October 2009

Breast carcinoma grading, estimation of tumor size, axillary lymph node status, staging, and nottingham prognostic index scoring on mastectomy specimens.

Zubair Ahmad
Aga Khan University, zubair.ahmad@aku.edu

Amna Khurshid
Aga Khan University

Asim Qureshi
Aga Khan University

Romana Idress
Aga Khan University, romana.idress@aku.edu

Nasira Asghar
Aga Khan University

See next page for additional authors

Authors
Zubair Ahmad, Amna Khurshid, Asim Qureshi, Romana Idress, Nasira Asghar, and Naila Kayani Naila Kayani

Indian Journal of Pathology & Microbiology

Previous Article ToC Next Article

ORIGINAL ARTICLE

Year : 2009 | **Volume** : 52 | **Issue** : 4 | **Page** : 477-481

Breast carcinoma grading, estimation of tumor size, axillary lymph node status, staging, and nottingham prognostic index scoring on mastectomy specimens

Zubair Ahmad, Amna Khurshid, Asim Qureshi, Romana Idress, Nasira Asghar, Naila Kayani
Department of Pathology and Microbiology, The Aga Khan University, Hospital, Karachi, Pakistan

Click **here** for correspondence address and email

Date of Web Publication 1-Oct-2009

Download Article (pdf) Email Article Print Article Read / Write a Comment Citation Manager

Abstract

Introduction: Breast carcinoma is the most common malignant tumor and the leading cause of cancer death in women. In western countries, a sharp increase in the detection of breast carcinoma, largely due to widespread use of mammography, has recently led to a fall in breast cancer mortality. This, however, is not true for less developed countries, in which mortality continues to rise. **Objective:** The aim of this study was to acquire information about the extent and spread of breast carcinoma in our patients by grading the tumors, determining the tumor size, and axillary lymph node status, staging of the tumors and Nottingham Prognostic Index (NPI) scoring on the available material. **Materials and Methods:** One hundred and twenty consecutive mastectomy specimens with axillary lymph node sampling removed for breast carcinoma and received in the section of histopathology, Aga Khan University, in the year 2005, were included in the study. Standard protocols were used for the processing of the specimens, and reporting was done using a standard format incorporating all relevant tumor parameters. NPI was applied to the cases. **Results:** Out of the 120 cases, 5 (4.17) were grade 1, 91 (75.83) were grade 2, and 24 (20%) were grade 3. Also, 9 cases (7.5%) were T1 (4 were T1b, and 5 were T1c); 53 (44.16%) were T2; 50 (41.66%) were T3; and 8 (6.66%) were T4. Axillary lymph nodes were available in 107 cases. In 13 cases, no lymph nodes were recovered. Out of 107 cases 27 (25.23%) lymph nodes were negative for metastases pN0; 29 (27.10%) cases were pN1; 26 (24.30) were pN2; and 25 cases (23.36%) were pN3. Extranodal spread was present in 56 (70%) out of the 80 cases in which lymph nodes were positive. The average microscopic size of nodal metastasis was 1.7 cms. Significant statistical association was found between the number of positive nodes and perinodal extension ($P = 0.001$). Tumor necrosis was present in 76 out of 120 cases (63.33%). Vascular invasion was present in 43 out of 120 cases (35.83%). NPI scores were greater than 5.4 in 60 out of 107 cases (56.1%) indicating poor prognosis. **Conclusion:** The large majority of the cases were grade 2 tumors. Most cases (all grades) were T2 or T3, and were axillary lymph node positive. Large majority of cases with nodel metastases showed extra nodal spread. The majority of patients had NPI scores greater than 5.4 indicating poor prognosis. Significant statistical association was found between the number of positive nodes and perinodal extension ($P = 0.001$). The findings show extensive and advanced disease trends in our patients.

Keywords: Breast carcinoma, mastectomy, tumor size, grade, axillary lymph node status, stage, Nottingham Prognostic Index

How to cite this article:

Similar in PUBMED
Search Pubmed for

- Ahmad Z
- Khurshid A
- Qureshi A
- Idress R
- Asghar N
- Kayani N

Search in Google Scholar for

- Ahmad Z
- Khurshid A
- Qureshi A
- Idress R
- Asghar N
- Kayani N

Related articles

- Breast carcinoma
- mastectomy
- tumor size
- grade
- axillary lymph node status
- stage
- Nottingham Prognostic Index

Email Alert *
Add to My List *
* Registration required (free)

Abstract
Introduction
Materials and Me...
Results
Discussion
References
Article Figures
Article Tables

Article Access Statistics

Viewed	9407
Printed	147
Emailed	5
PDF Downloaded	786
Comments	[Add]

Ahmad Z, Khurshid A, Qureshi A, Idress R, Asghar N, Kayani N. Breast carcinoma grading, estimation of tumor size, axillary lymph node status, staging, and nottingham prognostic index scoring on mastectomy specimens. Indian J Pathol Microbiol 2009;52:477-81

How to cite this URL:
Ahmad Z, Khurshid A, Qureshi A, Idress R, Asghar N, Kayani N. Breast carcinoma grading, estimation of tumor size, axillary lymph node status, staging, and nottingham prognostic index scoring on mastectomy specimens. Indian J Pathol Microbiol [serial online] 2009 [cited 2018 Mar 13];52:477-81. Available from: http://www.ijpmonline.org/text.asp?2009/52/4/477/56123

Introduction

Carcinoma of the breast is the most common malignant tumor and the most common cause of death from carcinoma in females. [1] In the West, widespread use of mammography has resulted in a marked increase in early detection of this carcinoma, when it is still localized and small in size. [2] As a result of early detection and improvement in therapy, breast carcinoma mortality is now beginning to fall. [3] This, however, unfortunately is not the case for developing countries in which breast cancer mortality is still rising. [4]

The therapy for carcinoma of the breast includes surgery (mainly mastectomy along with axillary lymph node sampling) hormonal therapy and chemotherapy [5] depending on the extent of the disease.

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.

Thus, a pathologist on receiving a mastectomy specimen must report all the above mentioned parameters, in order to provide adequate information to the clinician. The aim of this study was to acquire information about the extent and spread of invasive breast carcinoma in our patients, by incorporating all the important prognostic factors mentioned above, and to see how extensive and advanced the disease is in our population. The Nottingham Prognostic Index (NPI) [6] was constructed for patients with primary, operable breast cancer. We also applied the NPI in our cases to get an idea of the position of females suffering from breast cancer in our population stand in terms of chances of cure following mastectomy.

Materials and Methods

A total of 120 consecutive mastectomy specimens, received in the Section of Histopathology of a major referral center during the year 2005, were included in the study. All specimens were fixed in 10% buffered formalin and allowed to stay overnight. Specimens were grossed the next day, and representative sections were submitted according to established protocols. The sections were processed under standardized conditions for paraffin embedding. Section were then cut, and stained with Hematoxylin and Eosin using standard procedures. The reporting was done using a standard format incorporating all relevant tumor parameters. Grading and staging were done according to the Nottingham modification of the Bloom and Richardson Grading System [7] and TNM staging system, [8],[9] respectively. Cases were scored according to the NPI.

Data was analyzed using SPSS version 14.0.

Results

Age range of the patients was between 22-75 years (mean age, 47 years). Out of the 120 cases, there were 113 cases of infiltrating ductal carcinoma, NOS. There were two cases of invasive papillary carcinoma, one case of metaplastic carcinoma, two cases of invasive lobular carcinoma (including one case of pleomorphic lobular carcinoma, and one case of mixed ductal and lobular carcinoma), and one case of apocrine carcinoma [Figure 1], [Figure 2], [Figure 3], [Figure 4].

The tumor size ranged from as large as 13 X 12 cm^2 to as small as 1 X 1 cm^2 ; average tumor size was 5 X 4 cm^2 .

Out of the 120 cases, five cases (4.17%) were grade 1, 91 (75.83%) were grade 2, and 24 (20%) were grade 3.

The staging of the tumors was done according to the TNM system. The results of the T and N components are given in [Table 1].

Out of the 80 cases in which axillary lymph nodes were positive for tumor, extranodal spread was present in 56 cases (70%). The average microscopic size of the largest lymph node metastasis was 1.7 cm^2 in the largest dimension.

Tumor necrosis was present in 76 out of 120 cases (63.33%). Vascular invasion was present in 43 out of 120 cases (35.83%).

No statistically significant association was seen between tumor size and microscopic size of the largest lymph node metastasis ($P = 0.384$); or between size of the tumor and number of positive lymph nodes ($P = 0.314$). Similarly, there was no significant statistical correlation between tumor size and perinodal extension of metastatic tumor ($P = 0.310$); or between the number of positive nodes and the microscopic size of the largest node metastasis ($P = 0.085$). However, significant statistical association was found between the number of positive nodes and perinodal extension ($P = 0.001$).

NPI was applied to 107 cases (in which lymph nodes were present). The results are shown in the [Table 1].

Discussion

Cancer statistics of 2005 and 2006 [10],[11] compiled by the American cancer society, rated breast cancer as the most common cancer in females. Similarly, multiple studies done in Pakistan [12],[13],[14],[15] showed breast cancer to be the most common cancer in the females in India. One of these studies comprised 32% of all cancers in women. [12] A study conducted in our own department showed that breast cancer is the most common cancer comprising a staggering 33.5% of all cancers in the women, and dwarfing the next most common i.e., carcinoma of the oral cavity (7.06%). [16] Another study in our department showed that breast cancer is so common that the absolute number of cancers is greater in females than males in the fourth, fifth, and sixth decades. [17] These studies emphasized the importance of breast cancer as a leading cause of cancer morbidity and mortality in our population. As shown above, mortality from breast cancer in developing countries is still rising. [4]

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. [18],[19] In our study, as shown in the results, most tumors were T2 (44.16%) or T3 (41.66%). According to TNM staging system for breast carcinoma, [9] T2 are tumors greater than 2 cm^2 but not more than 5 cm^2 in greatest dimension; while T3 are tumors greater than 5 cm^2 in the greatest dimension. Only 7.5% tumors were T1 (i.e. tumors 2 cm^2 or less in the greatest dimension), while 6.66% were T4 (4.17% T4b and 2.5% T4d). T4b are tumors of any size with direct extension to the skin of breast causing ulceration; while T4d are inflammatory carcinoma, tumors of any size with dermal lymphatic permeation on microscopic examination (a sign of ominous prognosis). These results show that in the large majority of our patients, the tumors are already of large size when women first seek medical attention.

As shown in our results, axillary lymph nodes were positive in 80 out of 107 cases in which these were recovered i.e., 74.77%, while in 27 cases (25.23%), lymph nodes were negative for metastases. Of the 80 cases with positive lymph nodes: 27.10% were pN1a (metastasis in 1 to 3 axillary lymph nodes; 24.30% were pN2a (metastasis in 4 to 9 axillary lymph nodes); and 23.36% were pN3 (metastasis in 10 or more axillary lymph nodes). These results show that in the large majority of our cases, axillary lymph nodes are already positive for metastatic tumor when the patients first seek medical attention, and infact, majority of patients with positive nodes have pN2 or pN3 disease. The positivity of axillary lymph nodes for metastases is one of the most important prognostic parameters in carcinoma of breast [20] with sharp differences in survival rates between those with negative and positive nodes. In addition, the absolute number of nodes involved, the presence or absence of extranodal spread, and the amount of carcinoma in the positive nodes (measured by the microscopic size of the largest nodal metastases) are also prognostically important with survival rates falling with increased number of nodes involved (less than 4 versus 4 or more), presence of extranodal spread and increased amount of tumor in positive nodes. [21],[22],[23],[24] In our study, extranodal spread was present in 56 out of 80 cases with axillary node metastases (70%), and the average microscopic size of largest lymph node metastases was 1.7 cm^2, which is quite significant. Again, these findings show that disease is already present in advanced stage in the majority of our patients when it first comes to clinical attention.

Various studies have analyzed the importance of histologic grade (based on the Modified Bloom and Richardson grading system) as a prognostic factor in carcinoma of the breast. It has been shown that patients with high grade tumors treated by mastectomy have significantly high frequency of lymph node metastases with four or more positive nodes, develop more systemic recurrences, and more of such patients die of metastastic disease compared to patients with low grade tumors. [25],[26]

Histologic grade has also been found to be useful predictor of prognosis in patients with different stages of disease especially among those with negative axillary lymph nodes. [26] It has been found to be significantly related not only to increased recurrence and death in breast carcinoma patients, but also to disease free interval and overall length of survival after mastectomy regardless of clinical stage with early treatment failures occurring more commonly in high grade tumors. [27] For these reasons, accurate grading of invasive breast carcinomas is extremely important and our cases have been graded according to the modified Bloom and Richardson grading system [7] which measures three parameters i.e. tubule formation, nuclear pleomorphisim, and mitotic rate. Each of these is given a score of 1 to 3; final grade is determined by adding scores of all three categories i.e., grade 1 (score 3-5), grade 2 (score 6 or 7), grade 3 (score 8 or 9).

In our study, as shown in the results, only 4.17% cases were grade 1, while the large majority were grade 2 (75.83%) or

grade 3 (20%). Among tumors of all histologic grades, the majority were T2 or T3 with positive axillary lymph nodes, and increasing number of positive nodes with high grade tumors. Similarly, perinodal extension was more commonly seen in the tumors of higher grades.

Tumor necrosis, especially when extensive, correlates with increased histologic grade, increased incidence of lymph node metastases and decreased survival rates. [28] It was present in a large percentage of our cases (63.33%).

Vascular invasion shows, according to several studies, a high correlation with grade of the tumor, tumor size, and lymph node status. [29],[30] It was also present in a significant percentage (35.83%) of our cases.

The NPI has been widely adopted as a prognostic tool in breast cancer. [6] It was constructed for patients with primary operable breast cancer. Based on three factors (tumor size, tumor grade, and stage of the disease), the index defined three subsets of patients with different chances of dying from breast cancer. These three subsets are: good prognosis (score up to 3.4) comprising 29% patients with 80% five year survival; moderate prognosis (score 3.4 to 5.4) comprising 54% patients with 42% five year survival; and poor prognosis (score greater then 5.4) comprising 17% patients with 13% five year survival. [6] Various studies have shown its usefulness and utility in predicting outcome in treated patients with breast cancer. [31],[32],[33],[34] D' Eredita *et al*. [34] conclude that their improved survival rates may be attributed to the administration of adjuvant therapies to a larger number of patients after applying NPI. They argue that NPI allows them to accurately predict prognosis and recommend its more common use.

According to our results [Table 1], surprisingly, 56% patients are in the poor prognosis category with NPI scores greater than 5.4. Less than 3% are in the good prognosis category. This further emphasizes the advanced nature of disease and poor prognosis for this most common cancer in our population.

References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden. Globocan 2000, Int J Cancer 2001;94:153-6.
2. Garfinkel L, Boring CC, Heath CW Jr. Changing trends. An overview of breast cancer incidence and mortality. Cancer 1994;74:222-7.
3. Jatoi I, Miller AB. Why is breast cancer mortality declining? Lancet Oncol 2003;4:251-4.
4. Parkin DM, Bray F, Devesa SS. Cancer Burden in the year 2000. The global picture. Eur J Cancer 2001;37:4-66.
5. Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thurlimann B, Senn HJ. Meeting highlights: Updating international expert consensus on the primary therapy of early breast cancer. J Clin Oncol 2003;21:3357-65.
6. Galea MH, Blamely RW, Elston CE, Ellis IO. The Nottingham Prognostic Index in Primary breast cancer. Breast Cancer Res Treat 1992;22:207-19.
7. Frierson HF Jr, Wolber RA, Berean KW, Franquemont DW, Gaffey MJ, Boyd JC, Wilbur DC. Interobserver reproducibility of the Nottinghamm modification of the Bloom and Richardson histologic grading scheme for infiltrating ductal carcinoma. Am J Clin Pathol 1995;103:195-8.
8. Sobin LH. TNM: Principles, History and relation to other prognostic factors. Cancer 2001;91: 1589-93.
9. UICC International Union Against Cancer. Breast Tumors. In: Sobin LH, Wittekind C, eds. TNM classification of malignant tumors, 5th ed. New York: Wiley -Liss 1997:123-30.
10. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, *et al*. Cancer statistics, 2005. CA Cancer J Clin 2005;55:10-30.
11. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ. Cancer statistics, 2006. CA Cancer J Clin 2006;56:106-30.
12. Bhurgri Y, Bhurgri A, Hasan SH, Usman A, Faridi N, Malik J *et al*. Cancer patterns in Karachi division (1998 - 1999). J Pak Med Assoc 2002;52:244-6.
13. Bhurgri Y, Bhurgri A, Pervez S, Bhurgri M, Kayani N, Ahmed R, *et al*. Cancer profile of Hyderabad, Pakistan 1998-2002. Asian Pac J cancer Prev 2005;6:474-80.
14. Bhurgri Y, Pervez S, Kayani N, Bhurgri A, Usman A, Bashir I, *et al*. Cancer profile of Larkana, Pakistan (2000-2002). Asian Pac J Cancer Prev 2006;7:518-21.
15. Jamal S, Moghal S, Mamoon N, Mushtaq S, Luqman M, Anwar M. The pattern of malignant tumours: tumour registry data analysis, AFIP, Rawalpindi, Pakistan (1992-2001). J Pak Med Assoc 2006;56:359-62.
16. Zubair Ahmad, Najamul Sahar Azad, Nausheen Yaqoob, Akhtar Husain, Aamir Ahsan, Ambreen Nasir Khan, *et al*. Frequency of primary solid malignant neoplasms in both sexes, as seen in our practice. J Ayub Med Coll Abbotabad 2007;19:53-5.
17. Zubair Ahmad, Najamul Sahar Azad, Fouzia Rauf, Nausheen Yaqoob, Akhtar Husain, Aamir Ahsan, *et al*. Frequency of primary solid malignant neoplasms in different age groups as seen in our practice. J Ayub Med Coll Abbottabad 2007;19:56-63
18. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. Cancer 1989;63:181-7
19. Russo J, Frederick J, Ownby HE, Fine G, Hussain M, Kirckstein HI, *et al*. Predictors of recurrence and survival of patients with breast cancer. Am J Clin Pathol 1987;88:123-31.
20. Hutter RVP. The influence of pathologic factors on breast cancer management. Cancer 1980;46:961-76.
21. Fisher B, Bauer M, Wickerham L, Redmond CK, Fisher ER. Relation of number of positive axillary nodes to the prognosis of patients with primary breast cancer. An NSABP update. Cancer 1983;52:1551-7.
22. Rosen PP, Saigo PE, Braun DW, Weathers E, Fracchia AA, Kinne DW. Axillary micro- and macrometastases in breast cancer. Prognostic significance of tumor size. Ann Surg 1981;196:585-91.
23. Goldstein NS. The significance of extracapsular axillary lymph node extension by metastatic breast cancer. Int J Surg Pathol 1995;3:65-6.

24. Leonard C, Corkill M J. Tompkin J, Zhen B, Waitz D, Norton L, Kinzie J. Are axillary recurrence and overall survival affected by axillary extranodal tumor extension in breast cancer? Implications for radiation therapy. J Clin Oncol 1995;13:47-53.
25. Henson DE, Histological grading of breast cancer: Significance of grade on recurrence and mortality. Arch Pathol Lab Med 1988;112:1091-6.
26. Hopton DS, Thorogood J, Clayden AD. Histological grading of breast cancer: significance of grade on recurrence and mortality. Eur J Surg Oncol 1989;15:25-31.
27. Yoshimoto M, Sakamoto G, Ohashi Y. Time dependency of the influence of prognostic factors on relapse in breast cancer. Cancer 1993;72:2993-3001.
28. Gilchrist KW, Gray R, Fowble B, Torme DC, Taylor SG 4 th , Tumor necrosis is a prognostic predictor for early recurrence and death in lymph node-positive breast cancer. A 10 year follow-up study of 728 Eastern Cooperative Oncology Group Patients. J Clin Oncol 1993;11:1929-35.
29. Fisher ER, Anderson S, Tan-Chin E, Fisher B, Eaton L, Wolmark N. Fifteen Year prognostic discriminants for invasive breast carcinoma: National Surgical Adjuvant Breast and Bowel Project Protocol-06. Cancer 2001;91:1679-88.
30. Pinder SE, Ellis IO, Galea M, O' Rourke S, Blamey RW, Elston CW. Pathological prognostic factors in breast cancer. III Vascular invasion. Relationship with recurrence and survival in a large study with long term followup. Histopathology 1994;24:41-7.
31. Lee AH, Ellis IO. The Nottingham prognostic index for invasive carcinoma of the breast. Pathol Oncol Res 2008;14:113-5.
32. Balslev I, Axelsson CK, Zedeler K, Rasmussen BB, Carstensen B, Mouridsen HT. The Nottingham Prognostic Index applied to 9, 149 patients from the studies of the Danish Breast Cancer Cooperative Group (DBCG). Breast Cancer Res Treat 1994;32:281-90.
33. Sundquist M, Thorstenson S, Brudin L, Nordenskjoid B. Applying the Nottingham Prognostic Index to a Swedish breast cancer population. South East Swedish Breast Cancer Study Group. Breast Cancer Res Treat 1999;53:1-8.
34. D' Eredita' G, Giardina C, Martellota M, Natale T, Ferrarese F. Prognostic factors in breast cancer: The predictive value of the Nottingham Prognostic Index in patients with a long-term follow-up that were treated in a single institution. Eur J Cancer 2001;37:591-6.

Correspondence Address:
Zubair Ahmad
Department of Pathology and Microbiology, Aga Khan University, Hospital, Stadium Road, PO Box 3500, Karachi 74800
Pakistan
Login to access the email ID

Source of Support: None, **Conflict of Interest:** None

DOI: 10.4103/0377-4929.56123

Figures

[Figure 1], [Figure 2], [Figure 3], [Figure 4]

Tables

[Table 1]

This article has been cited by

1 **MTA1 expression correlates significantly with ER-alpha methylation in breast cancer**
Xiao-yun Mao,Hao Chen,Huan Wang,Jing Wei,Chong Liu,Hua-chuan Zheng,Fan Yao,Feng Jin
Tumor Biology. 2012; 33(5): 1565
[Pubmed] | [DOI]

2 **Effect of Comprehensive Breast Care on Breast Cancer Outcomes: A Community Hospital Based Study from Mumbai, India**
Anita Gadgil,Nobhojit Roy,Rengaswamy Sankaranarayanan,Richard Muwonge,Catherine Sauvaget
Asian Pacific Journal of Cancer Prevention. 2012; 13(4): 1105
[Pubmed] | [DOI]

3 **Data mining technique for breast cancer detection in thermograms using hybrid feature extraction strategy**

Muthu Rama Krishnan Mookiah,U. Rajendra Acharya,E.Y.K. Ng
Quantitative InfraRed Thermography Journal. 2012; 9(2): 151
[Pubmed] | [DOI]

4 **Promoter methylation status and expression of estrogen receptor alpha in familial breast cancer patients**
Jing Wei, Bing Han, Xiao-yun Mao, Min-jie Wei, Fan Yao, Feng Jin
Tumor Biology. 2011;
[VIEW] | [DOI]

5 **Thermography Based Breast Cancer Detection Using Texture Features and Support Vector Machine**
U. Rajendra Acharya, E. Y. K. Ng, Jen-Hong Tan, S. Vinitha Sree
Journal of Medical Systems. 2010;
[VIEW] | [DOI]

Previous Article Next Article

Online since 5th April, 2008
Editorial and Ethics Policies
BY-NC-SA Open Access View mobile site
ISSN: Print -0377-4929, Online - 0974-5130