = 10 Her-2+ patients. T, taxane; AC, anthracycline and cyclophosphamide; FAC, fluorouracil, anthracycline, and cyclophosphamide; CMF, cyclophosphamide, methotrexate, and fluorouracil; RXT, radiation therapy; HT, hormone therapy; SCF, supraclavicular fossa; TMX, tamoxifen; ANZ, anastrozole.

lymph node involvement. Okamoto et al. [31] retrospectively analyzed patients with a T3 tumor size and found 35% lymph node involvement. In a limited sample of 20 patients with tumors >5 cm, Bedrosian et al. [27] identified 80% lymph node involvement. Bernardi et al. [28] evaluated a limited number of patients with locally advanced tumors and observed 56.2% lymph node involvement when analyzing T3 and T4b together. Takei et al. [32] analyzed 91 patients with T3 tumors and observed 59.3% SN involvement. In that same publication, the authors showed that the rate of SN metastasis was 45.8% in 24 cases of T4b tumors. Coroş et al. [33] observed 86.6% lymph node involvement in T3 tumors. Wong et al. [34]

Fig. 3. Actuarial survival. (a) Overall. (b) Specific.

Table 4. Synthesis of the main findings observed in the literature

Study	T stage	SLNB +	Cases, <i>n</i>	SLNB +, %	SLNB N0, %
Bedrosian et al. [27]	T3	16	20	80.0	20.0
Greer et al. [30]	T3	16	30	53.3	46.7
Okamoto et al. [31]	T3	7	20	35.0	65.0
Coroş et al. [33]	T3	117	135	86.6	13.3
Wong et al. [34]	T3	23	31	74.2	25.8
Takei et al. [32]	T3	54	91	59.3	40.7
	T4b	11	24	45.8	54.2
Bernardi et al. [28]	T3/T4b	9	16	56.3	43.7
Subtotal T3	T3	233	327	71.3	28.7
Total T3/T4	T3/T4	253	367	68.9	31.1

+, metastatic lymph node; N0, absence of metastasis.

identified 74.2% lymph node involvement in T3 tumors. Table 4 summarizes the main results. Briefly, in the absence of metastatic lymph node involvement, 6 studies evaluated 327 T3 patients, with 28.7% lymph node involvement (114 out of 327 patients; Table 4). Only 1 study evaluated T4b patients, with 54.2% lymph node involvement (13 out of 24 patients). One study grouped T3 and T4b patients together, with 43.7% lymph node involvement (7 out of 16 patients). Combining all 7 studies, considering 367 patients and T3 and T4b tumors together, the rate of absence of lymph node involvement was 31.1% (124 out of 367 patients).

Combining the 7 studies with the present case series, considering the absence of lymph node involvement and micrometastasis, the rate of absence of lymph node in-

volvement was 32.1% in 374 T3 patients, 61.0% in 41 T4b patients, and 32.5% for the whole case series (T3 and T4b) of 431 patients.

Discussion

Deescalation of surgery in breast cancer has been associated with a significant reduction of morbidity. Measurement of this impact should consider the disease's epidemiological profile, which corresponds to the most frequent cancer in women, representing approximately 25% of cancers in women, with an increasing incidence and prevalence. Thus, small changes in practices, even in restricted subgroups, determine actions in larger numbers

of patients, making it important to individualize treatment scenarios [2, 11, 35].

Regarding tumor size, axillary lymph node involvement is more likely in tumors larger than 5 cm and with skin involvement, although the benefit of not performing ALND is unavailable to this population. However, the initial contraindications for SLNB have become debatable and relative over time [25], mainly because of the current association of the method with neoadjuvant chemotherapy and because prognostic/molecular staging has become as important as tumor TNM staging (tumor-node-metastasis) for defining treatment.

Regarding tumor size for determining axillary treatment, the staging may be clinical, radiological, or pathological, which may influence selecting patients for SLNB. Disagreement is often observed between clinical and pathological examinations as well as for imaging tests. Such variations in clinical/radiological sensitivity for determining tumor size [36] may interfere with the indication for SLNB, which can have clinical repercussions since initial clinical decisions are based on the clinical-radiological evaluation but can be modified via the anatomopathological evaluation. Thus, in the present study, 9 patients initially considered to have T3 tumors were shown to have T2 tumors. Thus, if the initial option had been ALND, most (6 out of 9 patients) would have undergone an unnecessary procedure.

One study evaluated surgeons' behaviors regarding axillary preservation in different settings and found that surgeons who had treated more breast cancer patients and participated in multidisciplinary teams had a greater tendency for axillary preservation. Further, many patients were overtreated with ALND, especially due to a lack of updating or training the surgeons [37]. Our service is located in an oncologic hospital that treats approximately 2% of the women with breast cancer in Brazil.

For pathologically confirmed tumors larger than 5 cm, the negative SN rate was 55.3%; however, the systematic review yielded a rate of 28.7%, with a range of 13.3–65.0%, although no articles described the patient selection process, the presence of an axillary ultrasound evaluation, or the tumor size considered, whether clinical, radiological, or pathological [27, 30–34]. In the present study, multiple criteria were used to select patients, such as axillary ultrasounds, FNAB, and intraoperative frozen sections, which was the reason for the high absence rate of axillary metastatic disease (46.8%). Ultrasonography elevates the axillary evaluation accuracy [38]. Likewise, ALND currently has no benefit in the presence of micrometastasis [22], and, as such, ALND can be avoided in 55.3% of patients, which we consider a very high number.

Larger tumor sizes yield higher rates of axillary involvement, and discussions are ongoing regarding the

acceptable and tolerable size for considering SLNB. A previous study of patients with clinically negative axilla who had undergone ALND considered up to 8 cm to be an acceptable size limit, with a negativity rate of 25% [39]. In evaluating this case series, the negativity rate decreased as the tumor size increased, being 26 out of 38 (68.4%) in tumors of 5.1–6.0 cm, 8 out of 12 (66.7%) in tumors of 6.1–7.0 cm, 4 out of 8 (50.0%) in tumors of 7.1–8.0 cm, and 1 out of 6 (16.7%) and 1 out of 4 (25.0%) in tumors larger than 8 cm. The literature on tumor size is scarce; thus, measuring tumor size is suggested in later studies, but in this study the use of SLNB in tumors up to 8.0 cm seems acceptable, since the only case without metastatic disease in tumors >8.0 cm was from the cT2pT3 group.

Patients with T4b tumors are candidates for neoadjuvant chemotherapy, but some patients with localized skin invasion, limited clinical conditions, or no conditions suitable for neoadjuvant chemotherapy are candidates for primary surgery. In these cases, SLNB was considered in the absence of axillary disease. Thus, combining the studies, and even with a restricted number of patients ($n = 41$) [32], the study showed the importance of axillary preservation in this patient group, where the rate of absence of metastatic disease was 61.0%.

The limitations of the present study do not diminish its importance regarding the paradigm shift in the axillary approach in tumors not previously subjected to SLNB. With rigid criteria for indicating SLNB, that is, without clinical or radiological suspicion, by selecting patients with low axillary tumor burdens, the benefit of SLNB can be evidenced without impacting ipsilateral axillary recurrence. The limited number of patients in the case series ($n = 73$) became expressive with the systematic review ($n = 431$). Although the systematic review was performed as a case series with an evidence level of 4, it allowed numerical transformation of the data into a relevant number. In the present study, multiple selection criteria were used with a selection bias, which may have influenced the high rate of T4b tumors without axillary metastatic involvement as well as the reasonable rate of T3 tumors. This can be reproduced, allowing many patients in similar conditions to be considered suitable for undergoing SLNB. Another limitation was the limited follow-up time for some patients (17.5 months), but the mean was considered acceptable (45 months), and no patients were lost to follow-up or had ipsilateral axillary tumor recurrence.

Several studies have shown the possibility of axillary preservation in the presence of a low axillary tumor burden [40, 41], if the patient undergoes adjuvant treatment with promising results in terms of axillary local recurrence, even with long follow-up times. In the present study, only patients without axillary metastatic disease in

SLNB did not undergo ALND, and all patients underwent adjuvant treatment with no axillary recurrence observed. The present study indicated that SLNB can be considered in selected patients and serves as a basis for discussion and implementation of this treatment in selected cases, a possibility that can be strengthened by analyzing more studies.

Conclusion

In selected patients with T3 and T4b tumors, the absence of axillary metastatic disease was >32.1%, and no ipsilateral axillary recurrence was observed. This indicates the feasibility of using SLNB in these patients.

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Statement of Ethics

The study protocol was approved by the Barretos Cancer Hospital committee on human research (No. 1244/2016). All of the patients signed the consent form for performing surgical treatment. Informed consent was not applied for this study because it evaluated retrospective data.

Disclosure Statement

The authors have no conflict of interests to declare.

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Author Contributions

I.O.J. and R.A.C.V.: substantial contributions to the conception or design of this work and acquisition, analysis, and interpretation of data for this work. E.A.P.N., A.C.C., and J.N.-N.: drafting this work or revising it critically for important intellectual content. I.O.J., R.A.C.V., E.A.P.N., A.C.C., and J.N.-N.: final approval of the version to be published.

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