

CLINICAL ASSESSMENT OF 324 BREAST CANCER CASES IN TWO CENTERS BETWEEN THE YEARS OF 1992 AND 2002

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Summary: The records of the 324 patients with breast cancer; diagnosed and followed in two different University Hospital between years of January 1992 and January 2002 were reviewed retrospectively. The median age of the patients was 49.0 ± 12.5 years, with the range of 18 and 90 years. The most frequently seen age interval of the patients was 40 and 49 years. The most frequently seen symptom and physical examination finding of the patients were breast mass. Breast cancer was diagnosed in 324 women, 173 in the left breast and 151 in the right breast. At the hospital admission percentages of the patients' disease stages were as follows: I (2.8 %), IIA (30.0 %), IIB (24.0 %), IIIA (19.8 %), IIIB (11.4) and IV (12.0 %). The most frequently seen histopathological diagnosis was infiltrative ductal carcinoma (84.4 %). Axillary lymph node metastasis was found in 61.7 % of the patients. Primary therapeutic options and percentages were surgical therapy (78.5 %), systemic chemotherapy (17.5 %) and radiotherapy (4 %). Systemic chemotherapy was given to 81.2 % of the patients. From the files, estrogen receptor status was known in 311 and positive in 128 (41.2 %) of them. Tamoxifen was given patients who had positive estrogen receptor. The five-year survival rate of the patients was calculated as 75.9 %.

Key words: Breast cancer; Stage; Treatment; Survival

Introduction

Today breast cancer is the most commonly seen cancer among women. The death due to breast cancer among women comes as the second leading cause after lung cancer. The risk of developing breast cancer is one in eight women in developed countries (1).

There are more than 1,000,000 breast cancer cases each year, and almost half of these are in less developed countries (20).

In the United States of America (USA) the rate of breast cancer and other cancers increased between 1973 and 1990. All-sites cancer incidence and mortality fell in the period 1991 through 1995. After the rapid increase in breast cancer incidence rates that accompanied the widespread introduction of the mammography in the 1980s, breast cancer mortality is now decreasing at a rate of approximately 1 % per year (16).

There is not enough information about cancer statistics and outcomes for our country. In this study we aimed to analyze breast cancer cases retrospectively followed in two different University Hospital in Turkey within the last ten years.

Patients and methods

The records of women with diagnosis of breast cancer that followed in Hospitals of Selcuk University and Kocaeli University were examined in a retrospective way. The age of the patients, their first complaints or symptoms, physical examination findings, used diagnostic methods, localization of the tumors, axillary lymph node status, histopathological types of the tumors, clinical stages and survival periods of the patients were recorded.

Results

The median age of the cases was 49.0 ± 12.5 (range: 18–90 years) and distribution according to the age groups are shown in Table 1. Breast cancer was observed more common in the patients between the ages of 40–49 (32.5 %).

Generally the patients (80.8 %) were admitted to the hospital as a result of the lump in the breast. The lumps were painless in most of the cases (80.9 %). The other complaints of the patients are shown in Table 2.

While mass was palpated in 275 (85 %) cases, axillary lymph nodes were palpated only in 174 (50 %) cases. Peau

D'orange appearance and nipple retraction were seen in 44 (13.6 %) and 27 (8.3 %) cases, respectively. Physical examination findings of the patients are shown in Table 3.

Tab. 1: The distribution of the cases according to the age groups.

Age	Number of the cases	%
0-29 years	9	2.8
30-39 years	51	15.7
40-49 years	105	32.5
50-59 years	80	24.7
60-69 years	61	18.8
70-79 years	16	4.9
80-89 years	1	0.3
90+ years	1	0.3
Total	324	100.0

Tab. 2: The clinical symptoms of the patients at hospital admission.

Symptoms	Number of the cases	%
Lump within the breast	262	80.9
Breast pain	91	28.1
Axillary swelling	69	21.3
Pain in axillary region	63	19.4
Discharge from the nipple	27	8.3
Ulcerous wound	18	5.6
Swelling and/or pain of breast	11	3.4
Nipple retraction	16	4.9
Back pain	3	0.9

Tab. 3: Physical examination findings of the patients at hospital admission.

Findings	Number of the cases	%
Lump within the breast	275	84.9
Axillary mass	174	50.0
Peau D'orange	44	13.6
Retracted nipple	27	8.3
Diffuse swelling of the breast	10	3.1
Supraclavicular mass	14	4.0
Hepatomegaly	6	1.9
Edema of upper extremity	5	1.5
Ascitis	4	1.2
Satellite nodule	4	1.2

Tab. 4: Clinical staging of the patients according to TNM classification.

Stage	Number of the cases	%
I	9	2.8
IIA	98	30.2
IIB	78	24.0
IIIA	64	19.8
IIIB	37	11.4
IV	38	12.1
Total	324	100.0

Tab. 5: Tumor localization in breast cancer patients.

Localization	Right	Left	Total	%
Areola	23	30	53	16.4
Upper exterior	73	80	153	47.2
Upper interior	23	25	48	14.8
Lower exterior	19	17	36	11.1
Lower interior	9	14	23	7.1
Diffuse	4	7	11	3.4
Total	151	173	324	100.0

Tab. 6: Performed surgical operation procedures in breast cancer patients.

Surgical operation	Number of the cases	%
Modified Radical Mastectomy and axillary dissection	216	85.7
Simple mastectomy and axillary dissection	15	5.9
Simple mastectomy	12	4.8
Partial mastectomy and axillary dissection	5	1.9
Partial mastectomy	2	0.8
Lump excision	2	0.8
Total	252	100.0

Tab. 7: Histopathological diagnosis of the patients.

Histopathological type	Number of the cases	%
Infiltrative ductal carcinoma	273	84.4
Lobular carcinoma	38	11.7
Mucinous adenomatous carcinoma	4	1.2
Medullary carcinoma	3	0.9
Inflammatory carcinoma	4	1.2
Comedo carcinoma	1	0.3
Papillary carcinoma	1	0.3
Total	324	100.0

According to TNM classification the most commonly seen stage was IIA, 98 cases (30.2 %) and followed by IIB, 78 cases (24.0 %). The clinical stages of the patients according to TNM classification are shown in Table 4.

Complete blood count and biochemical parameters including electrolytes, liver and renal function tests were checked in all cases. Co morbid diseases like hypertension in 58 (17.9 %) cases, heart disease in 7 (2.2 %), diabetes mellitus in 15 (4.6 %) cases, gallbladder stone in 7 (2.2 %) cases, anemia in 35 (10.8 %) cases, renal insufficiency in one case and Parkinson disease in one case were recorded. Elevated liver function tests in 20 cases (6.2 %) and hypercalcaemia in 12 (3.7 %) cases were established.

Bilateral mammography, abdominal ultrasonography and chest X-ray were done in all cases and computed tomography of thorax and abdomen were done in necessary situations. Scintigraphy of all bones in the body were taken

in 87 (26.9 %) cases in whom bone metastasis were suspected. Cranial tomographies of eight (2.5 %) cases were taken due to the suspicion of brain metastasis. The exact diagnosis of breast cancer was established histopathologically in all cases. For this purpose fine needle aspiration in 15 (4.6 %) cases and open biopsy in the rest of the cases were done. Diagnoses were established in 12 (3.7 %) cases with frozen section during operation.

At the first examination distant metastasis were found only in 38 (12.1 %) patients. Metastasis locations were found as bone in 11 cases, supraclavicular region in 11 cases, liver in 10 cases, lung in 3 cases, both liver and lung in 2 cases and both liver and bone in 2 cases. The tumor mass localizations were more in the left breast of the patients (53.4 %). When the all quadrants examined the tumors were established mostly in upper external quadrants of the breasts (47.6 %). The second most often established localization of the tumors was beneath areola region (16.4 %). In 73 of the cases (22.5 %) clinically inoperable breast cancer were present. After the biopsy, neoadjuvant systemic chemotherapy was given to 60 cases and 12 cases were referred to radiotherapy (RT) first. Initial surgical procedure and then systemic chemotherapy was applied to the rest of the 252 (77.8 %) cases. As systemic chemotherapy CMF (Cyclophosphamide, Methotrexate, 5-Fluorouracil) or CAF (Cyclophosphamide, Adriablastina, 5-Fluorouracil) were given to 81.2 % of the patients according to breast cancer stage and patient's clinical situation. Tamoxifen was given to the patients in whom estrogen receptor positivity shown in breast biopsy specimen. Modified radical mastectomy and axillary dissection were performed in 216 (85.7 %) patients as the most frequent surgical operation procedure. Performed surgical operations to the patients are shown in Table 6. In 13 cases (4.0 %) surgical operations were performed after down staging of the cancer by neoadjuvant chemotherapy or radiotherapy.

In 273 cases (84.4 %) infiltrative ductal carcinoma and in 38 cases (11.7 %) lobular carcinoma were diagnosed histopathologically. Histopathological results of the tumors are shown in the Table 7. In three cases in which infiltrative ductal carcinoma was diagnosed (1 %) also Pagets disease were found at the nipples of the breasts. Axillary dissection was done in 236 cases and metastases were found in 201 of them.

Primary surgery was performed in 76.5 % of the patients, systemic chemotherapy was given to 19.5 % of the patients and radiotherapy was employed to 4 % of the patients. Estrogen receptor status was positive in 41.16 % of the cases. Tamoxifen was given to the patients as 20 mg/day in whom estrogen receptor status was found as positive.

One or more postoperative complications was developed in 70 (21.6 %) cases and the most frequent complication was seroma and seen in 69 (21.3 %) cases. The other complications were skin necrosis in 29 (8.9 %) cases, infection of incision line in 15 (4.6 %) cases and nerve damage in 15 (4.6 %) cases.

We were able to contact with the patients or relatives through the telephone and recorded the last visits of the patients from the files. It was seen that 246 (75.9 %) patients were still alive and 78 (24.1 %) patients were died during 5 years period. When the died patients analyzed according to the their clinical stages at admission; it was found out that 4 of them in stage IIA, 5 of them in stage IIB, 7 of them in stage IIIA, 9 of them in stage IIIB, 53 of them in stage IV.

Discussion

Breast cancer is the second most frequent cause of cancer death among women and accounts for 15 % of all cancer deaths among women; only lung cancer causes more deaths (11). It is assumed that in year 2000 one million new cases and over 400,000 deaths would appear in the world (8). The American Cancer Society estimated that 192,000 cases and 40,000 deaths would occur among U.S. women during 2001 (13). Although the frequency of breast cancer varies from region to region, in recent years there is a significant increase in allover the world (8). Difference in the frequency of breast cancer between the developed and rest of the world have decreased. USA, Canada, Spain, and Sweden were countries in which breast cancer is highest. As one of the leading cause of cancer death among all women worldwide, breast cancer accounted for more than 300,000 deaths In 1990: 174,100 deaths occurred in developed countries and 139,500 occurred in developing countries (21). Death rates due to breast cancer were low in Asia, Africa and central America; intermediate in South America and southern Europe; and highest in western Europe and North America (13). This difference is most significant among the women after menopause. Likewise, there are differences between the different ethnic groups.

Probability of having breast cancer and dying from it for an American woman is calculated as 10 % and 3-4 % respectively. This assessment was approximated between the birth and 110 years old. It is known that the illness increases with the age. Breast cancer is rare in woman younger than 30 year-old, however rapidly increases after these ages. Although there is a slight decrease through the menopause period, following these years slow but an increasing tendency is seen (22). These differences are related to the effects of the environment, life styles, and socio-economical conditions of the women (9,19).

In our study group, most of the patients were between the ages of 40-49 (30.9 %). Genetical, environmental, hormonal, sociological and psychological factors have effect on breast cancer development (9,14). Socio-cultural levels of women have an important role in mortality of the breast cancer patients. The high stage level is more prevalent in low educated people and high rate of death is observed among them (4,24).

The frequency of breast cancer rises two-three times in women who have relative with breast cancer. This risk is doubled if the mother had history of breast cancer and 2.5

times greater if their sisters had the disease. The existence of cancer in one breast, early menarche, late menopause, late first pregnancy age, being subjected to radiation, obesity, extreme alcohol intake, high fatty diet have been researched risk factors for breast cancer (3,17). Because of the inadequate records and laboratory results of our patients, the role of these factors could not be established in this study. The association of breast cancer with pregnancy is rare. It is defined as the occurrence of breast cancer during pregnancy or during the year following delivery (15). In our series, a case with inoperable breast cancer was diagnosed and referred for chemotherapy and another had a history of full term childbirth of 4 months ago and breast mass complaint during the third trimester of the pregnancy.

The leading first complaint of our breast cancer patients was painless and hard lump within the breast. In addition to breast lump, skin changes like orange peel appearance, satellite nodules, ulceration, nipple discharge, lesions similar to eczema, lymph nodes in axillary and supraclavicular regions were found in clinical examination of the patients. In our patients lump within the breast and lymph nodes in axillary region could be palpated in 86 % and 53 % of the cases, respectively, by physical examination.

Breast cancer was diagnosed more often in upper exterior quadrant (47.2 %) and beneath the areola region (16.4 %). The excessive breast mass in upper exterior quadrant and connection point of the nipples are the reasons for this distinction pattern.

According to the clinical stage, the most common one stage IIA (30.2 %) and the least one stage I (2.8 %) in our patients. It was established that 74 % of the cases had one of the stages of IIA, IIB or IIIA. Seventy-two cases (23.5 %) were assessed as inoperable.

Established prognostic and predictive factors in breast cancer patients are age, race, tumor size, nodal status, tumor subtype, standard pathological grade, estrogen receptor, progesterone receptor, mitotic rate (1). The standard prognostic factors that are used in treatment of the breast cancer are the status of axillary lymph nodes, histological subtype, the tumor size, nuclear and histological grade, the presence of estrogen and progesterone receptors, the measurement of the proliferation. It was stated that the other factors other than these has no clinical benefit (18).

Axillary region is the main drainage area for the breast. In the 50 % breast cancer cases that are diagnosed clinically, axillary lymph node metastasis was observed histopathologically. The status of axillary lymph node metastasis is not directly related to the dimension of the primary tumor. Even in the small tumors like 0.5 cm diameter, the risk of axillary lymph node metastasis is as 20 %. Localization of the tumor within the breast helps to determine the risk of axillary lymph node metastasis. It was known that tumors of external quadrant cause the axillary lymph node metastasis more than one of internal quadrant. In addition, it was shown that the number of the lymph nodes with metastasis is independent from the size of the tumor and directly re-

lated to disease outcome (6,23). Axillary lymph node metastasis in our patient group was found out as 66.7 %. This number is apt with the data in the literature.

In early postoperative period the most common morbidity was found as seroma in the patients (22.4 %). Other complications of our cases were appropriate with the literature knowledge.

Surgical treatment, systemic chemotherapy, radiotherapy, hormonal therapy can be used for treatment of breast cancer. One of these treatment options or combinations might be preferred according to the patient's clinical status, tumor stage and characteristics of the tumor. It has been advised to use Tamoxifen in all estrogen-receptor-positive premenopausal and post-menopausal women (2,5,7,10,12). Primarily 76.5 % of our patients were undergone surgery, 19.5 % undergone systemic chemotherapy and 4 % undergone through radiotherapy. Surgical procedure was performed in 4 % of the cases after neoadjuvant chemotherapy or radiotherapy in whom down staging was achieved. After the surgery, systemic chemotherapy was given to 81.2 % of the cases. Estrogen-receptor was found positive in 41.16 % of the cases and Tamoxifen was given to them as hormonal therapy.

Five-year relative survival rates of breast cancer patients improved from 75 % during mid-1970s to 86 % during 1990s. Survival rates varied markedly by stage at diagnosis, from 89 % or more in women with localized disease to 22 % or less in women whose tumors have distant spread (13). In our cases, 5-year relative survival rate was found as 75.9 %. Breast cancer screening is not established in our country. So that the number of breast cancer patients with early stages is lesser than the patients with higher stages in our series. The patients apply to the hospitals when the disease has been progressed and give more complaints to them.

Conclusion

As a conclusion it can be predicted that breast cancer, as in the world generally, show the tendency of increase in our country and in our region. The object must be to go beyond the predictions with the real data and analyze the situation we are in, know the risk factors well and enlighten the people under the threat of this disease. The small number of the cases, which diagnosed in early stage shows that breast cancer is not yet well known by the people (especially women) in the region. The aim of this study is to put down the insufficiency in this matter. We are in the opinion that information and data insufficiency would be put away with the countrywide studies about breast cancer.

Both international and intranational breast cancer incidences and mortality rates are different. Incidence rate differences between countries show the importance of inherent genetic risk in breast cancer etiology and lifestyle factors can dramatically affect risk. Incidence rate differences within countries arise in part because of differential access to and utilization of health care resources such as

screening and diagnosis. We should extend therapeutic advances to all segments of the population.

References

1. Aapro MS. Adjuvant therapy of primary breast cancer: A review of key findings from the 7th international conference, St. Gallen, February 2001. *The Oncologist* 2001;6:376-85.
2. Aebi S, Gelber S, Castiglione-Gertsch M et al. Is chemotherapy alone adequate for young women with oestrogen-receptor-positive breast cancer? *Lancet* 2000;355:1869-74.
3. Anderson DE. Breast: Genetic study of breast cancer: Identification of a high risk group. *Cancer* 1974;34:1090-7.
4. Baquet CR, Commiskey P. Socioeconomic factors and breast carcinoma in multi-cultural woman. *Cancer* 2000;88:1256-64.
5. Cardoso F, Di Leo A, Lohrisch C et al. Second and subsequent lines of chemotherapy for metastatic breast cancer: what did we learn in the last two decades? *Ann Oncol* 2002;13:197-207.
6. Carter C, Allen C, Henson D. Relation of tumor size, lymph node status and survival in 24,740 breast cancer cases. *Cancer* 1989;63:181-7.
7. Cuzick J. A brief review of the current breast cancer prevention trials and proposals for future trials. *Eur J Cancer* 2000;36:1298-302.
8. Forbes JF. The control of breast cancer: the role of tamoxifen. *Semin Oncol* 1997;24(1Suppl 1):S1-5-S1-19.
9. Freeman HP. Cancer in economically disadvantaged. *Cancer* 1989;64(1Suppl 1):324-34; discussion 342-345.
10. Goldhirsch A, Glick JH, Gelber RD et al. Meeting highlights: International Consensus Panel on the Treatment of Primary Breast Cancer-V Update 1998. *J Natl Cancer Inst* 1998;90:1601-8.
11. Greenlee RT, Murray T, Bolden S et al. Cancer statistics, 2000. *CA Cancer J Clin* 2000;50:7-33.
12. Hortobagyi GN. Treatment of breast cancer. *N Engl J Med* 1998;339:974-84,20.
13. Lacey JV Jr, Devesa SS, Brinton LA. Recent trends in breast cancer incidence and mortality. *Env Mol Mutagenesis* 2002;39:82-8.
14. Martin AM, Weber BL. Genetic and hormonal risk factors in breast cancer. *J Natl Cancer Inst* 2000;92:1126-35.
15. Mathieu E, Merviel P, Barranger E et al. Breast cancer and pregnancy: review of the literature. *J Gynecol Obstet Biol Reprod (Paris)* 2002;31:233-42.
16. McKean-Cowdin R, Feigelson HS, Ross RK et al. Declining cancer rates in the 1990s. *J Clin Oncol* 2000;18:2258-68.
17. Morrison AS, Brisson J, Khalid N. Breast cancer incidence and mortality in the Breast Cancer Detection Demonstration Project. *J Natl Cancer Inst* 1988;80:1540-7.
18. National Institute of Health Consensus Development Conference Statement: Adjuvant therapy for breast cancer, November 1-3, 2000. *J Natl Cancer Inst* 2001;93:979-89.
19. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancer in 1990. *Int J Cancer* 1999;80:827-41.
20. Peto R, Boreham J, Clark M et al. UK and USA breast cancer deaths down 25 % in year 2000 at ages 20-69 years. *Lancet* 2000;355:1822.
21. Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. [published erratum. *Int J Cancer* 83:18-29;1999]. *Int J Cancer* 1999;83:870-3.
22. Seidman H, Mushinski MH, Gelb SK, Silverberg E. Probabilities of eventually developing or dying of cancer. *United States CA Cancer J Clin.* 1985;35:36-56.
23. Smith J, Gamez-Araujo JJ, Gallager HS et al. Carcinoma of the breast: Analysis of total lymph node involvement versus level of metastasis. *Cancer* 1977;39:527-32.
24. Wingo PA, Ries LA, Rosenberg HM, et al. Cancer incidence and mortality, 1973-1995: a report card for the U.S. *Cancer* 1998;82:1197-207.

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