

Epidemiology and Survival Analysis of Jordanian Female Breast Cancer Patients Diagnosed from 1997 to 2002

Mohammed Tarawneh*, Kamal Arqoub, Ghazi Sharkas

Non-communicable Disease Directorate, Ministry of Health, Amman , Jordan

Abstract

Background: Breast cancer is the most common cancer among Jordanian women, yet survival data are scarce. This study aims to assess the observed five-year survival rate of breast cancer in Jordan from 1997 to 2002 and to determine factors that may influence survival.

Methods: Data were obtained from the Jordan Cancer Registry (JCR), which is a population-based registry. From 1997-2002, 2121 patients diagnosed with breast cancer were registered in JCR. Relevant data were collected from JCR files, hospital medical records and histopathology reports. Patient's status, whether alive or dead, was ascertained from the Department of Civil Status using patients' national numbers (ID). Statistical analysis was carried out using SPSS (version 10). Survival probabilities by age, morphology, grade, stage and other relevant variables were obtained with the Kaplan Meier method.

Results: The overall five-year survival for breast cancer in Jordan, regardless of the stage or grade was 64.2%, meanwhile it was 58% in the group aged less than 30 years. The best survival was in the age group 40-49 years (69.3%). The survival for adenocarcinoma was 57.4% and for medullary carcinoma, it was 82%. The survival rate approximated 73.8% for well-differentiated, 55.6% for anaplastic, and 58% for poorly differentiated cancers. The five-year survival rate was 82.7% for stage I, 72.2% for stage II, 58.7% for stage III, and 34.6% for stage IV cancers.

Conclusion: According to univariate analysis, stage, grade, age and laterality of breast cancer significantly influenced cancer survival. Cox regression analysis revealed that stage, grade and age factors correlated with prognosis, while laterality showed no significant effect on survival. Results demonstrated that overall survival was relatively poor. We hypothesized that this was due to low levels of awareness and lack of screening programs.

Keywords: Breast cancer, Jordan, Survival, Epidemiology.

Introduction

Breast cancer in women is a major health burden worldwide. It is the

most common cause of cancer among women in both developing and developed countries, and is

♦Corresponding Author:
Mohammed Tarawneh, MD
Ministry of Health, Amman,
Jordan
Tel/Fax: +96-266-565489
Email: amman992001@yahoo.com



responsible for over one million of the estimated 10 million neoplasms diagnosed worldwide each year in both sexes.¹ It is the primary cause of cancer death among women globally, responsible for about 375,000 deaths in the year 2000.¹ Statistics about breast cancer show that about 700,000 cases are reported annually, of which 57% are in developing countries.¹

In Lebanon, breast cancer is the most common cancer, which accounts for one third of all cancer cases. Of these, 49% are less than 50 years of age.² Breast cancer is the most frequent cancer among Saudi women, accounting for 19.8% of cancers in females.³ The prevalence of breast cancer in Europe and the USA is estimated between 8%-10%, however the lowest prevalence is seen in Asian countries, at about 1%.⁴ In Iran, the prevalence of breast cancer has been reported as 6.7/1000 in 2002.⁵ In Jordan, breast cancer is the most commonly diagnosed cancer among females (34.8% of the total female cancers) and represents about 18.2% of cancers that affect both sexes.⁶ As a cause of cancer mortality in women, it is second only to leukemia (24.5% vs. 9.9%).⁷

Patient survival is the most important measure of cancer patient care. Population-based studies on cancer survival, using data from population-based cancer registries, are essential for monitoring and evaluating the effectiveness of cancer management (diagnosis and treatment). Cancer survival is an essential component of a cancer surveillance system that supports cancer prevention and control.

The objective of this study is to measure the observed five-year survival rate of female breast cancer diagnosed from 1997 to 2002 in Jordan, and to investigate the impact of a wide range of factors on breast cancer survival. These factors include age of patient at diagnosis, histopathology, laterality, grade and stage of the tumor, and treatment modalities .

Materials and Methods

This historical cohort study included all Jordanian females with breast cancer diagnosed and registered in the Jordan Cancer Registry

(JCR) from 1997 to 2002. For each registered patient, socio-demographic characteristics were obtained from JCR files and hospital medical records. We obtained patients' clinical characteristics from hospital medical records. Data on morphology, grade and stage of cancer were obtained from histopathology reports submitted to JCR from public and private laboratories, in addition to medical records from private hospitals. The JCR is a population-based registry that receives cancer notification forms from all health sectors in Jordan by utilizing active and passive data collection..

Vital status of included patients (whether alive or dead) and dates of their last visits were obtained from medical records. Vital status was ascertained from the Department of Civil Status using patients' national Identification numbers (ID).

Patients were observed for five years from the date of diagnosis to the last date of follow up. The cut off point was 31/12/2007 for those diagnosed in 2002. Patients diagnosed in 1997 were observed until 2002. The follow up end point was death from any cause. Each patient was followed until death, loss of follow up, or until the end of the data collection period (alive). A data collection form was designed to collect data about all the above-mentioned variables and was completed by trained personnel.

Data management and statistical analysis

Data was analyzed using the Statistical Package for Social Sciences Software (SPSS), version ¹⁰. Frequencies and percentages of demographic and clinical characteristics of the patients particularly age, gender, tumor morphology, stage, grade, and treatment were analyzed. The Kaplan Meier method was used to determine survival probability over time where the effect of age, grade, laterality, stage and type of treatment on five years survival of the patients was determined in addition to the survival curves of these variables by generating the characteristic "stair step" survival curves.⁸

Overall survival rate was estimated by Kaplan-Meier, using the exact survival time (differentiated from life table actuarial method) univariate

analysis. Log rank test was used to estimate P values to determine significant associations between the variables and survival rate. P less than 0.05 was considered statistically significant. Survival probabilities by age, morphology of cancer, laterality, grade, stage and treatment were obtained. Multivariate analysis as Cox proportional hazard regression was used to assess the independent effect of each variable after simultaneously controlling for the effects of potential confounders.

Breast cancer cases were coded as C50.0-C50.9 according to the International Classification of Diseases (ICD-O-3). Tumor laterality was divided by right, left, bilateral or classed as unknown.

Tumor morphology was categorized as ductal, lobular, medullary, adenocarcinoma, mixed carcinoma, and other. The tumor grade was divided into well, moderate, poorly differentiated, and anaplastic. Cancer stage was classified according to the American Joint Committee on Cancer (AJCC) staging of tumor (T), node (N), and metastasis (M), which was classified into four stages: stage I, stage II, stage III, stage IV, and unknown.

Results

Age distribution of patients

Table 1 shows the distributions of breast cancer patients by age group & clinical characteristics of the studied patients. Approximately half of the patients were above age 50 years and 28% were

in the age group of 50-59 years. Those below the age of 30 years accounted for 2.7% of cases, meanwhile those above age 70 years accounted for 7%. The mean age of patients was 50.1 ± 12.1 years and the median age at cancer diagnosis was 50.6 years.

Clinical characteristics

The left breast was affected more than the right (49.2% vs. 46.5%), and 1.8% of cases had bilateral cancer. According to tumor morphology, 74.6% of cases were diagnosed as ductal carcinoma, 6.9% were lobular carcinoma, 7.3% were not otherwise specified (NOS) carcinoma, and the remaining 1.6% were diagnosed as medullary carcinoma. According to the tumor grade, it was noted that 46.1% were moderately differentiated carcinomas, 43.5% were poorly differentiated, and 6.6% were well differentiated. A total of 17.7% of the cases were diagnosed at stage I, 34.6% at stage II, 29.6% at stage III, and 16.5% were diagnosed at stage IV.

According to treatment received, about 60.5% received triple therapy (surgery, chemotherapy and radiotherapy); 20.7% received combined surgery and radiotherapy; 11% received combined surgery and chemotherapy; and only 4.1% received surgery alone.

Survival analysis

Cases that could be followed were included in the study, however for reasons previously

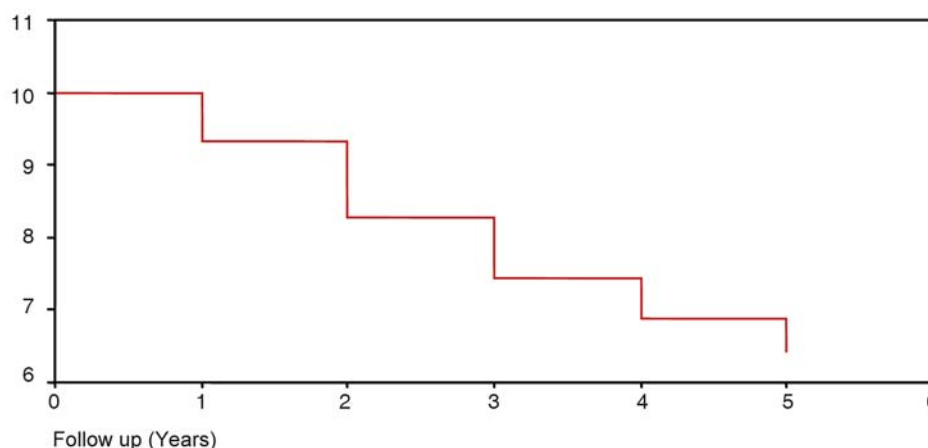


Figure 1. Overall survival rate of breast cancer patients in Jordan 1997-2002

Table 1. Distribution of Breast cancer cases registered from 1997 to 2002 by age group, clinical characteristics & vital statistic of the patients.

Demographic and clinical variable	Frequency	%
Age group (years)		
<30	58	2.7
30-39	372	17.5
40-49	570	26.9
50-59	595	28.0
60-69	376	17.7
≥70	150	7.1
Tumor laterality		
Right	986	46.5
Left	1044	49.2
Bilateral	39	1.8
Unknown site	52	2.5
Morphological type		
Ductal carcinoma	1583	74.6
Lobular carcinoma	146	6.9
Mixed lobular and ductal carcinoma	41	1.9
Medullary carcinoma	33	1.6
Carcinoma NOS (not otherwise specified)	155	7.3
Adenocarcinoma	54	2.5
Other types	109	5.1
Tumor grade		
Well differentiated	141	6.6
Moderately differentiation	977	46.1
Poorly differentiated	922	43.5
Anaplastic	36	1.7
Unknown grade	45	2.1
Tumor stage		
Stage I	376	17.7
Stage II	734	34.6
Stage III	625	29.5
Stage IV	350	16.5
Unknown	36	1.7
Treatment received		
Surgery	88	4.1
Surgery and radiotherapy	440	20.7
Surgery and chemotherapy	235	11.1
Surgery, radiotherapy and chemotherapy	1285	60.5
Unknown	73	3.4
Vital Status		
Alive	1363	64.3
Dead	758	35.7

mentioned there was some missing data of the study population. The total number of patients registered from 1997 to 2002 that included in the survival analysis were 2121 out of approximately 3000 patients registered in the JCR, the remaining cases were not eligible for the study as too many missed variables were present which made the follow up of those patient very difficult.

At the time of data analysis, we had survival information from 1363 patients of which 758 had expired (35.4%) as shown in Table 1. The period of follow up ranged from one day to five years.

The overall survival rates of patients are presented in Table 2 and Figure 1. The five-year survival rate of breast cancer in Jordan was 64.2%. The survival rates for the first year was 93.1%, for

the second year it was 82.7%, the third year was 74.33%, and the fourth year survival rate was 68.7%. This table represents the survival by 6 month intervals from 6-60 months duration.

Tables 3,4, and Figures 2-6 show the five-year survival of patients by age group, laterality, morphology, grade, tumor stage and treatment. Only the age group, laterality, grade and stage showed statistically significant associations with survival by the univariate analysis log rank test ($P < 0.05$). Table 5 shows the Cox proportional hazard regression analysis that was performed to assess the independent effect of different prognostic factors after simultaneously controlling for the effect of potential confounders. Initially the following variables were entered in this model: age group, morphology, laterality, grade, stage, and treatment modalities. Cancer morphology and treatment modalities did not significantly affect survival rate ($P \geq 0.05$). Age group, laterality, grade and stage of cancer significantly affected the survival rate and were retained in the final model of analysis. Table 5 shows the hazard ratio and significance of the above mentioned four variables. The best survival rate was observed in patients diagnosed at stage I when compared with other stages, which was statistically significant ($P \leq 0.000$). Tumor grade affected survival, but to a lesser extent than tumor stage ($P = 0.01$). Patients with well differentiated tumors had better survival than other grades ($P \leq 0.05$); age group also affected survival significantly but to a lesser extent than

tumor stage ($P = 0.01$). With regards to laterality of the cancer, we found that when both breasts were affected, patients survived less than when the right or the left breast alone were affected, however the difference was not statistically significant ($P = 0.06$).

Discussion

This study provides substantial information about epidemiology of breast cancer in Jordan; it reports the survival rate of female breast cancer patients registered during 1997-2002. The five-year survival rate for breast cancer in Jordan regardless of the stage or grade of tumor was 64.2% compared with 59.6% reported from a previous study conducted in Jordan during 1997-1998.⁹ This could be explained by improved health care facilities and cancer management.

A study conducted in Oman reported the overall survival rate to be 64%¹⁰ which was similar to the results reported from Iran (62%).¹¹ The survival rate of breast cancer among Malaysian women was 59.1%.¹² Similar results have been reported from Saudi Arabia where breast cancer is the most frequent cancer and accounts for 19.8% of all female cancers. In Saudi Arabia, the observed survival probability at one year was 93.3%, at three years it was 79.2%, and at five years it was 59.6%.³ Survival from breast cancer in developed countries approached 80%. The Surveillance Epidemiology and End Results (SEER) five-

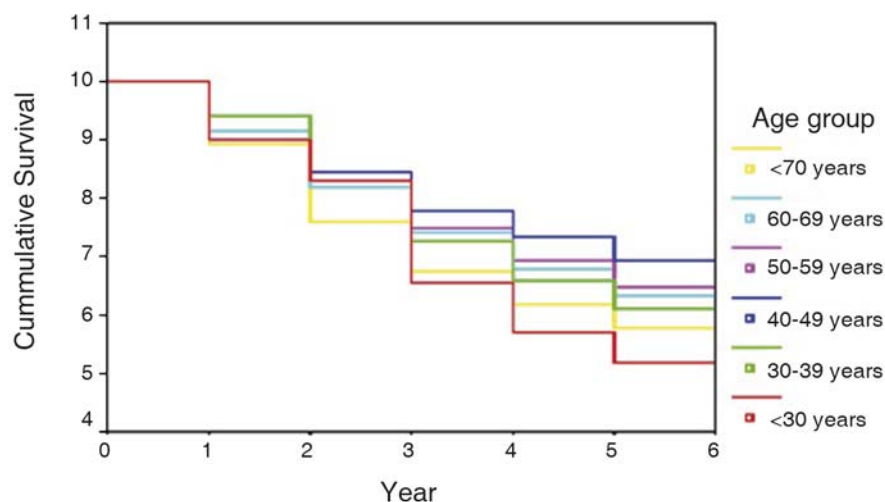


Figure 2. Overall survival rate of breast cancer patients in Jordan 1997-2002 by age group.

Table 2. Overall survival rate of female breast cancer patients during the period from 1997 to 2002 (N=2121).

Follow up (months)	Number of cases	Number of deaths	Cumulative survival (%)
0-5	2121	51	97.6
6-11	2070	89	93.3
12-17	1981	98	88.7
18-23	1883	117	83.2
24-29	1766	103	78.3
30-35	1663	75	74.7
36-41	1588	77	71.1
42-47	1511	41	69.2
48-53	1470	54	66.6
54-59	1420	57	64.2

year survival rates in the United States in 1990 was 89%, in European countries the rate was 79%,¹³ and in less developed countries it was 59.6%.³ In Bahrain, the survival rates were 68.6% after five years, 57.3% after seven years, and 36.4% after ten years which was slightly higher than our results. This could be due to national screening programs and early detection of breast cancer in Bahrain.¹⁴ Consistent with other studies,¹⁵ this study reported that the overall survival rate was low in the age group less than 30 years (58%), which could be explained by more aggressive disease (faster metastasis, short lead time, higher recurrence rate) as more cases were diagnosed at stages II and III; incomplete inclusion of other causes of death; and higher frequency of undifferentiated tumors. On the contrary, Milena et al. reported that in the United States breast cancer

patients less than 35 years of age had an overall five year survival rate of 65%, whereas the ten year survival rate was 49%.¹⁶

Our study revealed that TNM staging at diagnosis, laterality, grade and age group had an important, significant effect on survival rate for breast cancer in Jordan. Cox Proportional Regression analysis showed that tumor stage was the most important factor that influenced survival analysis after controlling for other factors. Grade and age were less important for survival rate and laterality did not affect survival in regression analysis. Meanwhile, tumor morphology and treatment showed no statistically significant effect on survival rate according to univariate analysis. A statistical association between survival rate and laterality on univariate analysis was seen; the five-year survival rate was 65% in the right breast,

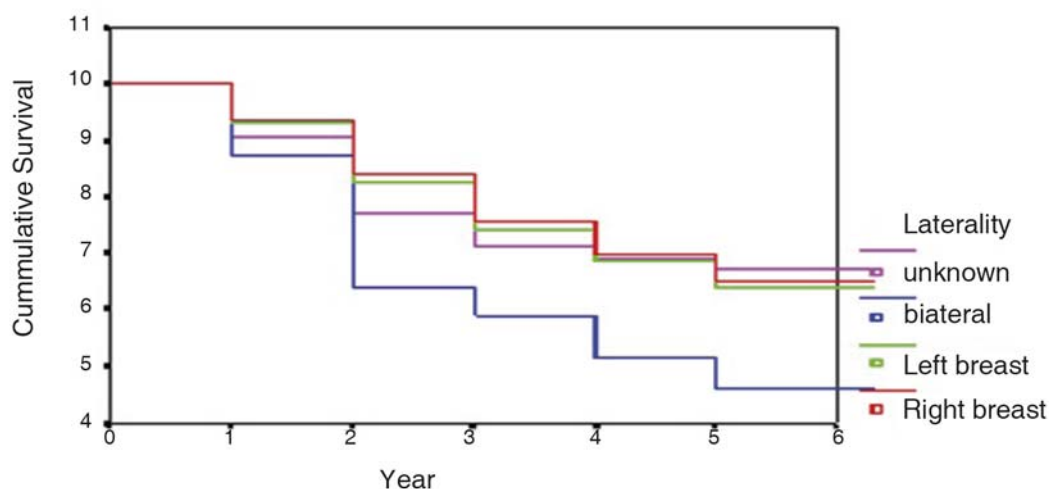
**Figure 3.** Overall survival rate of breast cancer patients in Jordan 1997-2002 by laterality.

Table 3. Overall survival rate of breast cancer patients from 1997 to 2002 by age group, morphology, grade and laterality.

Variable	No. of cases	No. of deaths	Mean survival time years (C.I.)	Cumulative Survival rate (%)
Age group (years)				
<30	58	28	3.8 (3.4-4.2)	51.7
30-39	372	145	4.0 (3.8-4.2)	61.0
40-49	570	175	4.2 (4.1-4.3)	69.3
50-59	595	209	4.1 (4.0-4.2)	64.9
60-69	376	138	4.0 (3.9-4.2)	63.3
≥70	150	63	3.8 (3.5-4.1)	58.0
Tumor morphology				
Ductal carcinoma	1583	572	4.1 (4.0-4.2)	63.9
Lobular carcinoma	146	49	4.2 (3.9-4.4)	66.4
Mixed lobular and ductal	41	17	3.9 (3.4-4.4)	58.6
Medullary carcinoma	33	6	4.6 (4.1-5.0)	81.8
Carcinoma	155	61	3.8 (3.6-4.1)	60.7
Adenocarcinoma	54	23	3.7 (3.2-4.1)	57.4
Other types	109	30	4.3 (4.0-4.6)	72.5
Tumor grade				
Well differentiated	141	37	4.4 (4.2-4.6)	73.8
Mod. differentiated	977	318	4.2 (4.1-4.3)	67.5
Poorly differentiated	922	387	3.9 (3.8-4.0)	58.0
Anaplastic	36	16	3.7 (3.1-4.0)	55.6
Laterality				
Right	986	345	4.1 (4.0-4.2)	65.01
Left	1044	375	4.1 (4.0-4.2)	64.08
Bilateral	39	21	3.4 (2.8-4.0)	46.15

Log rank test (age group) 14.98 *P* value 0.01 , Log rank test 11.16 , *P* value 0.08 (morphology)
 Log rank test 47.7 *P* value 0.000 (grade), Log rank test 14.9, *P* value 0.04 laterality.

64% in the left breast and only 46% for bilateral breasts. This was probably explained by more aggressive disease in patients with bilateral breast tumors. The TNM stage proved to be the most significant independent prognostic factor for determining survival rate. In our study,

approximately 52.3% of patients were diagnosed at stages I and II while in a study conducted in Canada about 75% of the patients were diagnosed at stages I and II.¹⁵ This could probably be explained by the implementation of screening programs for high risk groups through regular

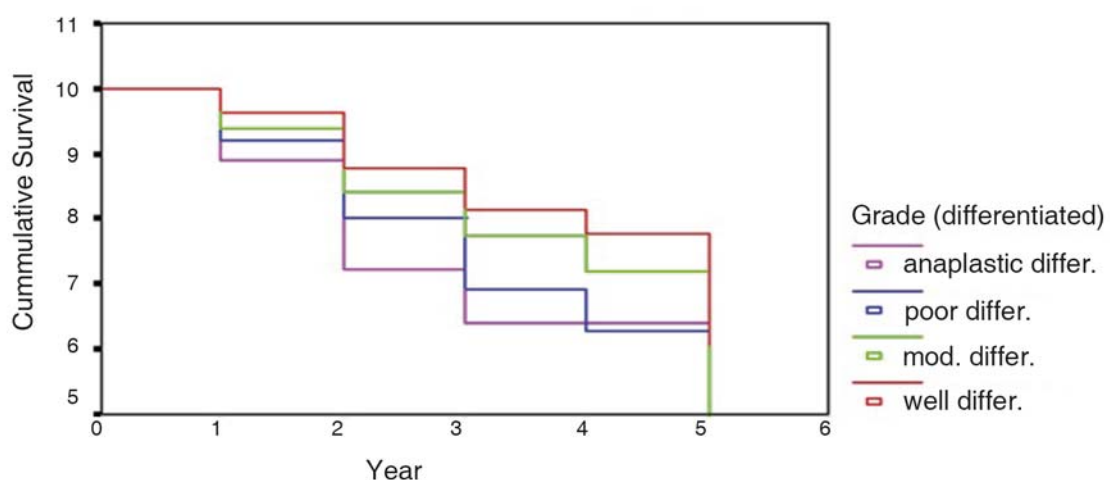
**Figure 4.** Overall survival rate of breast cancer patients in Jordan 1997-2002 by grade.

Table 4. Overall survival rate of breast cancer patients from 1997 to 2002 according to tumor stage and treatment.

Variable	No. of cases	No. of deaths	Mean survival time years (C.I)*	Cumulative survival rate (%)
Tumor stage				
Stage I	376	65	4.6 (4.5-4.7)	82.7
Stage II	734	204	4.4 (4.3-4.5)	72.2
Stage III	625	258	3.9 (3.8-4.0)	58.7
Stage IV	350	229	3 (2.8-3.2)	34.6
Type of treatment				
Surgery	50	15	4.2 (3.8-4.7)	70.00
Surgery and radiotherapy	229	77	4.0 (3.8-4.2)	66.38
Surgery and chemotherapy	121	55	3.6 (3.3-4.0)	54.55
Surgery, radiotherapy, and chemotherapy	690	279	4.0 (3.9-4.1)	59.57

Stage: Log rank test 291 *P* value 0.001Treatment :Log rank test 6.7 *P* value 0.083

mammography in combination with regular clinical examinations, which may increase the detection rate of cancer in its early stages. In our study, it was found that the five-year survival rate was 82.7% for stage I, 72.2% for stage II, 58.7% for stage III, and 34.5% for stage IV. Data from Bahrain showed that the five-year survival rate ranged from 87.5% for stage I to 48% for stage IV which differed from our study results. This could be explained by the different types of treatments provided for patients.¹⁴ A study from southern Iran has shown a survival rate of 58%, which considered relatively low when compared with our results. Results from other countries have explained this due to delayed diagnosis which resulted in patients presenting with late stage disease that was most probably due to low level of awareness and cultural barriers.¹⁷

The strength of this study is that it is a population-based study comprising virtually all histologically verified cases registered in JCR. Cases have not been subjected to selection bias, which occurs in studies dependent upon sample selection. The sample size was sufficiently large to examine the effect of modifications and to perform survival analysis across different subgroups of breast cancer. The study limitations included inadequate medical documentation and incomplete data in some patients files, and detailed causes of death were not reported for some patients. Since the exact cause of death in population-based studies is not usually clearly determined, thus we have considered cancer to be the cause of death unless otherwise specified.

This study proves that tumor stage is an important factor that influences survival of the

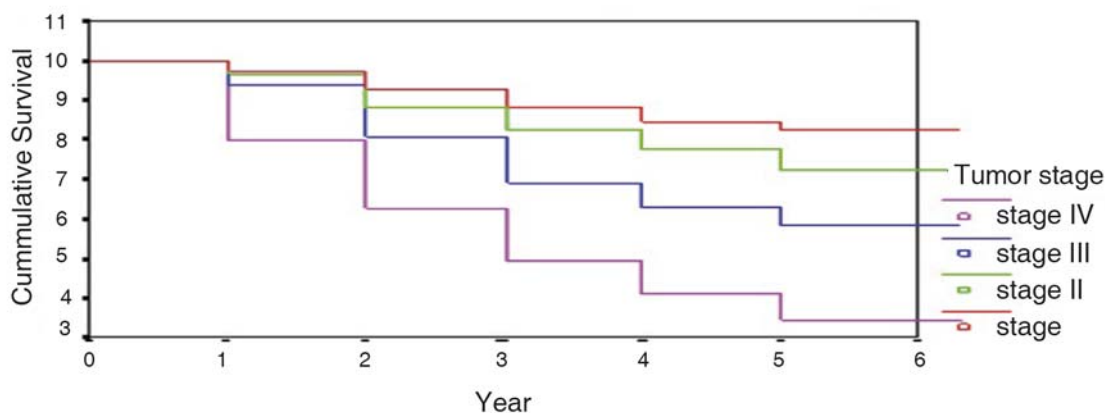
**Figure 5.** Overall survival rate of breast cancer patients in Jordan 1997-2002 by Tumor stage.

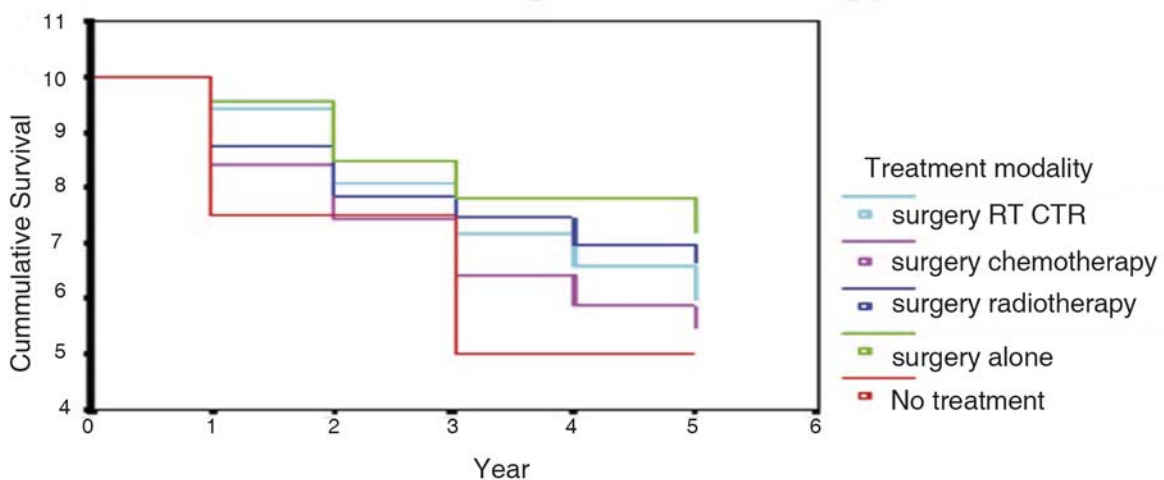
Table 5. Cox regression analysis (multivariate analysis) of surviving breast cancer cases from 1997-2002 by different factors.

Variable	Hazard ratio	95% Confidence interval	P value
Stage			0.00
Stage I	2.7	0.67-11.2	0.02
Stage II	4.5	1.1-18.3	0.03
Stage III	7.5	1.8-30.1	0.005
Stage IV	15.5	3.8-62.6	0.000
Grade			0.017
Well	1.2	0.8-1.7	0.23
Moderate	1.5	1.09-2.1	0.03
Poor	1.7	0.98-3.1	0.013
Anaplastic	2.7	1.4-6.5	0.011
Laterality			0.06
Right	1.059	0.93-3.31	1.7
Left	1.333	.61-1.6	0.997
Bilateral	1.1	.59-1.5	0.962
Age group(years)			0.01
< 30	1.1	0.74-1.8	0.51
30-39	0.89	0.66-1.19	0.43
40-49	0.66	0.499-0.89	0.006
50-59	0.78	0.59-1.03	0.088
60-69	0.83	0.61-1.12	0.224
≥70	0.97	1.2-2.2	0.32

cancer patient, therefore early diagnosis and detection is an important issue in improving patient survival. Since early diagnosis and prompt treatment have an important role in improving survival rate, therefore a screening program for high risk groups (women above 40 years) may improve early detection, survival, and eventually reducing mortality. Secondly, public health education programs and training courses regarding breast self-examinations for all high risk groups

in co-operation with all health sectors are essential. Complete documentation of cancer patients' files and medical records in hospitals and laboratories (histopathology reports) are important issues for survival studies.

Further population-based studies are recommended to identify other variables that may affect the survival rate such as demographics, clinical variables (estrogen and progesterone receptors), and the number of lymph nodes

**Figure 6.** Overall survival rate of breast cancer patients in Jordan 1997-2002 by treatment.

affected with the intent to compare if there is improvement in survival in the future.

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