# RESEARCH ARTICLE

# Survival of Patients with Stomach Cancer and its Determinants in Kurdistan

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## Abstract

**Background:** Stomach cancer is the fourth most common cancer and the second leading cause of death from cancer in the world. In Iran, this type of cancer has high rates of incidence and mortality. This study aimed to assess the survival rate of patients with stomach cancer and its determinants in Kurdistan, a province with one of the highest incidence rates of stomach cancer in the country. **Materials and Methods:** We studied a total of 202 patients with stomach cancer who were admitted to Tohid Hospital in Sanandaj from 2009 to 2013. Using Kaplan-Meier nonparametric methods the survival rate of patients was calculated in terms of different levels of age at diagnosis, gender, education, residential area, occupation, underweight, and clinical variables including tumor histology, site of tumor, disease stage, and type of treatment. In addition, we compared the survival rates using the log-rank test. Finally, Cox proportional hazards regression was applied using Stata 12 and R 3.1.0 software. The significance level was set at 0.05. **Results:** The mean age at diagnosis was 64.7 ± 12.0 years. The survival rate of patients with stomach cancer was 43.9% and 7% at the first and the fifth year after diagnosis, respectively. The results of log-rank test showed significant relationships between survival and age at diagnosis, education, disease stage, type of treatment, and degree of being underweight (P<0.05). Moreover, according to the results of Cox proportional hazards regression model, the variables of education, disease stage, and type of treatment were associated with patient survival (P<0.05). **Conclusions:** The survival rate of patients with stomach cancer is low and the prognosis is very poor. Given the poor prognosis of the patients, it is critical to find ways for early diagnosis and facilitating timely access to effective treatment methods.

**Keywords:** Stomach cancer - survival rates - risk factors - Iran

## Introduction

Stomach cancer is the fourth most common cancer and the second leading cause of death from cancer worldwide(Ferro et al., 2014). The type and survival rate of stomach cancer have undergone some changes in developed countries however it is still one of the cancers with a high incidence rate(Ferlay et al., 2015). The symptoms of this cancer not only are non-specific but also emerge with a delay; as a result, they are usually diagnosed only after being metastasized to other organs. For this reason, the prognosis of patients with stomach cancer is generally poor(Han et al., 2013). Recently, this disease has received more attention and its mortality rate has decreased by 6-14% however the five-year survival rate of these patients has not changed much(Arnold et al., 2013; Matsuda and Saika, 2013; Peleteiro et al., 2014). The low survival rate in these patients is generally due to tumor recurrence and late diagnosis. Nevertheless, different countries have reported diverse survival rates for this type of cancer. According to different reports,

the five-year survival rate of stomach cancer patients is 22% in Switzerland, 29.6% in China, 30% in France, and 37% in the United States. This controversy may be due to differences in the quality of services and the level of people's access to the related facilities (Nomura et al., 2003; Verdecchia et al., 2003; Tian et al., 2004; Matsuda and Saika, 2013).

Several variables can affect the survival of patients with stomach cancer. Many researchers introduced age as a factor affecting the prognosis of the disease because younger patients have lower survival rates than older patients (Belcastro et al., 1990; Allgayer et al., 1997; Angelov et al., 2013; Coimbra et al., 2015). This may be due to progression of the disease at diagnosis because younger patients are less suspected to being affected by a malignancy. In addition, due to physical conditions, the symptoms of the disease may emerge with a delay in younger people, thus the malignancy may not be diagnosed at the time of examination. Another likely reason is the biologic activity of the tumor at younger ages which results in poor differentiated grade of the disease

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in younger people. Other studies have shown that age at diagnosis and gender, have a significant effect on the survival of patients (Casariego et al., 2001; Heise et al., 2009; Li et al., 2013; Kim et al., 2014).

Women have a better prognosis of the disease. Men have higher mortality rate and lower survival rate (Takahari et al., 2011; Zhang and Ma, 2013). Surgery is known as an effective treatment for stomach cancer. Compared with those who did not undergo a surgery, the one-year and two-year survival rates are higher among people undergoing surgery(Nielsen et al., 1984; Li et al., 2014).

The incidence of stomach cancer in Iran has been increasing over the past three decades. Stomach cancer is the most common cancer among Iranian men and the third most common cancer among Iranian women after breast cancer and colorectal cancer. It is also the main cause of mortality in both sexes(Malekzadeh et al., 2009; Shadi Kolahdoozan MD et al., 2010).

Kurdistan province which is located in the western part of Iran is one of the provinces with a high incidence and prevalence of stomach cancer(Amori et al., 2016).

Given the high prevalence of the disease in the North West and West regions, especially in Kurdistan, this study aimed to evaluate the survival rate of patients with stomach cancer and its determinants in Sanandaj.

## Materials and Methods

This study was a retrospective cohort which was conducted on patients with a histological diagnosis of stomach cancer who were admitted to Tohid Hospital in Sanandaj from 2009 to 2013. Using complete enumeration method, a total of 202 patients with stomach cancer were enrolled in the study. To collect the required data, we reviewed the files and history of the patients and using their contact information recorded in their files we called the patients and their families. Part of the data about the cancer patients were collected from cancer registry system. The addresses and phone numbers of all the patients were available in hospital records and cancer registry system; those contact information were used to call the patients and their families to collect the required data. The studied variables included age at diagnosis, gender, education, residential area, occupation, underweight, and clinical variables including tumor histology, site of tumor, disease stage, underlying diseases, type of treatment, and existing complications. To determine the survival time, the time from the onset of disease until March 2014 (per months) was calculated. The patients who did not die during the mentioned period or died for reasons other than stomach cancer were considered as censored observations. The median survival time was reported in terms of the studied variables. In addition, the analysis was conducted in two steps. In the first step, using Kaplan-Meier nonparametric method and Log-rank test the survival curves were measured and calculated for all the studied variables. In the second step, the variables that according to the results of the first step were significant at a level of 0.1 were entered into the multivariate Cox regression models fitted with risks in order to study their effects on the presence of the other variables. In this step, the significance level

**Table 1. Results of Evaluation of the Tactors Affecting the Survival of Patients with Stomach Cancer Using Kaplan-Meier Nonparametric Method**

| Variable | Levels | Frequency (percentage) | Median survival per month | Probability |
|---|---|---|---|---|
| Sex | Male | 156 (77.2) | 16.55 | 0.67 |
| | Female | 46 (22.8) | 14.44 | |
| Age at diagnosis | < 55 years | 37 (18.3) | 12.36 | 0.037 * |
| | 55-65 years | 54 (26.7) | 13.43 | |
| | > 65 years | 111 (55) | 7.5 | |
| Education | Literate | 153 (75.7) | 13. 3 | 0.011 * |
| | Illiterate | 49 (23.3) | 37.35 | |
| tumor histology | Adenocarcinoma | 182 (90.1) | 15.27 | 0.083 |
| | Other | 20 (9.9) | 28.12 | |
| tumor site | Upper | 72 (35.6) | 15.15 | 0.078 |
| | Lower | 104 (51.5) | 15.7 | |
| | Unknown | 26 (12.9) | 23.8 | |
| Disease stage | Stage 1 | 18 (8.9) | 39.23 | 0.000 * |
| | Stage 2 | 46 (22.8) | 18.93 | |
| | Stage 3 | 10 (5) | 12.24 | |
| | Stage 4 | 77 (38.1) | 6.79 | |
| | Unknown | 43 (25.2) | 14.3 | |
| Type of treatment | Chemotherapy(CH) | 54 (26.7) | 10.9 | 0.000 * |
| | Radiotherapy(R) | 10 (5) | 17.46 | |
| | Surgery(S) | 9 (4.5) | 9.61 | |
| | CH + S | 28 (13.9) | 13.76 | |
| | CH + R | 57 (28.2) | 24.62 | |
| | CH + S + R | 28 (13.9) | 11.96 | |
| | None | 13 (7.9) | 4.69 | |
| Amount of underweight | < 10 kg | 122 (60.9) | 18.57 | 0.021 * |
| | 10-20 kg | 30 (14.9) | 9.44 | |
| | > 20 kg | 25 (12.4) | 15.05 | |

* Significance level: 0.05

was set at 0.05. Analyses were carried out using Stata 12 and R 3.1.0 software.

## Results

During the period of the study the files and records of 202 patients were reviewed and evaluated. The mean age of patients at diagnosis was 64.76±11.95 years. Of all, 156 patients (77.2%) were male, 50.5% of patients were living in rural areas, and 75.7% were illiterate. Moreover, 177 patients (87.6%) were underweight, among whom 12.4% were more than 20 kg underweight. By the end of the study period 155 patients (76.7%) had died, of whom 122 persons (78.7%) were male. The survival rate of stomach cancer patients was 43.9% in the first year of diagnosis, 24.7% in the second year of diagnosis, 10.7% in the third year of diagnosis, 8.9% in the fourth year of diagnosis, and 7% in the fifth year of diagnosis. The median survival time of the studied patients was 9.867 months (95% CI: 7.27-12.45) and the mean duration of survival was 16.62

months (95% CI: 13.47-19.77). The curve of survival probability per month is plotted in Figure 1. As shown in the graph, the curve has a sharp steep until about 10 months after the diagnosis of the disease; although the steep continues but its slope is reduced. Table 1 presents the results of the analysis of the median survival time in terms of the studied variables which were calculated using Kaplan-Meier nonparametric method; additionally it shows the likely differences between the curves of each of the variables which were calculated using the Log-rank test. As the results of Table 1 and Figure 2 show there were significant differences between the survival rates of patients at different age groups; the patients aged less than 55 years had higher survival rates (P=0.037). There was no significant differences between the survival of patients living in urban and rural areas and patients working at different jobs (P>0.05). In addition, illiterate people had lower survival rates than other educated people (P=0.011). Patients who underwent all the three methods of chemotherapy, surgery, and radiotherapy had
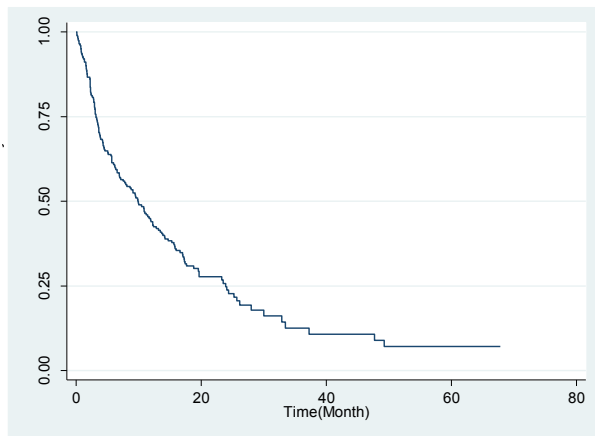


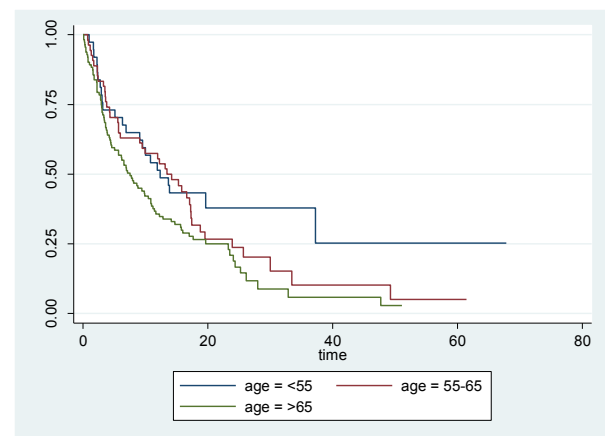**Figure 1. Survival Rate of Patients Calculated Using Kaplan-Meier Nonparametric Method**



**Figure 2. Survival Rate of Patients with Stomach Cancer Calculated for Different Age Groups**

**Table 2. Results of Evaluation of the Factors Affecting the Survival of Patients with Stomach Cancer Using Cox Proportional Hazards Model**

| Variable | Levels | Odds ratio | Limit less than 95% | Limit more than 95% | Probability |
|---|---|---|---|---|---|
| Age at diagnosis | 55-65 years | 1.281 | 0.65 | 2.52 | 0.47 |
| | > 65 years | 1.57 | 0.78 | 3.13 | 0.2 |
| Education | Literate | 0.51 | 0.24 | 0.93 | 0.04 * |
| tumor histology | Other | 0.85 | 0.4 | 1.81 | 0.69 |
| tumor site | Lower | 0.93 | 0.61 | 1.41 | 0.73 |
| | Unknown | 0.81 | 0.41 | 1.59 | 0.55 |
| Disease stage | Stage 2 | 1.95 | 0.77 | 4.92 | 0.15 |
| | Stage 3 | 3.47 | 1.11 | 1.88 | 0.03 * |
| | Stage 4 | 6.51 | 2.53 | 16.75 | 0.00 * |
| | Unknown | 2.32 | 0.9 | 5.97 | 0.07 |
| Type of treatment | Chemotherapy(CH) | 0.48 | 0.25 | 0.92 | 0.02 * |
| | Radiotherapy(R) | 0.56 | 0.22 | 1.45 | 0.24 |
| | Surgery(S) | 0.84 | 0.31 | 2.23 | 0.73 |
| | CH + S | 0.72 | 0.34 | 1.48 | 0.37 |
| | CH + R | 0.41 | 0.21 | 0.81 | 0.01 * |
| | CH + S + R | 0.56 | 0.28 | 1.13 | 0.1 |
| Amount of underweight | 10-20 kg | 1.3 | 0.79 | 2.13 | 0.28 |
| | > 20 kg | 1 | 0.59 | 1.68 | 0.9 |

* Significance level: 0.05

higher survival rate; on the other hand, patients who did not undergo any of the treatment methods had the lowest survival rate (P=0.000). Moreover, the underweight patients with less than 10 kg of weight loss had a significantly higher survival rate than other underweight patients. It is also worth mentioning that the patients with different tumor sites and different sexes had similar survival rates (P>0.05).

The variables of age at diagnosis, education, tumor histology, tumor site, disease stage, type of treatment, and the amount of underweight were entered into the Cox proportional hazards model to assess the impact of each of these variables on the survival time in the presence of other variables. The results of this model are presented in Table 2.

The software usually showed the smaller numbers to the base level, hence the results of Table 2 follow the same trend. The results of multivariate Cox model analysis showed that the variables of education, disease stage, and type of treatment influenced the survival of the patients. The hazard ratio in patients at disease stage 3 was 3.47 times higher than that in patients at disease stage 1 (P=0.03). In addition, the hazard ratio in patients at disease stage 4 was 6.51 times higher than that in patients at disease stage 1 (P=0.000). The hazard ratio in a literate patient was almost half the hazard ratio in an illiterate patient (P=0.04). The hazard ratio in patients undergoing chemotherapy or chemotherapy and radiotherapy, respectively, was 0.48 and 0.41 times higher than that in a patient who did not receive any treatment.

## Discussion

Stomach cancer is one of the most fatal cancers with a low survival rate (Matsuda and Saika, 2013). The most notable results of this study showed that survival rate of patients with stomach cancer was 43.9% and 7% at the first and the fifth year of diagnosis, respectively. The mean duration of survival was 16.62 months. The results of multivariate Cox model analysis showed that the variables of education, disease stage, and type of treatment had an impact on the survival of patients.

Our findings about the five-year survival rate and mean survival time were in line with the results of some other studies. Hansson et al. conducted a population-based study in Sweden from 1960 to 1989; according to the results of their study, the five-year survival rate of patients with stomach cancer was about 13% (Hansson et al., 1999). According to the results of a study by Mitry et al. the five-year survival rate in the decades before the 1990s of the last century was approximately 10% in the UK (Mitry et al., 2008). As Karimi et al. reported the five-year survival rate of patients with stomach cancer in the US before 1970 was less than 15%(Karimi et al., 2014).

It seems that the current status of survival of patients with stomach cancer in Iran is similar to the status of world's developed countries about thirty years ago. The similarity in the five-year survival rate may be due to the fact that the treatment and care facilities which are now available to the patients with stomach cancer in Kurdistan is much similar to those available to people in developed countries more than thirty years ago. Compared with the developed countries, the treatment services for patients with stomach cancer have not become properly available for the patients in Iran yet.

Nevertheless, our findings about the five-year survival rate and mean survival time are inconsistent with the results of following studies. According to the results of a study by Khedmat et al. the highest rate of five-year survival i.e. 89.4% has been reported in Japan, especially in the groups that undergo screening; moreover, the five-year survival was 32.6% in France, 26% in the US, and 30% in China (Khedmat et al., 2011). According to the results of the same study, the five-year survival in a referral hospital in Iran was more than 20% (Khedmat et al., 2011). These differences are probably due to differences in people's access to treatment and care facilities and services; the controversies might be also attributed to the utilization of screening programs and early diagnosis of patients.

In Japan, which is suffering from a high prevalence of stomach cancer, the screening programs have been run since many years ago, and their five-year survival is higher than other parts of the world. Screening and the utilization of techniques that are effective in early diagnosis of stomach cancer have improved this condition (Inokuchi, 1991).

The results of multivariate analysis showed that education had an impact on survival. In this study, the odds ratio of a literate patient was approximately half of the odds ratio of an illiterate patient. Our results are consistent with the findings of a study by Heise which reported the important role of social issues(Hsieh et al., 2012). According to Arnold et al. socioeconomic issues and behavioral characteristics had a very important effect on the survival of patients with stomach cancer(Arnold et al., 2011) . The results of these studies are consistent with our findings. The consistency in the results is probably due to the fact that educated people have better health behaviors. In addition, these people have better access to health services and usually they have better socioeconomic conditions.

The results of multivariate analysis showed that disease stage had an impact on survival. This finding is consistent with the results of a study by Heise who evaluated different stages of the disease among patients with stomach cancer from 1998 to 2002 in Chile; according to Heise's findings disease stage was the most important factor for the prognosis of the disease (Heise et al., 2009). In another study that was conducted in China, disease stage was introduced as the most important factor influencing the survival of the patients (Tian et al., 2004). These results are consistent with our findings. These results were expected, because the patients who are diagnosed in advanced stages of the disease have surely shorter survival.

The results of multivariate analysis showed that type of treatment affected the survival of the patients. It is consistent with the results of a study by Berezkin, et al. who reported the positive effects of a combination of treatment methods including surgery and radiotherapy(Berezkin et al., 1988). In addition, our finding was consistent with the

results of a study by Tian who reported that a combination of treatment methods could increase the survival of the patients(Tian et al., 2004). Appropriate use of treatment methods could increase the survival of stomach cancer patients.

According to some studies, there is a relationship between sex and survival of patients with stomach cancer. The differences between the two sexes have been reported by various studies. For example, a study in Japan has shown that the five-year survival of patients with stomach cancer was higher males than females(Sato et al., 2009). However, a study by Hiripi et al. reported that the five-year survival rate of stomach cancer patients was higher in females than males. The difference might be attributed to the fact that men usually neglect their general health status and thus are at more advanced stages of the cancer at the time of diagnosis(Hiripi et al., 2012). However, in our study the results of multivariate analysis showed no relationship between sex and five-year survival.

As one of the limitations of this study, it was difficult to access the data about the patients and we used the hospital data to identify patients with stomach cancer. Hence, to reduce the likely biases in the future studies on survival it is recommended to use population-based data and utilize prospective study designs.

In conclusion, The survival rate of patients with stomach cancer in our country is lower than that in developed countries. Delayed diagnosis, diagnosis at the advanced stages of the disease, and low levels of education are among the factors leading to lower survival of the patients with stomach cancer. Screening people in areas with a high prevalence of the disease (as performed in Japan), utilization of early detection methods, increasing people's access to effective treatment methods, and paying special attention to people with lower education levels can increase the survival of the patients with stomach cancer.

## Acknowledgements

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