Determining the Clinicopathologic Features of Breast Lesions in Iranian Army Families

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Abstract

Background: Breast cancer is the most common disease of women around the world. On the other hand, benign breast diseases also constitute a wide range of breast pathologies that precise information on them is important. This study is conducted aiming to examine the breast pathology reports and determine the frequency of various breast diseases and its relationship with some clinicopathologic parameters in Imam Reza Hospital of army of the Islamic Republic of Iran in a period of 4 years.

Methods: Imam Reza Hospital is a referral center for Army employees in Iran. This study is a retrospective descriptive study on patients who undertook biopsy or breast surgery during 2012-2015 in Imam Reza Hospital. After reviewing pathology reports and patient records and completing the required information, a total of 188 patients with 230 samples of breast tissue were included in this study.

Results: During the period, 230 samples of breast tissue from 188 patients were sent to the pathology department. 195 samples (84.8%) were related to female patients and 35 samples (15.2%) to males. 112 samples (48.7%) were related to the left breast and 118 samples to the right (51.3%). The average size of tissues was 11.82 ± 8.64 cm. The mean age of patients was 42 ± 14.

Conclusions: In this study, a statistically significant relationship exists between the patient sex and final diagnosis, patient age group and final diagnosis, and cell differentiation grade and lymph node metastasis along with samples. In the pathology reports in the center, cell differentiation grade of tumor was completely matched with Nottingham Grading System.

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Introduction

Breast cancer is the most common disease of women around the world. After skin cancer, breast cancer is the most common malignancy in women (1), after lung cancer, it is the second leading cause of cancer death in women aged 20-59 years old (2). According to the statistics of the World Health Organization, more than 1.2 million patients are annually diagnosed with breast cancer and more than 500 thousand people die of the disease, and the risk is increasing in developing countries unlike the United States (3). The incidence of cancer rises with aging so that we reach from 1 in 230 cases in the fourth decade of life to 1 in 30 in the seventh decade (4). Previous studies in Iran's population indicate the prevalence of 17 in 100 thousands of women with peak prevalence in the age group 45-54 years old (5). However, breast cancer is the most common cancer in Iran and includes 21.4% of all cancer malignancies among women (6).

The incidence of breast cancer in Iranian women occurs a decade sooner than the developing countries. It also reveals the importance of study and research in this area more than before (7). Breast diseases affect not only women but also men. Male breast cancer makes up 1% of all breast cancer cases in Western countries (8). Breast cancer treatment requires a widespread recognition of the disease at the time of diagnosis (9). Although clinical examination and radiological findings play an important role in providing information about the types of breast diseases, making treatment decisions is largely dependent on pathological findings and data from the sample examination. Determining principled and correct therapeutic method requires accurate and precise data from tissue, type of tumor, surgery and a

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full description of histologic evaluation such as calcification, necrosis, grade, perineural and vascular invasion, and lymphatic involvement (10).

On the other hand, benign breast diseases also constitute a wide range of breast pathologies that precise information on them is important. For example, fibroadenomas form 68% of all breast lumps to 44-94% of all breast biopsies diagnose fibroadenoma (11). According to available reports, from one out of every six women in society undergoes biopsy due to breast problems and diagnostic results in about 75-80% of cases are reported to be benign (12). Precise differentiation of benign lesions from malignant by physical examination is difficult to a large extent, and this signifies the importance of the precise histological diagnosis (13). Another important point that must be noted is if the breast benign lesions increase the risk of breast cancer in the future or not. Many experts in the field of breast diseases know that certain types of benign breast changes are more related to malignant lesions (14). Simple hyperplasia increases cancer risk partly while atypical hyperplasia increases absolute cancer risk by 29% in 25 years; therefore, precise pathological diagnosis and its correlation with clinical parameters in follow-up of patients with breast lesions is very important (15). Hence, this study has been designed and conducted to investigate pathological reports of patients with different types of breast lesions. It is hoped the results of this study provide a correct view of the types of breast diseases and their clinical and histological characteristics.

Materials and Methods

Imam Reza Hospital (501 Artesh of Islamic Republic of Iran) is a referral center for Army employees in Iran. Hence, the patients who refer to this center can make a good sample of all Army employees. This study is a retrospective descriptive study on patients who undertook biopsy or breast surgery during 2012-2015 (since early 2012 to late 2015) in Imam Reza Hospital (501 Artesh of Islamic Republic of Iran). To do this, referring to the hospital pathology ward and examining samples' registries, all pathological reports of the patients in this period available in hospital pathology ward were studied, and samples prepared from breast tissue were separated. Then, data collection form was completed based on the information in pathology reports, including patients' age, sex, tumor location, sample size, final diagnosis and tumor size, tumor grade, Nottingham score, lymph node involvement and vascular, or perineural invasion in the case of tumoral tissues. Meanwhile, a number of samples were deficient in information that was corrected and completed by referring to patients' admission records at the archives and phone call to patients. Finally, 188 patients were included into the study with 230 samples. The reason for this difference is in the number of patients and the number of samples, sending multiple samples from one patient. At least two samples were sent to the pathology ward from 43 patients, and the number of samples of some patients also reached 4. Collected data were analyzed using SPSS (version 23, IBM Corporation, Armonk, NY, USA) and chi-square test.

Results

During the period, 230 samples of breast tissue from 188 patients were sent to the pathology department for pathological evaluation. 195 samples (84.8%) were related to female patients and 35 samples (15.2%) to males. 112 samples (48.7%) were related to the left breast and 118 samples to the right (51.3%). Among all tissue sent to pathology regardless of the patient, 62 fibrocystic changes (27%), 55 non-specific tissues (23.9%), 50 cases of invasive ductal carcinoma (IDC) (21.7%), 26 cases (11.3%) of gynecomastia, 22 cases (9.6%) of fibroadenomas, 8 cases (3.5%) of ductal carcinoma *in situ* (DCIS), 5 invasive lobular carcinoma (ILC) (2.2%), and 2 cases (0.9%) of papillary carcinoma were reported. The average size of tissues was 11.82 cm with a standard deviation of 8.64. The largest sample was about 40 cm. The size of sent samples and patients' age by the final diagnosis is given in Table 1. In the meantime, the size of tumors with a diagnosis of DCIS had the most, and the size of tumors with fibroadenoma had the lowest average size. The highest mean age was related to the patients with papillary carcinoma and lowest average age to the patients with gynecomastia.

On the relationship between patients' gender and final diagnosis of the sent tissue, it can be noted that all patients who were diagnosed with gynecomastia, were male. Among patients with IDC, there was also a male patient. In fact, 1 out of 50 samples with IDC was related to male patient (2%). Among the tissues with non-specific diagnosis, 47 samples (85.5%) were related to the female patients and 8 (14.5%) to males (Table 1). No significant correlation was found in the relationship between the lesion location and final diagnosis of the tissue (Table 1).

Following results were obtained on the relationship between patients' age and final diagnosis after dividing the patients into two age groups under 50 years of age and patients over 50 which were statistically significant ($P < 0.001$): Among 62 cases of tissue with fibrocystic changes, 48 cases (77.4) were under 50 years old and 14 (22.6%) above 50. Among 22 samples with fibroadenoma, 21 samples (95.5%) were under 50 years old and 1 sample (4.5%) was above 50. Among 26 gynecomastia samples, 24 samples (92.3%) were under 50, and 2 samples (7.7%) were above 50. Among 50 samples with IDC diagnosis, 25 samples (50%) were under 50 years old and 25 samples (50%) were above 50.

Among 8 DCIS samples, 3 samples (37.5%) were under 50 and 5 samples (62.5%) were above 50. Among 5 ILC samples, 3 samples (60%) were under 50 years old and 2 samples (40%) were above 50. Among 48 samples with non-specific diagnosis 37 samples (67.3%) were under 50 and 18 samples (32.7%) were above 50. Among 2 papillary carcinoma samples, 1 sample (50%) was under 50 years old and 1 sample (50%) was above 50.

In studying samples with a diagnosis of malignant breast tissue, from 65 samples, 8 samples (12.3%) were DCIS, 50 samples (76.9%) IDC, 5 (7.7%) ILC, and 2 (3.1%) papillary carcinoma.

On the tumor size in sent samples in the final diagnosis, the maximum size was related to the samples with DCIS with an average size of 4 cm and the minimum size related to two papillary carcinoma samples with an average size of 2.45 cm (Table 2).

In relation to the grade of tumoral tissues, 6 samples (9.2%) were grade 1, 32 (49.2%) grade 2, and 27 (41.5%) grade 3.

On the relationship between the final diagnosis of tumoral tissue and grade, in 8 samples with a diagnosis of DCIS, 5 samples (62.5%) had a grade 2, and 3 samples (37.5%) grade 3. In 50 samples with a diagnosis of IDC 6 samples (12%) were grade 1, 20 samples (40%) were in grade 2, and 24 samples (48%) were in grade 3. In 5 samples with ILC diagnosis and 2 samples with the diagnosis of papillary carcinoma, all samples were in grade 2. There was not any statistically significant relationship between final diagnosis of tumoral tissue and their stages (Table 2).

In the case of metastasis of sent lymph nodes in patients with breast cancer, 36 samples (55.4%) were along with lymph node metastasis with malignant cells and 29 samples (44.6%) without lymph node metastasis.

In the case of vascular or perineural invasion, it was reported in 25 cases (38.5%) and in about 40 samples (61.5%), the invasion was not reported.

On the relationship between final diagnosis and lymph nodes involvement by tumor tissue, 2 lymph node metastases were reported out of 8 DCIS. Among 50 IDC, in 32 samples (64%) involvement of lymph nodes was reported. Among 5 ILC, 2 samples (40%) had lymph node involvement, and both papillary carcinomas lacked lymph node involvement. In general, from 65 samples of breast cancer tissue, 36 cases (55.4) had lymph node metastasis and 29 cases (44.6%) without lymph node metastasis. No significant relationship was found between final diagnosis of tumor and lymph node metastasis (Table 2).

On the relationship between vascular or perineural invasion and final diagnosis, from 8 DCIS cases, only 2 cases of vascular or perineural invasion have been reported. Among 50 ILC in 23 samples (46%) perineural or vascular invasion was reported. From 5 samples with ILC diagnosis, none had vascular or perineural invasion, and both either papillary carcinoma lacked vascular or perineural invasion. Finally, among 65 malignant samples, 25 samples (38.5%) had vascular or perineural invasion and 40 samples (61.5%) lacked it. No significant relationship was found between final diagnosis of tumor and vascular or perineural invasion (Table 2).

About the relationship between the lesion site and the lymph nodes involvement by tumoral tissue, 14 out of 29 samples (48.3%) from the left breast had lymph node metastasis and 22 out of 36 samples (61.1%) sent from the right breast, had lymph node metastasis. This difference was not statistically significant in the samples (Table 3) (P value Fisher's Exact test = 0.327).

About the relationship between lesion site and the vascular or perineural invasion, 11 out of 29 samples (37.9%) from the left breast had vascular or perineural invasion and 14 out of 36 samples (38.9%) sent from the right breast had such a situation. This difference was not statistically significant in the samples (Table 3) (P value Fisher's exact test = 1.000).

On the relationship between tumor grade and lymph node metastasis, 5 out of 6 samples (83.3%) with grade 1 had lymph node metastasis and 1 was reported without involvement. Among 32 grade 2 samples, 13 samples (40.6%) were reported with lymph node involvement and 19 samples (59.4%) lacked that. Among 27 samples with grade 3 diagnosis, 18 samples (66.7%) were reported with lymph node involvement and 9 samples (33.3%) lacked that. The relationship between tumor grade and lymph node metastasis was statistically significant (P = 0.047).

On the relationship between tumor grade and vascular or perineural invasion, 3 out of 6 samples with grade 1 were involved and 3 were reported without involvement. Among 32 grade 2 samples, 8 samples (25%) were reported with vascular or perineural involvement and 24 samples (75%) lacked that. Among 27 samples with grade 3 diagnosis, 14 samples (51.9%) were reported with vascular or perineural involvement and 13 samples (48.1%) lacked that. There was not any statistically significant relationship between tumor grade and vascular or perineural invasion (Table 3).

On the relationship between patient age and lymph node metastasis, the average age of patients with lymph node metastasis was 48 with a standard deviation of 12 and the average age of the patients without lymph node metastasis was 55 with standard deviation of 13 that the results were not statistically significant (Table 3) (P = 0.058).

On the relationship between patients' age and vascular and perineural invasion, mean age of patients with invasion was 50 with a standard deviation of 13 and mean age of patients with no invasion was 52 with standard deviation 13 that was not statistically significant.

Table 1. Clinicopathologic features of breast lesions

Variables	Non-S	Fad	Gyn	FCC	IDC	ILC	DCIS	PC	Total	P-value
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	
Frequency										
Patient	44 (23.4)	21 (11.2)	17 (9)	43 (22.9)	49 (26.1)	5 (2.7)	7 (3.7)	2 (1.1)	188 (100)	
Sample	55 (23.9)	22 (9.6)	26 (11.3)	62 (27)	50 (21.7)	5 (2.2)	8 (3.2	2 (0.9)	230 (100)	
Location										
R	26 (47.3)	11 (50)	13 (50)	32 (51.6)	27 (54)	2 (40)	6 (75)	1 (50)	118 (51.3)	0.920
L	29 (52.7)	11 (50)	13 (50)	30 (48.4)	23 (46)	3 (60)	2 (25)	1 (50)	112 (48.7)	
Sex										
F	47 (85.5)	22 (100)	0 (0)	62 (100)	49 (98)	5 (100)	8 (100)	2 (100)	195 (84.8)	< 0.001
M	8 (14.5)	0 (0)	26 (100)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	35 (15.2)	
Age group										
< 50	37 (67.3)	21 (95.5)	24 (92.3)	48 (77.4)	25 (50)	3 (60)	3 (37.5)	1 (50)	162 (70.4)	< 0.001
> 50	18 (32.7)	1 (4.5)	2 (7.7)	14 (22.6)	25 (50)	2 (40)	5 (62.5)	1 (50)	68 (29.6)	
Size										
Mean ± SD	12.30 ± 9.34	3.07 ± 1.81	6.73 ± 3.19	13.66 ± 8.94	14.51 ± 8.30	10.80 ± 5.97	17.75 ± 7.55	15.5 ± 2.12	11.82 ± 8.64	
Age										
Mean ± SD	43 ± 12	30 ± 22	28 ± 13	42 ± 11	50 ± 12	54 ± 19	55 ± 14	59 ± 28	42 ± 14	

Non-S: Non-specific tissues; IDC: Invasive ductal carcinoma; Gyn: Gynecomastia; Fad: Fibroadenomas; DCIS: Ductal carcinoma *in situ*; ILC: Invasive lobular carcinoma; SD: Standard deviation

Table 2. Clinicopathologic features of malignant samples

Variables	IDC	ILC	DCIS	PC	Total	P-value
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	
Grade						0.122
1	6 (12)	0 (0)	0 (0)	0 (0)	6 (9.2)	
2	2 (40)	5 (100)	5 (62.5)	2 (100)	32 (49.2)	
3	24 (48)	0 (0)	3 (37.5)	0 (0)	27 (41.5)	
Lymph node involvement						
+	32 (64)	2 (40)	2 (25)	0 (0)	36 (55.4)	0.059
-	18 (36)	3 (60)	6 (75)	2 (100)	29 (44.6)	
Vascular or perineural invasion						
+	23 (46)	0 (0)	2 (25)	0 (0)	25 (38.5)	0.103
-	27 (54)	2 (100)	6 (75)	2 (100)	40 (61.5)	
Mass size						
Mean ± SD	14.51 ± 8.30	10.80 ± 5.97	17.75 ± 7.55	15.5 ± 2.12	11.82 ± 8.64	
Tumor size						
Mean ± SD	3.176 ± 2.970	3.80 ± 3.17	4.00 ± 3.61	2.45 ± 2.89	3.30 ± 3.01	
Age						
Mean ± SD	50 ± 12	54 ± 19	55 ± 14	59 ± 28	51 ± 13	

IDC: Invasive ductal carcinoma; DCIS: Ductal carcinoma *in situ*; ILC: Invasive lobular carcinoma; SD: Standard deviation

Table 3. Relationship between invasion of tumor and tumor grade, lesion site and age

Variables	Lymph node involvement			Vascular or perineural invasion		
	+	-	P-value	+	-	P-value
	Frequency (%)	Frequency (%)		Frequency (%)	Frequency (%)	
Grade						0.086
1	5 (83.3)	1 (16.7)	0.047	3 (50)	3 (50)	
2	13 (40.6)	19 (59.4)		8 (25)	24 (75)	
3	18 (66.7)	9 (33.3)		14 (51.9)	13 (48.1)	
Total	36 (55.4)	29 (44.6)		25 (38.5)	40 (61.5)	
Location						
Right	22 (61.1)	14 (38.9)	0.327	14 (38.9)	22 (61.6)	1.000
Left	14 (48.3)	15 (51.7)		11 (37.9)	18 (62.1)	
Total	36 (55.4)	29 (44.6)		25 (38.5)	40 (61.5)	
Age						
Mean ± SD	48 ± 12	55 ± 13	0.058	50 ± 13	52 ± 13	0.618
Age group						
< 50	21 (65.6)	11 (34.4)	0.136	12 (37.5)	20 (62.5)	1.000
> 50	15 (45.5)	18 (54.5)		13 (39.4)	20 (60.6)	

SD: Standard deviation

After dividing patients into two age groups above 50 and younger than 50 years old and examining its relationship with the lymph node invasion and vascular or perineural invasion, following results were obtained: 21 samples (65.6%) out of patients under the age 50 years had lymph node metastasis and 11 samples (34.4%) without lymph node metastasis. Among patients older than 50 years, 15 samples (45.5%) had lymph node metastasis and 18 (54.5%) without lymph node metastasis. The results from this study were not statistically significant (P = 0.136). 12 out of 32 patients (37.5%) younger than 50 years had invasion and 20 (62.5%) without it. Among patients older than 50 years, 13 cases (39.4%) had invasion and 20 (60.6%) had no invasion. The results of this survey were not statistically significant (Table 3) (P = 1.000).

About the Nottingham score in the samples, 1 sample (1.5%) obtained score 3, 5 samples (7.7%) score 5, 24 (36.9%) score 6, 8 samples (12.3%) score 7, 21 samples (32.3%) score 8, and 6 samples (9.2%) score 9. About tubular formation, 1 sample (1.5%) obtained score 1, 31 samples (47.7%) score 2 and 33 sample (50.8%) score 3. About mitotic rate in malignant tissues 11 samples (16.9%) had score 1, 38 samples (58.5%) had score 2 and 16 samples (24.6%) had score 3. About nuclear grade in malignant tissues, 2 samples (3.1%) obtained score 1, 39 samples (60%) score 2 and 24 samples (36.9%) had score 3 (Tables 4 and 5). As shown in table 5, the samples with scores 3 to 5 in Nottingham Score have a grade 1, score 6 and 7 grade 2 and scores 8 and 9 grade 3 that are fully consistent with the Nottingham grading system or the Elston-Ellis modification of the Scarff-Bloom Richardson grading system.

Discussion

Complete and accurate pathology report has an important role in the treatment and determining the prognosis of patients with various breast lesions (10). Importance of factors such as tumor size, cell differentiation grade, lymph node metastasis, vascular or perineural invasion in the prognosis and life expectancy, and survival of patients with breast cancer is well understood (16). In several studies conducted in different countries, addressing these factors was different and most studies in this field through reviewing pathological reports were like the present study (17). This study is conducted aiming to examine the breast pathology reports and determine the frequency of various breast diseases and its relationship with some clinicopathologic parameters in Imam Reza Hospital of army of the Islamic Republic of Iran in a period of 4 years. The problem with this study is the small sample size with DCIS and ILC diagnosis and given that this study was conducted on samples collected over 4 years, this is partly justified.

The mean age of patients was 42 ± 14, which was consistent with the studies conducted in Iran and other studies (18).

Table 4. Nottingham scores in malignant samples

Variables	1	2	3	Total
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
Tubular formation	1 (1.5)	31 (47.7)	33 (50.8)	65 (100)
Mitotic rate	11 (16.9)	38 (58.5)	16 (24.6)	65 (100)
Nuclear grade	2 (3.1)	39 (60)	24 (36.9)	65 (100)

Table 5. Relation between Nottingham score and tumor grade

Score	Frequency (%)	Grade	Frequency (%)
3	1 (1.5)	1	6 (9.2)
4	0 (0)		
5	5 (7.7)		
6	24 (36.9)	2	32 (49.2)
7	8 (12.3)		
8	21 (32.3)	3	27 (41.5)
9	6 (9.2)		

After dividing patients into two age groups below and above 50, it was observed that the frequency of non-specific tissue, fibroadenoma, fibrocystic, and gynecomastia changes was significantly more common in age group under 50. This was consistent with similar studies in this field (11,12). The mean age of patients with breast cancer was 51 which are higher compared to a mean age of patients with benign lesions that are 38 years old.

As you can see in table 1, the gender of patients with gynecomastia is male and in other cases, the number of female patients is significantly greater than the results are consistent with studies by Swerdloff and Makki in this field (19,20).

Only two papillary carcinomas existed from all tumoral tissues that it was expected due to the spread of the tumor among the types of breast cancer (20).

There was no relationship between the breast tumor site and final diagnosis, lymph node metastasis, vascular or perineural invasion that it was consistent with previous similar studies (21).

There was no relationship in tumoral tissue between the final diagnosis and tumor grade, lymph node metastasis, vascular perineural invasion that this case was in previous studies (22).

A significant correlation existed between tumor grade and lymph node metastasis so that tumors with higher grades were more involved in lymph nodes. This was consistent with previous similar studies, but there was no significant relationship between higher tumor grade and vascular or perineural invasion. This was not consistent with previous studies in this area (23-27).

Checking the histological differentiation of malignant samples showed that about 90% of the samples had grades 2 and 3 and given the direct impact of the tissue differentiation grade on patient survival and prognosis of the disease, if we can diagnose the disease at earlier stages by developing the necessary training in relation to breast cancer screening and self-examination, the burden of disease and adverse effects of breast cancer in society can be dramatically reduced, and the survival of patients can be increased.

In this study, a statistically significant relationship exists between the patient sex and final diagnosis, patient age group and final diagnosis, and cell differentiation grade and lymph node metastasis along with samples. In the pathology reports in the center, cell differentiation grade of tumor was completely matched with Nottingham Grading System. Since only 9.2% of samples were diagnosed in grade 1, it is hoped to focus more on breast cancer screening methods and breast cancer self-examination and help to a large extent to the early detection of the disease in earlier stages. It is hoped to look at this study as a prospective study with a larger sample size and more variables of clinicopathologic parameters, so to better know the preventive factors and factors affecting the prognosis of the types of breast diseases with the help of data from these studies.

Conflict of Interests

Authors have no conflict of interests.

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