



# The survival rate of Iranian breast cancer patients with focus on prognostic factors

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## Abstract

**Introduction:** Breast cancer is the most prevalent cancer in women. Several studies showed that TNM stage, grade cancer, lymph node involvement, and the status of hormone receptors are the most important factor of breast cancer prognosis.

**Objectives:** To evaluate the clinical characteristics, prognostic factors, and survival rate in patients with breast cancer who underwent surgery in Ahvaz, Southwest of Iran.

**Patients and Methods:** This historical cohort study was conducted on 561 patients who underwent surgery for breast cancer between May 1997 and June 2016. Clinical characteristics, pathological profile, stage, and treatments of the patients were recorded. The prognostic factor, two and five-year overall survival (OS) rates, disease-free survival (DFS) were evaluated by the Cox proportional hazards model and the Kaplan-Meier test, respectively.

**Results:** The two and five-year OS rates were 92.1% and 81.7%, respectively. The most important prognostic factors in breast cancer survival were age, the size of the tumor, regional lymph node involvement, metastasis, stage, relapse, estrogen receptor (ER), progesterone receptor (PR), and hormone therapy. There was no significant relationship between tumor type, tumor site, metastasis, surgery kind, chemotherapy, radiation therapy, and the status of human epidermal growth factor receptor 2 (HER2) and the five-year survival rate.

**Conclusion:** This study showed that the most important factors affecting the high survival rate of patients with breast cancer are hormonal receptors, non-involvement of the lymph nodes, early-stage cancer, no recurrence, and no metastasis.

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## Introduction

Breast cancer is the leading cause of death due to cancer in women and also the most common cancer identified in women. It is also ranked as the fifth most important cause of mortality (1). The age-standardized incidence rate (ASR) of breast cancer in Iran was 23.1 per 100 000 populations (2). Five-year survival is one of the most important indicators to evaluate the quality of care and treatment in breast cancer. The overall survival (OS) refers to the time between the diagnosis of the disease and the death of the patient or last visit. The survival depends on factors, such as race, socioeconomic status, age, genetic background, and quality of care (3-6). In a study on 441 breast cancer patients in Iran from 1994 to 2007, the 5- and 10-year survival rates were 81% and 77%, respectively (7). In recent years, deaths from this cancer have declined, especially in developed countries (8). However, the survival rate of women with breast cancer in Iran stands between western and eastern

## Key point

In a historical cohort study on 561 patients who underwent surgery for breast cancer between May 1997 and June 2016, we found most important factors affecting the high survival rate of patients with breast cancer are hormonal receptors, non-involvement of the lymph nodes, early-stage cancer, no recurrence and no metastasis.

European countries (9). Breast cancer is classified according to different histological and clinical criteria for different purposes. The main divisions are based on histological features, tumor grade, tumor staging, receptor status, and gene expression (10). Several studies showed that high cancer grade and its stage, more lymph node involvement, hormone receptor-negative, metastasis, poor socioeconomic status, premenopausal status, different fertility status and high body mass index are factors associated with breast cancer with a poor prognosis (11). It has also shown that breast cancer patients with positive human epidermal growth factor

receptor 2 (HER2) have a higher recurrence and mortality rate, as well as faster-growing and more aggressive nature than other types (12-15).

### Objectives

The aim of our study was to determine the survival rate and its related prognostic factors in patients with breast cancer in Ahvaz, Southwest of Iran.

### Patients and Methods

#### Study design

This investigation was a historical cohort study conducted on 561 patients who underwent surgery for breast cancer in Ahvaz city between May 1997 and June 2016. Ahvaz city is the province center, the largest city of the Khuzestan province in the southwest of Iran, and also the proper diagnostic and therapeutic facilities are available in the city. Therefore, the patients in this study were those referring to the Khuzestan province and neighboring provinces. The inclusion criteria were all patients with a definitive diagnosis of breast cancer who underwent surgery for breast cancer. The exclusion criteria were patients with incomplete records, lack of follow-up, no access to patients, and lack of consent to participate in the study. The patients' demographic data, including age, gender, and family history and prognostic factors such as tumor characteristics, the status of hormone receptor (ER and PR), HER2 expression, regional lymph node involvement, metastasis, stage, and therapeutic interventions were recorded. Additionally, two and five-year OS and disease-free survival (DFS), metastasis, and recurrence, were collected based on the patients' medical records and last follow-up using a telephone interview by trained staff and supervised by an expert surgical oncologist.

#### Statistical analysis

The qualitative variables were expressed as frequency and percentage, whereas quantitative variables were reported as mean  $\pm$  SD and range. The mean and median of two and five-year OS and DFS in each group of variables were also reported using the Kaplan-Meier method. Then, Cox regression was used to investigate the factors affecting the survival of patients, which examined the significance of variables on survival rate. The *P* value  $<0.05$  was considered significant. Data were analyzed using SPSS 16 software.

### Results

A total of 561 patients were studied, out of the 557 patients (99.3%) were female and others were male with the mean age of  $53.27 \pm 12.29$  years (age range, 27-90 years) with most cases (58.2%) being 40-60 years. The most common breast complaints were breast mass (87.0%) followed by pain, nipple discharge, ulcer, edema, dimpling, and thickening of the skin, respectively. In addition, 46.4% of the patients had right breast cancer, 51.8% left breast cancer, and others

were bilateral. The most common type of tumor (89.7%) was invasive ductal carcinoma, followed by invasive lobular carcinoma (6.2%) and others (3.6%) and 35.0% of patients were diagnosed at stages I and II. In terms of hormone receptors, 65.2% and 56.2% of cases were ER-positive and PR-positive, respectively. Also, most patients (75.1%) with breast cancer had HER2-negative breast cancer. Among all patients undergoing surgery, 84.5% of the patients were subjected to modified radical mastectomy (MRM), and the rest were subjected to breast conservative treatment (BCT) and radical mastectomy, respectively. The other demographic and baseline tumor characteristics were shown in Table 1. The two and five-year OS rates were 92.1% and 81.7%, respectively. Likewise, the two and five-year DFS were 86.3% and 70.3%, respectively (Table 2). In

**Table 1.** Clinical and treatment characteristics in breast cancer patients

Variables	Number	Percent		
Age	20-29	5	0.9	
	30-39	61	11.0	
	40-49	159	28.3	
	50-59	168	29.9	
	60-69	109	19.4	
	>70	59	10.5	
Tumor size	1	75	21.6	
	2	177	51.0	
	3	59	17.0	
	4	36	10.4	
	Total	347	100.0	
Regional lymph node involvement status	0	133	38.3	
	1	96	27.7	
	2	71	20.5	
	3	47	13.5	
Metastasis	Yes	332	87.8	
	No	46	12.2	
Stage	I	44	7.6	
	IIA	108	18.6	
	IIB	49	8.8	
	IIIA	69	12.0	
	IIIB	26	4.5	
	IIIC	39	6.7	
	IV	30	5.2	
	Unknown	213	36.9	
Receptor status	ER	Negative	110	19.0
		Positive	206	35.6
	PR	Negative	139	24.0
		Positive	178	30.8
	HER2	Negative	227	39.3
		1+	13	2.2
		2+	79	13.7
	3+	106	18.3	
Surgery kind	MRM	443	84.5	
	BCT	79	15.1	
	Radical mastectomy	2	0.4	
Chemotherapy	Done	512	98.3	
	Not done	9	1.7	
Radiotherapy	Done	390	77.1	
	Not done	116	22.9	

MRM, Modified radical mastectomy; BCT, Breast conserving therapy.

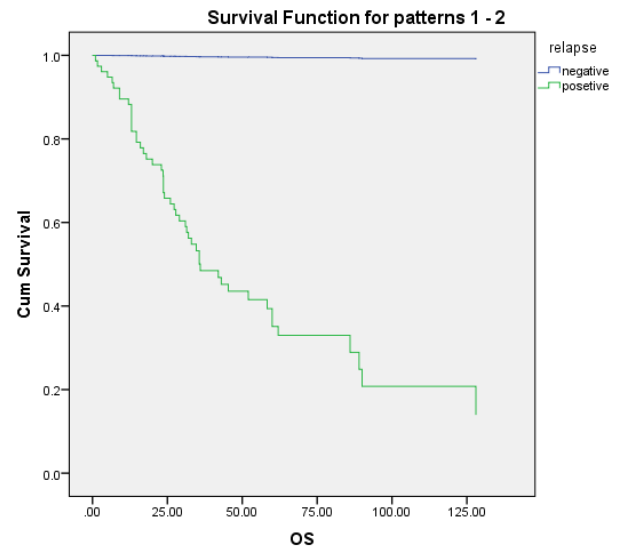
addition, the recurrence occurred in 80 (20.4%) patients, and unfortunately, 55 (14.0%) cases died. Based on the results of the Kaplan-Meier analysis and Cox regression model, the five-year survival was 32% in patients with recurrence and 100% in patients without recurrence, (HR=200.77, 95% CI: 27.71-1454,  $P<0.001$ ). As well, the lowest survival rate was observed in cases with stage IV breast cancer (HR=14.58, 95% CI: 1.90-111.48,  $P=0.01$ ) (Figures 1 and 2; Table 3). It seems that recurrence and cancer staging is the most important prognostic factors in survival rate. Other results of our investigation indicated that the regional lymph node involvement (HR=4.86, 95% CI: 1.84-12.88,  $P=0.001$ ), larger tumor size ( $P<0.001$ ), negative ER ( $P=0.03$ ), negative PR ( $P=0.008$ ) play a key role in the prediction of poor survival rate in breast cancer patients (Table 3). Additionally, no significant relationship between the five-year survival rate and tumor site ( $P=0.68$ ), surgical method (HR=0.75, 95% CI: 0.34-1.62,  $P=0.46$ ), tumor type ( $P=0.70$ ), HER2 overexpression ( $P=0.67$ ), chemotherapy (HR = 0.90, 95% CI: 0.12-6.78,  $P=0.92$ ), radiation therapy (HR = 0.92, 95% CI: 0.45-1.86,  $P=0.82$ ) and trastuzumab therapy were detected (Table 3).

## Discussion

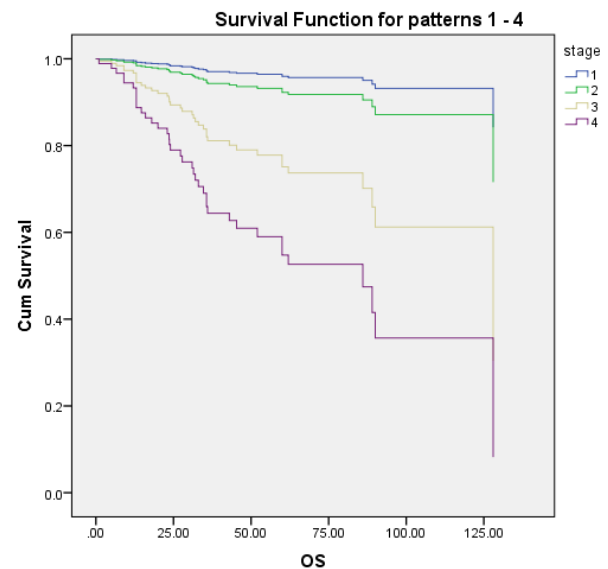
Disease survival is an important indicator that helps physicians and policymakers identify appropriate prognosis rates, and employ appropriate methods to prevent and treat the disease. In this study, the two and five-year survival rates were 92.1% and 81.7%, respectively. These values for two and five-year DFS were 86.3% and 70.3%, respectively, and at the end of the study, approximately 14.0% of the patients experienced death. The 5-year survival rate of breast cancer has been studied in several studies. According to the report by Colditz and Beers, the 5-year survival rate of breast cancer in the United States is 86%. According to the study by Sant et al, survival in Finland and Sweden was 82% and 83%, respectively (11,16), which is almost consistent with our

**Table 2.** Clinical and treatment outcomes in breast cancer patients

Outcome	No. of Patients	Percent
<b>Relapse</b>		
No	312(392)	79.60
Yes	80(392)	20.40
<b>Death</b>		
Yes	55(392)	14.04
No	337(392)	85.96
<b>DFS (n=385)</b>		
Range (months)	0-264	-
2 year DFS	-	86.3
5 year DFS	-	70.3
<b>OS (n=385)</b>		
Mean (months)	200.6 (95% CI: 172.7-228.4)	-
Range (months)	1-272	-
2 year OS	-	92.1
5 year OS	-	81.7



**Figure 1.** The relationship between tumor recurrence and overall survival in patients with breast cancer.



**Figure 2.** The relationship between staging and overall survival in patients with breast cancer.

results. In addition, in studies by Haghghat and Akbari et al, the five-year survival rate was 76.6% which is almost in line with our findings (81.7%) (17,18). It should be noted that most studies in Iran have shown lower levels of breast cancer survival than the above-mentioned studies, which can be due to referral to the healthcare quality provided in different health centers, as well as the lack of subsequent follow-up. Compared with other developing countries, the five-year survival rate of breast cancer in Turkey, Thailand, India, Singapore, and Korea has been reported 77.0%, 62.9%, 0.48%, 76.4%, and 0.77%, respectively (19). These rates are somewhat less than the survival of our patients, which may be due to the different settings of studies,

**Table 3.** Evaluation of factors affecting the survival rate of patients with breast cancer

Covariate	5 years OS (%)	Risk ratio	95% CI	P
<b>Family History</b>				
Yes/No	91/82	1.358	0.99-1.85	0.05
<b>Age</b>	-	1.041	1.017-1.06	0.001
<b>Tumor site</b>				0.68
Right	83	-	-	-
Left	80	1.21	0.69-2.13	0.50
Bilateral	-	1.94	0.26-14.49	0.51
<b>Tumor Size</b>				0.000
T1	93	-	-	-
T2	90	1.80	0.39-8.23	0.44
T3	66	6.04	1.30-28.02	.022
T4	63	10.50	2.26-48.77	0.003
<b>Lymph node</b>				
Yes/No	74/90	4.86	1.84-12.88	0.001
<b>Metastasis</b>				
M1/M0	84/66	2.84	1.32-6.08	.007
<b>Stage</b>				0.000
I	92	-	-	-
II	90	1.95	0.24-15.83	0.53
III	73	6.94	0.92-52.46	.06
IV	52	14.58	1.90-111.48	0.01
<b>Relapse</b>				
Relapsed/Not relapsed	32/100	200.77	27.71-1454	.000
<b>Surgical method</b>				
BCT/MRM	88/80	0.75	0.34-1.62	0.46
<b>Radiotherapy</b>				
Yes/No	82 /84	0.92	0.45-1.86	.82
<b>Chemotherapy</b>				
Yes/No	81/86	0.90	0.12-6.78	.92
<b>ER</b>				
Positive/Negative	85/72	0.45	0.22-0.93	0.03
<b>PR</b>				
Positive/Negative	87/72	0.36	0.17-0.77	0.008
<b>HER2</b>				0.67
Negative	78	-	-	-
1+	86	0.71	0.09-5.24	0.71
2+	90	0.47	0.14-1.59	0.47
3+	77	0.91	0.45-1.84	0.91
<b>Tumor type</b>				0.70
Invasive ductal carcinoma	80	-	-	-
Invasive lobular carcinoma	78	1.0	0.35-2.81	0.99
Others	89	0.04	0.05-3.09	0.39
<b>Hormone therapy</b>				
Yes/No	86/71	0.40	0.19-0.83	0.01
Trastuzumab therapy				
Yes/No	77/80	1.02	0.51-2.03	0.95

especially different stages of breast cancer patients at the time of diagnosis. Therefore, in our study, the five-year survival rate from stage I to IV cancer was 92.0%, 90%, 73.0%, and 52.0%, respectively, with the lowest survival rate in cases with stage IV cancer (HR = 14.58%). In this study, lymph node involvement, negative hormone receptor, metastasis, T3 and T4 tumors, and recurrence of the disease were important factors that significantly reduced survival in patients, which has been confirmed in other studies (11). Lymph node involvement increased the

risk of death by 4.86 times which is confirmed in other studies (20). Likewise, patients with hormone receptor-positive tumors (ER+ and PR+) had a significantly higher five-year survival compared with those with hormone receptor-negative tumors. In general, the status of hormone receptors is one of the most important prognostic and preventive factors of cancer, which has been confirmed in other studies (11,21-25).

Considering the factors affecting the survival of patients, the five-year survival rate in cases with and without

chemotherapy was 86% and 82%, and 84% and 82% in cases with and without radiotherapy, respectively. No significant relationship was found between these values. Also, in other studies, the positive effect of radiotherapy and chemotherapy on survival has sometimes been rejected (17,23) or confirmed (11,24). This inconsistency in different studies could be due to different treatment options by physicians for adjuvant treatment, patients' personal opinions, or differences in health care facilities (18).

Regarding tumor type, the five-year survival in invasive ductal carcinoma, invasive lobular carcinoma, and other types was 80%, 78%, and 89%, respectively. Accordingly, no significant relationship was found between tumor type and survival (20). Besides, no significant relationship was found between surgical methods and survival (26). Although in our study there was no association between tumor site and survival, in a study among Egyptian patients despite right-sided tumors seemed more aggressive, Left-sided ones tend to confer worse survival than right-sided tumors (27). Regarding age at diagnosis, there was no significant difference in survival (20) although there is a controversy pointed out in the literature regarding its effect on the prognosis of the disease (28,29).

It is worth saying the impact of some prognostic factors on breast cancer survival has been shown to vary with time since diagnosis (30).

### Conclusion

The results of this study showed that the most important factors affecting the high survival rate of patients with breast cancer include the existence of hormonal receptors (ER+, PR+), no involvement of lymph nodes, early-stage disease, and no recurrence. In our country, due to the correct and timely diagnostic process and timely surgical treatment, and optimal use of adjuvant treatments, patients are in a better condition and have a longer life expectancy compared to other developing countries. The lifespan of our patients is similar to western countries and in some cases, it is even better than theirs. Although, the need for further use of appropriate methods for the prevention and early treatment of breast cancer and the subsequent follow-up is mandatory.

### Study limitations

The lack of access to all patients' records, not answering the phone to complete the data by patients, the relatively small sample size, missing some patients in the follow-up, and unawareness of some patients about the treatment process were the limitations of this study.

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### Authors' contribution

All authors listed have made a substantial, direct, and intellectual

contribution to the work, and approved it for publication.

### Conflicts of interest

The authors report no conflict of interest.

### Ethical issues

The voluntary and informed consent was obtained from all participants in accordance with the Declaration of Helsinki. The research protocol was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. The institutional ethical committee at Ahvaz Jundishapur University of Medical Sciences approved all study protocols (Ethical code # IR.AJUMS.HGOLESTAN.REC.1399.022). This study is extracted from M.D., thesis of Saghar Babadi at this university. Besides, ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors.

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