Review Article

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Survival Rate and Average Age of the Patients with Breast Cancer in Iran: Systematic Review and Meta-Analysis

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ABSTRACT

BACKGROUND AND OBJECTIVE: Breast cancer is one of the most common and worrying health problems in women around the world. In predicting of survival rate in patients with breast cancer several factors such as age, breed and spread of disease, stage of diagnosis and lymph node involvement are involved. This study was aimed to determine the mean age and survival rate of women with breast cancer in Iran.

METHODS: This systematic review and meta-analysis was based on searching in iranian databases as SID, Magiran, Irandoc, Noormag, IranMedex and Medlib and international databases as Ebsco, Cochrane, CEBM, Google Scholar, Scopus, Web of Sciences, Jama, were published 1990-2016. Researched keywords were, breast cancer, age, survival rate, Iran and compound of them. The obtained documents analyzed based on appropriate checklist through a random effects model.

FINDINGS: In 52 studies, 332991 samples were tested. Average of 5-years survival rate, and mean age of women with breast cancer estimated 68.84% in total (CI-95%: 64.9-72.72) and 48.59 years (CI-95%: 50.72-46.47). Lowest and the highest average of 5-years survival rate of them were calculated in northern of Iran 60.65%(CI-95%: 53.58-67.72) and in Tehran with 73.99%(CI-95%: 64.76-83.22), respectively. Lowest and highest average age of patients were calculated in North, 45.46(CI-95%: 35.10-55.83) years and in West with 49.83(CI-95%: 32.71-66.95) years.

CONCLUSION: Survival rate and mean age are tow essential variables in treatment management of breast cancer. These tow essential variables in north of Iran, were the lowest. Therefore, consider these factors and screening exam for early diagnosis are recommended.

KEY WORDS: *Iran, Breast, Cancer, Neoplasm, Survival Rate, Age, Meta-analysis, Systematic Review*.

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Introduction

Breast cancer is one of the most common and worrisome health problems in the world (1-4) and includes 30% of female cancer (5, 6). Breast cancer is the second cause of death in developed countries and is the third leading cause of death in less developed countries (8, 7, 3) and approximately 41,000 women die from breast cancer in year (9,10). According to the World Health Organization predicts by 2050, up 2.3 million women will be diagnosed with breast cancer (11, 12). The incidence of breast cancer mortality was reported in the countries of northern Europe and North America the highest, and in Asian and African countries the lowest and in South America and southern Europe as average (13).

Aging, genetic predisposition, personal history of breast cancer, exposure to types of radiation, cigarette (14), geographic influences, number of pregnancies, late menopause, early menstruation, obesity (15) and first childbirth after age 30 could be as risk factors for breast cancer (19-16). There are various methods for the treatment of breast cancer, according to the grading, staging, physical condition of the patient and his wishes (16). Overall 5-year survival rate is considered as a criterion in the assessment of cancer services and the undertaken work representing the survival of patients with a type of cancer is in the fifth year of diagnosis (20).

In predicting survival in patients with breast cancer factors such as age (23-21), race (24, 25) and the spread of disease, diagnosis (28-26, 10) and lymph node involvement (29, 30) are involved. Age at menarche, age at first pregnancy and menopause are important dates influencing the occurrence of breast cancer in women (32, 31). The main goals of meta-analysis studies are the increased sample size due to the increased number of relevant studies, reduced difference in existing parameters and reduced confidence interval (34, 33). In fact, these studies are a vital link between research studies and decision-making at the bedside (35, 34).

Despite relatively high stats of breast cancer in the country (36, 16) and the importance of evaluating the survival rate and the average age of the patients involved in breast cancer to evaluate therapeutic strategies and better control of risk factors for breast cancer, there is no rough estimate of the average survival age of breast cancer in Iran. This study was conducted to review studies on breast cancer survival rate and the average age of the patients involved in the entire country, from 1990 to 2016 using systematic review and meta-analysis.

Methods

This study is the first systematic review and meta-analysis to evaluate the survival rate and an average age of breast cancer patients involved in Iran from 1990 to 2016. This study is included all papers published in national and international journals, congress abstracts, conference papers, books, dissertations and reference sites. Articles were selected from internal databases such as SID, Magiran, Irandoc, Noormag, IranMedex and Medlib and international data banks including Ebsco, Cochrane, CEBM, Google Scholar, Scopus, Web of Sciences, Jama and Bandolier. The search of articles was done using Persian keywords: Iran, cancer, breast, age, survival, longevity and meta-analysis and using English keywords: Iran, Cancer, Neoplasm, Breast, Age, Survival and Meta-analysis and their compounds. Database searching was carried out with high sensitivity (High Sensitive Searching) by the researcher and senior expert in the field who were searching databases. At first, the titles of papers by the research team with the keywords were searched as it was 927. To avoid biased, the search was conducted by two researchers independently, and then the same query, and duplicates were excluded. Finally, based on mentioned inclusion and exclusion criteria, 52 article (5.6%) were analyzed (Fig 1). Then based on previous studies and surveys, the country was divided and studied into six geographical regions (38, 37).

Tehran was separately investigated because of the health, welfare and economic elite as well as a reference medical center for the other provinces. Checklist includes: name of author, year of publication, study location, time, sample size, the average age of the patients involved in breast cancer, the 1 to 5 and 10-year survival rate, survival rates based on the type of breast cancer and breast cancer stage. Because articles related to 2 to 4 years' survival and the survival rate based on the type and Stage of cancer was very low, these two factors were not examined.

Statistical analysis: In each study, after considering the age of the patients involved in breast cancer and survival rate as binomial distribution, the variance of the binomial distribution was calculated. Cochran test (Q) and I2 index were used to assess heterogeneity of

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studies. Due to the heterogeneity of studies, the random effects model for combining the results of both studies was used. Data analysis was done using specialized software for meta-analysis (Cochrane Collaboration company) called Review Manager ver: 5.3.5 and $p<0.05$ was considered significant.

Results

In this study, 927 papers were identified and after review and final assessment in accordance with designed checklist, a total 52 article containing 332,991 samples were listed. The number of articles with the subject of breast cancer survival rate was 26 and their sample size was 226,093 people. Of these, 125267 patients were (55.4 %) from Tehran, 3084 (1.36%) from the north, 3147 people (1.4%) from the south, 53855 people (23.8%) from Center, 1165 people (0.51%) from the west, 630 people (0.03%) from the east and 38812 people (17.16%) from national studies and not mentioned place (table 1). The number of articles with the subject of average age of patient with breast cancer was 41 and their sample size was 106898 people. Of these, 8358 patients (7.81%) from Tehran, 3028 patients (2.83%) from the north, 68315 cases (63.9%) from the south, 2231 cases (2.08%) from the center, 1429 people (1.33%) of the West, 8712 patients (8.15%) of the East of Iran and 14825 patients (13.86%) from national studies and not mentioned place (table 2). Based on the random effects model, 5-year survival rate for breast cancer was calculated 68.84 percent (CI-95% from 64.95 to 72.72), respectively.

As the number of studies is insufficient data for 1-year and 10-year survival rate for breast cancer, these data of survival rate has not been analyzed. Also, the average age of the patients involved in breast cancer was calculated 48.59 years (CI-95% from 46.47 to 50.72). Due to the heterogeneity of the studies (heterogeneity index for five-year survival rate: I^2= 94% and the mean age of the patients involved in breast cancer I^2 = 0%), confidence intervals for individual studies and in terms of geographic regions and by year, based on a random effects model was estimated (Fig 2).

The lowest percentage of 5-year survival rate for breast cancer was reported in the north of the country 60.65% (CI-95% from 53.58 to 67.72) and highest in Tehran 73.99% (CI-95% from 64.76 to 83.22). 5-year survival rate for breast cancer in south of the country was calculated 68.65 percent (CI-95% from 66.08 to 71.22) using a random effects model which was very close to this amount in the country (68.84%). The lowest average age of the patients involved in breast cancer in the north of the country was 45.46 years (CI-95% from 35.10 to 55.83) and the highest in the West 49.83 years (CI-95% from 32.71 to 66.95) and the mean age of patients with breast cancer in center of the country was calculated 48.42 years using random-effects model (CI-95% from 43.55 to 53.28) (Fig 2).

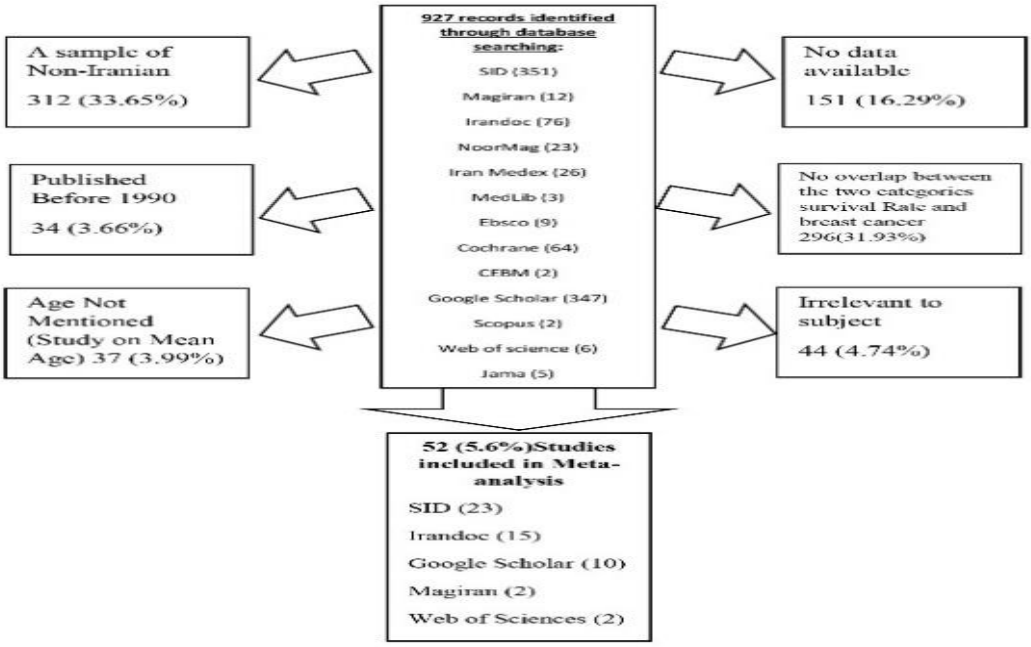

Figure 1. Flowchart of entry procedures and criteria for selecting studies in systematic review and meta-analysis

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Table 1. Profile of investigated studies related to 1, 5 and 10-year survival rate of breast cancer

Authors' name	Publication year	Place of study	Time of study	Sample size	1-year survival rate	5-year survival rate	10-year survival rate	Mean (month)
Akbari et al (39)	2006	Tehran	1995-97	154	95	76.6		
Fallahzadeh et al (36)	2014	Yazd	2002-07	200		70		
Fooladi et al (40)	2011	Ardebil	2003	161		51±0.05		
Haghighat et al (41)	2013	Tehran	1997-2006	623		87		
Yaghmaie et al (16)	2008	Semnan	1991-2001	50	86.9	58	47	
Vojdaninia et al (20)	2003	Tehran	2003	167	93	62±0.04		47.3
Makarian et al (42)	2013	Tehran	1999-2009	685				106.77
Moosavi Naeini (3)	2007	Tehran	1997-2007	242	100			
Fazeli et al (43)	2014	Markazi	2007-11	400	98	87		
Fardmal et al (44)	2013	Tehran	2004-11	542	96.8	68	31	109.7
Salehi et al (45)	2013	Tehran	2005-12	344		67.3		44.6
Bakhtiari et al (46)	2007	Babolsar		403				36
Movahedi et al (38)	2012	Top of northeast	2001-06	728	94.4±0.009	76.2±0.025		
Movahedi et al (38)	2012	North central	2001-06	625	95.2±0.005	75.3±0.015		
Movahedi et al (38)	2012	Center	2001-06	359	94.8±0.007	73.3±0.018		
Movahedi et al (38)	2012	East central	2001-06	437	91.9±0.014	69.6±0.036		
Movahedi et al (38)	2012	North	2001-06	294	96.3±0.007	69.6±0.028		
Movahedi et al (38)	2012	The lower part of the South West	2001-06	1974	95.2±0.01	68.9±0.032		
Movahedi et al (38)	2012	South Central	2001-06	221	96.4±0.013	67.4±0.052		
Movahedi et al (38)	2012	East	2001-06	430	95.3±0.01	65.7±0.046		
Movahedi et al (38)	2012	North west		1078	92.5±0.015	62.1±0.043		
Khadivi et al (47)	2012	Shahrkord		52200		62		
Akbari et al (48)	2008			441		81	77	
Rezaeian et al (49)	2099	North of Iran	2000-05	1148		58		
Moosavi et al (2)	2009	National review	1998-2005	36871		65-73		
Heidari et al (50)	2009	South of Iran	2001-06	863	97	67	45	
Gohari et al (51)	2006	Tehran	1990-2003	117				49.6
Vojdaninia et al (52)	2004	Tehran	1997	128		75		
Ghavam nasiri et al (53)	2005	Mashhad	1995-9	133		47.7		
Mosavi Naeini (54)	2009	Tehran	2009	242		89		
Rajaee fard et al (55)	2005	Shiraz	1993-2002	310		70		
Asadzadeh vostakolaei, et al (56)	2012	National	1999-2001	1500		72		
Akbari et al (57)	2014	National		122000		82		
Hedayati et al (58)	2014	Tehran	1998-2014	23		75		

*Listed numbers at the front of authors' names indicating the reference number.

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Table 2. Characteristic of the investigated studies regarding to average age of breast cancer

Authors' name	Publication year	Place of study	Time of study	Sample size	The average age of breast cancer patient
Akbari et al (39)	2006	Tehran	1995-97	154	48.11±0.5
Fallahzadeh et al (36)	2014	Yazd	2002-2007	200	48.11±29.7
Fooladi et al (40)	2011	Ardebil	2003	161	45.12±5.3
Haghighat et al (41)	2013	Tehran	1997-2006	623	46.11±3.05
Yaghmaie et al (16)	2008	Semnan	1991-2002	50	51.14±5
Vojdaninia et al (20)	2003	Tehran	1997	167	47.13±2.5
Makarian et al (42)	2013	Tehran	1999-2009	685	47.11±9.08
Moosavi Naeini (3)	2007	Tehran	1997-2007	242	48.11±3.1
Fazeli et al (43)	2014	Markazi	2007-11	400	50.1±28.36
Fardmal et al (44)	2013	Tehran	2004-11	542	46.10±6.82
Salehi et al (45)	2013	Tehran	2005-12	344	49.10±9.93
Movahedi et al (38)	2012	The top of northwest	2001-06	728	49.12±83.36
Movahedi et al (38)	2012	North central	2001-06	625	50.12±9.28
Movahedi et al (38)	2012	central	2001-06	359	49.12±83.36
Movahedi et al (38)	2012	East central	2001-06	437	49.12±83.36
Movahedi et al (38)	2012	North	2001-06	294	49.12±83.36
Movahedi et al (38)	2012	The lower part of southwest	2001-06	1974	49.12±83.36
Movahedi et al (38)	2012	South central	2001-06	221	49.12±83.36
Movahedi et al (38)	2012	East	2001-06	430	49.12±83.36
Movahedi et al (38)	2012	North west	2001-06	1078	47.11±5.58
Heidari et al (50)	2012	South of Iran	2001-06	863	46.11±3.5
Gohari et al (51)	2006	Tehran	1990-2003	117	46.11±3.5
Asadzadeh vostakolaei et al (56)	2012	National	1999-2001	1500	46±12
Yavari et al (59)	2005	Tehran	2004	203	48.9±8.8
Ebrahimi et al (60)	2002	Tehran	1997-8	266	47.12±5.5
Fathinejad et al (61)	2004	Mashhad	2002	170	41.5±5.6
Pesaran et al (62)	2003	Shahrkord	2003	176	49.11±0.3
Talei et al (63)	1997	Shiraz	1994-5	12894	>53
Asadi et al (64)	1998	Bushehr	1996-7	2842	30-65
Mahbubi et al (4)	2004	Babol	1998-99	100	39.11±7.02
Dabiri et al (65)	2002	Kerman	1998-2000	75	50.1
Naderi et al (66)	2000	Kerman	1999	2000	20-98
Omranpour et al (67)	2003	Tehran	2000-01	100	29-76
Modir et al (68)	2001	Yazd	2001	110	19-64
Hasani esfahani et al (69)	2001	Tehran	2001	110	48.10±9.4
Abbas alizadeh et al (70)	2002	Tabriz	2001	842	>30
Zakavi et al (71)	2004	Mashhad	2002-03	110	20-79
Chokar et al (72)	2000	Ilam	1998	264	>20
Ramezani et al (73)	2001	National	2000	13325	20-49
Dadkhah et al(74)	2002	Ardebil	2001	150	20-50
Abedzadeh et al (75)	2003	Kashan	2001	400	29.7±7.9
Hajimahmoodi et al (76)	2002	Tehran	2001	410	32.9±9.5
Mahoori et al (77)	2003	Shiraz	2002	1000	>35
Harirchi et al (78)	2005	Tehran	1996-2000	2343	48.8
Nafisi et al (50)	2012	Tehran	2010	650	40.9±72.58
Almasi Nokiaee et al (80)	2005	Kermanshah	2000-03	48742	45.9±66
Bakhtiari et al (46)	2007	Babolsar	2007	403	45.12±97.03
Montazeri et al (81)	2008	Tehran	2008	1402	43.14±4.4
Baeradeh et al (82)	2014	Khorasan razavi	2008	5617	18±61.5

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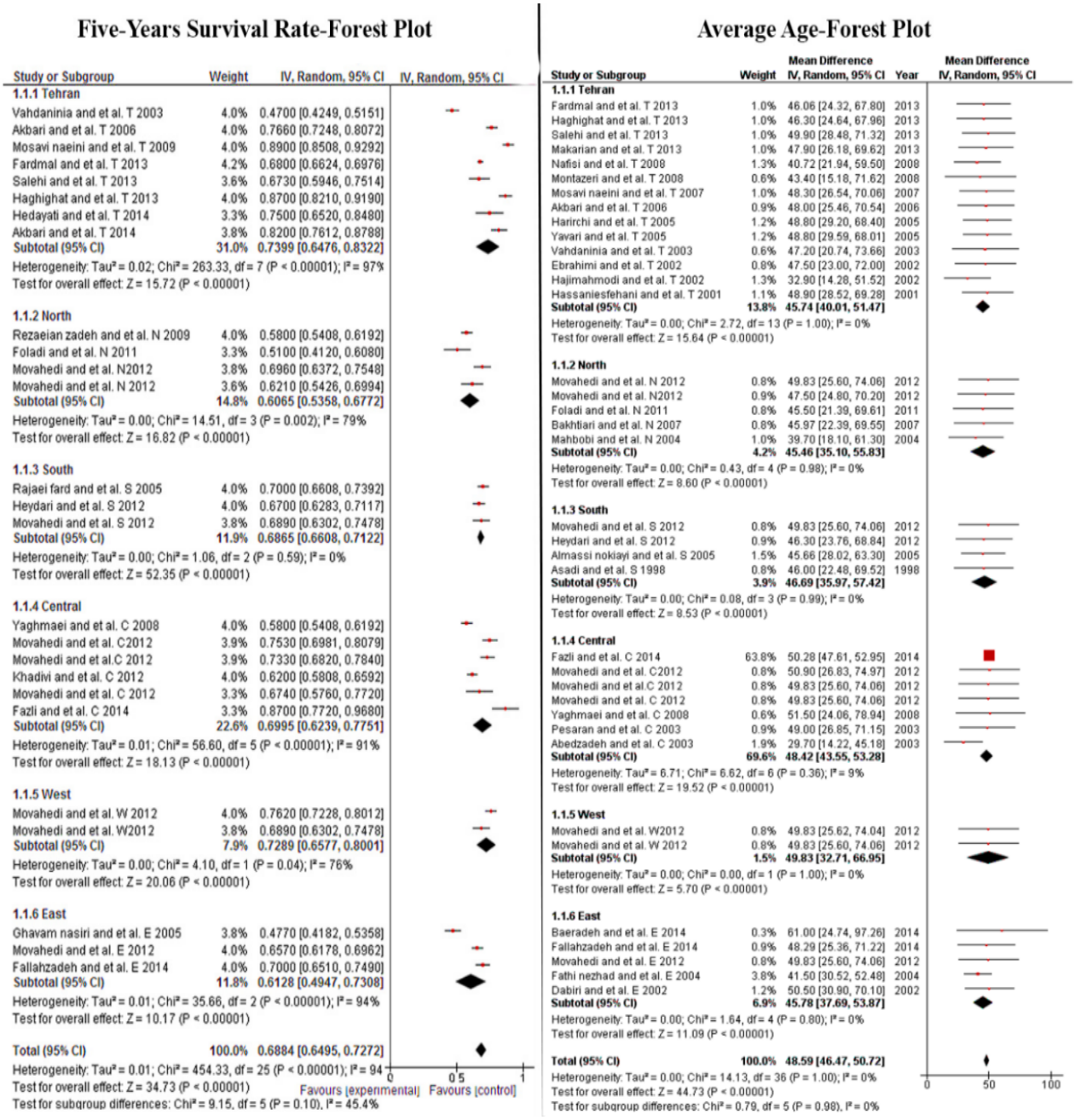

Figure 2. The estimated 5-year survival rate (left) and average age (right) in patients with breast cancer and their 95% confidence interval in the investigated studies based on authors' name and geographical regions separately (six regions: Tehran, north, south, Central, west and east) in order of year based on a random effects model. The left graph midpoint of each segment is the estimation of the 5-years survival rate, and in the right graph is the average age of the patients involved in breast cancer and the length of segment is 95% confidence interval in each geographic region. Diamond symbols in the left graph shows the overall 5-year survival rate and in the right graph shows the mean age of patients.

Discussion

This is the first systematic review and meta-analysis study aimed to investigate the survival rate and the average age of the breast cancer patients in Iran. In all 52 article, the 5-year survival rate of breast cancer in women was estimated 68.84% (CI-95% from 64.95 to 72.72) and the mean age of the breast cancer patients was calculated 48.59 years (CI-95% from 46.47 and 50.72). Protani and colleagues in their systematic review concluded that the survival rate of women with breast cancer decreases along with obesity increased body mass (1.47 and 1.21: CI-95%; HZ =1.33) (83). Radiation therapy can decrease also 10-year mortality risk of 35% to 19.3% and 15-year mortality risk from 25.2% to 21.4%, respectively (84). Results of Iranian studies (38, 2) with a survival rate of 65-72 percent, as well as the results of foreign studies (85-89) a survival rate of 72-53% confirm the results of this study. According to the report of National

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Cancer Institute of America, 5-year survival rate for breast cancer based on stage 0, 1, 2, 3, 4 are 100, 100, 93, 72 and 22 percent, respectively (90).

This difference could be due to gross disparities in health indices of the community. Results for Iranian Studies (56, 38), with a mean age range 46±12-49.83±12.36 years, although exactly is not match to the average age of the present study, but accounted for the confidence interval of this study. In addition, the results of foreign studies (92, 91), with an average age of 58.8±12.7 years, was corresponded with these results. Differences in health indicators can be one of the most important factors is the difference in the results of the above countries. Key and colleagues also showed an increased risk of breast cancer with age. During pregnancy the risk of breast cancer is higher and after that (menopause), after 50 years old was reported slower (93). The total sample size in this study were 332991 people.

The heterogeneity in 5-year survival rate of breast cancer was 94% and the mean age of patients involved in breast cancer 0% was obtained. In study of 5-year survival rate for breast cancer, it is assumed that the observed differences are due to different sampling as well as differences in the measured parameters in different societies. Based on the conducted studies, the lowest 5-year survival rate for breast cancer was reported in the north of the country 60.65% (CI-95% from 53.58 to 67.72) and highest in Tehran 73.99% (CI-95% of 64.76 to 83.22). The lowest average age of the breast cancer patients in the north of the country was obtained 45.46 years (CI-95% from 35.10 to 55.83) and highest average age in the West was 49.83 years (CI-95% from 32.71 to 66.95), respectively. According to the report of Ministry of Health and Medical Education (2011), the percentage of breast cancer in northern provinces is higher compared to other provinces (7).

However, given the importance of this issue, no study was done in Guilan province as one of the northern provinces. Some studies in the north of the country have reported a higher incidence of cancer (especially gastric cancer and esophageal squamous cells) compared to other parts of the country (94-96, 37). In this regard, in accordance with development plan policies and national health officials, healthcare, large cohort studies on cancer types in the north of the country are running by the researchers.

These studies will be discussed the major causes of a higher incidence of cancer than other places in the north of the country as well as methods of screening, prevention and treatment. According to studies, the average age and survival rate are two key factor in the management of patients with breast cancer. According to previous studies, exploration and consideration of breast cancer using different ways in the early stages of the disease and prior to lymph node involvement can cause a significant reduction in mortality and health of women (97, 89, 28).

Investigations also indicated an increased awareness and community education, the establishment of screening programs (breast self-examination (98), clinical breast examination, mammography, ultrasound and magnetic resonance imaging (MRI)) (99) and providing diagnostic and therapeutic facilities for the public especially in lower levels of society is associated with the early stage diagnosis (100-104). Thus providing the above-mentioned cases in each province based on the presence of risk factors for early detection and effective treatment of breast cancer can be placed in the health policy agenda.

Limitations: Due to a systematic review of studies, regular and systematic review of evidence, summing up of different results and providing a general interpretation resulting from studies and create a vital link between research studies and important decisions at the bedside are the points of this study. In contrast, indetermination of the qualitative value of these studies, individuals referred to treatment centers were not randomly selected, the lack of survival rate review based on breast cancer stage, the more studies from Tehran province compared to other provinces are the limitations of this study.

In addition, because the average age of the patients referred to the hospital was considered and the exact average age of breast cancer was not available due to misdiagnosis and lack of timely referral, can be considered as other limitations of this study. Breast cancer is preventable and early detection among all cancers that applying specific strategies can reduce the delay and provide effective treatment to increase patients' survival, reduce mortality and improve quality of life of patients. The average age and survival rate of breast cancer are two important factors in the management of these patients.

In addition, because the average age of the patients referred to the hospital was considerable and the exact average age of breast cancer due to misdiagnosis and timely referral was not available, can be considered as

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limitations of this study. Therefore, further studies in this area can improve the health of women and mothers in the country's socio-economic cycle and can be taken effective steps in achieving to the goal of healthy humans' sustainable development.

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