

What has changed in the clinical presentation of breast carcinoma in 15 years?

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ABSTRACT

Objective: The aim of this study is to investigate if there was a change in time in terms of age at diagnosis, menopausal status, pathologic tumor size, lymphatic metastasis and pathologic stage in patients with surgical treatment for breast carcinoma.

Material and Methods: The clinical and pathological characteristics of 1223 patients with breast carcinoma who underwent surgical treatment between January 1994 and December 1998, and of 1346 patients who underwent surgical treatment with the same diagnosis between January 2004 and December 2008 were retrospectively reviewed.

Results: The median age at diagnosis was 48 (20-78) years during the first period, and 50 (20-91) years during the second period. While 27% of patients were 40 years of age or younger in the first period, this ratio decreased to 20% during the second period ($p=0.0001$). The rate of premenopausal patients was 54% in the first period and 46% in the second period ($p=0.0001$). The median tumor size at diagnosis was 3 cm at the first period, and 2.5 cm at the second period. The number of patients with tumor size ≤ 2 cm increased in time from 391 (32%) to 531 (39%) ($p=0.0001$). Among young patients (aged ≤ 40 years), the number of patients with tumor size 2 cm or smaller were 81 (24.5%) and 92 (33.8%) at the first and second periods, respectively ($p=0.001$). Lymphatic metastases rate of patients aged ≤ 40 years was higher than patients aged >40 years, in both study periods ($p=0.0001$). The number of patients staged as pN1 at the first period increased from 356 (50.8%) to 441 (56.3%) at the second interval, while those staged as pN3 decreased from 251 (35.8%) to 175 (22.3%) ($p=0.0001$).

Conclusion: It may be concluded that recently, breast cancer is diagnosed at older ages, the rate of young and premenopausal patients and size on diagnosis has decreased, and breast-conserving surgery is used more often.

Keywords: Breast cancer, age, menopausal status, tumor size, lymphatic metastasis, stage

INTRODUCTION

Breast cancer, which is the most common cancer in women, is one of the leading disorders affecting adult women. It also is an important public health problem with screening, research and treatment related health care costs (1).

There have been significant changes over time in the incidence of breast cancer, diagnosis and treatment approaches, as well as mortality and survival rates. The clinical presentation of breast cancer has also altered in time (2). The incidence of breast cancer has reached a plateau in developed countries, with even a decreasing trend in recent years, while it continues to increase in developing countries and Asia (1-3). There are studies suggesting a recent increase in the prevalence of breast cancer in young women (4).

Increased awareness on breast cancer in the community, dissemination of screening programs, and frequent use of mammography resulted in detection of smaller lesions with less rates of lymph node involvement. Early diagnosis enables higher rates of surgical treatment, especially breast conserving surgery, thus yielding more successful treatment outcomes (5, 6).

However, studies on the demographic and clinical characteristics of breast cancer, which is also the most common cancer among women in our country, and the changes occurring over time are limited.

In this study, we aimed to evaluate age, menopausal status, pathologic tumor size, lymph node involvement and stage in surgically treated breast cancer patients in 5-year periods that are a decade apart, and determine if there have been changes regarding these parameters.

MATERIAL AND METHODS

1223 patients who underwent surgical treatment in our clinics with a diagnosis of breast cancer between January 1994 and December 1998, as well as 1346 patients operated for the same diagnosis between January 2004 and December 2008 were enrolled in the study, regardless of the presence/absence of diagnostic or screening mammography. Patients with metastatic disease or did not undergo surgery, patients with neoadjuvant treatment and male patients were excluded from the study. The study was

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designed as a retrospective assessment of patient files. Data on age, sex, menopausal status, complaints, diagnostic procedures, and pathologic features such as tumor size, lymph node involvement, and stage were extracted from files.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL, USA) 15.0 software package was used for statistical analysis. Continuous variables between groups were compared with Student t test, and categorical variables with chi-square test. Analysis of $p < 0.05$ was considered statistically significant.

RESULTS

Clinico-pathologic characteristics of patients according to the study period are summarized in Table 1. The median age of patients operated for early-stage breast cancer was 48 (20-78) in the first period, and 50 (20-91) in the second period. The rate of patients under 40 years of age was 27% in the first 5-year period, while this rate decreased to 20% in the second five years ($p=0.0001$). The rate of premenopausal patients was identified as 54% in the first period, and 46% in the second period ($p=0.0001$).

The median tumor diameter at diagnosis was 3cm in the first period, and 2.5 cm in the second period. The number of patients with tumor size less than 2 cm was 391 (32%) in the initial 5-year period, while it increased to 531 (39%) in the second period ($p=0.0001$). The number of patients with 2-5 cm tumors in the first period was 713 (58%), and was 723 (53%) in the second period. Similarly, the number of patients with tumors greater than 5 cm decreased from 119 (9.7%) to 92 (6.8%) ($p=0.0001$).

The number of patients who were 40 years old and younger with tumor size less than 2 cm was 81 (24.5%) in the initial 5-year period, and 92 (33.8%), in the second period, while these values were 310 (34.8%) and 439 (40.9%) in patients who were older than 40 years of age, respectively ($p=0.001$, $p=0.037$).

The rate of patients with axillary metastases was 57% in the first, and 58% in the second period. The proportion of patients with pathologic stage I-II disease was 70% in the first, and 72% in the second period. There was no significant difference between the periods for both parameters ($p=0.689$, $p=0.163$). There was no statistically significant difference between patients younger or older than 40 years old between periods in terms of axillary lymph node metastasis ($p=0.375$), but lymphatic metastasis rate in patients younger than 40 years of age was significantly higher in both periods. During the first period 224 (68%) of the young patients, and 477 (53.5%) of those over 40 years had axillary lymphatic metastasis ($p=0.0001$), while in the second period these figures were 194 (71%) and 589 (55%), respectively ($p=0.0001$).

In terms of axillary lymph node involvement, the number of patients with pN1 tumors was 356 (50.8%) in the first period, and 441 (56.3%) in the second interval, while the number of patients with pN3 tumors decreased from 251 (35.8%) to 175 (22.3%) ($p=0.0001$).

Modified radical mastectomy was performed in all patients during the initial 5-year period because breast-conserving sur-

Table 1. Clinico-pathologic features of patients according to time periods

Patient number	1994-1998	20042-2008	p
Total	1223	1346	
≤40 years	331 (27.1%)	272 (20.2%)	0.0001
>40 years	892 (72.9%)	1074 (79.8%)	
Menopausal status			
Premenopausal	668 (54.6%)	624 (46.4%)	0.0001
Postmenopausal	555 (45.4%)	722 (53.6%)	
Tumor size (pathologic)			
pT1	391 (32.0%)	531 (39.5%)	
pT2	713 (58.3%)	723 (53.7%)	0.0001
pT3	119 (9.7%)	92 (6.8%)	
Axillary lymph node involvement			
Negative	522 (42.7%)	563 (41.8%)	$p=0.689$
Positive	701 (57.3%)	783 (58.2%)	
Stage			
I-II	853 (69.7%)	973 (72.3%)	$p=0.163$
III-A-C	370 (30.3%)	373 (27.7%)	

gery was not routine at that period. In the second period, 148 patients (11%) underwent breast-conserving surgery.

DISCUSSION

Changes in the clinical characteristics and natural history of breast cancer over time may be associated with differences in the demographic structure of the country, geographical and racial characteristics, as well as socio-economic and cultural factors. In addition, new technologies and developments in the diagnosis and treatment of breast cancer also influence natural disease course.

In this study, changes in clinical characteristics of breast cancer on admission were evaluated over 10 years of admission to our hospital. There was an increase in median patient age, and a decrease in the rate of young (40 years and under) and premenopausal patients. In addition, decrease in median tumor size; increase in the number of patients with tumor size less than 2 cm was detected along with a decrease in large tumors, and a decrease in extension of lymph node involvement not showing statistical significance. Looking at the overall trends these results reflect, the widespread implementation of mammography in the screening and diagnosis of breast cancer could explain all these changes. However, lack of identification of data on the frequency of diagnosis and screening mammography in our study period is one of the most important limitations of this study. Among other limitations are the retrospective nature of the study, as well as inclusion of patients from a single institution, and the likelihood of not representing the whole country. The present patient group is compatible with the National Breast Cancer Database, which is one of the largest breast cancer series in our country, in terms of mean and median age, rate of patients younger than 40 years and premenopausal patients, tumor size on diagnosis and rate of pathological early stage (7). Especially results of the second

term patients are nearly identical with the database results between the years 2005-2009, except for the rate of lymph node involvement. This suggests that although this is a single center study, this patient group's characteristics are similar to the whole country.

On the other hand, it is clear that the number of mammography devices across the country and the ability to access mammography have increased recently, thereby increasing community awareness on mammography and breast cancer. Although not included in this study data, mammography use in our country is reported to increase annually. According to the Ministry of Health Cancer Control Department data, there is a 63% increase in the number of screening mammographies in 2013 as compared to 2012 (8).

Breast cancer is the most common cancer in women and the second leading cause of cancer deaths in our country, as the rest of the world (1, 9). Although there is possible curative treatment in early-stage patients, currently it is not possible to provide cure in metastatic disease. This explains the vital role of screening programs that are essential for early diagnosis. The main purpose of breast cancer screening is applying the national screening program particularly created for that country to the target population in order to detect cancer development before emergence of clinical signs, in the initiation stage, as small and early as possible, and to reduce the mortality rate. That is why, the introduction of mammography that can be used for both diagnosis and screening is one of the most important milestones in the diagnosis and treatment of breast cancer.

The results of this study suggest that lately tumors are being identified at smaller sizes. Reduction of the tumor size in the second period, decreased rate of patients with larger tumor size, increased rate of patients with tumor size less than 2 cm can be related to the increased frequency of mammography as well as increased awareness of the community.

The proportion of patients diagnosed early is high in developed countries with screening programs (10, 11). Early diagnosis allows increased treatment options, more breast conserving surgery, better cosmetic results and survival. Therefore, the use of screening mammography has increased significantly in our country, as all over the world in recent years. The rate of obtaining mammography in the last 2 years in women 40 years and older in the USA increased from 29% in 1987 to 71% in 2003, had a slight decline between 2003-2005 and stabilized to 67% by 2010 (1, 12, 13). In consequence, there was an increase in the incidence of breast cancer; this increase since 1987 is thought to be due to the widespread screening mammography allowing detection of occult breast cancer, without any clinical symptoms (1).

Another effect observed with the extensive use of screening mammography is the increase in median age at diagnosis followed by a decrease. It was originally shown that screening mammography over the age of 40 caused an increase in the incidence in this age group (2). In our study, the median age of 48 in the initial period increased to 50, which may be due to the increased incidence of getting breast cancer in women over 40 years of age associated with the widespread use of mammography.

Breast cancer is an age-related disease, in other words increasing age is a major risk factor for the development breast cancer in women. Breast cancer incidence in Western countries increases up to 80 years. Breast cancer in young women is rare. The median age of patients diagnosed with breast cancer in 2002-2006 was found to be 61 in the USA (14). A median age of 50 years reported both in our study during the period 2004-2008, and in the National Breast Cancer Database indicates that half of patients with breast cancer were under 50 years of age, which is a major difference from the Western reports. The proportion of women with breast cancer before 40 years of age in the Western countries is less than 10% (6, 15). The American Cancer Society (ACS) reported that only 5% of new breast cancer patients were younger than 40 years of age, in 2002-2006 (13).

The rate of young breast cancer in our country and Asian-African countries is high, reaching up to 30%, which is different from Western countries (16). Findings in our series also support this opinion. The rate of breast cancer under the age of 40 was 27% in the first period of our study and 20% in the second period. The National Breast Cancer Database reported this rate as 17%, indicating that despite a reduction the rate of young breast cancer is still high as compared to Western countries. Similarly, the proportion of pre-menopausal women with breast cancer in our study was 55% in the first period, and 46% in the second period, and was reported as 45% in the National Breast Cancer Database. In Western countries, only 25% of women diagnosed with breast cancer were premenopausal. One of the possible causes of this high rate of young and premenopausal breast cancer patients may be the high young population density. According to the Turkish Statistical Institute data, the female population of our country under the age of 40 years accounts for 64% of the total female population, while this figure is lower in Western countries (17).

Breast cancer at a young age is known to behave more aggressively with worse results. Tumors in young people have larger sizes, and increased possibility of lymphatic metastases and hormone receptor negativity (18, 19). The lack of decrease in stage despite detecting smaller tumors in the second period in our study can be related to the high rate of young breast cancer patients and higher rates of lymph node metastases in these patients. Indeed, the axillary lymph node metastasis rate in our series is higher than the National Breast Cancer Database (50%) as well as Western countries (30-40%), and shows a significant decrease in the second period of the study (6, 7, 13). The rates of lymph node metastasis in young patients during both study periods appear to be significantly higher as compared to patients over 40 years of age. Although there was no significant difference between periods in terms of lymph node metastasis and pathological stage, the increase in pN1 rate along with reduction of pN3 rate support that lymphatic metastasis extension is reduced although the rate has not changed.

Although there was an increase in the rate of patients with small tumors, the relatively lower rate of breast conserving surgery in the second period as compared to present practice may be related to cautious application of the then newly applied technique with very selectively use. It is obvious that one of the most important advantages of detecting smaller tumors is increasing the rate of breast conservation.

Study Limitations

Retrospective nature of analysis including patients from a single institution is the main limitation of our study.

CONCLUSION

At the end of a decade, it may be concluded that breast cancer diagnosis age is increasing, the rates of young and premenopausal breast cancer patients are decreasing, breast cancer is diagnosed at smaller sizes and breast-conserving surgery is applied more frequently.

Ethics Committee Approval: This study was designed retrospectively so the ethics committee approval was not needed.

Informed Consent: We did not need the patient's consent since this study was retrospective and no personal information and document were shared.

Peer Review: Externally peer-reviewed.

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