Ten-Year Survival of Breast Cancer in Iran: A National Study (Retrospective Cohort Study)

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Abstract

Purpose: This study aimed to estimate the 5- and 10-year survival rates of breast cancer in Iran. *Methods:* This retrospective cohort study was performed in 2019 on breast cancer patients registered in the national cancer registry system of Iran during 2007–2014. The patients were contacted to collect their information and status (alive or dead). Age and pathological type of tumor were categorized into five groups, and the place of residence was divided into 13 regions. The Kaplan-Meier method and the Cox proportional hazards model were used for data analysis. *Results:* A total of 87,902 patients were diagnosed with breast cancer during the study, 22,307 of whom were followed-up. The 5- and 10-year survival rates of the patients were 80% and 69%, respectively. The mean age of the patients was 50.68 ± 12.76 years (median age, 49 years). About 2.3% of the patients were male. The 5- and 10-year survival rates were 69% and 50% in men, respectively. The highest survival rate was reported in the age group of 40–49 years, and the lowest rate was found in the age group of ≥70 years. Of all pathological types, 88% were found in the invasive ductal carcinoma group; the highest survival rate was reported in the noninvasive carcinoma group. The highest survival rate was reported in the Tehran region and the lowest in the Hamedan region. Based on the results, the Cox proportional hazards model, sex, age group, and pathological type were statistically significant differences. *Conclusion:* This nationwide study performed on breast cancer patients indicated an improvement in the overall survival rate of these patients over the past years (the 5-year survival rate increased from 71% in 2011 to 80% in the present study), which might be attributed to advances in cancer management.

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Introduction

Breast cancer (BC) is the most common cancer in women worldwide, although it occurs in both sexes. In 2020, it was identified as the fifth cause of cancer death in both sexes and the leading cause of mortality due to cancer in women worldwide [1]. Nevertheless, the prognosis of BC is more favorable than that of other common malignancies. In Iran, BC is the most common type of cancer in women (and also in both sexes), with an age-standardized incidence rate of $32.63/10^5$ in 2015 [2]. It is also the fifth and first cause of cancer death in both sexes and females, respectively [3].

There has been an increasing trend in the incidence of BC in recent years [4]. In a nationwide study performed in Iran in 2011, the 5-year survival rate of BC was estimated at 71% [5]. In this study, data was collected from

Table 1. The baseline characteristics of the total registered and followed-up patients with BC

Variable	Patients, N (%)	Followed up, n (%)	p value
Sex			
Female	85,880 (97.7)	21,860 (98)	>0.05
Male	2,022 (2.3)	447 (2)	
Age group			
<40 years	19,259 (21.9)	4,974 (22.3)	>0.05
40–49 years	24,788 (28.2)	6,446 (28.9)	
50–59 years	23,381 (26.6)	5,866 (26.3)	
60–69 years	12,745 (14.5)	3,167 (14.2)	
≥70 years	7,735 (8.8)	1,851 (8.3)	
Pathologic type			
IDC	77,529 (88.2)	19,786 (88.7)	>0.05
ILC	4,395 (5)	1,115 (5)	
Noninvasive tumors	3,516 (4)	801 (3.5)	
Mixed	1,494 (1.7)	405 (1.8)	
Others	967 (1.1)	226 (1)	
Region			
Alborz	3,685 (4.2)	892 (4)	>0.05
Azerbaijan	1,951 (2.2)	402 (1.8)	
Fars	9,496 (10.8)	2,365 (10.6)	
Guilan	3,476 (4)	1,093 (4.9)	
Hamedan	3,045 (3.5)	781 (3.5)	
Isfahan	10,911 (12.4)	2,833 (12.7)	
Kerman	3,506 (4)	959 (4.3)	
Kermanshah	2,973 (3.4)	647 (2.9)	
Khorasan	9,145 (10.4)	2,476 (11.1)	
Khuzestan	6,663 (7.6)	1,718 (7.7)	
Markazi	6,995 (8)	1,829 (8.2)	
Qom	2,682 (3.1)	781 (3.5)	
Tehran	23,374 (26.6)	5,531 (24.7)	

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

BC patients, registered in the national cancer registration system, and used for comprehensive cancer control planning [6]. Survival is one of the most important indices in epidemiological cancer studies. The 5-year survival rate generally refers to the percentage of patients who live at least 5 years after the cancer is diagnosed [7]. This indicator was estimated at 90% in women with breast carcinoma in the USA [8] and 85% in the UK [9]. According to published reports, the survival rate ranges from 85% or higher in North America and Europe to 66–69% in Asia [10].

The early detection of BC remains the main strategy for BC management by improving the outcomes of disease and survival [11]. Many factors, such as demographic, clinical, and biological factors or treatment protocol, can affect the survival rate of patients with BC [12]. Because survival rate is one of the most important indicators of health management, the present study aimed to estimate the 5- and 10-year survival rates of patients with BC, registered in the Iranian National Cancer Registry System during 2007–2014.

Methods

This retrospective cohort study examined the data of patients diagnosed with BC, registered in the Iranian National Cancer Registry System from 2007 to 2014. This registry system was pathology-based until 2014, with a coverage rate of approximately 93% of pathological reports. Since 2014, it became population-based, collecting the data of new cancer patients from pathology laboratories, hospitals, and death certificates; the coverage rate was estimated at 75% of all cancer patients [2].

The collected data consisted of demographic (i.e., name, age, sex, and address) and pathological characteristics of the patients and tumors. Inclusion criteria was patients ≥15 years old and BC cases <15 years old were excluded.

It should be noted that the Ministry of Health and Medical Education (MOHME) omitted duplicate data during 2007–2009 and in 2013. Accordingly, we removed duplicate data for other years, as well (2010–2013); the applied method is described in detail in the literature [13]. After cleaning the database, a trained team of nurses conducted the patient follow-ups via phone calls by available telephone number to determine their current status (alive or dead) in 2019. If no one answered the call, contact repeated at different times in order to collect patients' information (online suppl. Table 1; see www.karger.com/doi/10.1159/000526746 for all online suppl. material).
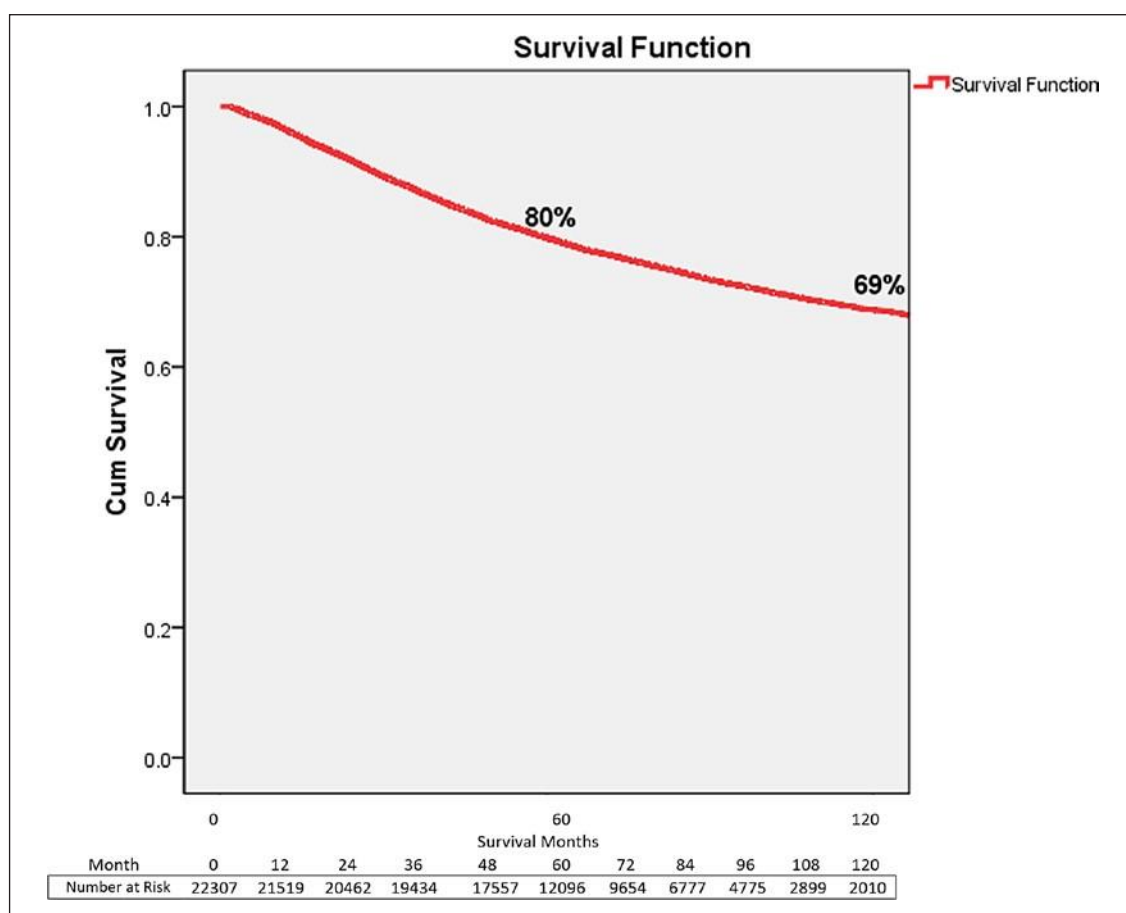
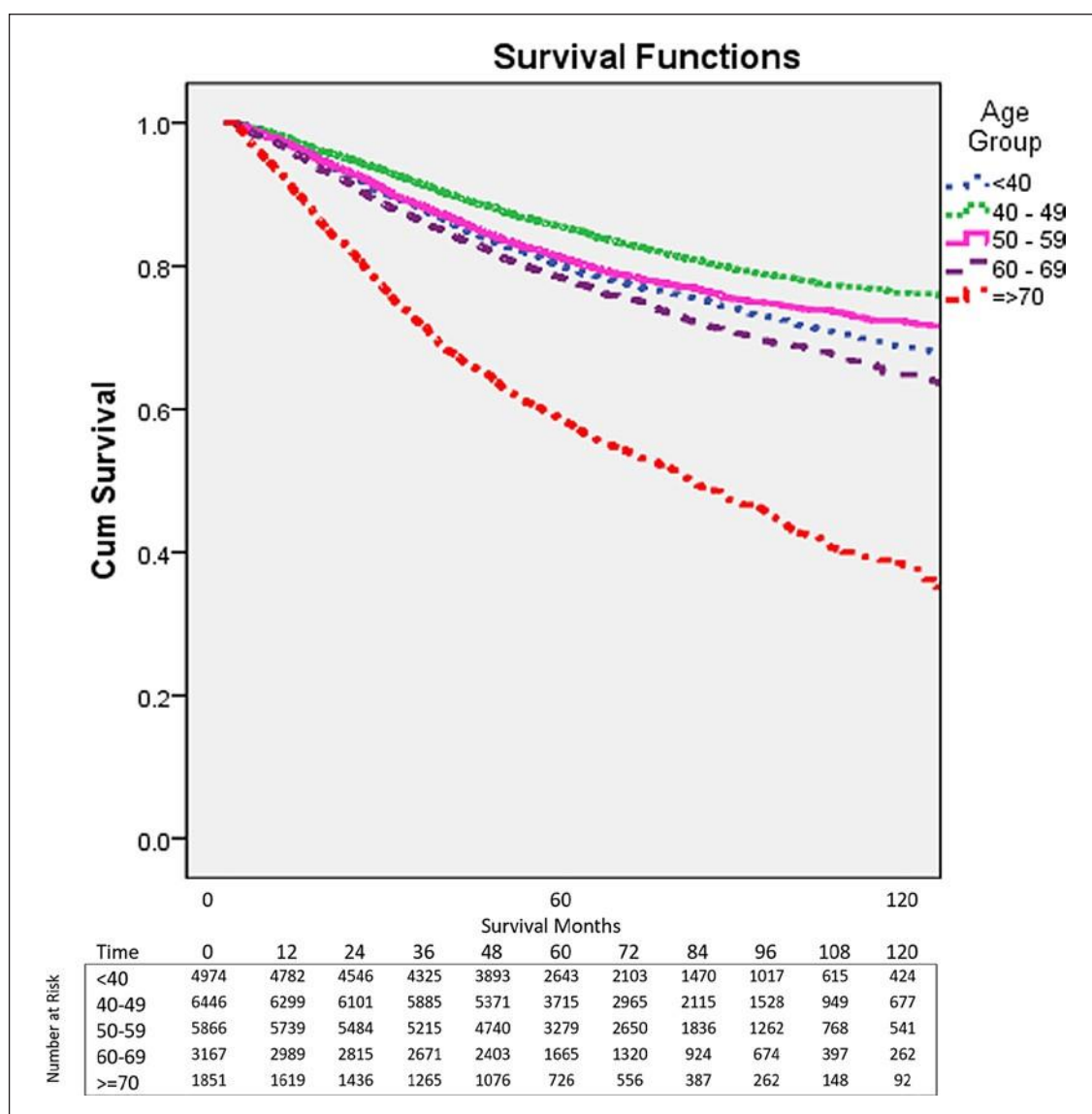**Fig. 1.** Survival rate of patients with BC from 2007 to 2014.

The survival rate was measured from the time of cancer diagnosis until the time of death or the final follow-up. Age was categorized into five groups (<40, 40–49, 50–59, 60–69, and ≥70 years) for survival analysis. The pathological type of tumor was registered in 160 figures. The patients were classified into five groups, including invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), noninvasive BC, mixed, and others (i.e., carcinomas, sarcomas, lymphomas, inflammatory BC [IBC], and Paget's disease). Moreover, the patients were divided into 13 groups according to the place of residence, using the geographic segmentation strategy suggested by the MOHME (online suppl. Table 2).

Variables were described using indices, such as mean, standard deviation, median, percentage, and frequency. Moreover, t test was used to measure the mean age of the patients stratified by sex, while ANOVA and Dunnett's test were used to estimate the mean age of the patients based on the place of residence in different geographical regions. Since Tehran is the capital city of Iran, with the majority of BC patients and also the highest mean population age, it is considered as the control group in Dunnett's test. χ^2 test was used to compare characteristics between total registered and followed-up patients. The Kaplan-Meier estimate was measured to determine the survival rate of the cohort and investigate differences between sexes, age groups, pathological types, and place of residence. The log-rank test was used to estimate survival differences between the groups, and the Cox proportional hazards model was used to determine the effects of covariates on survival. p value <5% was considered statistically significant. Data analyses were performed in SPSS version 24.

Results

In this study, the data of 87,902 BC patients, registered in the Iranian National Cancer Registry System during 2007–2014, were examined. The baseline characteristics of the total registered and followed-up patients are presented in Table 1.

From 2010 to 2013, nearly 10% of all cases were duplicates, which were excluded after cleaning the data; the remaining 87,902 cases were included in the final analysis (inclusion criteria was patients ≥15 years old and BC cases <15 years old were excluded). All of the patients were contacted via phone calls to determine their status (alive or dead). However, we could only contact 22,307 patients (25% of total patients) while others were unavailable (they had moved to a new house, or their phone numbers had changed, or they did not answer several calls consecutively). The characteristics of the total registered and followed-up patients were compared regarding the main variables. There were no significant differences between the two groups; therefore, the patients who were followed-up were considered as a representative sample of the total patient population (Table 1).

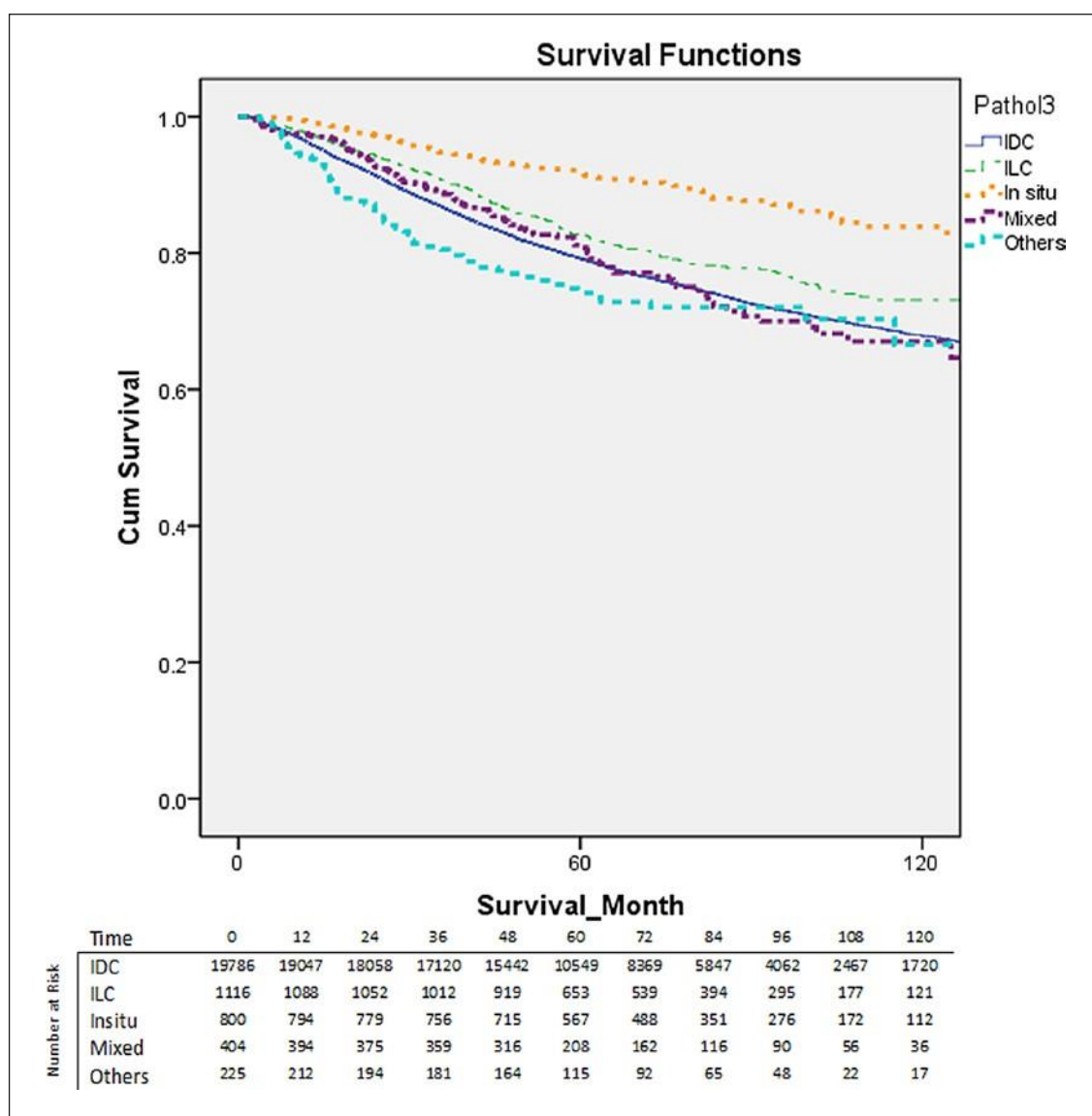**Fig. 2.** Survival rate of patients with BC based on the age group.

Nearly 22,307 patients were followed-up, 5,371 of whom had expired due to BC, while 16,936 were alive in the follow-up time. The 5- and 10-year survival rates for the followed-up population were estimated at 80% ± 0.005 and 69% ± 0.007, respectively (Fig. 1). Survival curve based on the year of diagnosis is shown in online suppl. Fig. 1.

The 5- and 10-year survival rates were 80% and 69% in females and 69% and 50% in males, respectively ($p < 0.001$). The mean and median age of the total population (after excluding patients <15 years old) were 50.68 ± 12.76 and 49 years, respectively. The mean age of male and female patients was 58.63 ± 14.84 and 50.50 ± 12.65 years, respectively ($p < 0.001$). Age was categorized into five groups, including <40, 40–49, 50–59, 60–69, and ≥70 years. About 54.8% of the total patients were in the age

group of 40–59 years, while 21.9% were younger than 40 years. The highest survival rate was reported in the age group of 40–49 years, and the lowest rate was found in the age group of ≥70 years (Fig. 2). There were significant differences in the survival rate between the age groups ($p < 0.001$).

As shown in Figure 3, considering the pathological type, the highest survival rate was attributed to noninvasive tumors, and the lowest rate was attributed to other pathological types (Fig. 3). Overall, 88% of the tumors were observed in the IDC group, and the 5- and 10-year survival rates were 79% and 68%, respectively. There were significant differences in the survival rate between different pathological types of tumor ($p < 0.001$).

The patients' survival rates in terms of place of residence, based on the geographic segmentation by

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Fig. 3. Survival rate of patients with BC based on the pathological type of tumor.

MOHME, are presented in Table 2. The highest 5- and 10-year survival rates were reported in Tehran in central Iran, while the lowest rates were found in Hamedan province in the west. There were significant differences in terms of survival between different places of residence, based on the geographic segmentation ($p < 0.001$).

Based on the Cox proportional hazards model, female patients had a better prognosis than males. The highest and lowest survival rates were reported in the age groups of 40–49 and ≥70 years, respectively. Also, noninvasive BC had a significantly higher survival rate compared to other pathological types. According to the results, the age group of 40–49 years was considered as the reference group because the best survival rate belonged to this age group (Table 3).

The mean age of the patients in different geographical segmentations is shown in Table 4. The highest and the lowest mean ages were found in Tehran and Kermanshah regions, respectively. There were significant differences in the mean age of the patients between Tehran and other geographical regions ($p < 0.001$), except Guilan ($p = 0.372$).

Discussion

Overall Survival
In this nationwide study, the 5- and 10-year survival rates of patients with BC were 80% and 69%, respectively. In a previous nationwide study performed in 2011, the 5-year survival rate was 71% [5]. In the USA in 2019, the

Table 2. The 5- and 10-year survival rates of patients with BC based on the geographic segmentation

Region	Survival rate (5 years)	Survival rate (10 years)	p value
Isfahan	87	71.5	<0.001
Tehran	86	73.5	
Alborz	79	72	
Fars	79	70.5	
Kermanshah	78	67	
Khorasan	78	67.5	
Khuzestan	78	65.5	
Azerbaijan	77	68	
Kerman	77	67	
Qom	77	67	
Mazandaran	76	67	
Guilan	73	62	
Hamedan	68	61	

Table 3. HRs (95% CI) estimated by the Cox proportional hazards model for BC

Variable	HR (95% CI)
Sex	
Female	1
Male[a]	1.25 (1.07–1.47)
Age group	
40–49	1
<40[a]	1.36 (1.25–1.48)
50–59[a]	1.26 (1.16–1.36)
60–69[a]	1.54 (1.41–1.69)
>70[a]	3.43 (1.14–3.74)
Pathology type	
Invasive ductal carcinoma	1
Noninvasive[a]	0.79 (0.69–0.90)
ILC (pure)[a]	0.40 (0.33–0.49)
Mixed	0.97 (0.79–1.18)
Others	1.11 (0.86–1.43)

CI, confidence interval; ILC, invasive lobular carcinoma; HR, hazard ratio. [a]Threshold of the *p* value.

Table 4. Mean age of BC patients in different geographical regions in Iran

Region	Mean age, years	SD of age	p value
Alborz	50.60	12.664	<0.001
Azerbaijan	49.01	12.156	<0.001
Fars	50.28	12.984	<0.001
Guilan	51.90	12.702	0.376
Hamedan	49.76	13.122	<0.001
Isfahan	51.14	13.006	<0.001
Kerman	49.39	13.050	<0.001
Kermanshah	48.94	12.369	<0.001
Khorasan	50.26	13.067	<0.001
Khuzestan	49.29	12.663	<0.001
Mazandaran	49.56	12.143	<0.001
Qom	50.59	13.117	<0.001
Tehran[a]	52.43	12.650	<0.001

SD, standard deviation. The mean difference is significant at the 0.05 level. [a]Dunnett *t* tests treat Tehran as a control, and compare all other groups against it.

5- and 10-year survival rates were 90% and 83% in female patients with BC, respectively [8]. In the UK, the 5- and 10-year survival rates were 85% and 75%, respectively, during 2013–2014 [9]. The highest 5-year survival rate of BC was reported in developed countries, while the lowest rate was reported in developing countries [10]. The 5-year survival rate, based on the registry systems of different Asian countries, was 83.2%, 40–62%, and 86% in China [14], India [15], and Turkey [16], respectively. Also, the 5-year survival rate was 85–87% in Western Europe and 84–88% in Southern Europe, followed by Central and Eastern Europe [17]. In Europe, the highest survival rate of BC was reported in Nordic countries, such as Sweden and Finland (89%), while the lowest rate was found in Romania (75%) [18].

The survival rate of cancer patients based on the geographical region showed the efficiency of local health services in providing affordable, accessible, and effective early detection, treatment, and follow-up care services [19]. The highest survival rate for cancer patients was reported in countries with appropriate healthcare services, early detection, adequate access to medical facilities, and sufficient treatment [20]. The lower survival rate of BC in Iran, which is estimated in this study, may be due to the late referral of patients or diagnosis in advanced clinical stages as compared to developed countries [21].

Comparison of the survival rates between two nationwide studies performed in Iran ([5] and present research) indicates a considerable improvement in the 5-year survival rate (nearly 9%), which might be related to earlier diagnosis and better management of the disease in recent years. This improvement could be relevant to increase population awareness about BC due to extensive education in mass media and also development in the health system according to more trained physicians and specialists and adequate access to medical facilities in different parts of the country (more than previous years).

Age at the Time of Diagnosis

The onset of BC is associated with age. A small increase in BC incidence rate was observed in the age groups of 15–19, 20–24, and 25–29 years, and a sharp increase was found after the age of 30 years in Iran [22]. In the present study, the mean age at the time of diagnosis was 50.68

years. The mean age of BC patients was 49.84 years in another nationwide study in Iran [5], 51.5 years in Turkey [23], 49.8 years in Pakistan [24], 48 years in Africa [25], 52.5 years in Lebanon [26], 56–62 years in Central and South America [27], and 67 years in the UK [28]. The peak age varied across the world (40–50 years in Asian countries and 60–70 years in Western countries) [29]. The large number of patients below 40 years (21.9%) and the lower mean age of patients in Iran compared to Western countries might be related to differences in the population pyramid (a larger youth population in Iran and shapes of the age pyramid).

Evidence shows that age at diagnosis of BC varies among populations. In a previous study on patients with BC in Egypt, the median age at diagnosis was 49 years, and 19.2% of the patients were below 40 years [30]. In another study in Saudi Arabia, female patients aged 40 years or less accounted for 25.2% of all BC cases, with a median age of 47 years. On the other hand, a retrospective cohort study performed in the USA on BC patients showed that 6.4% of them were below 40 years [31]. This discrepancy between the findings might be related to differences in the population structures, as Egypt and Saudi Arabia have younger populations, similar to Iran. The recurrence rates were higher in most female patients with advanced BC, as well as young female patients [32].

Survival Based on Age Groups

In this study, the best and worst survival rates were found in the age groups of 40–49 and ≥70 years, respectively. In a study using the Surveillance, Epidemiology, and End Results (SEER) 18 Database, the 5- and 10-year survival rates were the highest in patients aged 40–49 years (92% and 86%, respectively) and the lowest in those above 80 years (62% and 28%, respectively) [33]. Additionally, in a study performed in Malaysia, the highest survival rates were reported in the age groups of 40–59, <40, and >60 years, respectively [34]. In young patients' factors such as a higher tumor grade of differentiation, more aggressive subtypes included triple negative or HER-2 positive biological subtypes, presentation in advanced stages and lymphovascular invasion maybe the reasons for a lower survival rate than elder groups of patients [35]. Young age is considered as an independent adverse prognostic factor in patients with BC [34, 36].

BC in Males

In this research, the 5- and 10-year survival rates of male patients with BC were 69% and 50% respectively. In other studies, the mentioned indices were about 63–85.5% (5 years) and 41–76% (10 years), respectively [37]. Our results were in concurrence with the previous findings. The lowest survival rate in male patients was related to the development of disease in older age or diagnosis in advanced stages [38]. An interesting finding of this study was the higher rate of BC in men in Iran compared to other parts of the world (2.3 vs. 1%); however, further investigations are necessary to obtain more conclusive results. It is worth mentioning that the male-to-female ratio in the total Iranian population was similar to the global ratio (M/F ratio: 1.01).

Survival Based on Pathological Type

In this study, 88.2% of tumors were IDC and 5% were pure ILC, accounting for the highest number of tumors. In a study performed in Haiti, IDC accounted for 87.3% of all detected tumors, whereas ILC accounted for 4% of all tumors [39]. IDC, ILC, noninvasive, and "other" tumors accounted 87%, 3%, 4%, and 6% of BC malignancies in a study performed in China [40] and were 84.73%, 8.81%, and 6.47% for IDC, ILC, and "others" in diagnosed breast malignancy cases in Brazil [41].

In the present study, the 5-year survival rates were 79%, 82%, 91%, 81%, and 74% for IDC, ILC, noninvasive tumors, mixed tumor, and other breast malignancies, respectively. "Other" tumors included IBC that might be poor prognosis because these types of tumors are more common in young women and spread faster than other type of BCs. So, this type of tumor is usually diagnosed in advanced stages because cancer cells have grown in the skin before the symptoms appear. The 5-year survival rate for patients with IBC is estimated about 30% [42]. Breast sarcoma is an invasive and aggressive disease with poor prognosis and high recurrence rate. A range of 5-year overall survival rate for primary breast lymphoma has been reported from 49 to 67% [43]. Moreover, 5-year survival rates in breast lymphoma were estimated 77% [44]. According to these explanations, the lowest survival rate estimated in the "other cancers" group can be justified.

In Germany, the 5-year survival rates were 83%, 82%, and 93% in patients with IDC, ILC, and mixed carcinoma, respectively [45]. Moreover, according to a meta-analysis in Iran, the relationship between the pathological type of tumor and BC survival was confirmed in three studies [46]. On the other hand, in a study performed in Brazil, there was no significant difference in the survival of patients with IDC and ILC [47]. Besides, a Korean study showed no significant difference in the 5-year survival rate of patients between different pathological types of BC (i.e., IDC, mucinous carcinoma, papillary carcinoma, and medullary carcinoma) [48]. So, except the last study, the results of other mentioned researches were consistent with our findings on the relationship between the pathological type of tumor and the survival rate.

Survival Based on Region

The patients' place of residence affected the survival rate of BC due to differences in the socioeconomic status

and access to healthcare services [5]. In the present study, Tehran and Isfahan provinces (two of the largest provinces in Iran) showed the highest survival rates, while the lowest rate was reported in Hamedan. The present findings are inconsistent with our similar nationwide study in 2011 [5]. Overall, the survival rates reported in Iran varied significantly from 52% to 88% [49]. However, it should be noted that these results were reported in studies with a small sample size and limited geographical regions.

In a study performed in northwest of Iran, the 5- and 10-year survival rates were 77% and 65%, respectively [50]. The 5-year survival rate was 81% in Tehran [51] and 70% in Yazd [52]. Moreover, a meta-analysis in Australia reported the lowest survival rate and different clinical management protocols for BC in rural areas. The place of residence, signifying socioeconomic factors, such as income, level of education, and treatment method, might affect the survival rate [53].

The survival of patients with BC had a significant relationship with different clinical and socioeconomic prognostic factors. Clinical prognostic factors include the stage of tumor, tumor size, nodal status, tumor grade, age at diagnosis, and estrogen receptor status [54]. Other important prognostic factors include the population structure (age and ethnicity), socioeconomic status, level of education, and accessibility of health services including screening programs and promotion of early detection and accessibility of high-quality treatments [55]. Generally, ethnicity is an important factor influencing the survival rate. According to the results presented in Table 2, the overall survival rate varied across geographical areas, this could be related to the level of education or other social factors. Cultural factors and accessibility of health facilities might also affect the overall survival rate.

Strengths and Limitations

This is the first and only study to estimate the 10-year survival rate of BC patients based on national data. Second, the consistency of data collected from the followed-up patients and the total registered cases revealed that this study was performed on a representative sample of all registered patients in this period. Third, this study had a large sample size.

On the other hand, this study had some limitations. First, the data of the cancer registration system did not include the clinical data of patients, such as tumor stage and pathological grade; therefore, it is not possible to estimate survival based on these variables. Second, despite our many efforts, a large number of patients were not accessible. Third, different qualities of data registration systems forced us to spend significant amounts of time on cleaning the databases.

Conclusion

This Iranian nationwide study on the survival of BC patients indicated an overall improvement over the past years, with 5- and 10-year survival rates of 80% and 69%, respectively, which might be due to advances in cancer management. The rate of BC in the male population of Iran was twice higher than the global rate (2.3 vs. 1%), despite a similar M/F ratio in the Iranian and global populations. The mean age of BC patients was 5–10 years lower than that of Western countries and 5 years higher than that of Asian countries.

Statement of Ethics

The study protocol was reviewed and approved by the Ethics Committee of Cancer Research Center of Shahid Beheshti University of Medical Sciences (approval number: IR.SBMU.CRC.REC.1398.005). This research was explained for followed-up patients. All of them agreed to use their information in this study and written informed consent was obtained from participants.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

Author Contributions

Mohammad Esmaeil Akbari and Maryam Khayamzadeh designed and performed the study. Maryam Khayamzadeh and Reza Salmanian analyzed the data. Reza Salmanian managed the data. Mohammad Esmaeil Akbari, Maryam Khayamzadeh, Atieh Akbari, Reza Salmanian, and Mohammad Akbari interpreted the results, prepared the manuscript, and read and approved the final version of the manuscript. Mohammad Esmaeil Akbari supervised this study.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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