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A Retrospective Study on Correlation between Sentinel Node Biopsy, Axillary Node Sampling and Type and Grade of Tumour in Breast Cancer Patients

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Abstract

Lymph node metastases are the most significant prognostic factors in patients with breast carcinoma. A lymph node defined as sentinel lymph node (SLN) would be the first to receive tumoral drainage. A positive sentinel lymph node (SLN) biopsy is followed by an axillary lymph node clearance (ANC). In sentinel lymph node negative cases, the risk of positive non-sentinel lymph nodes (ANS: Axillary node sampling) is very low. The aim of this retrospective study was to determine the rate of sentinel lymph node (SLN) positivity, number of SLN harvested, grade, size and type of the tumour in SLN positive cases and the percentage of ANS positivity, in addition to ANC complications. Patients and Methods— Between January 2009 and May 2010, 223 female patients with breast cancer who underwent wide local excision and the SLN biopsy were reviewed. 222 patients of them had SLN biopsy. Results— SLNs were positive in 44 of 223 (19.82%) The mean number of SLNs removed was 2.35; the median was 2. ANSs were positive in 5 of 117 cases. The mean number of ANSs removed was 2.25, the median was 2. The Commonest grade of tumour in cases of positive SLN was grade 2. The Commonest type of tumour was invasive ductal carcinoma (73.99%) followed by invasive lobular carcinoma (10.3%).The complications of ANC were seen in 25 patients (60.97%) out of 41 patients Conclusion—SLN positivity was 19.82% and the median SLN collected was 2. ANS positivity was 4.3%. The commonest grade was grade2. The Median size of tumour with positive SLN is 17mm.

Keywords

Sentinel Lymph Node (SLN), Axillary Node Sampling (ANS), Axillary Node Clearance (ANC), Tumour Grade

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1. Introduction

The Sentinel lymph node (SLN) biopsy is a simple, minimally invasive technique which uses subareolar or peritumoral injection of vital blue dye or radio-labelled colloid, or both substances together, to identify the first lymph node(s) draining the primary tumor. It has been shown to predict accurately the axillary node status in patients with clinically node-negative breast cancer (1–4). Tumour location, multifocality, tumour size, neoadjuvant systemic therapy, and prior breast surgery do not seem to reduce the accuracy of the SLN biopsy technique (6–12). Moreover, prospective observational studies have indicated that the technique is not associated with an increase in axillary recurrence, and have confirmed that it has a low overall morbidity (1–4). The sentinel lymph node(s) can be examined intraoperatively by frozen section (5), one step nucleic acid amplification (OSNA) technique or imprint cytology. Axillary node clearance can be subsequently performed if intraoperative examination of the node is positive for malignancy, thus avoiding the need for a second surgical procedure. Lymph node metastases are the most significant prognostic factors in

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patients with breast carcinoma. A positive sentinel lymph node (SLN) biopsy is followed by an axillary lymph node clearance (ANC) with or without adjuvant radiotherapy (RT) . In sentinel lymph node negative cases, the risk of positive non-sentinel lymph nodes (ANS) is very low though not absent. Axillary lymph node Clearance (ANC) is an important procedure in the staging of breast cancer patients. However, it is associated with a significant morbidity rate.

2. Patients and Methods

Between January 2009 and May 2010, 223 female patients with breast cancer who underwent wide local excision and the SLN biopsy procedure in the unit were reviewed. 222 patients of them had SLN biopsy. The SLN biopsy was performed using the vital blue dye method alone, or the combination of the dye and the radioactive isotope technique. The tracers were injected in subareolar and/or peritumoral locations. The sentinel node had been defined as a blue node, a node receiving a blue lymphatic and/or hot, and the node with the radioactivity detected by a gamma probe.

3. Results

3.1. Sentinel Lymph Nodes

A total of 223 sentinel breast cancer patients identified, 222 of them had SLN biopsy, SLN wasn't done in 1 patient (ANS +ve) (Table l). SLNs were positive in 44 of 223 (19.82%) carcinomas, 38 (86.4%) with macrometastases and 6 (13.6%) with micrometastases. Totally there were 45 positive lymph nodes patients .The mean of SLNs removed per patient was 2.35, and the median of the SLNs was 2 (range: 1–7). Overall 19.82% (44/223) of patients were found to be SLN-positive on histology. Out of 45 patients with positive nodes, 41 patients had ANC and 4 patients had radiotherapy alone. In RT group, 3 patients had macrometastasis (patients choice in 2 cases and 1 patient had pulmonary embolism) and 1 patient had Micrometastasis (radiotherapy was decided by clinician).

Of these positive 45 patients, 39 patients had macrometastasis, and 6 patients had micrometastasis. In micrometastasis group, 5/6 had ANC: 3 patients had no further LN metastasis, 1 patient with 1 LN metastasis, and 1 patient with 8 LN metastasis, and 1 patient had radiotherapy alone

Table 1. Summary of Sentinel Node Biopsy

The total number of cases	- 223
SLN was done	- 222
SLN wasn't done	- 1 (ANS +ve)
SLN was done but no LN	- 4 (ANS was also done in all four cases and were –ve for tumour).

Table 2. Total number of SLNs positive for metastasis

1 node	28	63.64%
2 nodes	12	27.27%
3 nodes	4	9%
4 nodes	1	0.09%

3.2. Axillary Node Sampling (ANS)

The Axillary node sampling was done in 117 patients. It was positive in 5 patients (4.27%). 4 of the 5 patients had 1 LN metastasis, and 1 patient had 2 LN metastasis. The mean of ANS collected was 2.25, the median was 2 (range: 1-9)

3.3. Grade of Tumour

The commonest Grade in the all cases was grade 2 and also, the commonest grade with positive SLN is grade 2 rather than grade 3.

Table 3. Tumour grade in SLN positive cases

Grade	Number of cases	Percentage
Grade1	57	25.6
Grade2	98	43.9
Grade3	61	27.35
In Situ	6	2.7

3.4. Type of Tumour

Table 4. Tumour type in all cases

Type of Tumor	Number of Cases
Invasive Ductal Carcinoma	165
Invasive Lobular Carcinoma	23
Invasive Ductal and Lobular Carcinoma	13
DCIS	6
Invasive Non-keratinizing SCC	1
Benign Papilloma with Implantation	1
Others (Papillary, Medullary, Mucinous)	14

3.5. Size of Tumour

The median of tumour size was 19.725 mm and the mean was 18 mm, the range was 2-85 mm .The median of tumour size in positive SLN was 17mm, the mean was 16.95 mm.

3.6. Complications of Axillary Node Clearance

The complications of ANC were seen in 25 patients (60.97%) out of 41 patients who had ANC.

Table 5. Complications of Axillary Node Clearance

Complications	Number of cases
seroma	18
wound infection	5
haematoma	2

4. Discussion

The concept of sentinel lymph node biopsy in breast cancer surgery relates to the fact that the tumor drains in a logical way through the lymphatic system, from the first to upper levels. Therefore, the first lymph node met (the sentinel node) will most likely be the first to be affected by metastasis, and a negative sentinel node makes it highly unlikely that other nodes are affected. Because axillary node dissection does not improve prognosis of patients with breast cancer (being important only to stage the axilla), sentinel lymph node biopsy might replace complete axillary dissection to stage the axilla in clinically N0 patients. Sentinel lymph node biopsy would represent a significant advantage as a minimally invasive procedure, considering that, after surgery, about 70% of patients are found to be free from metastatic disease, yet axillary node dissection can lead to significant morbidity. Furthermore, histologic sampling errors can be reduced if a single (sentinel) node is assessed extensively rather than few histologic sections in a high number of lymph nodes per patient.

The term "sentinel node"—that is the first lymph node encountered by lymphatic vessels draining a tumor—was coined in 1960 by Gould et al. (13) for cancer of the parotid gland. The value of lymphatic mapping was highlighted in 1977 by Cabanas (14) with his studies of patients with penile cancer.

Mammographic screening procedures result in early detection of breast cancer, when the tumor is around 1 cm in diameter (15,16) and the probability of axillary metastasis is relatively low (20%–30%) (17-19). A negative axilla at clinical examination has a poor predictive value concerning cancer involvement of lymph nodes; therefore, histologic examination of any nodes is important in identifying metastatic involvement. Unfortunately, this implies the risk of some significant side effects, resulting, for example, from axillary node dissection. These considerations explain the ongoing debate about whether to routinely perform axillary dissection in breast cancer (20,21), which still represents the standard surgical treatment for breast cancer irrespective of tumor size.

The 20%–30% likelihood of axillary nodal metastases in early breast cancer (T1a-b, tumor size, ≤1 cm), which rises to 30%–40% when including also patients with T1c cancer (size, 1–2 cm), has maintained axillary node dissection as part of the staging procedure in patients with a clinically negative axilla (22). Regrettably, axillary dissection is associated with a relatively high incidence of immediate and late postsurgical complications, especially lymphedema and sensory-motor disturbances. Because these occur in many patients who are found to have no nodal disease after surgery, these distressing outcomes fuel the debate on routine axillary node dissection in all patients with breast cancer (23).

Focusing on just 1 or a few sentinel lymph node(s) for extensive histologic evaluation increases the accuracy of histopathologic staging of the axilla in patients with breast cancer (24). Thus, the availability of a minimally invasive procedure for defining axillary node status in patients with early breast cancer whose disease is clinically N0 is particularly attractive to surgeons and to patients.

To have real impact in the management of breast cancer patients, histologic examination of the sentinel lymph node(s) must be extremely careful and extensive. The nodes must be entirely and serially sectioned at reduced intervals. Computer simulations and the current practice have shown that, to identify small micrometastatic foci (size, ≤2 mm), the nodes must be sectioned at 50- to 200-µm intervals, thus evaluating up to 60 or more sections per node (25). Most macrometastases in a sentinel node are detected in few sections starting from the hilus: about 77% in the first section, 84% within the first 3 sections, and 93% within the first 5 sections. Distribution of micrometastases in a sentinel node is much more dispersed, with only about 53% detected within the first 5 sections and 91% within the first 10 sections; a no negligible 9% will be found in sections 11–20 (G. Viale, data, December 2000); after all, tumor cell clusters giving rise to metastases nest initially in the most peripheral sinusoid spaces of the lymph node. On the other hand, detecting micrometastases is crucial because their presence in the sentinel lymph node is associated with additional metastatic disease of the axilla in about 25% of the patients (25).

Histological grade and type, tumour size and presence or absence of axillary node metastases is well-recognised prognostic factors of breast cancer. Tumour grade, size and nodal involvement are three factors considered in Nottingham Prognostic Index [26]. Histological grade and type on their own can be helpful in predicting the biological behaviour of the tumour as regards to local recurrence and overall survival Green Hough (1925) was the first to categorise the breast tumours into three grades according to its differentiation. He also assessed the association of grades with "cure" though the term cure was not clearly defined [27]. Since then a clear association between grades and prognosis has been established .Higher the grade, greater is the chance of the tumour relapsing [28]. It has also been noted that oestrogen receptor (ER) negative tumours are usually of higher grade [29]. Higher the tumour grade more aggressive is the tumour and nodal involvement too is directly related to aggressiveness of the tumour [29]. All these factors suggest that higher the grade of tumour more radically should it be managed.

5. Conclusion

SLN biopsy can accurately determine whether axillary metastases are present in patients with breast cancer with clinically negative axillary nodes. Both success and accuracy of SLN biopsy are optimised by the combined use of blue dye and isotope. Our results support previous observations except that grade-2 tumours had maximum metastasis to sentinel lymphnode.

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