ASSESSMENT OF CLINICAL & MORPHOLOGICAL PROGNOSTIC FEATURES ON
MASTECTOMY SPECIMEN

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ABSTRACT

Objective: To assess clinical and morphological prognostic features of breast cancer, to
evaluate and determine the prognostic usefulness of Nottingham prognostic index (NPI) and
its components. Methods: A prospective and retrospective study was conducted on 123
consecutive modified radical mastectomy specimens received in our department during
period from January 2013 to June 2014 (retrospective and prospective study). We evaluated
the significance of the various prognostic features like age, stage at diagnosis,
histopathological grade, and number of axillary lymph nodes retrieved and involved. The
Nottingham Prognostic Index was also calculated. Results: The age range was 20-75 years
with a mean (±SD) of 49 ±11.5 years. Infiltrating duct carcinoma NOS (IDC NOS) was the most
common type of carcinoma breast seen in 86.2% and BR Grade 2 was seen in 85.7% patients.
Maximum number of cases (95.12%) had TNM stage II (47.15%) and III (47.97%). Majority of
cases i.e.47% were classified under poor prognostic group with NPI Score more than 5.41.
Conclusion: Based on the findings of the present study it may be concluded that assessment of
tumor size, histological grade and lymph node involvement along with NPI Score are important
determinants of breast carcinoma prognostication and should be incorporated in planning
therapy of patients with breast carcinoma. The Nottingham grading system when adequately
executed gives a simple, non-expensive, accurate and validated method for assessing
patients prognosis.

Breast cancer is the most commonly occurring female cancer in
the world with a lifetime risk of up to 12%, a risk of death of up to
5%[1] & with an age-standardized incidence rate (ASR) of 39.0
per 100,000, which is more than double that of the second ranked
cancer (cervical cancer ASR=15.2 per 100,000)? [2,3]

The most important morphologic prognostic factors in invasive
carcinoma of breast include size of the primary tumor,
microscopic grade, axillary lymph node metastases, blood and
lymph vessel emboli, tumor necrosis, skin invasion, and nipple
invasion. The prognostic factors are indicators of the inherent
aggressiveness of the tumor as well as of the extent of the disease
and based on these factors, treatment decisions are being taken

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The Nottingham Prognostic Index (NPI) [8] was constructed for patients with primary, operable breast cancer which was used for prognostic stratification of patients. It comprises of 3 strong predictors of prognosis grade, number of LN and size of tumor. The NPI not only predicts prognosis with a level of accuracy but also help to distinguish groups of patients suitable for different forms of therapy [4].

The purpose of this study is to study the prevalence of various clinical and morphological features in patients having mastectomy for breast cancer, their role in prognostication and guiding clinicians for therapy and review the relative importance of various prognostic and predictive factors.

MATERIAL & METHOD

Source of Data:

All the modified radical mastectomy (MRM) specimens received in histopathology section during the period from January 2013 to June 2014 (retrospective and prospective study). A total of 122 cases with 123 mastectomy specimens were included in the present study.

Methods of Collection of Data:

Clinical data of retrospective cases were obtained from the case files retrieved from the Medical Records and requisition forms received with the MRM specimen in the department. In prospective cases the mastectomy specimen received in Department of pathology were included. Specimens were sliced at 1cm thickness and fixed in 10% buffered formalin for at least 24 hours before giving sections. The specimens were then examined for gross details like nipple, areola and skin, size of growth, its cut surface, type of tumor margin, margin of resection and number of lymph nodes in axillary tail, their size and cut surface. The sections were given from all representative areas. They were processed routinely in automated tissue processor followed by paraffin embedding and block formation. Then 3 to 5 micron thick sections were made from paraffin embedded blocks. These sections were routinely stained with Haematoxylin and Eosin followed by mounting. Finally slides were examined microscopically.

TNM staging was done based on tumor size, node positivity and distant metastasis. NPI score was calculated for 119 cases (Table 7). Maximum number of cases i.e.47% were classified under poor prognostic group with NPI Score more than 5.41 (Table 8).

Inclusion Criteria:

All modified radical mastectomy specimen with axillary dissection received in the department irrespective of age were included in the study.

Exclusion Criteria:

1). History of previous lumpectomy ;
2). Patient who had taken preoperative chemotherapy ;
3). Conservative surgery of breast ;
4). Biopsy samples of recurrent cases.

The data was analysed using percentage while continuous data was expressed as Mean ± SD.
Table 3. Histological Type of Carcinoma Breast

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDC NOS</td>
<td>106</td>
<td>86.2</td>
</tr>
<tr>
<td>ILC</td>
<td>6</td>
<td>4.9</td>
</tr>
<tr>
<td>Medullary</td>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td>Apocrine</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Intracystic Papillary</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Tubular</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>IDC-ILC</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>DCIS</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>LCIS</td>
<td>1</td>
<td>0.8</td>
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Table 4. Nottingham Modification of Scarff-Bloom Richardson Grading in Carcinoma Breast

<table>
<thead>
<tr>
<th>BR Grade</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>4.2</td>
</tr>
<tr>
<td>2</td>
<td>102</td>
<td>85.7</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>10.1</td>
</tr>
<tr>
<td>Not Done</td>
<td>4</td>
<td>-</td>
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Table 5. Involvement of Deepest Resected Margins

<table>
<thead>
<tr>
<th>Deepest Resected Margins</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Positive</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>CLOSE(&lt;2mm)</td>
<td>31</td>
<td>25</td>
</tr>
<tr>
<td>Negative</td>
<td>77</td>
<td>63</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 6. TNM Staging

<table>
<thead>
<tr>
<th>T</th>
<th>Frequency</th>
<th>Percentage</th>
<th>N</th>
<th>Frequency</th>
<th>Percentage</th>
<th>M</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>12</td>
<td>5.8</td>
<td>N0</td>
<td>37</td>
<td>30.3</td>
<td>M0</td>
<td>121</td>
<td>50.4</td>
</tr>
<tr>
<td>T2</td>
<td>69</td>
<td>56.1</td>
<td>N1</td>
<td>41</td>
<td>33.3</td>
<td>M1</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>T3</td>
<td>32</td>
<td>26.0</td>
<td>N2</td>
<td>31</td>
<td>25.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>10</td>
<td>8.1</td>
<td>N3</td>
<td>14</td>
<td>11.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>100</td>
<td>123</td>
<td>100</td>
<td>123</td>
<td>100</td>
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</table>

Table 7. TNM Stage

<table>
<thead>
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<th>Stage</th>
<th>TNM</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1N0M0</td>
<td>4</td>
<td>3.25</td>
</tr>
<tr>
<td>IIA</td>
<td>T1N1M0</td>
<td>25</td>
<td>20.32</td>
</tr>
<tr>
<td>IIB</td>
<td>T1N2M0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T2N1M0</td>
<td>33</td>
<td>26.83</td>
</tr>
<tr>
<td>IIB</td>
<td>T2N2M0</td>
<td>37</td>
<td>30.08</td>
</tr>
<tr>
<td>IIC</td>
<td>T3N1M0</td>
<td>9</td>
<td>7.32</td>
</tr>
<tr>
<td>IV</td>
<td>T3N2M0</td>
<td>13</td>
<td>10.57</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>100</td>
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</table>

Table 8. NPI Prognostic Groups

<table>
<thead>
<tr>
<th>NPI</th>
<th>Score</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>&lt;3.4</td>
<td>32</td>
<td>26.9</td>
</tr>
<tr>
<td>Moderate I</td>
<td>3.41-4.4</td>
<td>17</td>
<td>14.3</td>
</tr>
<tr>
<td>Moderate II</td>
<td>4.41-5.4</td>
<td>14</td>
<td>11.8</td>
</tr>
<tr>
<td>Poor</td>
<td>&gt;5.41</td>
<td>56</td>
<td>47.0</td>
</tr>
<tr>
<td>Not Possible</td>
<td>-</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>123</td>
<td>100</td>
</tr>
</tbody>
</table>

Figure 1. IDC NOS BR Grade 3 with Comedopattern in intraductal component (A); marked Nuclear Pleomorphism and Mitosis (B) (H&E 200X & 400X)
Figure 2. Infiltrating Duct Carcinoma BR Grade 2 showing nuclear pleomorphism and mitosis (H&E 400X)
DISCUSSION

The present study was done over a period of one and a half year (January 2013 to June 2014) which included 122 cases of carcinoma breast who underwent modified radical mastectomy.

Male breast cancer is extremely rare, accounting less than 1% of all breast cancers, and less than 1% of all cancer deaths in men. In the present study 99% patients were females and the males accounted for only 1% of the primary invasive breast carcinoma diagnosed. Many population based descriptive studies held internationally such as in US[9], Israel[10], Scandinavia[11], Central Italy[12], Iceland[13] reported comparable findings with respect to male breast cancer incidence <1%.

Age of the cancer patient is an important factor both for occurrence and management of the cases. It is the strongest risk factor for breast cancer after gender. Indian women are prone to develop breast cancer at earlier age than their western counterparts and it peaks from 45-50 years in India. In the present study, mean age of presentation of patients with breast cancer was 49 ± 11.5 years. The age range was 20 - 75 years with maximum number of patients in age group 41-50 years (34.4 %) followed by 31-40 years (25.41%). Our results were comparable to studies done in south India [14,15] The results of present study were also comparable to the various studies on breast cancer done in other countries.[16-20] Our results for mean age were lower than a report from Spain[21] which showed mean age 59±13 years.

In the present study left breast cancer (54.1%) outnumbered the right breast cancer (44.3%). This results correlated with a study from south India.[15] Our result were also supported by Ekanem and Aligbe’s report.[22] In contrast studies by Adeniji KA et al.[23] had shown that breast cancer is occurring more frequently in the right than the left.

Breast cancer usually presents with a unilateral single hard lump as is evident in the present study with occurrence of bilaterality in only 2 out of total 122 cases which is 1.6%. Bilateral cases reported in some studies were 0.88% [24] and 3%.[23]

In present study 48% patients had growth in upper outer quadrant which was followed by upper inner quadrant in 20% cases. The present study has confirmed previously reported findings that the distribution of breast cancer is not even throughout the breast but is higher in the Upper outer quadrant. Our results were in concordance with various studies in India[25] and other countries like Great Britain[26], the West Indies[27] and Italy[28] and irrespective of race within any one country.[29]

Conservative nature of our society and lack of awareness play a role in the advanced stage of presentation at the time of diagnosis. Various studies have shown that the gross size of tumor is one of the most significant prognostic factors in breast carcinoma and there is increased incidence of axillary lymph node metastases and decreased survival with increasing size of the tumor.[30,31]

In the present study mean tumor size was 4.6 ± 2.5 cm and was ranging from 0.5 to 13 cm in size. Our results were almost similar to Sharif MA et al.[32] (4.4 cm). Lower results for mean tumor size were reported by Albegeria et al.[31.1 ± 2.00 cm].[21] Majority of cases in our study had tumor size ranging between 2-5 cm (49.6%) which was comparable to Sharif MA et al.[32] and Albegeria et al.[21] But various studies in developing countries like Pakistan[33,34] showed a tumor size > 5 cm in majority of cases. In other Muslim countries like Indonesia and Jordan, the mean tumour size reported was between 2-5 cm by Arryandono et al.[19] and 5 cm by Almasri et al.[35] respectively.

Histological typing has been proved to be an important prognostic factor. Patients with Infiltrating duct carcinoma (IDC-NOS) (Figure 1,2) have a poor survival compared to other types.[36] In the present study the commonest histological subtype was infiltrating duct carcinoma (86%) followed by infiltrating lobular carcinoma (4.9%) (Figure 3). The special histological types were diagnosed in 9% of patients comprising medullary carcinoma (Figure 4) in 2.4%, apocrine carcinoma (Figure 5) in 1.6%, tubular carcinoma in 0.8%, intracyctic papillary carcinoma in 0.8%, IDC-ILC in 0.8%, DCIS in 1.6%, LCIS in 0.8% of cases. Our results were supported by Chandrika Rao et al.[14] with Infiltrating ductal carcinoma in 88%. This presentation is similar to earlier local studies by Malik et al.,[37] Siddiqui et al.[34] and Wahid et al.[33]

Histologic grade has also been found to be useful predictor of prognosis in patients with different stages of disease.[38] Higher tumour grade is associated with poor prognosis. Subramaniam Sivakumar et al.[15] Siddiqui et al.[34] and Sharif MA et al[32] showed majority of cases in grade 2 which is in consonance with the present study where grade 2 tumours constituted the highest number of cases at 85.7% followed by grade III (10.1%) and grade I (4.2%). In contrast to this study high grade tumor i.e. grade III was more common according to reports by Chandrika Rao et al.[14] Malik et al.[37] and Albegeria et al.[21] (Figure 2)

The status of resected margins and the definition of a positive or close surgical margin following surgical therapy for breast cancer has been a subject of substantial debate.[39,40] In this study only 15 (12%) patients were positive for tumor at deepest resected margins which was comparable to some study (Figure 6).[41] Only a single case had muscle invasion in this study.

The present study showed maximum number of cases in pT2 stage (56.1%) which was followed by pT3 (26%) and only 9.8% and 8.1% cases were seen in pT1 and pT4 stage respectively. A study from Pakistan[42] showed comparable results with pT2 seen in maximum number of patients (44.16%) followed by pT3 (41.66%). Similar results were also reported by several studies with pT2 being the most common stage.[21,43] These results show that when large majority of our patients seek medical attention for the first time they had tumors of large size.
The positivity of axillary lymph nodes for metastases is one of the most important prognostic parameters in carcinoma breast [44] with sharp differences in survival rates between those with negative and positive nodes. Patients with increased number of metastatic lymph nodes represent a higher stage of presentation. Axillary lymph nodes were positive in 86 out of 123 cases (69.9%), while 37 (30.1%) cases were negative for metastasis. (Figure 7)

Our results were almost similar to Chandrika Rao et al. [14] Earlier, Malik et al. [37] had reported 74% cases with lymph node metastasis in their study out of which 30% had more than 3 positive lymph nodes. Arhyandono et al. [19] reported 38.3% and Sharif MA et al. [32] 46% patients with more than 3 positive lymph nodes.

Among cases with positive lymph nodes 33.3% were pN1a (metastasis in 1-3 axillary lymph nodes), 25.2% were pN2a (metastasis in 4-9 axillary lymph nodes) and 11.4% were pN3 (metastasis in ≥ 10 axillary lymph nodes). Our results were comparable to a study done in Pakistan by Ahmad et al. [42] showing maximum number of cases in pN1a (27.1%) and pN2a (24.3%). These results show that most of the patients axillary lymph nodes are positive for metastatic tumor when they seek first medical attention and majority being pN2a and pN3a.

Out of 123 cases only 2 (1.6%) patients had distant metastasis with M1 stage. In the present study 47.97% cases were in poor prognostic category followed by 26.9% and 26.1% in good and moderate prognostic categories respectively. Our results were supported by Hamza et al. [51] with poor NPI 48.0% of patients. But were in contrast to Subramaniam Sivakumar et al. [15] and Lokhettey MD et al. [20] who had 50% and 53.6% patients respectively in the moderate prognosis category with NPI scores in between 3.4 – 5.4.

Histological grading is an important determinant of breast cancer prognostication and should be incorporated in algorithms to define therapy in patients with breast cancer. [52] Tumor size and lymph node involvement along with NPI Score are also the important determinants of breast carcinoma prognostication.

The present study demonstrated the meticulous implementation and application of NPI in stratifying patients in various prognostic groups. It also provides simple, inexpensive, accurate and validated method for assessing the prognosis in patients with primary epithelial breast malignancy.

CONCLUSION

Based on the findings of the present study it may be concluded that assessment of tumor size, histological grade and lymph node involvement along with NPI Score are important determinants of breast carcinoma prognostication and should be incorporated in planning therapy of patients with breast carcinoma. The Nottingham grading system when adequately carried out provide a simple, non-expensive, accurate and validated method for assessing patients prognosis.

LIMITATIONS OF THE STUDY

This study did not cover hormonal receptors determination i.e. estrogen and progesterone receptors due to lack of reagents at our histopathology laboratory, the funding for the dissertation research is not enough to cover the costs for these reagents which are very expensive. Long term survival could not be studied because of time bound nature of the study.

References


