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The correlation of estrogen and progesterone receptor expression with prognostic parameters in women with breast cancer

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Abstract

Introduction: Progesterone and estrogen receptor (PR and ER) expression are considered the oldest biomarkers. The presentation of these markers can guide the treatment in breast cancer patients because of their predictive value in hormonal therapy responsiveness and prognosis.
Objectives: This study investigated the correlation between estrogen and PR expression with prognostic parameters of breast cancer, including age, grading, staging, tumor size, and lymph node spread.
Patients and Methods: This cross-sectional study included 245 cases of breast tumors. Characteristics of patients, including age, the status of ER and PR biomarkers, tumor type, pathological features of cancer, and staging, were documented from case files. Accordingly, SPSS version 27 software was conducted for data analysis. The collected data were analyzed using the Spearman's correlation, Mann-Whitney U and chi-squared tests. A P value < 0.05 is considered statistically significant.
Results: High ER and PR expression (>50%) were found in 56.7% and 40.4% of cases, respectively. Most of the tumors in patients belonged to grade 2 (56.3%) and staging IIA, IIB, and IIIA. We found a significant correlation between ER expression, breast cancer grading, and patients' age. PR expression was significantly associated with breast cancer staging, grading, size, and lymph node spread.
Conclusion: These results highlight the value of ER and PR expression as they can determine the clinicopathological parameters of the tumor, which can be helpful for better-managing breast cancer.

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Introduction

Breast cancer is the most common type of cancer in women, and each year more than one million females are diagnosed with breast cancer, which compromises 16% of all female cancers (1-3). The prognosis of breast cancer depends on factors such as the tumor size, lymph node spread, staging, grading, and hormone receptor tumor markers. (4).

Progesterone receptor (PR) and estrogen receptor (ER) expressions are considered as the oldest biomarkers. A large number of tumors are estrogen receptor-positive (ER+) and progesterone receptor-positive (PR+), which most probably leads to the progression of breast cancer (1,5). A significant development in managing breast cancer is the expression of hormone receptors and the responsiveness to hormonal therapy (3). The presentation of ER and PR is of great importance as it can guide the treatment of patients because of their predictive value in hormonal therapy responsiveness and prognosis (5).

Key point

The expression of progesterone receptor (PR) and estrogen receptor (ER) as the oldest biomarkers in breast cancer can guide the treatment and prognosis of breast cancer patients. Therefore, this study was conducted on 245 breast cancer cases to correlate ER and PR expression with various prognostic features of breast cancer in Isfahan, Iran. Our study found high ER and PR expression in 56.7% and 40.4% of cases, respectively. Most of the tumors belonged to grade 2 (56.3%). A significant correlation between ER expression and the grade of the tumor and the age of the cancer patients was also found. PR expression was significantly associated with the grade, stage, tumor size, and number of involved lymph nodes.

Objectives

Given the importance of these two markers in breast cancer, understanding the correlation of these two markers with other prognostic parameters of breast cancer can help us better determine the prognosis and hormonal therapy in patients. This study was conducted to correlate ER, and PR expression

with various prognostic features of breast cancer, including age, grading, staging, tumor size, and lymph node spread in patients referred to Al-Zahra hospital, Isfahan, Iran.

Patients and Methods

Study design

This cross-sectional study included 245 cases with breast tumors referred to Al-Zahra hospital, Isfahan, Iran, over five years (2013-2018). These patients underwent surgery, and the specimens were examined in the pathology department of the hospital. Patients' characteristics, including age, ER and PR biomarkers status in immunohistochemistry (IHC) staining, tumor type, pathological features of the tumor size, lymph node spread, histopathological grading, and staging, were documented from case files.

Statistical analysis

SPSS version 27 software was used for data analysis. The collected data were analyzed using the Spearman's correlation, Mann-Whitney U and chi-squared tests. A P value < 0.05 is considered statistically significant.

Results

Our study cohort comprised 245 breast cancer patients aged 26-88 (mean = 51.7 and standard deviation =12.1). The ER and PR were expressed in more than 50% of the tumor tissue in 56.7% and 40.4% of the patients, respectively (Table 1). Most of the tumors in patients belonged to grade 2 (56.3%) and staging IIA, IIB, and IIIA (Table 2). Table 3 shows the frequency of histopathological types of breast cancer in our patient cohort, where invasive ductal carcinoma is our cohort's most common breast cancer (87.8%). In addition, a tumor size of 1-5 cm was the most frequent size (76.7%) observed in our patient cohort (Table 4).

Spearman's correlation coefficient showed a reverse correlation between breast cancer grading and ER expression ($P=0.002$) and PR ($P=0.01$). While the staging of breast cancer showed a reverse correlation with the presentation of PRs ($P=0.03$), it did not show any correlation with the expression of ERs ($P=0.16$). Moreover, in our patient cohort, the tumor size was between 1-17 cm. The tumor size had a significant reverse correlation with the expression of PRs ($P=0.04$). There is no significant relationship with the ER ($P=0.26$). Our study showed a direct correlation between age and the presentation of the ER ($P=0.037$). However, there is no significant relationship with the PR ($P=0.50$, Table 5). The average lymph node spread was 3.1, with a standard deviation of 0.3. The lymph node spread had a reverse correlation with the expression of PRs ($P=0.042$). Still, it did not significantly correlate with the presentation of ERs ($P=0.4$, Table 5).

Table 1. Frequency of estrogen receptor and progesterone receptor expression of breast cancer

Variant	Status	Number	Percent
Estrogen receptor	Negative	61	24.9
	Positive in <50%	45	18.4
	Positive in >50%	139	56.7
Progesterone receptor	Negative	82	33.5
	Positive in <50%	64	26.1
	Positive in >50%	99	40.4

Table 2. Frequency of grading and staging of breast cancer

Variant		Number	Percent
Grading of tumor	1	45	18.4
	2	138	56.3
	3	41	16.7
	4	1	0.4
	Unknown	20	8.2
Staging of tumor	IA	31	12.7
	IIA	68	27.8
	IIB	57	23.3
	IIIA	63	25.7
	IIIB	4	1.6
	IIIC	22	9

Discussion

Estrogen and progesterone receptors are potent predictors of breast cancer. Since the outcome of hormonal therapy depends on these receptors' expression, assessing these two receptors' expressions will allow us to determine the response to hormone therapy in patients. We aim to resolve if the expression of progesterone and ERs correlates with the staging, grading, tumor size, lymph nodes involved, and age in 245 patients who were referred to Al-Zahra hospital, Isfahan, Iran.

Our study showed a high ER and PR expression in

Table 3. Frequency of histopathological types of breast cancer

Histopathological type	Number	Percent
Invasive ductal carcinoma	215	87.8
Invasive lobular carcinoma	18	7.3
Invasive tubular carcinoma	2	0.8
Metaplastic breast carcinoma	1	0.4
Invasive papillary carcinoma	1	0.4
Invasive medullary carcinoma	1	0.4
Mixed invasive ductal and lobular carcinoma	4	1.6
Mucinous carcinoma	1	0.4
Comedocarcinoma	2	0.8

Table 4. Frequency of tumor size of breast cancer

Tumor size	Number	Percent
1-5 cm	188	76.7
6-10 cm	45	18.4
11-15 cm	8	3.3
16-20 cm	2	0.8
Unknown	2	0.8

Table 5. Correlation between the staging, grading, tumor size, age, and lymph nodes involved with the expression of estrogen and progesterone receptors

Variant	Estrogen receptor		Progesterone receptor	
	P	*r**	*P*	*r**
Grading of tumor	0.002	-0.209	0.01	-0.170
Staging of tumor	0.16	-0.090	0.03	-0.121
Tumor size	0.26	-0.072	0.04	-0.113
Age	0.037	0.133	0.50	0.043
Number of involved lymph nodes	0.40	-0.053	0.042	-0.111

the (>50%) in 56.7% and 40.4% of cases, respectively, which is similar to previous studies (6-8). Similar to a survey conducted by Bansal et al, most of our cases had a tumor size of 1-5 cm and belonged to grading II (2). In our study, the most common histologic type was invasive ductal carcinoma, as reported previously (2). Due to the low number of cases with different histologic types, it was impossible to study the correlation of PR and ER expression with the histopathological type. However, studies have already shown that ER and PR expression do not correlate with the histopathological types of breast tumors (2).

The results did not correlate the ER's expression with tumor size, staging, and lymph node spread. Other studies supported these findings but did not find a significant relation between ER expression and tumor size (7,9,10) and also lymph node status (8,11-13). However, a reverse and a direct correlation were observed between the expression of ERs with the grading and age of patients, respectively. In the study by Bansal et al, ER positivity significantly correlated with tumor grading (2). Previous studies show that in older women, the expression of ER is higher, and there is a significant correlation between age and the presentation of ER (2,3).

While the PR expression showed a significant reverse relationship with tumor size, lymph node spread, staging, and grading, it did not correlate with the patient's age. A previous study showed a significant correlation between PRs with tumor grading, but not with other parameters such as tumor size, age, and lymph node spread (2). However, other studies showed a correlation between PR expression and age, and the expression increased with age (3,14).

Conclusion

The study's results showed a significant relationship among ER expression, tumor grading, and patient age and a significant association between the expression of PR, the grading, staging, tumor size, and lymph node spread. These results further highlight the prognostic value of ER and PR expression as they can determine the clinicopathological parameters of the tumor, which can help manage breast cancer.

Limitations of the study

The limitation of the study was the documents and limited study population. We also suggest that more studies with extended follow-up periods should be performed.

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Authors' contribution

Conceptualization: SE, SG, AB.
Methodology: AB, SE, SG and PM.
Validation: AB, SE.
Formal ش‌nalysis: SG.
Investigation: AB, SE, SG and PM.
Resources: AB, SE, SG.
Data ژuration: AB, SE, SG.
Writing–original draft preparation: SG
Writing–review and editing: AB, SE
Visualization: AB, SE, SG.
Supervision: AB, SE.
Project ش‌dministration: SE, SG, AB.
Funding ش‌cquisition: AB, SE, SG.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan University of Medical Sciences approved this study (Ethical code#IR.MUI.MED.REC.1399.885). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from the M.D., thesis of Sarah Ghorbani (Thesis#399804) at this university. Ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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