



# Breast Cancer Survival Rate in Mashhad, Iran: A 10- Year Population-based Study

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### ABSTRACT

**Introduction:** The breast cancer burden is still increasing, both in developing and developed countries. The present study was conducted to determine the survival rate of breast cancer based on tumor biological subtypes in patients referring to three referral oncology centers at Mashhad University of Medical Sciences, Mashhad, Iran.

**Methods:** The present population-based study was conducted at Imam Reza Hospital, Omid Hospital, and Reza Oncology Center, Mashhad University of Medical Sciences, Mashhad, Iran. Demographic information, the status of biomarkers in immune-histochemical evaluation, clinical and pathological features of the tumor, type of therapy, recurrence, or death was recorded for each eligible patient.

**Results:** In total, 247 patients were included in the study. The mean age of patients was  $48.8 \pm 1.3$  years. The mean time of survival was  $2.64 \pm 0.13$  years. In detail, the survival rate from the first year to the fifth year was reported as 100%, 96%, 91%, 90%, and 89%, respectively. The survival rate of the luminal B subtype was higher than other subtypes but the difference was not significant ( $P=0.7$ ). Only in terms of metastasis, there was a significant difference between the alive and dead patients ( $P=0.0001$ ).

**Conclusion:** Despite no significant relationship between biological markers, the breast cancer subtype, and its survival rate, the overall survival rate of the patients decreased lightly through five years. However, further studies are required to indicate more accurate data about the breast cancer survival rate in our region.

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## Introduction

Breast cancer is the most common cancer in women, affecting 2.1 million women annually and causing the most cancer-related deaths among women in the US. In 2018, about 627,000 women died due to breast cancer, as this disease accounts for approximately 15% of all cancer

deaths in women (1). The burden of breast cancer continues to increase in both developed and developing countries. Inadequate early screening and expensive treatment contribute to significant variations in breast cancer survival rates between countries (2). The age-standardized incidence rate of breast cancer is

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33.21 per 100,000 according to the latest national database; however, breast cancer mortality has not changed over the past 30 years in Iran; Thus, the age-standardized mortality rate was 14.2 per 100,000, with a median age of 49.84 years (3, 4).

To improve breast cancer outcomes and survival, early detection is critical (4). Traditional clinical and pathologic factors such as age, histological grade, tumor type, tumor size, and hormone receptors are often used to stratify patients into high-risk groups for treatment with adjuvant hormone therapy, radiation therapy, and/or chemotherapy. These factors accurately classify patients based on long-term follow-up studies. However, it is acknowledged that traditional prognostic factors are limited in their ability to provide reliable stratification in all patients (5). Recently, morphologic and immune-histochemical analyzes have been integrated to determine patient prognosis (6). Breast cancer has been divided into five molecular subtypes based on gene expression patterns found to have significant differences in clinical outcome including Luminal A, Luminal B, HER2, Basal-like, and normal basal-like (7). Molecular subtypes are predictive for responses to specific therapies and are prognostic for clinical outcomes (8-10).

According to the current situation, Breast cancer is a major concern in public health, and patient survival is a key indicator of overall health globally. This study aimed to determine the survival rate of breast cancer patients based on tumor biological subtypes in whom referring to Imam Reza Hospital, Omid Hospital, and Reza Oncology Center, Mashhad University of Medical Sciences, Mashhad, Iran.

## Materials and Method

### Study Design

The present population-based study was conducted at Imam Reza Hospital, Omid Hospital, and Reza Oncology Center, Mashhad University of Medical Sciences, Mashhad, Iran. The study utilized the medical records of breast cancer patients who underwent mastectomy between 2008 to 2018. Patients with measured levels of biomarkers (HER2, PR, and ER) were included in the study. Patient data was extracted from archives and their survival time was calculated. All eligible patients were included in the study by census sampling method. All extracted data analyzed confidentially without mentioning the patient's name and the research has been approved by the Organizational Ethics Committee of Mashhad University of Medical Science with the code IR.MUMS.fm.REC.1396.32.

### Measurements

Demographic information, the status of biomarkers (ER, PR, HER-2) in immune-histochemical evaluation, clinical and pathological features of tumors (such as type, size, degree of histology, number of lymph nodes, presence of primary metastasis), type of therapy, recurrence or death were recorded during follow-up.

### Statistical Analysis

The data was analyzed by SPSS software (version 11). The t-test was applied to compare quantitative variables, while Chi-square test was applied to compare qualitative variables between two groups (dead and alive). Patient survival analysis was performed using the Kaplan-Meier method. The significance level was set at  $<0.05$ . Cox regression model was used to predict factors affecting survival.

## Results

Among the 400 breast cancer patients who were referred to Imam Reza Hospital, Omid Hospital, and Reza Oncology Center, Mashhad University of Medical Sciences, Mashhad, Iran, from the beginning of 2008 to the end of 2018, 247 cases met the inclusion criteria and the information were registered. Then contacted them and their living conditions were recorded. The mean age of patients was  $48.8 \pm 1.3$  years and the mean weight was  $67.5 \pm 1.6$  kg. The participants' demographic characteristics are represented in Table 1. In terms of disease status, 202 participants (81.78%) were early stage, 24 (9.71%) recurrence of disease, and 21 (8.50%) were metastatic. Table 1 indicated the pathological status of the studied population in detail.

In immune-histochemical studies, 188 (92.6%) of patients were positive for estrogen receptor (ER) and 15 (7.4%) were negative. Progesterone receptor was negative in 23 (11.3%) of patients and positive in 181 (88.7%) of patients (Table 3). The classification of patients based on the results of the immune-histochemical test showed that most subtypes was related to luminal B ( $n=107$ ; 52.5%) and then luminal A ( $n=66$ ; 32.4%). In staging of disease according to table 7, the most patients were in STAGE IB ( $n=47$ ; 27.3%). Metastasis was observed in 21 (10.4%) of the patients. Additionally, 172 (84.3%) of the studied population were alive (table 2).

Comparison based on demographic status showed no significant difference between living and deceased groups ( $P \geq 0.05$ ). Comparison between living and dead groups based on biological subtype, grade, hormonal receptors, familial history, Breastfeeding history, and

**Table 1.** Demographic and pathological characteristics of Studied Population

Variable	Mean± SD	Min-Max	
Age (year)	48.78±1.34	25-84	
Weight (kg)	67.55±1.61	60-168	
BMI (kg/m <sup>2</sup> )	27.77±5.11	16.38-44.37	
Body surface (m <sup>2</sup> )	1.37±0.29	1-2.42	
Age at menarche (year)	12.76±1.01	10-16	
Age at first pregnancy (year)	19.72±3.40	14-36	
Age at last pregnancy (year)	34.48±4.17	20-43	
Survival (year)	5.6±2.53	1-10	
Characteristics	Frequency	%	
Marital status	Single	43	17.3
	Married	204	82.7
Addiction	Drugs	1	0.4
	Cigarettes and Hookahs	4	1.6
	Alcohol	0	0
Menstrual Status	Pre-menopause	129	52.4
	Post-menopause	118	47.6
	Regular menstrual cycle	225	90.9
	Irregular menstrual cycle	22	9.1
Familial History	Positive	31	12.6
	Negative	216	87.4
Breast feeding History	Have	232	94.1
	Not have	15	5.9
Variable	Frequency	%	
Disease Status	Early stage	202	81.78
	Relapsed	24	9.71
	Metastatic	21	8.50
Organ	Right breast	82	41.2
	Left breast	85	42.7
	Lymph node	2	1.0
	Unknown	30	15
Pathology	Invasive ductal carcinoma	226	91.4
	Invasive lobular carcinoma	19	7.8
	Others	2	0.8
Grade	I	31	15.5
	II	125	62.5
	III	44	22.0
Type of surgery	Modified radical mastectomy	190	77.1
	Breast conserving surgery	55	22.4
	Others	1	0.4

menstrual (pre/post menopause) status showed no considerable difference between the two groups ( $P \geq 0.05$ ). Only in terms of metastasis, there was a significant difference between the two groups ( $P < 0.05$ ) (Table 3).

Additionally, the trend in overall survival of patients is shown below in Table 4. In survival assessment based on subtypes, it was found that the survival of luminal B was higher than other subtypes. But this difference was not significant ( $p > 0.05$ )

## Discussion

The present study was performed on 247 cases of breast cancer patients between 2008 and 2018.

The mean age of patients was about 48 years. About 42% of patients had cancer in the left and 41% had it in the right breast. Invasive ductal carcinoma was reported in 91.4% of patients. In the immuno-histochemical assessment, 92.6% of participants were positive for estrogen, 88.7% for progesterone, 62.3% for HER2, and 74.9% for K167 receptor, and the most subtype was related to luminal B and then luminal A. Most treatments were neo-adjuvant-chemotherapy. 15.7% of all patients had died by the end of the study and the rest were alive.

The results showed two groups (alive and dead) were not significantly different in terms of demographic variables, family history, history

**Table 2.** Hormone receptor test findings and breast cancer characteristics in the studied population

Receptor type Frequency	Negative		Positive	
	%	Frequency	%	Frequency
Estrogen (ER)	15	7.4	188	92.6
Progesterone (PR)	23	11.3	181	88.7
HER2	77	37.7	127	62.3
K167	50	25.1	149	74.9
Variable	Frequency		%	
Immuno-histochemical classification				
luminal A	66		32.4	
luminal B	107		52.5	
Triple negative	13		6.4	
Unknown	18		8.8	
Clinical stage				
STAGE IA	23		13.4	
STAGE IB	47		27.3	
STAGE IIA	48		27.9	
STAGE IIB	44		25.6	
STAGE IIIA	5		2.9	
STAGE IIIB	2		1.2	
STAGE IIIC	3		1.7	
Metastasis & Local Relapse				
Have	21		10.4	
Not have	181		89.6	
Medication				
Neo adjuvant	Chemotherapy	124	54.4	
	Hormone therapy	8	3.3	
Adjuvant	Chemotherapy	76	30.9	
	Hormone therapy	5	2	
	Radio therapy	20	8.1	
Target therapy	4		1.6	
Follow up	1		0.4	

of breastfeeding, and menstruation. There was no significant difference between the two groups in terms of tumor receptors status. Only in terms of metastasis, there was a significant difference between the two groups. The mean time of survival was 2.6 years. The survival rate of the luminal B subtype was higher than other subtypes but the difference was not significant.

A study of 309 women between the ages of 18 and 40, in the USA, found that the frequency of luminal B tumors (35%) was higher than luminal A (33%) and triple negative (21%) tumors, also the triple-negative subtype had a worse prognosis than other subtypes and the frequency of grade 2 was higher than other cases (11). In a study by Bucky et al. On 909 cancer patients (12), and in a study by Alvarado Cabrero et al. In Mexico on 1,320 women with cancer, similar to our findings, the frequency of the luminal B subtype was higher than other subtypes (13).

A study by Tiffanie Jones et al. Conducted in 2013 on 453 patients with grade 1 and 2 breast cancer without lymph node involvement, showed

that the luminal A subtype was the most common subtype in patients, and the mean survival time in triple-negative patients was significantly lower than luminal A (6). In the study of Jenkins et al., Which was performed on 4621 patients between 1980 and 2010, the survival time of triple-negative patients was significantly less than the other two groups (14). A study published in 2017 in India reported 45.7% of patients were in the advanced stage (15). In a study in Pakistan, 60.7% of cases were in the second stage of the cancer (16). A study conducted in northeastern Iran with 797 patients found that 48.4% of them had early-stage breast cancer and 51.6% had advanced breast cancer. This result is similar to the CRC result with 54.5% early breast cancer and 45.5% late-stage cancer (17, 18). Also, several studies in Iran evaluated the prognostic value of breast cancer biomarkers (4, 19, 20). These studies showed no significant relation between tumor prognosis and biological markers. However, a recently published study showed that negative biomarkers (ER-, PR-, HER2-) were associated with worse prognosis in

**Table 3.** Comparison of patients based on demographic and clinical characteristics

Variable	Living Status	Frequency	Mean±SD	P-value*
Age	Alive	172	48.2093±10.62615	0.179
	Dead	32	51.875±14.42165	
BMI	Alive	170	27.547±4.73772	0.246
	Dead	31	29.0469±6.79061	
Age at onset of disease	Alive	18	46.5±15.65905	0.662
	Dead	7	43.5714±12.14986	
Age at menarche	Alive	170	12.7529±1.0252	0.788
	Dead	31	12.8065±0.98045	
Age at first pregnancy	Alive	153	19.8497±3.5444	0.233
	Dead	27	19±2.41788	
Age at last pregnancy	Alive	153	34.5098±3.9969	0.873
	Dead	27	34.3704±5.14519	

Variable	Living status		P-value**	
	Sub index	Frequency (%)		
Index	Alive	Frequency (%)	0.7	
	Dead	Frequency (%)		
Biologic sub type	Luminal A	54(35%)	12(40%)	0.7
Luminal B	90(58%)	17(57%)		
Triple negative	12(8%)	1(3%)		
Grade	I	25(14.9%)	6(18.8%)	0.85
	II	106(63.1%)	19(59.4%)	
	III	37(22%)	7(21.9%)	
ER	Negative	15(8.8%)	0(0%)	0.08
	Positive	156(91.2%)	32(100%)	
PR	Negative	19(11%)	4(12.5%)	0.81
	Positive	153(89%)	28(87.5%)	
HER2	Negative	65(37.8%)	12(37.5%)	0.97
	Positive	107(62.2%)	20(62.5%)	
K167	Negative	39(22.9%)	11(37.9%)	0.08
	Positive	131(77.1%)	18(62.1%)	
Metastasis	No	161(94.7%)	20(62.5%)	0.0001
	Yes	9(5.3%)	12(37.5%)	
Familial history	No	151(87.8%)	25(78.1%)	0.14
	Yes	21(12.2%)	7(21.9%)	
Breastfeeding history	No	9(5.6%)	2(7.1%)	0.75
	Yes	151(94.4%)	26(92.9%)	
Menstrual (pre/post menopause) status	Pre	79(55.2%)	10(40%)	0.15
	Post	64(44.8%)	15(60%)	

\* Independent T-test / \*\*Chi-square test

**Table 4.** Overall survival based on life table results

Survival type	First year	Second year	Third year	forth year	Fifth year	Mean years of survival	SD
Overall survival	100%	96%	91%	90%	89%	2.64	0.13

all 4 subgroups. ER-HER2+ has a shorter survival time than ER+HER2- cases (21). Akbari et al. reported that in the absence of ER and Lympho-Vascular Invasion (LVI), the probability of tumor recurrence increased (22-25).

## Conclusion

According to the frequency of disease progression in different Iranian studies (30-36%), it appears that the health system reported to strengthen early detection programs needs improvement. Given the key role of biomarkers such as steroid receptor, and C-erb (HER2) in adequately managing this disease, the importance of further research and standardized evaluation

of biomarkers should focus on different regions of Iran (4).

This study evaluated the recurrence and survival pattern based on different subtypes of breast cancer in patients referred to the clinic of Imam Reza Hospital, Omid Hospital, and Reza Oncology Center, Mashhad University of Medical Sciences, Mashhad, Iran, from 2008 to 2018. The strength of this study was its access to relatively accurate patient records.

There was no significant difference between biological subtypes in terms of prognosis in our study which may be due to the small population we were studying which is the limitation of our study. Additionally, a large number of missed

data was another limitation of our study. The use of more samples in different regions can show this pattern in the whole country and develop a suitable guideline for the patients' diagnosis and treatment. Designing a study without time constraints, with an adequate and equal sample of each subtype can make a more accurate comparison between different subtypes in terms of recurrence and survival.

### Ethics approval and consent to participate

The protocol for conducting the present study was approved by the ethics committee of Mashhad University of Medical Sciences, Mashhad, Iran (IR.MUMS.fm.REC.1396.32). Written informed consent was obtained from all of the participants.

### Consent for publication

Not applicable.

### Availability of data and material

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### Competing interests

The authors have no competing interests to declare.

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### Author contributions

M.M, H.E.G, and A.T: Conducted the main idea of the study. M.M: Supervision. A.S: Data gathering. H.E.G: Data analysis. A.M & A.S: Drafting of the manuscript. All authors reviewed and accepted the manuscript.

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