Evaluation of the Relation between Lymph Node Status and Estrogen and Progesterone Receptors Status in Breast Cancer Patients in Ahvaz Hospitals

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ABSTRACT

Breast cancer is one of the most common cancers in Iranian women. Estrogen and progesterone receptors have been described as a prognostic factor in breast cancer. Axillary lymph node status is also one of the most powerful prognostic factors for patients with breast cancer. The relationship between Estrogen receptor (ER) and progesterone receptor (PR), and axillary lymph node is still controversial. This study aims to investigate the relationship of ER and PR with axillary lymph node among women with breast cancer. Estrogen and progesterone receptors were evaluated by immunohistochemistry assessments in 200 breast cancer patients. Statistical comparison was performed between ER and PR and nodal status. Of the 200 carcinoma tissue samples (mean age. 51.34 years), 133 cases (66.5%) were positive for estrogen receptor, of them 94 cases (70.7%) were positive for axillary nodal involvement. Sixty seven cases (33.5%) were negative for ER, of them 41 cases (61.2%) were positive for axillary nodal involvement. One hundred-eighteen cases (59%) were positive for progesterone receptor, of them 82 cases (69.5%) were positive for axillary nodal involvement. Eighty two cases (41%) were negative for PR, of them 53 cases (64.6%) were positive for axillary nodal involvement. There is no significant relationship between ER and axillary nodal involvement (P=0.397). In addition, there is no significant relationship between PR and axillary lymph node involvement (P: 0.825). There is no relationship between ER and PR status and axillary nodal involvement.

Key words: Estrogen receptor, Progesterone receptor, Breast cancer, Axillary lymph node.

INTRODUCTION

Breast cancer is the most common site specific cancer among women and the leading cause of death in women of 20-59 years old. It comprises 26% of all women's cancer and is responsible for 15% of cancer deaths in women. Increased incidence of cancer happens in women aged 55 years or more in parallel to increase in the percentage of mammograms in women. In these women, the incidence of regional metastasis has declined mortality due to breast cancer has reduced.

The women living in the less industrialized societies have lower risk of breast cancer than those in industrialized countries (1).

It is also the most common cancer among Iranian women. During the years 1968 to 1998 the proportion of breast cancer among common cancers among women has increased from 12.6% to 25.3%.

Despite of the development of new predicting techniques for early diagnosis of breast cancer (1), late diagnosis of breast cancer is a

major health problem in Iran. Seventy percent of patients are patients referring with high levels due to the delay in the diagnosis (3).

Age is probably the most important risk factor for breast cancer. Other risk factors include obesity, first childbirth at old age, increased exposure to estrogen, early menarche, late menopause and Knoll's Party (4,2).

Many patients are identified in the later stages of the disease: 18% in stage I, 75% in stage II and 25% in stage III (2). Sixty three percent of patients have lymph node involvement at the time of diagnosis. The most important factor associated with disease-free survival and overall survival of patients is lymph nodes situation. The recurrence rate in patients without lymph nodes involvement is 30% and with lymph nodes involved is 75% (2).

The results of several studies on patients with primary breast cancer who underwent ALND and investigated the relationship between hormone receptors and axillary lymph nodes involvement status showed a significant correlation between the negative status of hormone receptor and underarm lymph node involvement (5,6,7,8,9). The results of several other studies did not show significant relation in the relationship between hormone receptor status and axillary lymph nodes involvement (10,11,12).

However, one very important factor that plays an important role in the prognosis of breast cancer is the status of estrogen and progesterone receptors whose negativity is associated with poor cancer prognosis. On the other hand, involvement of lymph node and the status of estrogen and progesterone receptors can influence the selection of therapeutic modalities in breast cancer. Determining the relationship between lymph nodes

and estrogen and progesterone receptors status is important as proving this relationship would alert the physician in choosing the therapeutic modalities and accurate prognosis of the patient. Due to the lack of conclusive proof of this relevance, this study will be an effective help in this regard.

MATERIALS AND METHODS

This study is a retrospective study conducted on 200 patients with breast cancer referred to health centers in Ahvaz during 2010 to 2011.

Patients studied had undergone surgery with axillary lymph nodes dissection. Samples sent to a pathology laboratory and the involvement of lymph nodes had been checked. For each patient, at least 10 lymph nodes had been examined. In cases where one or more lymph nodes were involved, it was considered as positive. The samples were checked by IHC staining for positive ER and PR.

After data collection, a checklist was designed and completed based on variables of interest and then analyzed using SPSS17 software.

At first, using descriptive statistical techniques such as frequency tables and diagrams, the variables were described and then by using the chi-square test, mean comparison test (T-test) the relationship between the variables was compared (for all statistical analyses $P < 0.05$ was considered as statistically significant).

RESULTS

In this study, 200 women with breast cancer, with an average age of 51.34 years participated.

Table 1: Distribution of age in patients

	Abundance	Percent
Less than 40 years	46	23%
years 40-60	115	57.5%
Over 60 years	39	19.5%
Total	200	100%

Table 2: Distribution of ER in patients

Positive		Negative		
Frequency	Percent	Frequency	Percent	ER
133	66.5	67	33.5	

In this study, patients were divided into 3 age groups: under 40 years, 40-60 years, and over 60 years (Table 1).

Three hundred thirteen patients (66.5%) were positive for estrogen receptor and 67 patients (33.5%) were negative for estrogen receptor (Table 2).

In addition, 118 patients (59%) had positive progesterone receptor and 82 patients (41%) had negative PR (Table 3).

In this study, 135 patient (67.5%) had pathological axillary lymph node involvement, and 65 (32.5%) did not have axillary lymph node involvement (Table 4).

Pathology of 152 patients (76%) was invasive ductal carcinoma, 28 patients (14%) infiltrative carcinoma, 11 patients (5.5%) invasive lobular carcinoma and 9 patients (5.4%) had medullary carcinoma (Table 5).

In this study, of 133 patients who were ER positive, 94 patients (70.7%) had pathological axillary lymph node involvement and 39 patients (29.3%) did not have pathological axillary lymph node involvement.

Moreover, out of 67 patients who were negative ER. 41 patients (61.2%) had pathological axillary lymph node involvement and 26 patients (38.8%) did not have axillary lymph node involvement (Table 6).

Table 3: Distribution of PR in patients

Positive		Negative		
Frequency	Percent	Frequency	Percent	PR
118	59	82	41	

Table 4: The frequency of pathological axillary lymph node involvement in patients

Positive		Negative		
Frequency	Percent	Frequency	Percent	Pathological involvement
135	67.5	65	32.5	of axillary lymph nodes

Table 5: Distribution of pathology in patients

Frequency	Percent	Frequency Pathology
152	76	Invasive ductal carcinoma
28	14	Infiltrative carcinomas
11	5.5	Invasive lobular carcinoma
9	4.5	Medullary carcinoma

According to this study, no association was found between estrogen receptor status and axillary lymph node involvement (P:0.397).

In our study out of 118 patients who had positive PR, 82 patients (69.5%) had axillary pathologic lymph node involvement and 36 (30.5%) did not have pathological axillary lymph node involvement. Moreover, out of 82 patients who had

Table 6: Axillary lymph node frequency separately for positivity of ER in patients

	Pathological involvement of axillary lymph nodes		Lack of involvement of axillary lymph nodes	
	Frequency	Percent	Frequency	Percent
Positive ER	94	70.7	39	29.3
Negative ER	41	61.2	26	38.8
total	135	67.5	65	5.32

negative PR, 53 (64.6%) had axillary lymph node involvement and 29 patients (35.5%) did not have axillary lymph node involvement (Table 7).

Statistical analysis performed by Chi-square test does not show a significant relationship between axillary lymph node involvement and progesterone receptor (P=0.825).

In this study, of 135 patients who had axillary lymph node involvement, 36 (26.7%) were less than 40 years of age.

Seventy four (54.8%) were between 40-60 years of age and 25 (18.5%) were over 60 years, and out of 65 patients without lymph node involvement 10 patients (15.4%) were under 40

years of age, 41 patients (63 %) were 40-60 and 14 (21.6%) patients were above 60 years of age (Table 8).

Statistical analysis performed by Chi-square test did not show a significant relationship between age and lymph node involvement (P:0.207).

In this study, out of 133 patients positive for ER, 109 patients (82%) had invasive ductal carcinoma, 14 patients (10.5%) had infiltrative carcinoma, 9 patients (6.8%) had invasive lobular carcinoma, and 1 patient (0.7%) had medullary carcinoma. Of 67 patients with ER negative, 43 patients (64.2%) had invasive ductal carcinoma, 14 patients (20.8%) had infiltrative carcinoma, 2

Table 7: Axillary lymph node involvement distribution separately for the positive PR in patients

| | Pathological involvement of axillary lymph nodes | | Lack of involvement of axillary lymph nodes | |
	Frequency	Percent	Frequency	Percent
Positive PR	82	69.5	36	30.5
Negative PR	53	64.6	29	35.4
Total	135	67.5	65	32.5

Table 8: The age distribution of patients separately for axillary lymph node involvement

| | Younger than 40 years | | 40-60 years | | Age over 60 years | |
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Involvement of axillary lymph nodes	36	26.7	74	54.8	25	18.5
Lack of involvement of axillary lymph nodes	10	15.4	41	63	14	21.6
Total	46	23	115	57	39	19.5

Table 9: Distribution of frequency of pathologic findings in patients with ER positive

| | Invasive ductal carcinoma | | Infiltrative carcinomas | | Lobular carcinoma | | Medullary carcinoma | |
	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
Positive ER	109	82	14	10.5	9	8.6	1	0.7
Negative ER	43	64.2	14	20.8	2	3	8	12
Total	152	76	28	14	11	5.5	9	4.5

patients (3%) had invasive lobular carcinoma, and 89 patients (12%) had medullary carcinoma (Table 9).

There was a significant relationship with regard to the pathology results of the distribution of invasive ductal carcinoma and positive ER (P = 0). Because of low frequency of other types of pathology investigating their relationship with estrogen receptor status was not possible.

In this study, out of 118 patients with positive PR, 96 patients (81.4%) had invasive ductal carcinoma, 13 (11%) had infiltrative carcinoma, 8 (6.8%) had invasive lobular carcinoma, and 1 (0.8%) had medullary carcinoma.

Out of 82 patients who were PR negative, 56 (68.3%) had invasive ductal carcinoma, 15 (18.3%) had infiltrative carcinoma, 3 (3.65%) lobular carcinoma, and 8 (9.75%) had medullary carcinoma (Table 10).

There was a statistically significant relationship between pathology results of the distribution of results of invasive ductal carcinoma and PR positive (P=0.006). Because of low frequency of other types of pathology, their investigation to determine their relationship with estrogen receptor status was not possible.

In Pishrou's study, of 135 patients who had axillary lymph nodes involvement, 108 patients (80%) had invasive ductal carcinoma pathology, 15 patients (11.1%) had infiltrative carcinoma, 10 patients (7.4%) lobular carcinoma, and 2 patients (1.5%) had medullary carcinoma. Out of 65 patients without lymph node involvement, 44 patients (67.7%) had invasive ductal carcinoma, 13 patients (20%) infiltrative carcinoma, 1 patient (1.5%) lobular carcinoma, and 7 patients (10.8%) had medullary carcinoma (Table 11) .

A statistically significant relationship is seen between invasive ductal carcinoma and axillary lymph node involvement (P=0.002). Due to

Table 10: The frequency of the distribution of pathologic findings separately for patients with positive PR

	Invasive ductal carcinoma		Infiltrative carcinomas		Lobular carcinoma		Medullary carcinoma	
	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
Positive PR	96	81.4	13	11	8	6.8	1	0.8
Negative PR	56	68.3	15	18.3	3	3.65	8	9.75
Total	152	76	28	14	11	5.5	9	4.5

Table 11: Distribution of pathologic findings separately for patients with lymph node involvement

	Invasive ductal carcinoma		Infiltrative carcinomas		Lobular carcinoma		Medullary carcinoma	
	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent
Involvement of axillary lymph nodes	108	80	15	1.11	10	4.7	2	5.1
Lack of involvement of axillary lymph nodes	44	7.67	13	20	1	5.1	7	8.1
Total	152	76	28	14	11	5.5	9	5.4

low rates of other types of pathology, determining their correlation with axillary lymph node involvement was not possible.

In this study, mean age of patients with ER-positive and ER-negative was compared and the average age of patients with ER positive was 2.5 years higher (Table 12), but there was no statistically significant relationship (P=0.5).

Moreover, mean age of patients with negative PR is 1.7 years more than PR positive patients, but no statistically significant relationship was observed (P=0.397) (Table 13).

The average age of the patients, separately for lymph node involvement and no lymph node involvement, was compared with the mean age of patients with lymph node involvement being 3.17 years higher and there was no significant correlation (P=0.6) (table 14).

In this study, out of 133 patients with ER positive, 29 (21.8%) were under 40 years, 74 patients (55.6%) between 40 and 60 years and 30 patients (22.6%) were over 60 years old. Of 67 patients with negative ER 17 (25.4%) were younger than 40 years and 41 (61.2%) between 40 and 60 years and 9 (13.4%) were over 60 years old. Statistical analysis showed no significant relation between age and estrogen receptor status (P=0.303) (Table 15).

Table 12: Comparing the average age of ER positive and ER negative patients separately

Frequency	Average age (years)	
133	ER positive	52.18
67	ER negative	49.67

Table 13: Comparing the average age of patients with PR positive and PR negative separately

Frequency	Average age (years)	
118	50.64	PR positive
82	52.35	PR negative

Table 14: Comparing the average age of the patients studied separately for lymph node involvement and lack of lymph node involvement

Frequency	Average age (years)	
135	50.31	Positive ALND
65	53.47	Negative ALND

Table 15: The age distribution of patients separately for ER positive

	Age under 40		40-60 years of age		Age over 60	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
ER positive	29	8.21	74	6.55	30	6.22
ER negative	17	4.25	41	2.61	9	4.13
Total	46	23	115	5.57	39	5.19

Table 16: The age distribution of patients in separation for positive PR

	Age under 40		40-60 years of age		Age over 60	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
PR positive	29	6.24	67	8.56	22	6.18
PR negative	17	20.7	48	6.58	17	7.20
Total	46	23	115	5.57	39	5.19

Of 118 PR positive patients, 29 (24.6%) were younger than 40 years, 67 (56.8%) between 40 and 60 years and 22 patients (18.6%) were over 60 years old. Out of 82 PR negative patients, 17 patients (20.7%) were younger than 40 years, 48 patients (58.6%) were between 40 and 60 years and 17 (20.7%) were over 60 years of age. Statistical analysis was performed by Chi-square test showed no significant correlation between age and progesterone receptor status (P=0.801) (Table 16).

DISCUSSION AND CONCLUSIONS

In this study, 200 women with breast cancer were studied regarding axillary lymph node involvement and estrogen and progesterone receptor status and the relationship between the two was investigated.

In this study, 133 patients (65%) regarding the estrogen receptor and 118 patients (59%) regarding progesterone receptor were positive. In the reference book *Diseases of the Breast* published in 2010, it is stated that in breast cancer patients, 75% have positive estrogen receptors and 55 percent are positive regarding progesterone receptor (13). Sixty percent of breast cancer patients are positive for ER or PR or both (4).

Comparing these statistics with findings of this study, we can conclude that the incidence of estrogen and progesterone receptors in our society is the similar to other studies (9,10).

In this study, of 200 patients, 135 (67.5%) had pathological axillary lymph node involvement. By comparing the present study and previous studies, it seems that pathological axillary lymph node involvement in breast cancer is slightly higher in our society (14,15,16, 17).

The average age of breast cancer patients in this study is 51.34 years. It seems that in our society, the average age of patients with breast cancer, according to studies conducted in other communities is 4-5 years lower (17,17).

The relationship between axillary lymph node involvement and estrogen receptor status was assessed using the chi-square test and was not significant (P=0.397). in addition, by using chi-square test axillary lymph nodes involvement with PR status was examined that was not significant (PR=0.825).

The relationship between involvement of axillary lymph nodes and hormone receptors in different studies is controversial.

The relationship between age and positivity of estrogen receptor was determined and there was no significant relationship (P=0.303). Moreover, there was no statistically significant relationship between age and progesterone receptor status (P=0.801). At the same time, there was no significant correlation between age and pathological lymph node involvement (P=0.207).

The relationship between pathology and axillary lymph node involvement was evaluated that was significant in invasive ductal carcinoma (P=0.002). The relationship between pathology and ER were evaluated that between invasive ductal carcinoma and ER positive status, there was a strong correlation (P=0.00). There was also a significant correlation between invasive ductal carcinoma and PR positive status (P=0.006).

According to the book Text Schwartz, the prevalence of invasive ductal and infiltrative carcinoma is 80%, medullary carcinoma is 4%, and lobular carcinoma is 10%, which is almost consistent with our community (1).

Finally, we suggest further studies with more patients and in subsequent studies, the relationship between estrogen and progesterone receptors involved with the number of lymph nodes be studied examined because prognosis of sickness is related to number of lymph nodes involved.

All breast cancer patients should be evaluated for estrogen and progesterone receptors, because determining the status of hormone receptors is effective in the treatment modality choice.

The average age of patients in our society is the lower, so screening of patients in lower ages is done by mammography. Other studies should also be conducted to study other tumor markers and pathological involvement of axillary lymph nodes.

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