

Breast carcinoma detected in breast specimens: A fifteen-year single-center experience

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Abstract

Aim: The aim of this study was to determine the incidence of breast carcinomas in our center, to examine their clinicopathological characteristics and to present our experiences.

Material and Methods: A total of 4309 breast biopsy cases whose histopathological examination was performed in the Pathology Clinic between 2003 and 2018 were retrospectively evaluated. The age, operation procedure, histopathological examination results and postoperative prognostic indices of breast carcinoma cases were presented and analysis results of these parameters were compared with literature data and discussed.

Results: Six hundred thirty five (14.7%) of the patients were administered with modified radical mastectomy + lumpectomy. Our cases of 65.2% were grade II, 21.3% of them were grade I, and 13.5% of them were grade III. Lymph node metastasis and recurrence were detected in 53.2% and 9.75% of the cases, respectively, the records of whom were reached. 6.41% of the patients had metastasis at the time of diagnosis. 12.54% of the patients who were followed up until 2019 died.

Conclusion: The incidence of breast carcinoma in our center is 37%. It is also quite common at a young age, and lymph node metastasis is common.

Keywords: Breast; carcinoma; clinicopathologic characteristics.

INTRODUCTION

Breast cancer is the most common malignant tumor among women and constitutes approximately 30% of all cancers observed in women. 180 thousand new cases in Europe and 184 thousand new cases in the United States of America (USA) are detected annually (1,2). Breast cancer is rarely observed before the age of 30 years and rapidly increases in the reproductive years following this age. This increase also continues to rise with a slow slope after menopause (3). Therefore, it is expected that breast cancer may develop in one out of every 9 women aged 85 years. Furthermore, 18% of cancer-related deaths in women are caused by breast cancer. Among all cancers, breast cancer-related deaths are in the third place after lung and colorectal cancers (2,4). Along with the increase in treatment modalities, and especially, with the fact that breast cancer has begun to be perceived as a systemic disease since its diagnosis, "neo-adjuvant" and "adjuvant systemic" treatments have come to the fore, which has

brought along the question of to which patients these treatments will be administered, as well. Thus, patients have begun to be staged, the prognostic factors related to survival have been found, and they have been reflected on clinical observations and treatments. The changes in knowledge and the improvements experienced primarily in the diagnosis and then the treatment of breast cancer especially in the last two decades have made significant contributions to patients' survival and disease-free survival time.

MATERIAL and METHODS

This study included 4309 patients whose breast biopsy was histopathologically examined in the Pathology clinic in our center between 2003 and 2018. Patient information was obtained from computer records and phone calls when required. The age of breast carcinoma cases, operation procedure, the location and size of the tumor, histological types, tumor grade according to the recommended

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classification of the World Health Organization (According to Scarff-Bloom-Richardson), the status of axillary lymph nodes, clinical and pathological stage distribution, and postoperative prognostic indices were evaluated.

The status of axillary lymph nodes was evaluated in three groups: those with no metastasis, those with 1-3 lymph node involvement, and those with 4 and more lymph node involvement (5). Estrogen, progesterone, HER-2 receptors are the parameters examined. As in similar studies, the value ER/PR $\geq 1\%$ was considered positive, and the value 3+ for HER-2 positivity or silver in situ hybridization (SISH) positivity in suspected cases was accepted (6).

Postoperative prognostic indices were investigated such as recurrence, metastasis, and survival. The follow-up period is from the date of diagnosis to the date of recurrence or the last follow-up. The records of the patients since 2003 started to be examined, and data were kept until the last month of 2018. The follow-up period of the patients who died was considered as the period from the time of diagnosis until the date of their death. While the mean follow-up period of the patients who died was 61.64 months (11-136), the mean follow-up period of the patients who were still alive was 85.33 months (1-198). The follow-up period of all patients was 82.19 months (1-198).

RESULTS

Among 4309 patients who underwent breast biopsy in our center between 2003 and 2018, 1596 (37.7%) patients were diagnosed with breast carcinoma. During the histopathological examination of the patients, invasive ductal carcinoma was detected in 1424 (89.2%) cases (Figure 1), lobular carcinoma was detected in 57 (3.6%) cases (Figure 2), and other carcinomas (mucinous carcinoma, mixed carcinoma, papillary carcinoma, medullary carcinoma, tubular carcinoma, invasive cribriform carcinoma, metaplastic carcinoma, etc.) in 115 (7.2%) cases (Table 1).

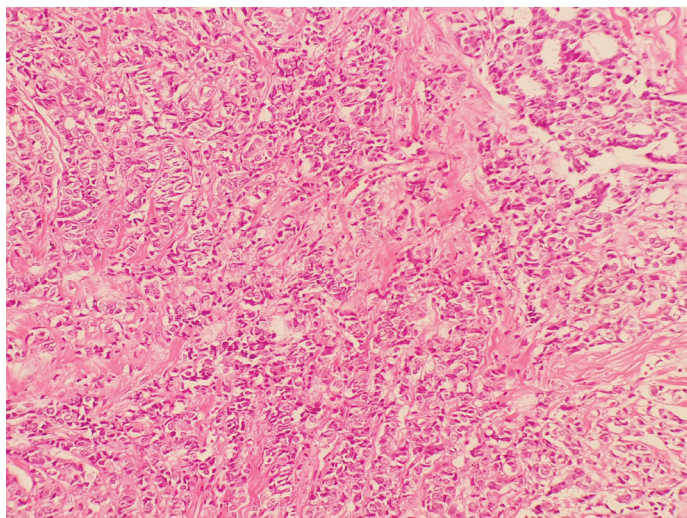


Figure 1. Invasive ductal carcinoma in which atypical cells form ductus structures (HE, X400)

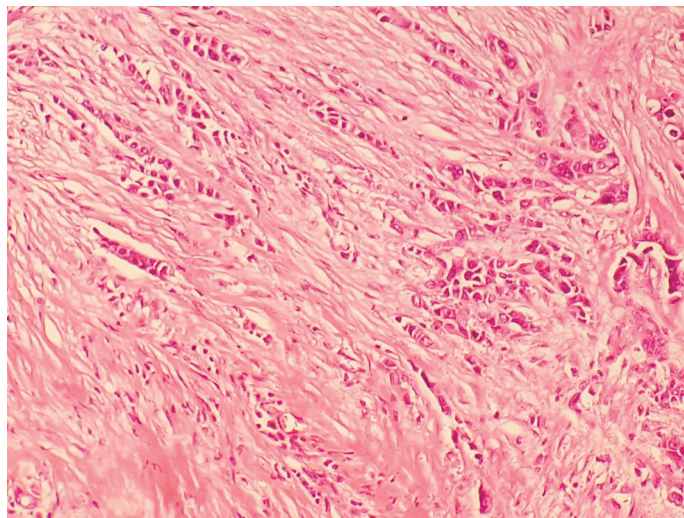


Figure 2. Invasive lobular carcinoma of atypical cells that do not form ductus and are arranged side by side.(HE,X400)

Table 1. Malign tumors detected in breast specimens

Malignancy	Total,n= 1596(%)
Invasive ductal carcinoma	1424(89.2)
Invasive lobular carcinoma	57(3.6)
Mixed carcinoma	18
Mucinous carcinoma	19
Medullary carcinoma	11
Atypical medullary carcinoma	15
Tubular carcinoma	5
Kribriform carcinoma	3
Other	39

The mean age of the diagnosis of breast cancer patients was 19-84. With respect to the age distribution of patients, when the age groups during diagnosis were examined, there were 381 cases under the age of 40 years (23.9%), 1004 cases between the ages of 40-60 (62.9%), and 211 cases aged 60 and above (13.2%). It was determined that the incidence of cancer reached the highest level with 1004 cases (62.9%) aged between 40-60 years and then decreased. 65.2%, 21.3%, and 13.5% of invasive breast cancers were histologically evaluated as grade II, grade I, and grade III, respectively. 65% and 35% of only invasive breast cancers were stage I & II and stage III & IV breast cancers, respectively. Estrogen, progesterone and HER-2 and positivity were found in 51.9%, 37%, and 9.6% of the cases, respectively. When we examined the location of the tumor according to the quadrants of the breast, it was found out that the tumor was located in the upper outer quadrant (74.1%) at the most and in the upper inner quadrant (1.7%) at the least. There was also multifocal localization by 15.5%.

When the status of lymph node metastasis was examined, the data of only 359 cases were reached. One hundred sixty-eight(46.8 %) of these cases had no lymph node metastasis. It was found out that 103 (28.7%) of the remaining cases had 1-3 metastatic lymph nodes and 85 (23.7%) of them had 4 and more metastatic lymph nodes

(Table 2). When the cases were examined in terms of tumor necrosis, necrosis was observed in 38.9% of them. On the contrary, 61.1% of the cases did not have necrosis.

Table 2. Patient and tumor characteristics Total, n= 1596(%)

Number of patients diagnosed with malignancy 37%

Under 40 years 23.9%
40 years and older 62.9%
Over 60 years 13.2%

Histological grade

Grade I 21.3%
Grade II 65.2%
Grade III 13.5%

Tumor localization

Upper outer quadran 74.1%
Upper inner quadran 1.7%
Multifocal quadran 15.5%

Hormone receptor status

Estrogen positive 55.2%
Progesterone positive 57.3%
CerbB2 positive 23.6%

Lymph node involvement

No metastasis 46.8%
1-3 lymph node involvement 28.7%
4 or more lymph node involvement 23.7%

Lymph node metastasis and recurrence were detected in 53.2% and 9.75% of the cases, respectively, the records of whom were reached. 6.41% of the patients had metastasis at the time of diagnosis, whose data could be achieved, had metastasis at the time of diagnosis while 34 (9.5%) of them had a recurrence after metastasis development. 1 case (0.3%) recurred with mass detection from the other breast, not with metastasis. 12.54% of the patients who were followed up until 2019 died. A total of 35 cases (9.7%) were observed to have a recurrence. In the determination performed until the last month of 2018, the death reports of 44 patients (12.3%) were achieved, and we are still following the other 315 cases (87.7%)(Table 3).

Table 3. Postoperative prognosis indices Total, n= 359 (%)

Recurrence 9.7%
Metastasis 15.9%
Ex 12.3%

DISCUSSION

Breast cancer is the most common malignancy in women. In the USA, 230.000 new breast cancer cases were detected in 2012, and approximately 40.000 of them resulted in death (1). The incidence of breast cancer is rapidly increasing in Turkey. Studies indicate that the incidence of breast cancer has doubled in Turkey over the last 20 years (6, 7, 8).

In the study by Özmen, in Turkey the average age was 51.6 years (± 12.6 ; 12-97) in a total of 13.240 breast cancer patients since 1992, 17% of them were under the age of 40 years, and 45% of them were premenopausal. It has been reported that the incidence of breast cancer significantly increased up to 50 years of age, and that this increase reached the peak in the 45-49 age group (17%) and then it

decreased to 7.6% between 65-69 years of age, and then it increased to 10% after 70 years of age (6).

In our study, similarly, the mean age of the diagnosis of female breast cancer patients was 19 years as the youngest and 84 as the oldest, and the average age was 53 ± 12 . With respect to the age distribution of patients, when the age groups during diagnosis were examined, there were 381 cases under the age of 40 years (23.9%), 1004 cases between the ages of 40-60 (62.9%), and 211 cases aged 60 and above (13.2%). It was also determined that the incidence of cancer, similarly to the literature, reached the highest level by 62.9% and then decreased.

Invasive ductal carcinoma is the most common type of invasive breast carcinomas, ranging from 70% to 75% in some series (1). In the study by Özmen, 78.7% of patients had invasive ductal carcinoma, 7.8% of them had invasive lobular cancer, 9.8% of them had invasive mixed cancer (invasive ductal + invasive lobular), and 4% of them had other histological types (e.g. inflammatory, intracystic papillary, mucinous, etc.) (6). In our study, as a result of the histopathological examination, 89.2% of the patients were diagnosed with invasive ductal carcinoma. The incidence of invasive lobular carcinoma, which was the second most common type by 3.6% in our study, is between 5% and 15% in the literature (8, 9). The reason for the variability in incidence is the use of different diagnostic criteria in different studies.

The determinations of tumor size, the status of axillary lymph node, histological subtype, histological grade, hormone receptor and HER2 status in breast cancer are the basic parameters in determining the prognosis and response to treatment (1, 2). In the study by Elston et al., the histological grade evaluated in 1831 patients showed a very strong correlation with prognosis; the patients with grade I tumors showed better survival than those with grade II and III tumors (10). These results indicate that this method provides important prognostic information for histological grading and that repeatable results can be obtained if the grading protocol is consistently followed (10).

The histological grade constitutes a part of the multifactorial Nottingham prognostic index. Histological grade is one of the parameters that should be necessarily specified in biopsy and resection materials (1, 2). In the study by Özmen, histological grades (HG) were evaluated as HG I 5%, HG II 45%, and HG III 50%. While HG III tumors were detected in half of the cases, HG decreased along with the advancing age (6).

Anders et al. found higher axilla positivity and HG ratio, lower ER and PR positivity and higher HER-2 positivity in young breast cancer patients (11). In the study by Özmen, it was reported that pN0 was 44%, HGIII ratio was 60%, ER positivity was 61%, PR positivity was 57%, and HER-2 positivity was 26.5% in patients under the age of 40, and that pN0 was 60%, HGIII ratio was 44%, ER positivity was 71%, PR positivity was 59%, and HER-2 positivity was 23%

in the older age group (6). In the same study, the estrogen receptor and CerbB2 ratio were found to be higher in the postmenopausal group and premenopausal group, respectively. 90.6% of progesterone negative cases were under the age of 50 years while 9.4% of them were above the age of 50 years. It was reported that progesterone receptor increased as the age increased (6). In our study, estrogen in 55.2% of cases, progesterone in 57.3% of them and HER-2 receptor in 23.6% of them were detected to be positive.

In the study by Ehinger et al., the researchers showed that the patients with ER-positive / HER2-negative / grade1 breast cancer had a good prognosis similar to "Luminal A-like" while the patients with ER-positive / HER2-negative / grade 3-breast cancer had a worse prognosis (12).

The size of the tumor is an important prognostic factor used to determine the stage of the disease. In the literature, the mean tumor diameter was reported to be 2.5 cm (\pm 1.6; range 0.1-20 cm) (6). In our study, the tumor diameter was most frequently between 2 cm and 5 cm. The number of lymph node metastases increases as the size of the tumors increases (13-18).

In our study, lymph node metastasis and recurrence were detected in 53.2% and 9.75% of the cases, respectively, the records of whom were reached. 6.41% of the patients had metastasis at the time of diagnosis, whose data could be achieved, had metastasis at the time of diagnosis while 34 (9.5%) of them had a recurrence after metastasis development. 1 case (0.3%) recurred with mass detection from the other breast, not with metastasis. 12.54% of the patients who were followed up until 2019 died. A total of 35 cases (9.7%) were observed to have a recurrence. In the determination performed until the last month of 2018, the death reports of 44 patients (12.3%) were achieved, and we are still following the other 315 cases (87.7%)(Table 3).

CONCLUSION

In conclusion, invasive ductal carcinoma was the most common, while invasive lobular carcinoma was the second most common carcinoma in our study. The incidence of invasive breast carcinoma reaches the peak between the ages of 40-60 years and reaches its second peak before the age of 40 years.

Competing interests: The authors declare that they have no competing interest.

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REFERENCES

- Lakhani S, Ellis I, Schnitt S, et al. WHO Classification of Tumours of the Breast 4th. Lyon: IARC Press; 2012.
- Tavassoli FA, Devilee P, editors. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. Lyon: IARC Press; 2003.
- Orvieto E, Maiorano E, Bottiglieri L, Maisonne et al. Clinicopathologic characteristics of invasive lobular carcinoma of the breast: results of an analysis of 530 cases from a single institution. *Cancer* 2008;113: 1511-20.
- Talman ML, Jensen MB, Rank F. Invasive lobular breast cancer. Prognostic significance of histological malignancy grading. *Acta Oncol* 2007;46: 803-80
- Dillon D A, Guidi AJ, Schnitt S.J. Pathology of invasive breast cancer. In: Harris JR, Lipmann ME, Morrow M, and Osborne CK, eds. *Diseases of the Breast*. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2010.
- Özmen V. Breast Cancer in Turkey: Clinical and Histopathological Characteristics (Analysis of 13.240 Patients). *J Breast Health* 2014;10:98-105.
- Fidaner C, Eser SY, Parkin DM. Incidence in Izmir in 1993–1994; First results from Izmir cancer registry. *Eur J Cancer* 2001;37: 83-92.
- Mollahaliloğlu S, Başara BB, Eryılmaz Z, eds. T.C. Sağlık Bakanlığı Sağlık İstatistikleri Yıllığı. Ankara: Kalkınma Bakanlığı; 2010.
- Ravdin PM, Cronin KA, Howlader N, et al. The Decrease in Breast-Cancer Incidence in 2003 in the United States *N Engl J Med* 2007; 356:1670-1674.
- Elston CW, Ellis I O. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology* 1991;19: 403-10.
- Anders CK, Hsu DS, Broadwater G, et al. Young age at diagnosis correlates with worse prognosis and defines a subset of breast cancers with shared patterns of gene expression. *J Clin Oncol* 2008; 26: 3324-3330.
- Ehinger A, Malmström P, Bendahl PO, et al. South and South-East Swedish Breast Cancer Groups. Histological grade provides significant prognostic information in addition to breast cancer subtypes defined according to St Gallen 2013. *Acta Oncol* 2017;56: 68-74.
- Sendto Makki J. Diversity of breast carcinoma: histological subtypes and clinical relevance. *Clin Med Insights Pathol* 2015; 8: 23-31.
- Henson DE, Ries L, Freedman LS, et al. Relationship among outcome, stage of disease, and histologic grade for 22,616 cases of breast cancer. The basis for a prognostic index. *Cancer* 1991;68:2142-9.
- Rosenberg J, Chia YL, Plevritis S. The effect of age, race, tumor size, tumor grade, and disease stage on invasive ductal breast cancer survival in the U.S. SEER database. *Breast Cancer Res Treat* 2005 ;89:47-54.
- 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.
- Ahmad Z, Khurshid A, Qureshi A, et al. 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.
- Yoshimoto M, Sakamoto G, Ohashi Y. Time dependency of the influence of prognostic factors on relapse in breast cancer. *Cancer* 1993;72: 2993-3001.