*Available online at* www.scholarsresearchlibrary.com

Scholars Research Library

**Der Pharmacia Lettre, 2015, 7 (8):232-236**
***(http://scholarsresearchlibrary.com/archive.html)***

ISSN 0975-5071
USA CODEN: DPLEB4

# Factors associated with survival of patients with breast cancer

**Mansour Rezaei[1], Omid Beiki[2], Amir Hossein Hashemiann[3], Afshin Almasi[4], *Elahe Saleh[5], Somayeh Bakhshi[6]**

*[1]Associate Professor of Biostatistics of Behdasht, Faculty, social development and health promotion Research Centre, University of medical sciences, Kermanshah, Iran.*
*[2]Assistant Professor of epidemiology Faculty of health, Kermanshah University of medical sciences, Kermanshah, Iran.*
*[3]Assistant Professor of Biostatistics, Faculty of health, Kermanshah University of medical sciences, Kermanshah, Iran.*
*[4]Doctoral course student in biostatistics, school of medical sciences, Tarbiatmodares University, Tehran, Iran.*
*[5]** Responsible author:Msc student of Biostatistics and epidemiologyDepartment, "Student Research Committee", Kermanshah University of Medical Sciences, Kermanshah, Iran, e. saleh3 @ ymail.com*
*[6]Msc student of Environmental Health Engineering Department, "Student Research Committee", Kermanshah University of Medical Sciences, Kermanshah, Iran*

---

**ABSTRACT**

*Breast cancer is the most common cancer and the second leading cause of death due to cancer in women after lung cancer.Breast cancer is a major public health problem all around the world. In cancer, patient's survival has been accepted as the main criteria for cancer control and measuring the treatment impact. There are different methods for survival estimation. Cox model is the most known statistical applied model for evaluating the relationship between survival time and other variables. In this historical cohort study, studied individuals in this group include breast cancer patients who their data exist in American Cancer registration system during the 1973to 2010. Totally 679967 patients were studied.The relationship between age, job, race, marital status and grade with the survival was evaluatedat the time of diagnosis and Cox model has been used for checking these variables with the individual survival. The variables including race, marital status, age in time of diagnosis, grade, and job were factors related to the patient's survival.(P<0.05) The initial training for timely detection of disease in first stages of disease increases the individuals` life length. Necessity ofexistingcancer registry system exists in Iran is inalienable.*

**Key words:** Breast cancer, Cox model, survival

---

## INTRODUCTION

Breast cancer is the most common cancer and the second leading cause of death due to cancer in women after lung cancer[1]. Breast cancer is a major public health problem all around the world [2]. According to the country`s total statistics, breast cancer is the most common cancer in women in Iran also and about 6160 cases show per year[3] and 1063 people dies of this disease[4]. In the United States, in 2003, more than 203500 new cases of breast cancer were found and 39600 women died of that. [5]The incidence of deaths caused by it has been reported the highest in North America and North European countries, the average in south America and south Europe, and the lowest in Asia and African countries that genetic , environmental and social factors can be named as the effective factors. [6]. In cancer disease, patience survival has been accepted as the main standard for cancer control and measuring the treatment impact. [7] Survival means the proportion of patients who stay live in a specified period of time that is such a simple concept, but there are different ways to estimate that. In general there are 3 Regression model for survival data: The Cox proportional hazards model as a half parameter method[8],speedy failure time methods such

as Vibel, viewing and normal stork as parametric methods [9] and Allen collective hazards model as a non-parametric method.

In survival data modeling, one of the main objectives is determining effecting factors survival period. Also with modeling, survival function for each individual in any time can be achieved. That's why in various studies, Cox proportional hazards models fitted with the length of patients lifetime, has been addressed.[11-13] Cox model is the most applicable and known statistical model for studying the relation between survival time with helping variables but there is an important and basic default in this model and that is the theory of the danger being fit for all independent variables existing in final model. In case of this theory establishment, resulted model commentary will be simpler than parametric models.[9, 10, 14]

In this study, the follow-up period is long [Almost 40 years], as well as the number of subjects is very high [679967]. Such features [long term follow-up and the large number of patients] have made this research distinctive fromsimilar researches in this field. The aim of this study was to evaluate different variables relation with the patient's survival by Cox model. Applied software in this research was spss16.

**Working method:**
This study has been carried out by historical cohort. The study group consisted of patients with breast cancer that theirdataexist in America cancer registration system during years 1973 to 2010 and their illness has been definitely recognized. This number equals to 679967 individuals.It should be noted that the license for data using has been acquired by Dr. Omid Beikiconcluding a contract with the American Cancer Institute and age, marital status, race, grade and involved part with the disease variables have been evaluated. Used model in this study, is Cox model. Cox regression model, assumes a half-parametric model for hazard function estimation that explanatory variables or factors` risk can be added to its model but the basic hazard function should be saved as the uncertain function but nonnegative time. Cox hazard function for X explanatory variable is as follow(15):

$$\lambda(t;x) = \lambda_0(t)\exp(X'\beta)$$

According to this model, basic hazard of $\lambda_0(t)$ is the function hazard for the individual who his explanatory variable is zero. As it is not assumed that this basic hazard function has a parametric form, Cox model is called a half-parametric model for hazard function. The survival function fit for this model will be as following (16):

$$S(t;x) = \exp\left[-\exp(X'\beta)\int_0^t \lambda_0(u)du\right]$$

This Integral is called basic hazard accumulating function which there are different methods for estimating it (9). Cox model is the most applicable for finding the relation between the explanatory variables with survival respond or other respondent variable which is censured from right (17). Yet this model has some limits too. One of the limits of this model is fitted hazard theory. This means that the hazard amount between two or more groups of explanatory variable should remain stable during survival period that the theory will be defined according to basic accumulating function.

Of the ethical considerations of this research in using these data, sometimes we faced with some deficiencies that their completeness was impossible. Therefore regarded to them as lot cases and did not enter them to the analysis. Of other problems we faced with in this research was incapability of evaluating other variables such as Estrogen, Progesterone receivers, treatment method and ….which had been evaluated in other researches, but because of failure in collecting these variables during this period, their evaluation was canceled.

## RESULTS

In table 1, distribution frequency of the studies patients'` characteristic, is displayed.

According to table 1, age average in time of diagnose is 61.42 and most of patients with breast cancer are white and married. Approximately the individual affluence by side involved with cancer (left or right breast) is the same and few of them are involved in both sides and as it can be seen in table 1, just few people are registered in America`s cancer registration system in grade 1 (seer) and most people are registered with high grades.

**Table1: Distribution frequency of characteristics of patients with breast cancer**

| Variable | frequency | Percent |
|---|---|---|
| Grade | | |
| Grade I | **79312** | 11.7 |
| Grade II | **174497** | 25.7 |
| Grade III | **155783** | 22.9 |
| Grade IV | **18424** | 2.7 |
| Unknown | **251951** | 37.1 |
| LATERALITY | | |
| Right | **328883** | 48.4 |
| Left | **343116** | 50.5 |
| both sides | **999** | 0.1 |
| Unknown | **6969** | 1 |
| Marital status at diagnosis | | |
| Single | **72203** | 10.6 |
| Married | **377302** | 55.5 |
| Divorced | **59995** | 8.8 |
| Widowed | **135451** | 19.9 |
| Unknown ,other | **35016** | 5.1 |
| Race | | |
| White | **576643** | 84.8 |
| Black | **56684** | 8.3 |
| Unknown ,other | **46640** | 6.9 |
| Age at diagnosis | Average | 61.42 |
| | Standard Deviation | 15.98 |

**Table 2: Cox model estimation results**

| Variable | HR | Standard Deviation | Z | P value | 0.95 CI FOR HR | |
|---|---|---|---|---|---|---|
| | | | | | Lower bound | Upper bound |
| LATERALITY | | | | | | |
| *Left | | | | | | |
| Right | 0.92 | 0.36 | -2.23 | 0.026 | 0.84 | 0.99 |
| both sides | 4.50 | 1.1 | 6.14 | <0.001 | 2.73 | 7.26 |
| Race | | | | | | |
| *Black | | | | | | |
| White | 1.71 | 0.18 | 5.12 | <0.001 | 1.39 | 2.11 |
| Marital status at diagnosis | | | | | | |
| *Married | | | | | | |
| Single | 0.8 | 0.05 | -3.47 | <0.001 | 0.71 | 0.91 |
| Divorced | 0.62 | 0.048 | -6.2 | <0.001 | 0.53 | 0.72 |
| Widowed | 0.37 | 0.03 | -14.14 | <0.001 | 0.32 | 0.43 |
| Age at diagnosis | 1.01 | 0.005 | 27.11 | <0.001 | 1.012 | 1.014 |
| Grade | | | | | | |
| Grade I | | | | | | |
| Grade II | 1.63 | 0.1 | 7.91 | <0.001 | 1.44 | 1.84 |
| Grade III | 1.46 | 0.09 | 5.98 | <0.001 | 1.29 | 1.66 |
| Grade IV | 1.39 | 0.16 | 2.84 | 0.005 | 1.11 | 1.76 |

*In table 2, the reference level, is signed by**

According to the results in table 2, all evaluated variables are in Alpha 0.05 significant level and are effective on individuals' survival period. The results in table 2 show the reality that respectively risk of death for the patients who both sides are involved with cancer (left and right) is 4.50 times more than the ones having cancer in left side and possibility of death for the patients with right side only involved with cancer, is less than the ones in left side (0.92). Possibility of death for white skinned is 1.71 more than blacks. Also possibility of death for patients who are in grades 2, 3 and 4 of the disease, in compare with the people in grade 1 of illness are: 1.63, 1.46 and 1.39. In other words as the patient is on highest grade of the illness, death risk increases.

Of other factors effective on individual`s survival, is marital status. Relative death risk for single people, divorced and widows in compare with the married ones is less and is 0.80T 0.62 and 0.37. Also regarding to the above table, age in time of diagnosis, is an effective factor on survival duration and as the age is lower in time of diagnosis, survival duration is higher.

## CONCLUSION

The research results showed that the age average of individuals involved with breast cancer is 61.42 that this is less than the age average in Iran which is between 45-53 years old and defines that in our country, women involve with

the disease in lower ages (3). Regarding to the results of table 2, most people are in grades 1-3 and just 0.02 of people are in grade 4 of the disease, the grade in which the disease has been improved and metastases to other parts and needs more critical and wider treatments that regarding to KhodaBakhshi`s study, most of the studied people in this research have been in grades 2 and 3. This research results define that there is a significant relationbetween the age in time of diagnosis and marital status with the patients' survival. This result complies with the results gained from the study of CK Gajalakshmi and colleagues. Also in CK Gajalakshmi study, marital status is also evaluated and marital status has been regarded as reference group. In this study the risk in widows is less than reference group but related death risk in singles is more than the reference group which is against this research result (19). In Cohoroti study performed by Rajayeefard and his colleagues, the results showed that the main factors effective on death are the disease stage and patient`s age. Relative death risk in patients with higher disease stage, had been 20.5 times more, in patients with a higher degree of malignancy,2.62 times, in patients with history of benign tumor 4.15times and 4.4 times in older patents. Between the survival periods of patients in above groups, a significant relation has been showed. The patients who were in the first stages of the disease, in compare with the patients in the improved stage or metastasis, were more hopeful. The death risk is more for patients in more advanced stage of the disease, higher malignancy degree, higher age and with history of benign tumor(20). In Cohort study performed by Gohari and his colleagues during years 2005 and 2007 on 133 women patients involved with breast cancer who had been referred to ShahidfayazBakhsh hospital in Tehran, showed that higher age and higher disease stage variables have more risk ratio with survival rate. Although, they were not statistically significant (22).

In partial study by Gohari, survival rate has relationship with the tumor malignancy degree and is defined as one ofsurvival prognosis providers. Patients with malignancy degree level 3, face death 1.69times more that patients in level 2. Tumor malignancy degree and number of involved groups is effective on survival but no reason was found on the prognosis providing role of tumor size and patient`s age (23).

In other researches performed by Akbari and his colleagues on 154 patients involved with breast cancer, the results showed that the patients with tumor in left breast lived longer than the ones with tumor in right part. 87.5% against 76.5%. Age less or more than 50 years, had no effect on life duration alone (24). According to the above results the disease grade is of effective factors on survival which shows that as the patient be informed about his(her) illness sooner, the risk is less and the possibility of survival is higher.It doubles the place of necessary training for timely detection of the illness by the individual.

Other necessity which is felt in our country is the cancer registry system existence that makes basic steps toward upgrading the knowledge of cancer improving phenomenon that should be implemented here.

**Acknowledgments**
The authors appreciated the Research council of Kermanshah university of medical science, Biostatistics Department, for the financial support Kermanshah, Iran." This article is based on theses of postgraduate students of Biostatistics-Elahe saleh-in Biostatistics Department, Kermanshah University of Medical Sciences, Kermanshah, Iran."

## REFERENCES

[1] Parkin DM, Bray F, Ferlay J, Pisani P. *CA Cancer J Clin* **2005**;55:74-108.
[2] Boy leP, Ferlay J.,(**2004)** .*Ann Oncol* **2005**:16:481-488.
[3] Collaborative Group on Hormonal Factors Breast Cancer. Breast cancer and hormonal contraceptives: Collaborative reanalysis of individual data on 53297 women with breast cancer and 100239 women without breast cancer from 54 epidemiological studies.*Lancet* (**1996**);347:1713-1727.
[4] Collaborative Group on Hormonal Factor in Breast Cancer. Breast cancer and hormonal replacement therapy: Collaborative reanalysis of individual data from 51 epidemiological studies of 52705 women with breast cancer and 108 411 women without breast cancer. *Lancet* (**1997)**;350:1047-1059.
[5] Chia KS, Du WB, Sankaranarayanan R, et al. *Int J cancer* (**2001)**;93:142-147.
[6] Kuru B. *Eur J Surg Oncol* (**2006**);32:1082-1088.
[7] Parkin DM. (**2000)**.*Lancet Oncol* 2001;2(9):533-43.
[8] Cox DR, *Stat Soc* (**1972)**;34:187-220.
[9] Klein JP, Moeschberger ML. Survival analysis techniques for censored and truncated data. New York: Springer-Verlag (**1997)**.
[10] HosmerDW,Lemeshow S. Applied survival analysis:Regression modeling of time to event data. New York, John Wiley & Sons, (**1999**).
[11] Kleinbaum GD, Muller EK, Nizam A. Applied regression analysis and multivariable methods. New York:Springer (**1998)**.

[12] Vahdaninia M, Montazeri A. *Asian Pac J Cancer Prev* (**2004)**;5(2):223-5[Persian].
[13] MousaviSM,MohagheghiMA,MousaviJerrahiA,NahvijouA,Seddighi Z. *Asian Pac J Cancer Prev* (**2008)**; 9(2):275-78[Persian].
[14] CollettD,Modelling survival data in medical research. London:Chapman& Hall, (**1994)**.
[15] Cox DR. *Journal of Royal Statistical Society* B (**1972)**; 34:187-220.
[16] Lawless J. Statistical models and methods for lifetime data. New. York,(**1982)**, Wiley.
[17] TherneauT, and Grambsch P. Modeling survival data: Extending the Cox model, (**2000)**; New York, Springer-Verlag
[18]khodabakhshi, Gohari,Foadsi, Mghdmifard, *Razi medical sciences journal*.(**2011)**, 89 (18): 28-311.
[19] Gajalakshmil CK. *British Journal of Cancer* **(1997)**; 75(5): 771-775.
[20]Rajayeefard. *Journal of medical research;* JMR, summer (**2005),** (4) 3.
[21] Gohari.the survival of breast cancer patients and influencing factors by using models of Allen collective risks. Journal of Medical Sciences University of North Khorasan, special letter of biostatistical and epidemiology, no 3, (**2011)**.
[22]VahdaniNiyam. Checking the survival rate of 5 years in women with breast cancer, referring to Imam Khomeini hospital.Quartely. **(2003)**, (2) 2.
[23]Gohari, *Razyaban Journal of medical sciences*. **(2011)**,(89)18.
[24]Esmaili. survival of breast cancer patients data analysis with the Cox proportional risks related for related censorship according to joint function.Journal of Medical Sciences University of North Khorasan, special letter of bio statistical and epidemiology (**2011)**; 3.