



Comparison of Estrogen Receptor and Progesterone Receptor in Ductal Carcinoma and Lobular Carcinoma With Regard to Age Prevalence

Seyed Morteza Mousavi Naeini¹, Shaban Mehrvarz¹, Ali Mohammad Madahian¹, Shahram Manoochehy^{1*}, Hamid Reza Rasuli¹

¹Trauma Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

*Corresponding Author: Shahram Manoochehy, M.D., Assistant Professor, Trauma Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran. Tel/Fax: +98-2188053766, Email: shahram.manoochehy@yahoo.com

Received May 3, 2017; Accepted July 16, 2017; Online Published August 6, 2017

Abstract

Background: Breast cancer is one of the most common women's cancers, and the number of cases is increasing worldwide.

Objective: The current study compared invasive lobular carcinoma (ILC) and invasive ductal carcinoma with regard to the prevalence of estrogen receptor (ER), progesterone receptor (PR), and age prevalence.

Methods: This cross-sectional study recruited 225 women diagnosed with invasive ductal or lobular carcinoma who were admitted to the Department of Surgery of Baqiyatallah hospital between March 2014 and March 2015. The ER and PR levels reported were based on the pathologists' interpretation of assay results; both ER and PR were estimated to be positive when immunoperoxidase staining of the tumor cell nucleus was more than 10%.

Results: The most common malignancy was invasive ductal carcinoma found in 213 patients (94.7%) with a mean age of 49.30 ± 12.25 years (0.706). The most common subtype of invasive ductal carcinoma was NOS (82.6%); patients of this type had a mean age of 49.68 ± 12.27 years. Among patients with infiltrative ductal carcinoma (IDC), 129 (60.6%) of them were ER positive. In patients with ILC, 11 cases (91.7%) were ER positive ($P < 0.03$). Among the patients who had IDC, 107 (50.2%) of them were PR positive. Also, 6 patients who had ILC (50.0%) were ER positive ($P < 0.98$).

Conclusion: The results of this study indicate that the age prevalence of breast cancer in Iran is about 10 years sooner than the rest of the world. In addition, the prevalence rates of positive estrogen and progesterone receptors were lower in this study than in the majority of other studies, and these 2 features worsen the prognosis in the treatment of Iranian patients.

Keywords: Estrogen Receptor, Progesterone Receptor, Ductal Carcinoma, Lobular Carcinoma Cancer

1. Background

Breast cancer is a common disease among women, and its incidence is increasing worldwide. This disease still has complex and vaguely-understood aspects. Hormonal disorders are one of the strong factors in the development of this disease. Accordingly, many studies have investigated estrogen and progesterone receptors (PRs) on breast cancer cell tissues, and researchers have achieved good progress in the control and treatment of this disease. Adjunctive therapies that are effective on hormonal receptors such as tamoxifen can be used for a better prognosis of breast cancer if the breast cancer tissue tests positive for progesterone and estrogen. This drug can significantly reduce the recurrence of breast cancer; its preventive effects for breast cancer in high-risk groups have also been proven.^{1,2}

Based on histological origin, invasive breast cancers are classified into different types such as invasive lobular carcinoma (ILC). This type is the second most prevalent breast cancer and forms about 10% of breast cancers.

ILC metastasizes through the blood stream. The most common type of breast cancer is invasive, or infiltrative ductal carcinoma (IDC), and forms about 80% of all breast cancers. IDC usually metastasizes through the local lymph nodes (especially axillary nodes). Other types of intraluminal cancer that are less common are mucinous ductal carcinoma, medullary ductal carcinoma, papillary ductal carcinoma, and tubular ductal carcinoma.¹

Age is one of the most significant predisposing factors for malignancies such as breast cancer; moreover, age at diagnosis is a known prognostic factor of breast cancer.²

ER-positive/PR-negative breast cancers are most prevalent after age 40 in all groups of breast cancer patients.³ It has been shown that growth-factor-activated pathways downregulate PR expression, and this explains the ER-positive/PR-negative phenotype.⁴⁻⁶

In breast cancer studies, tumor markers are of notable importance because of their role in prognosis. The status of ER in invasive breast cancers is important, and its

determination is a common practice in the management and prognosis evaluation of the disease.⁷

The ER-positive and/or PR-positive breast cancer patients have a lower disease-related mortality rate in comparison with ER- and/or PR-negative patients. It has been proven that adjuvant chemotherapeutic and/or hormonal therapies improve survival in hormone receptor-positive cancers.⁸⁻¹¹

2. Objective

The current study compared ILC and invasive ductal carcinoma considering the prevalence of estrogen, PRs, and age prevalence.

3. Methods

In this cross-sectional study, 225 women with a diagnosis of ILC or invasive ductal carcinoma were included. All patients were admitted to the Department of Surgery of Baqiyatallah hospital between March 2014 and March 2015.

Non-probability convenience sampling was used to select the subjects.

The data collection tool was a self-made checklist. This standard checklist was confirmed by five experts in the field of study.

The enrollment of patients in the current study was approved by the ethics committee of Baqiyatallah University of Medical Sciences, and written informed consent was obtained from each patient. ER and PR levels from the pathologists' interpretation of the assay are reported. Both ER and PR were estimated to be positive when immunoperoxidase staining of the tumor cell nucleus was more than 10%.

Descriptive statistics were calculated for the data presented herein. Categorical data was compared with either chi-square or Fisher exact test depending on the sample size. The nonparametric Mann-Whitney test was used to compare the groups. The Kolmogorov-Smirnov test was used for normality of data. The data was analyzed by SPSS 20 software (SPSS Inc., Chicago, IL, USA). The significance level for all the tests was considered 0.05.

4. Results

Overall, 225 eligible patients were evaluated for study participation. The most common malignancy was invasive ductal carcinoma found in 213 (94.7%) participants who had a mean age of 49.30 ± 12.25 years. The minimum and maximum ages of patients were 24 and 86 years, respectively. There were no significant differences in the ages of patients with various types of tumors (0.706).

The most common subtype of invasive ductal carcinoma was NOS; patients of this type had a mean age of 49.68 ± 12.27 years (Table 1).

Figure 1 depicts the distribution of age levels of the study samples. The most frequent was 74 patients (32.9%) ranging in age from 40 to 49 (Table 1).

Table 2 depicts a cross table of the study samples regarding outcomes of ER and pathology tests. Among the IDC patients, 129 (60.6%) were ER-positive. In patients

with ILC, however, only 11 cases (91.7%) were ER positive. There was a significant relationship between the outcomes of ER and pathology ($P < 0.03$).

Table 2 depicts a cross table of the study samples regarding outcomes of PR and pathology. Among patients with IDC, 107 (50.2%) of them were PR-positive. In patients with ILC, 6 cases (50.0%) were ER positive. There was no significant relationship between the outcomes of PR and pathology ($P = 0.98$).

In total, 140 (62.2%) patients were ER-positive, and 112 (80.0%) of them were PR-positive. Moreover, in total, 85 (37.7%) patients were ER Negative and 84 (98.8%) of them were PR Negative.

The average age of ER-positive patients was higher than that of ER-negative patients ($P = 0.036$). Also, the mean age of patients who were PR positive was significantly higher than that of patients with negative PR ($P = 0.020$; Table 3).

5. Discussion

Estrogen and PR tests are performed on the resected breast cancer tissues by Immunohistochemical (IHC) assay. If both tests are positive for receptors, the patient may benefit from adjuvant hormonal therapy, which leads to a better prognosis and better treatment outcome.¹² Obviously, if one or both receptors are negative, the treatment strategy will change, and the prognosis and treatment outcome will be worse. In studies performed in Iran, the most common age at which women are diagnosed with breast cancer is between 30-40 years; that is a decade earlier than international statistics.¹³

The prevalence rates of different types of breast cancer in the current study are like those of other studies.¹⁴ The

Table 1. Distribution of Patients Regarding Types of Cancer

Pathology	Number	Percent
Invasive ductal carcinoma		
Invasive ductal (NOS)	186	82.6
Medullary carcinoma	12	5.3
Mucinous carcinoma	6	2.66
Papillary carcinoma	4	1.77
Tubular carcinoma	5	2.22
Invasive lobular carcinoma		
	12	5.3
Total	225	100

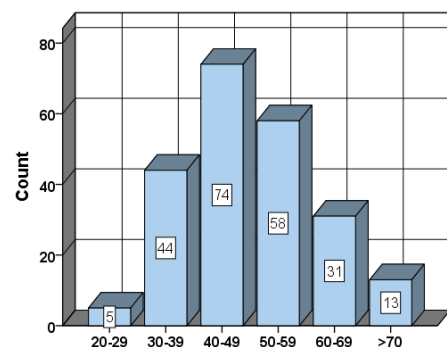


Figure 1. Distribution of Patients According to Age.

Table 2. Distribution of the Study Samples Regarding Outcomes of Estrogen Receptor, Progesterone Receptor, and Pathology Tests

Items		Pathology		Total, No. (%)	P Value
		Invasive Ductal Carcinoma (NOS)+etc, No. (%)	Invasive Lobular Carcinoma, No. (%)		
ER	Positive	129 (60.6)	11 (91.7)	140 (62.2)	0.03
	Negative	84 (39.4)	1 (8.3)	85 (37.8)	
PR	Positive	107 (50.2)	6 (50)	113 (50.2)	0.98
	Negative	106 (49.8)	6 (50)	112 (49.8)	

Abbreviations: ER, estrogen receptor, PR, progesterone receptor.

Table 3. Mean Ages of Patients Based on Estrogen Receptor and Progesterone Receptor Results

Items	Status	Number	Mean±SD	Min-Max	P Value
ER	Positive	140	50.43±11.82	26-85	0.036
	Negative	85	47.25±12.84	24-86	
PR	Positive	113	50.96±11.97	26-85	0.020
	Negative	112	47.49±12.41	24-86	
Total	225		49.23±12.29	24-86	

Abbreviations: ER, estrogen receptor, PR, progesterone receptor.

average age of ER-positive patients was higher than that of ER-negative patients.

This correlation was seen in both ductal and lobular carcinomas; it explains why aging breast cancer patients have a better response to hormonal therapy.

In the current study, only one patient had a positive PR, while her ER was negative. In almost all ER-negative patients, the PR was negative simultaneously. This particular topic was not found in any other studies, although in most studies the rate of (ER +, PR-) was low.¹⁵ It seems that the findings of the current study are unique, perhaps because of the ethnic characteristics of the Iranian population or an accidental finding. A systematic review of this issue in more studies is necessary.

6. Conclusion

Results of the current study indicate that the age prevalence of breast cancer in Iran is a decade earlier than the rest of the world. Moreover, the prevalence of positive estrogen and

PRs was lower in this study than in the majority of other studies, and these two features make a worse prognosis in the treatment of Iranian patients.

Authors' Contributions

Study concept and design: SMMN and SM; Acquisition of data: SMMN and AMM; Analysis and interpretation of data: SM, SM, and HRR; Drafting of the manuscript: SM, SM, and HRR; Critical revision of the manuscript for important intellectual content: SM, SM, and HRR; Statistical analysis: HRR; Administrative, technical, and material support: SMMN and AMM; Study supervision: SMMN.

Conflict of Interest Disclosures

The authors declare that there are no conflicts of interest in this study.

Ethical Approval

The protocol of this study was approved by the ethical committee of Baqiyatallah University of Medical Sciences.

Acknowledgments

The authors wish to thank Dr. Hasan Mohammad Hosseini Akbari and Dr. Seyed Mohammad Javad Pourkhayat for their kind cooperation in this study.

References

1. Pal SK, Lau SK, Kruper L, et al. Papillary carcinoma of the breast: an overview. *Breast Cancer Res Treat.* 2010;122(3):637-645. doi:10.1007/s10549-010-0961-5.
2. Yau C, Fedele V, Roydasgupta R, et al. Aging impacts transcriptomes but not genomes of hormone-dependent breast cancers. *Breast Cancer Res.* 2007;9(5):R59. doi:10.1186/bcr1765.
3. Arpino G, Weiss H, Lee AV, et al. Estrogen receptor-positive, progesterone receptor-negative breast cancer: association with growth factor receptor expression and tamoxifen resistance. *J Natl Cancer Inst.* 2005;97:1254-1261. doi:10.1093/jnci/dji249.

Research Highlights

What Is Already Known?

Patients with ER-positive and/or PR-positive tumors in breast cancer have lower risks of mortality after diagnosis compared to patients with ER- and/or PR-negative tumors. Age is one of the most significant risk factors for human malignancies, including breast cancer; moreover, age at diagnosis has been determined to be explanatory of breast cancer prognosis.

What This Study Adds?

Breast cancer in patients in Iran occurs a decade sooner than the international norm. Furthermore, the prevalence rates of positive estrogen and PRs, factors that worsen prognoses, were lower in this study than in the majority of other studies.

4. Cui X, Zhang P, Deng W, et al. Insulin-like growth factor-I inhibits progesterone receptor expression in breast cancer cells via the phosphatidylinositol 3-kinase/Akt/mammalian target of rapamycin pathway: progesterone receptor as a potential indicator of growth factor activity in breast cancer. *Mol Endocrinol*. 2003;17:575-588. doi:[10.1210/me.2002-0318](https://doi.org/10.1210/me.2002-0318).
5. Cui X, Schiff R, Arpino G, Osborne CK, Lee AV. Biology of progesterone receptor loss in breast cancer and its implications for endocrine therapy. *J Clin Oncol*. 2005;23:7721-7735. doi:[10.1200/JCO.2005.09.004](https://doi.org/10.1200/JCO.2005.09.004).
6. Kim H-J, Cui X, Hilsenbeck SG, Lee AV. Progesterone receptor loss correlates with human epidermal growth factor receptor 2 overexpression in estrogen receptor- positive breast cancer. *Clin Cancer Res*. 2006;12:1013s-1018s.
7. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)- negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California Cancer Registry. *Cancer*. 2007;109(9):1721-1728. doi:[10.1002/cncr.22618](https://doi.org/10.1002/cncr.22618).
8. Dunnwald LK, Rossing MA, Li CI. Hormone receptor status, tumor characteristics, and prognosis: a prospective cohort of breast cancer patients. *Breast Cancer Res*. 2007;9(1):R6. doi:[10.1186/bcr1639](https://doi.org/10.1186/bcr1639).
9. Fisher B, Redmond C, Fisher ER, Caplan R. Relative worth of estrogen or progesterone receptor and pathologic characteristics of differentiation as indicators of prognosis in node negative breast cancer patients: findings from National Surgical Adjuvant Breast and Bowel Project Protocol B-06. *J Clin Oncol*. 1988;6(7):1076-1087. doi:[10.1200/JCO.1988.6.7.1076](https://doi.org/10.1200/JCO.1988.6.7.1076).
10. Buzdar AU, Ibrahim NK, Francis D, et al. Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer. *J Clin Oncol*. 2005;23(16):3676-3685. doi:[10.1200/JCO.2005.07.032](https://doi.org/10.1200/JCO.2005.07.032).
11. Hugh J, Hanson J, Cheang MC, et al. Breast cancer subtypes and response to docetaxel in node-positive breast cancer: use of an immunohistochemical definition in the BCIRG 001 trial. *J Clin Oncol*. 2009;27(8):1168-1176. doi:[10.1200/JCO.2008.18.1024](https://doi.org/10.1200/JCO.2008.18.1024).
12. McPherson K, Steel C, Dixon JM. Breast cancer-epidemiology, risk factors, and genetics. *BMJ*. 2000;321(7261):624. doi:[10.1136/bmj.321.7261.624](https://doi.org/10.1136/bmj.321.7261.624).
13. Mousavi SM, Montazeri A, Mohagheghi MA, et al. Breast cancer in Iran: an epidemiological review. *Breast J*. 2007;13(4):383-391. doi:[10.1111/j.1524-4741.2007.00446.x](https://doi.org/10.1111/j.1524-4741.2007.00446.x).
14. Mousavi SM, Mofid B, Mohebi HA, et al. Comparison of local recurrence, metastasis and survival rate between the two surgical approaches in clinical stage I and II breast cancer. *Trauma Mon*. 2009;14(2):89-94.
15. Moghni M, Mokhtariyan K. Correlations of estrogen or progesterone receptors with grade of invasive ductal carcinomas of the breast in women referred to pathology center in Chaharmahal va Bakhtiari province Iran (Persian). *J Shahrekord Univ Med Sci*. 2009;11(3):40-45.