Identification of the sentinel lymph node stained with blue dye in breast cancer patients

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Summary

Purpose: This study aimed to evaluate the reproducibility of sentinel lymphadenectomy in breast cancer patients ($T_1N_0M_0$ and $T_2N_0M_0$) and its possibility of predicting the total axillary behavior.

Methods: A total of 25 patients were evaluated, all presenting palpable mammary nodes between 1.5 and 5 cm (T_1 and T_2), with clinically negative axillary lymph nodes (N_0). After an incisional biopsy of the tumor and histopathological confirmation of invasive breast carcinoma, a study of the sentinel lymph node took place with a peritumoral injeção of 4 ml of blue dye at 2.5%. After waiting for 15 to 20 minutes, a search for the blue stained lymphatic vase in the axillary fat was carried out, which would lead to the sentinel lymph node, stained or not. At that point, a mastectomy (20 patients) or a quadrantectomy (5 patients) was performed, both with axillary lymphadenectomy at grades 1, 2 and 3. The sentinel lymph nodes and the material from the axillary dissection were sent separately for an anatomicopathological test in paraffin.

Results: The lymph nodes were identified in 19 patients, which represented a 76% detection rate. There was a concordance between the sentinel lymphadenectomy and the standard axillary dissection in 68.4% of the patients. The false-positive and the false-negative rates observed were 10% and 55.5%, respectively. A higher detection rate was found in tumors larger than 2 cm and situated in external quadrants.

Conclusions: Sentinel lymphadenectomy identified the sentinel lymph node in the majority of the patients in this study, although the high rate of false-negatives observed prevented an accurate staging.

Key words: Sentinel lymph node; Breast cancer; Blue dye.

Introduction

The condition of the operable axillary lymph node chain remains as the most important prognostic factor of recurrence and survival [1-3].

In the last decades, the adoption of mammographic screening has enabled the diagnosis of smaller tumors and the questioning on the radicalism of surgical treatment, especially axillary emptying, whose complications are found to be directly proportional to its extension, which can be incapacitating [3].

Modifying radical axillectomy (levels I, II and III) towards a more limited dissection, normally of level I or, I and II, aims mainly at reducing potential morbidity, in addition to decreasing costs. Moreover, there is a clear incentive to avoid the performance of wide axillary surgery in patients with clinically negative axillas [1, 2].

The sentinel lymph node is defined as the first ganglion to receive lymphatic drainage of a tumor, and therefore, the most likely to contain metastasis [7, 8].

Sentinel lymphadenectomy is considered a less invasive method than complete axillary dissection or even axillectomy in levels I and II, resulting in less morbidity and lower costs [2, 4-6].

This study aimed at evaluating the reproducibility of sentinel lymphadenectomy in breast cancer patients ($T_1N_0M_0$ and $T_2N_0M_0$) and its possibility of predicting total axillary compromise.

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Patients and Methods

This study was developed with 25 patients presenting palpable mammary nodes measuring from 1.5 cm to 5 cm (T_1 and T_2) and clinically negative axillary lymph nodes (N_0), at the Mastology Division of the Obstetrics and Gynecology Service of the Hospital do Servidor Público Estadual – São Paulo, after the approval of the Institution's Ethics Committee in the period from March to September, 1998.

The age of the patients varied from 42 to 82 years, presenting a mean of 62.5 ± 13 years. There were 20 postmenopausal patients (80%) and five patients (20%) were in the menacme. Tumors up to 2 cm (T_1) occurred in eight (32%) patients. Those larger than 2 cm and smaller or equal to 5 cm (T_2) were found in 17 (68%) of them.

All the patients were informed about the study in question and after written consent, they were submitted to incisional biopsies of the tumors for the histopathological confirmation of invasive carcinoma in frozen exam.

After diagnostic confirmation and choosing the surgical approach, the search for the sentinel lymph node took place with a peritumoral injection of 4 ml of blue-violet dye at 2.5% and a posterior massage at the place of the injection for 3 to 5 minutes. After 15 to 20 minutes, the referred surgical procedure began.

A Patey modified radical mastectomy was performed in 20 (80%) patients. In five (20%) patients the surgery chosen was quadrantectomy. All the patients were submitted to axillary emptying at levels I, II and III.

During the Patey mastectomy or the quadrantectomy, a search for the blue stained lymphatic vase in the axillary fat took place, which would lead to the lymph node, stained or not.

The sentinel lymph nodes and the product of the axillary dissection were fixed in formol at 10% and sent separately for

histopathological exams. The positivity for lymph node metastasis was taken into consideration upon finding any size of tumor focus, either micro or macrometastases.

The sentinel lymph node detection rate was then calculated. It was defined as the proportion of these lymph nodes found in all the cases in which sentinel lymphadenectomy was performed followed by total axillary dissection.

The accuracy of the test (sentinel lymphadenectomy) was evaluated in relation to a procedure considered the "gold standard" (total axillary dissection).

Results

The sentinel lymph node was found in 19 out of the 25 patients studied, with a 76% detection rate (Table 1). The mean number of sentinel lymph nodes found was 1.7 per case (all in level I) and the mean number of dissected lymph nodes was 15.1 per case.

In six cases it was not possible to find the blue stained lymphatic vase or the sentinel lymph node. Four of these cases occurred in the first ten procedures performed. In three patients the tumors were bigger than 2 cm (Table 1). In all the cases (6/6), the mammary tumors were located in the upper medial quadrant (Table 2).

Among the 19 patients in which the sentinel lymph node was identified (19/25), there was concordance with the rest of the axilla in 13 of them (true-positive and true-negative), which meant a 68.4% accuracy (Table 3).

Table 1. — *Relationship between size of the tumor and identification of the lymph nodes.*

Sentinel lymph nodes	Number of cases	%	Size of the tumor			
			T_1	%	T_2	%
Identified	19	76	05	62.5	14	82.4
Not identified	06	24	03	37.5	03	17.6
Total	25	100	08	100	17	100

T_1: tumor ≤ 2 cm; T_2: tumor > 2 cm and ≤ 5 c.

Table 2. — *Relationship between location of the tumor and identification of the sentinel lymph nodes.*

Sentinel lymph nodes	Number of cases	%	Tumor localization			
			IQ	%	EQ	%
Identified	19	76	04	40	15	100
Not identified	06	24	06	60	–	–
Total	25	100	10	100	15	100

IQ: internal quadrants; EQ: external quadrants.

Table 3. — *Comparison between sentinel lymphadenectomy (test) and radical axillary emptying (gold standard) for the presence or absence of metastases in dissected lymph nodes.*

Sentinel lymphadenectomy		Radical Axillary Emptying Metastases		
		Yes	No	Total
Metastases	Yes	04	01	05
	No	05	09	14
	Total	09	10	19

Yes: presence of metastasis; No: absence of metastasis.

Five out of these 19 patients presented, after histopathological confirmation, lymph nodes positive for metastasis. In four cases (4/5), the sentinel lymph nodes were concordant with the material from the axillary dissection (true-positive). There was a case where the sentinel lymph node was the only one compromised (1/5), thus reflecting a 10% false-positive rate (1/10) (Table 3).

Fourteen patients presented negative sentinel lymph nodes after the pathological examination (14/19). In this group, the sentinel lymph nodes were concordant with the axillary dissection in nine cases (true-negative). In the five remaining cases, the sentinel lymph nodes did not contain metastases, while the material from the axillary dissection did show compromised lymph nodes (false-negatives). These data reveal a 55.5% false-negative rate (5/9) (Table 3).

Upon separating the tumors by size (T_1 and T_2), a higher detection rate was evidenced, as well as a lower false-negative rate in tumors larger than 2 cm. In small tumors (T_1), the false-negative rate represented 100% of the cases, where the sentinel node was identified (Table 4).

For the tumors located in the external quadrants, the detection rate was greater, if compared to the ones situated in the medial quadrants. The false-negative rates were higher in the internal quadrant tumors (Table 5).

Table 4. — *Relationship between size of the tumor and false-negative detection rates of the sentinel lymph nodes.*

Size of the tumor	Number of cases	Detection rate (%)	False-negative rate (%)
T_1	08	62.5	100
T_2	17	82.3	50

T_1: tumor ≤ 2 cm; T_2: tumor > 2 cm and ≤ 5 cm.

Table 5. — *Relationship between location of the tumor in the breast and false-negative detection rates of sentinel lymph nodes.*

Tumor localization	Number of cases	Detection rate (%)	False-negative rate (%)
EQ	15	100	50
IQ	10	40	100

IQ: internal quadrants; EQ: external quadrants.

Discussion

The data suggest that axillary lymph node metastases follow an orderly pattern of tumor progression [8, 9]. The sentinel lymph node concept reaffirms this process of tumor progression, from a primary location in the regional lymph node and that the first lymph node effectively filtrates the afferent lymphatic vase of tumor cells and is capable of confining them efficiently [7]. In this study, all the sentinel lymph nodes were found at level I, thus in agreement with the literature.

The biggest obstacle in defining the term the sentinel lymph node is to describe it in the singular, because it implies that only one ganglion receives all the drainage of a primary tumor [8]. Although this can occur, in a number of cases multiple sentinel lymph nodes may

exist, either grouped or in separate locations [10]. More than one sentinel lymph node per patient was found in the majority of the patients in this study (11/19) dispersed in the axillary fat below the lateral edge of the small pectoral muscle and not grouped (level I).

Of the 25 patients in this study, the detection rate of the sentinel lymph nodes was 76% (19/25). Four of the six cases in which the lymph node was not identified, were among the first ten patients. Other factors that are possibly associated with the difficulty in finding these lymph nodes were the presence of tumors located in the supermedial quadrant (5/6), a tumor size of 4.5 cm (1/6) and multicentricity (2/6).

The first study to search for the sentinel lymph node using a dye (isosulfan blue) in T_1, T_2 and T_3 tumors enabled its identification in 65.5% of the cases; the operation was performed by only one surgeon, with the aim of evaluating the learning curve of a new procedure. A 58.6% detection rate was demonstrated in the first 87 cases while in the final 50 patients the lymph node was found in 78% of the cases [4]. Subsequent studies utilizing the same technique have shown detection rates varying from 71% to 93.5%, thus emphasizing that the success in finding the sentinel lymph node is directly related to the experience of the researcher [11-14].

In this series, of 19 patients (19/25) where the sentinel lymph node was identified, it can be observed that sentinel lymphadenectomy was concordant with axillary dissection – in the presence or absence of metastases – in 13 cases (68.4%). In many studies involving the search for the sentinel ganglion with dye, the capability of sentinel lymphadenectomy in predicting the axillary status varied from 83% to 100% with the best results occurring after the mastery and confidence of the surgeon in an accurate performance of the technique [4, 11, 13, 14].

Finding the sentinel lymph node, the only one compromised by metastasis in breast cancer, validates the sentinel lymphadenectomy technique from a biological point of view [8]. Epidemiologically, this fact is represented by false-positive cases.

In the 19 patients where sentinel lymph nodes were identified, it was observed that nine cases had metastatically compromised lymph nodes and materials from axillary dissection. In five of the nine cases, the sentinel lymph node was not compromised, which led to a high rate of false-negatives (55.5%) in our case series. This reflects the fragility of sentinel lymphadenectomy in accurately predicting the true axillary status.

It should be noted that the small number of cases in this sample reflects indices which are not satisfactory to evaluate the efficacy of this test due to the false-negative rates.

There is a clear relationship between tumor size and the detection rates of false-negatives [15, 16]. In this study larger tumor size was associated with a higher detection rate of the sentinel lymph node. This could be due to a direct association between tumor size and axillary lymph node involvement, and based on the definition of the sentinel lymph node, a higher axillary lymph node effect could be expected, thus determining a higher facility in identifying this lymph node. Another factor to be taken into consideration is the probability of chance in determining this result due to the small case series.

This study found lower false-negative rates (50%) in T_2 tumors compared to T_1 tumors (100%). All the false-negative cases (T_1 and T_2) presented peritumoral lymphatic invasion. In the literature the number of false-negatives are especially associated, with the presence of peritumoral vascular invasion and also to multifocality [5].

Although some authors affirm no existing important differences in the axillary lymph node involvement such as the location of the breast tumor, sentinel lymphadenectomy, when the tumors are located in the internal quadrants, is found less efficient, thus presenting a higher number of false-negatives [5, 6].

The time the dye injection takes is also another extremely important factor, as there is be a bigger track to travel up to the axilla. The lesions located in the lower quadrants can drain to the internal mammary lymph nodes [6]. These factors could explain six cases in which the lymph node was not found in super-medial quadrant tumors.

Other factors that influence the detection of sentinel lymph nodes are multifocality and multicentricity [17]. Multifocal tumors frequently involve more than one lymphatic trunk of the mammary gland, propitiating the occurrence of "skip" metastases. Thus the consensus is that when the tumor focuses are found 3 cm apart or more, sentinel lymphadenectomy should not be carried out [5, 17]. This could explain the fact that no sentinel nodes were found in two cases of this study, where the anatomicopathological examination of the mastectomy material showed another tumor focus 3 cm material from the initial lesion.

As to conservative surgery for adequate evaluation of axillary node compromise in breast cancer, the projection for the future is based on the encouraging results of sentinel lymphadenectomy, especially, the decrease in morbidity and costs.

It is important to emphasize that for an accurate staging, it is necessary to have long-term follow-up of patients submitted to sentinel lymphadenectomy without complementary axillary dissection, in order to validate definitively the technique as to safety and also reliability, with less morbidity and costs.

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