Sentinel Lymph Node Detection in Early Carcinoma Breast: A Comparative Study Between Intraluesional and Perilesional Dye Injection

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ABSTRACT:
Background and objective: Axillary lymph node status is the most important prognostic indicator for patients with primary breast cancer. Recent introduction of intraoperative lymphatic mapping and sentinel lymph node dissection (SLND) for primary breast cancer allows directed and accurate assessment of axillary involvement with minimal morbidity. This study aims at comparing the routes for detection of sentinel lymph nodes for the better management of carcinoma breast.

Material and method: This was a prospective descriptive study of 60 patients admitted with carcinoma breast without palpable axillary lymph nodes from October 2013 to September 2015. After induction of general anesthesia, 5 ml of 1% methylene blue was infiltrated into the perilesional or intraluesional part of the tumour and sentinel nodes were identified, removed and sent for histopathological examination. Then results from both the groups were compared.

Observation and results: Among all the studied patients 55 (91.67%) patients got the lymph node stained with the methylene blue dye and 5 (8.33%) patients were not having stained lymph nodes. Out of these 28/30 (93.33%) were detected by the intraluesional route and 27/30 (90%) through the perilesional route. Among all the detected and surgically removed lymph nodes histopathological examination were done and 22 out of 55 (40%) patients were found to have metastasis in the lymph nodes. Depending upon the detection of metastasis in the sentinel lymph nodes, 22 patients underwent modified radical mastectomy.

Conclusion: No significant difference in the detection rate of sentinel lymph node between these routes. Axillary lymph node dissection (ALND) should be reserved for only those patients who were found to have metastasis to the lymph nodes.

Keywords: Axillary lymph node dissection (ALND), Histopathological examination (HPE), Intraluesional, Perilesional, Sentinel lymph node biopsy (SLNB).

Key message: Axillary lymph node status is the most important prognostic indicator for patients with primary breast cancer. Till date not a single non invasive method achieved a certain level of diagnostic accuracy for sentinel lymph node detection. Meanwhile intra operative detection of sentinel nodes is more directed and accurate with minimum morbidity.

1. INTRODUCTION

Sentinel lymph nodes are the nodes in a tumor bed that first receive lymphatic drainage from the tumor and are, therefore, the nodes most likely to harbor tumor cells, if tumor cells have indeed entered the lymphatics. William Halsted described lymph nodes as barriers to the spread of tumor cells, as vehicles for progression of tumor spread within lymphatics, and as vehicles for progression of tumor spread from lymphatics to more remote sites [1]. That description includes good precursors of the bases of our modern notion of sentinel node.

Axillary lymph node status is the most important prognostic indicator for patients with primary breast cancer [2]. Lymphatic mapping with sentinel lymph node biopsy (SLNB) has emerged as an effective method of detecting axillary metastases. At present, there are no adequate noninvasive techniques for assessment of axillary status in patients with primary breast cancer. Physical examination carries a 29%–38% false negative
rate, and radiographic methods (mammography, computed tomography, and positron emission tomography) have not achieved the level of accuracy on which to base clinical decisions [3-4].

Recent introduction of intraoperative lymphatic mapping and sentinel lymph node dissection (SLND) for primary breast cancer allows directed and accurate assessment of axillary involvement with minimal morbidity [5]. This study aims at comparing the routes for detection of sentinel lymph nodes and for the better management of carcinoma breast.

II. AIMS AND OBJECTIVES
To compare Intralesional and Perilesional routes of methylene blue dye injection for detection of sentinel lymph nodes in early carcinoma breast and to evaluate the most suitable route and impact of SLNB in prognosis.

III. MATERIAL AND METHOD
All patients [n=60] admitted with carcinoma breast without palpable axillary lymph nodes at Rajendra institute of medical sciences, Ranchi, India from October 2013 to September 2015 included in the study. Patients with Inflammatory breast cancer (T4d), Clinically N1 disease, Pregnancy, Prior axillary surgery and not willing for surgery or study participation were excluded from the study.

After induction of general anesthesia, 5 ml of 1% methylene blue is infiltrated into the perilesional or intralymphatic part of the tumour with special care to avoid injection into the skin or submammary connective tissue and muscle. Then breast is massaged gently for 5 minutes. All blue nodes and any node receiving a blue tinge was identified or not, number of Sentinel nodes. Total number of nodes removed should usually not exceed three, otherwise the benefits of the limited dissection required for SLNB could be compromised. The following variables were then recorded on to a pre-coded form: Mastectomy versus breast conserving surgery, site of injection, SLN identified or not, number of Sentinel nodes. Then Surgery is completed, including axillary lymph node dissection.

IV. OBSERVATION AND RESULT
Total of 60 patients who were admitted for breast lump without palpable axillary lymph nodes at Rajendra Institute Of Medical Sciences, Ranchi, and later diagnosed as a case of carcinoma breast were evaluated. Of these, 2 groups were created comprising of 30 patients in each group. One group was injected the methylene blue dye intralymphatically and the other group was injected the methylene blue dye perilesionally. It was found that carcinoma breast is more 54 (90%) common in females aged more than 40 years and rare 1 (1.67 %) only in less than 30 years of age [Table 1]. Most common site for the occurrence of tumor in breast was the upper outer quadrant 49 (81.67%) and rarest in the upper inner quadrant 3 (5%) [Table 2]. Most of the patients were in T1 53 (88.33% ) stage and rest in T2 stage 7 (11.67%) [Table 3]. Among all the patients 38 (63.33 %) were found to be ductal carcinoma and 22 (36.67%) was lobular carcinoma in nature by trucut biopsy. After Immunohistochemistry 49 (81.67%) of the tumour were found to be having estrogen receptor status positive, 17 (28.33%) were having progesterone receptor positive and 17 (28.33%) of the tumour were HER-2 NEU positive. Among all the studied patients 55 (91.67%) patients got the lymph node stained with the methylene blue dye and 5 (8.33%) patients were not having stained lymph node. Out of these 28/30 (93.33%) were detected by the intralesional route and 27/30 (90%) through the perilesional route [Table 4]. Among all the detected and surgically removed lymph nodes histopathological examination was done and 22/55 (40%) patients were found to have metastasis in the lymph nodes [Table 5]. Depending upon the detection of metastasis in the sentinel lymph node 22 patients underwent modified radical mastectomy, rest of the patient (38) went for breast conservative surgery followed by adjuvant radiotherapy. No any adverse reaction Of dye injection occurred in either of the patients. Although complication managed conservatively, 6 (10%) patient developed seroma and subsequently wound infection and 4 (6.67%) patients developed lymphedema and pain in the upper limb. All the studied patients followed till date and no any further recurrence of the carcinoma or any other complication developed.

V. DISCUSSION
Breast cancer patients routinely undergo surgical staging of the axilla because of primary tumor features are inadequate in predicting the presence versus absence of nodal positivity. The prognostic significance of axillary nodal involvement also extends to the number of nodes involved [1]. Axillary lymph node dissection (ALND) with histopathologic study of the axillary specimen remains the gold standard for detecting axillary nodal involvement and determining the number of nodes involved [6]. However, the low (<3%) rate of axillary recurrence in patients undergoing level I-II ALND [6-8]. The removal of level I and level II lymph nodes at axillary node dissection (ALND) is the most accurate method to assess nodal status, and it is the universal standard. Although complication rates may decrease by limiting the extent of axillary...
dissection, nondirected sampling of axillary nodes is associated with unacceptably high false negative rates: 40% for random axillary nodal sampling and 10%-15% for excision of level I nodes [9-10]. Axillary lymph node dissection has been part of the standard treatment of breast carcinoma since it was proposed by Halsted (1852-1922) [11]. The axillary lymph node status represents the most important information for the prognosis of patients with breast carcinoma and is one of the parameters that indicate the need for adjuvant systemic treatment. Axillary lymph node dissection also assures regional tumour control and improves survival [12].

This study was undertaken to compare between the intralesional and perilesional route of administration of methylene blue dye and to study the prognosis on management of the patients with early breast carcinoma. In this study of 60 patients, dye was injected through intralesional route in 30 patients and through perilesional route in another 30 patients. Among these 55 patients were identified with staining of the dye. Of these 28/30 (93.33%) were found through intralesional route and 27/30 (90.00%) through perilesional route. Similar detection rate was found ranging from 90%-98% in various studies conducted by Kapteijn et al (1998), Horgan et al (1998), Giuliano et al (1997), Miner et al (1998), Koller et al (1998) [13-17]. No significant difference was found in the detection rate of sentinel lymph nodes through both of these routes. All the sentinel lymph nodes detected, were sent for histopathological examination and it was found that 22 patients were having metastasis, out of which 12/28 (42.86%) were detected from the sentinel lymph nodes retrieved by the intralesional route, and 10/27 (37.03%) were detected from the sentinel node retrieved by the perilesional route. Similar detection rate was reported by MH Doting et al 2000 which says 49% of the sentinel lymph nodes retrieved by the intralesional route were found to have metastasis [18]. Similarly it was found that 36%-41% of the sentinel lymph node were found to have metastasis in the detected lymph node by John J Albertini et al(1996), Brian J Ohea et al (1998) [19-20]. Depending upon the presence of metastasis in the lymph node 22 patients were treated by Modified Radical Mastectomy which accounts for 36.67% of the patients whose treatment modality changed following the presence of metastasis in the lymph nodes, as they could have gone with Breast conserving surgery or with simple mastectomy as clinically no lymph nodes were palpable. According to american society of clinical oncology (2005), SNLB is an appropriate initial alternative to routine staging ALND for patients with early-stage breast cancer with clinically negative axillary nodes. Completion of ALND remains standard treatment for patients with axillary metastases identified on SLNB [21]. No adverse reaction was detected in both groups of patient following administration of the dye. Blue dye performed well as a single modality for SLN biopsy. Non-identification, axillary nodal recurrence and serious allergic reactions were uncommon [22]. SLN biopsy procedure has proven to be safe; serious allergic reactions to isosulfan blue dye are infrequent [23]. Out of all the 55 operated patients 6 patient developed seroma and wound infection and 4 patient developed lymphedema and pain following breast surgery. The axillary web syndrome, seroma formation, axillary paresthesia, axillary haematoma and wound infection can be found as complications after SLNB procedure. When compared with SLN/ALND, SLNB alone results in a significantly lower rate of lymphedema 5 years postoperatively. However, even after SLNB alone, there remains a clinically relevant risk of lymphedema [24].

Depositing the dye around the tumour is in theory as accurate as injecting the dye into the lesion but has several drawbacks. For instance, it is more difficult to distribute the dye all around the tumour. A theoretical problem is that the needle tip may end up underneath the fascia, when trying to inject around a deep lying tumour because the resistance of the tumour is not felt after insertion of the needle. Needle tract metastasis may occur at the fascia because the needle may pass through one or more of the tumour protrusions. The risk of local recurrence then is enhanced in patients who undergo breast conservative surgery. There is also a potential danger of needle tract seeding by intratumoural injection, but this needle tract is usually part of the mastectomy in breast conservation surgery.

### VI. TABLES

#### Table 1. Age of the patients

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Frequency</th>
<th>Percent(%)</th>
<th>Valid percent</th>
<th>Cumulative percent</th>
</tr>
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<tbody>
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<td>&lt;30</td>
<td>1</td>
<td>1.67</td>
<td>1.67</td>
<td>1.67</td>
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<tr>
<td>31-40</td>
<td>5</td>
<td>8.33</td>
<td>8.33</td>
<td>10</td>
</tr>
<tr>
<td>&gt;40</td>
<td>54</td>
<td>90</td>
<td>90</td>
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<tr>
<td>Total</td>
<td>60</td>
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#### Table 2. Tumor site

<table>
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<tr>
<th>Quadrant of Breast</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid percent</th>
<th>Cumulative percent</th>
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<tbody>
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<td>Upper Outer</td>
<td>49</td>
<td>81.67</td>
<td>81.67</td>
<td>81.67</td>
</tr>
<tr>
<td>Lower Outer</td>
<td>8</td>
<td>13.33</td>
<td>13.33</td>
<td>95</td>
</tr>
<tr>
<td>Upper Inner</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100</td>
<td>100</td>
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</tbody>
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Table 3. Tumor size

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 &lt; 2 cm</td>
<td>53</td>
<td>88.33</td>
<td>88.33</td>
<td>88.33</td>
</tr>
<tr>
<td>T2 &gt;2 to ≤ 5 cm</td>
<td>7</td>
<td>11.67</td>
<td>11.67</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100</td>
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</table>

Table 4. Detection of sentinel lymphnode

<table>
<thead>
<tr>
<th>Route of dye administration</th>
<th>Stained lymphnode (no. of patients)</th>
<th>Not stained lymphnode (no. of patients)</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Intralesional</td>
<td>28</td>
<td>02</td>
<td>30</td>
</tr>
<tr>
<td>Perilesional</td>
<td>27</td>
<td>03</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
<td>05</td>
<td>60</td>
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Table 5. HPE report of stained lymphnodes

<table>
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<th>Route</th>
<th>Sentinel node metastasis</th>
<th>Total</th>
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<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Intralesional</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Perilesional</td>
<td>10</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>33</td>
</tr>
</tbody>
</table>

VII. CONCLUSION

We came to conclude that, there are no significant differences in the detection rate of sentinel lymph nodes between these two routes. Both of these route is safe and non hazardous but technically perilesional route is easier to administer the dye. Approximately 40% of the patients were found to have locoregional metastasis to the axillary lymphnodes. Hence Axillary lymph node dissection should be reserved for only those patients who were found to have metastasis to the lymph nodes.

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