The Effects of Risk Factors on One- and Five-Year Survival of Patients with Gastric Cancer in Isfahan in 2016

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Abstract

Background:
Gastric cancer (GC) is a frequent and multifactorial malignancy worldwide. The aim of this study was to investigate the relationship between some risk factors of GC and the 1-year or 5-year survival rates in newly diagnosed patients in Isfahan in 2016.

Methods:
We included 274 newly diagnosed patients in this survival analysis from a database of 484 GC cases. We used a checklist to collect information. To inform about missed data, we call the patients or their families in non-survived cases. We evaluated each patient's age, sex, body mass index (BMI), education, salt, salty foods, and red meat consumption. In addition, we asked patients about the intake of fresh fruits and vegetables, tobacco smoking, opium usage, and alcohol consumption. We surveyed the patient's job, physical activity, *Helicobacter pylori* infection, family history of GC, history of gastric surgery, and survival status after 1 or 5 years. Variables were evaluated between survived and dead patients and compared for means and frequencies using the independent samples t-test or Mann-Whitney, or chi-square test. The univariate relationship of each risk factor, with 1- and 5-year survival, was examined by the log-rank test and the Kaplan-Meyer method and their multivariate relationship with Cox regression.

Results:
1- and 5-year survived patients were younger than dead patients with GC ($P<0.001$; HR for 1-year survival: 1.014, 95% CI: 0.997 to 1.030; HR for 5-year survival: 1.005, 95% CI: 0.994 to 1.017), and had more frequent higher educational levels ($P<0.05$; HR for 1-year survival: 1.887, 95% CI: 1.046 to 3.406; HR for 5-year survival: 1.482, 95% CI: 0.987 to 2.223). The death rate after 5 years was higher in men than in women ($P=0.009$; HR: 1.009, 95% CI: 0.593 to 1.717) and depended on the job status of the patients ($P=0.021$). The other studied variables were not significantly different between 1- or 5-year survived and dead patients.

Conclusion:
GC development depends on genomic changes, environmental factors, and lifestyle status. But all risk factors that play a role in its development are not notable for a patient's survival. We suggest that risk factors for these patients' survival become elucidated in future studies. It helps to gather the necessary pieces of evidence for the enhancement of survival in patients with GC.

Keywords: Gastric cancer, Survival, Hazard ratio, Lifestyle

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Introduction

Gastric cancer (GC) is the fifth most diagnosed cancer, with 1 033 701 new cases worldwide in 2018. It represents 5.7% of all diagnosed cases with different cancer types. It is also the third most common cause of cancer-related death worldwide after lung and colorectal cancers. GC was responsible for 8.2% of all deaths from cancer in 2018, equating to 1 in every 12 deaths.[1] GC has a high incidence in developing countries, and nearly two-thirds of GCs were detected in developing countries.[2] In Iran, GC is one of the most common cancers in men and the third most common cancer in women, after breast and skin malignancies.[3] Northern provinces of Iran have the highest rate of GC,[4] unlike the southern parts of Iran, such as Kerman province, which harbors the lowest rate.[5] GC is a multifactorial disease and is affected by genetic and environmental factors. Investigators have reported approximately 52 risk factors for GC.[6] Age is a known risk factor for GC, and it usually occurs in people between 60 and 80 years old.[7] About 70% of GCs occur in patients aged 65 years or older.[8] As World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) declared, salt is a known risk factor for GC.[9] Excessive salt and salty food consumption may act as a stimulant of gastric mucosa, leading to atrophic gastritis, increased DNA synthesis, and cell proliferation, thus providing a basis for GC. According to a study, 24% of stomach cancer cases in the UK (31% in men and 12% in women) were from individuals with 6 grams/day salt intake.[10]

Adequate consumption of fruits and vegetables is beneficial in the prevention of GC. Epplein et al discovered an inverse connection between fruit intake and GC in male smokers.[11] Fruit and vegetable consumption > 156 g/d was found to be protective in GC.[12]

Frequent intake of red meat increases the risk of GC.[13,14] A too large amount of red meat consumption promotes the synthesis of N-nitroso compounds by a direct interaction between nitric oxide and hemoglobin or myoglobin.[15] Red meat contains iron metal in high contents, which may induce free radical formation.[16] Tobacco smoking is another risk factor for GC development,[17,18] exerting destructive and permanent effects on gastric tissue and increasing the risk of GC.[19]

Alcohol consumption as a risk factor for GC was a controversy previously. But it has been implicated in the development of GC in the latest studies.[20] According to a study, those who had an alcohol consumption of more than 50 g/d had a 24% chance of developing GC, greater than non-drinkers or low drinkers.[21] The mechanism by which the alcohol affects gastric mucosa probably relates to the primary metabolites, acetaldehydes, which have a local toxic action that raises the risk of GC.[22-24]

Physical activity is associated with a lower incidence and mortality rate of some malignancies, most notably proximal and distal colorectal cancer, breast cancer, and endometrial cancer.[25-27] Singh et al have claimed that physical activity is related to a lower risk of GC. Concerning how physical activity protects against GC, it may act by counteracting the carcinogenic effects of obesity, enhancing insulin sensitivity, and lowering systemic inflammation. All of these contribute to positive immunomodulation.[28]

Helicobacter pylori infection is the most prevalent chronic infection globally, with a frequency of over 50%; nevertheless, a large percentage of infected patients remain asymptomatic.[29] This infection is a GC risk factor [30] that leads to precancerous lesions. Chronic atrophic gastritis or gastric intestinal metaplasia eventually changes to malignant growth in the gastrointestinal tract.[31] So far, researchers have discovered some *H. pylori* virulence factors. For example, cagA protein is one of the most notable factors, seen in 60-70% of *H. pylori* strains and associated with an elevated risk of GC in several populations.[32]

The prognosis of GC is poor, with a 5-year survival rate of less than 20% worldwide, and the main reason is the delay in diagnosis due to the silent nature of the disease in the early stages.[33] According to the results of a systematic review and meta-analysis of 22 studies conducted in Iran between 1990 and 2011, the 5-year survival of GC in Iran was 15%, and the minimum and maximum 5-year survival rates were 6% and 30%, respectively.[34]

This study aims to investigate the relationship between some risk factors of GC and the 1-year and 5-year survival rates in newly diagnosed patients in Isfahan in 2016.

Materials and Methods

Case selection

This study is a cross-sectional and retrospective study to identify GC risk factors and investigate their relationship with 1- and 5-year survival rate. The patients were new cases of GC in 2016 in Isfahan province, a city in the center of Iran. We used a data repository that was available in the Isfahan Health Center province. In total, 484 GC cases were diagnosed based on the clinicopathology findings. Detailed data were registered and documented in medical records. The death certificate and clinical data were explored precisely by investigators. We did not include all patients in the study due to some problems, such as incorrect information or missing data. The patients on stage 3 were entered the study because most of the patients entered the database in this stage and missing data of other stages were too much. Patients who diagnosed with stage 4 of GC were excluded from study due to risk of recall bias and their hesitancy. We used a checklist to collect information. In addition, we call patients or their families (if they were expired). Finally, we included only 274 series raw data in the statistical analysis.

Checklist

The checklist included the patient's full name, age, sex, education, salt and salty food consumption, intake of fresh fruits and vegetables, red meat consumption, tobacco smoking, opium consumption, alcohol consumption, job, physical activity, *H. pylori* infection, family history of GC, history of gastric surgery and patient's survival status after 1 year and 5 years. We divided education into three categories: pre-high-school education, high school diploma or bachelor's degree, Master's, or Ph.D. We categorized salt usage and salty food consumption into three categories: less than 5 g/d, 5-10 g/d, and more than 10 g/d salt intake.

We divide fresh fruits and vegetable consumption into three categories: less than 100 g/d, 100-500 g/d, and more than 500 g/d intake. We considered three groups for red meat consumption: less than 50 g/d, 50-150 g/d, and more than 150 g/d intake. We have defined physical activity as: it lasts more than 20 minutes or causes tachycardia or tachypnea and sweating. Walking, yoga, in-house or outdoor exercises, and aerobic training were supposed as physical activities. We supposed six categories included: no physical activity, once in the last 3 months, 1 to 3 times a month, 1 to 2 times a week, 3 to 4 times a week, 5 and more times a week.

Statistical analysis

The collected data were recorded and entered into SPSS software and analyzed at both descriptive and analytical levels. We have reported numerical variables as means and categorical variables by number and percentage. We have compared numerical variables between the living and the dead patients by t-test or Mann-Whitney test and non-numerical variables by chi-square test. We have examined the univariate relationship of each risk factor with 1-and 5-year survival by the log-rank test and the Kaplan-Meyer method and their multivariate relationship with Cox regression.

Results

We studied 273 patients with GC with mean±SD age=64.54±13.59 years, and mean±SD body mass index (BMI)=25.54±4.55. In total, 184 men (67.4%) and 89 women participated (32.6%) in our survey.

203 (74.4%) patients had pre-high school education, 66 (24.2%) had high school diplomas or bachelor's degrees, and 4 (1.5%) had Master's or Ph.D. certificates. 268 (98.2%) people were married. 81 (29.7%) patients used salt less than 5 g/d, 147 (53.8%) used 5-10 g/d, and 45 (16.5%) consumed salt more than 10 g/d. 70 (25.6%) patients consumed vegetables and fruits less than 100 g/d, 129 (47.3%) between 100-500 g/d and 74 (21.7%) more than 500 g/d. 43 (15.8%) participants consumed red meat less than 50 g/d, 168 (61.5%) between 50-150 g/d and 62 (22.7%) consumed it more than 150 g/d. In this study, 196 (71.8%) patients were non-smokers, 30 (11.0%) were past smokers, and 47 (17.2%) were current smokers. 248 (90.8%) patients were not consuming opium, 7 (2.6%) were consuming it in the past, and 18 (6.6%) were consuming it during their disease. 268 (98.2%) persons were not alcohol consumers, 1 (0.4%) was a past consumer, and 4 (1.5%) were current consumers. We also investigated patients' jobs, which were representative of their socio-economic conditions. Accordingly, 56 (20.5%) were self-employed, 100 (36.6%) were unemployed,

38 (13.9%) were labors, 34 (12.5%) were employees and 45 (16.5%) were farmers. For physical activity, 200 (73.3%) patients did not perform any physical activity, 3 (1.1%) individuals had one session in the last three months, 1 (0.4%) had between 1-3 times a month, 23 (8.4%) persons had between 1-2 times a week, 17 (6.2%) individuals had 3-4 times a week, and 29 (10.6%) had physical activities 5 or more times a week.

We investigated the history of *H. pylori* infection as another risk factor for GC. 27 (9.9%) participants had positive history, and 246 (90.1%) had negative *H. pylori* infection history. 58 (21.2%) patients had positive, and 215 (78.8%) had a negative familial history of GC. Finally, 2 (0.7%) patients had a positive history of gastric surgery, and 271 (99.3%) had a negative history.

For each one-year increment, the patient mortality rate increases by 1.4% (HR: 1.014, 95% CI: 0.997 to 1.030). Death likelihood within a year was 88.7% in patients with pre-high-school education compared with patients with high school diplomas or bachelor's (HR: 1.887, 95% CI: 1.046 to 3.406). Also, self-employed, unemployed, labor patients, and employed patients had 69.9% (HR: 0.699, 95% CI: 0.388 to 1.257), 95.6% (HR: 0.956, 95% CI: 0.575 to 1.588), 6.0% (HR: 1.060, 95% CI: 0.578 to 1.944), and 77.0% (HR: 0.770, 95% CI: 0.325 to 1.821) death likely within a year, respectively, compared with farmers. Those patients with a family history of GC were 71.4% more likely to die within a year than patients without it (HR: 1.714, 95% CI: 1.023 to 2.870).

After each 5-year age advancement, the patients' mortality rate increased by 0.5% (HR: 1.005, 95% CI: 0.994 to 1.017). Also, the death rate of men within 5 years was 0.9% higher than women (HR: 1.009, 95% CI: 0.593 to 1.717). The patients with pre-high-school education were 48.2% more likely to die within five years than patients with a high school diploma or bachelor's degree (HR: 1.482, 95% CI: 0.987 to 2.223). Self-employed, unemployed, labor, and employee patients were 70.6% (HR: 0.706, 95% CI: 0.461 to 1.079), 85.6% (HR: 0.856, 95% CI: 0.481 to 1.522), 6.0% (HR: 0.895, 95% CI: 0.565 to 1.419) and 41.0% (HR: 1.041, 95% CI: 0.588 to 1.842) more likely to die within a year, respectively, compared with farmers.

1-year-survived patients were younger than expired GC patients ($P<0.001$). They had more frequent higher educational levels ($P=0.012$). They had insignificant differences in BMI, sex frequencies, marital status, salt, fruit and vegetables, red meat usage, tobacco smoking, opium, and alcohol abuse ($P>0.05$). In addition, survived and expired patients had not had a significantly different frequency of the job types. The level of physical activity, history of *H. pylori* infection, familial history of GC, and gastric surgery were not different between one-year survived and expired GC patients ($P>0.05$). 1-year-survived patients had higher educational levels than expired patients ($P=0.012$) (Table 1).

5-year survived patients were younger than dead patients ($P<0.001$) and had more frequent higher educational levels ($P=0.007$). The death rate after 5 years was higher in men compared with women ($P=0.009$). The distribution of job types was significantly different between survived and dead patients ($P=0.021$). After 5 years of diagnosis, the surviving patients had insignificant BMI, marital status, salt, fruit/vegetables, and red meat intake frequencies compared with dead patients ($P>0.05$). Also, they had no considerable difference in tobacco smoking, opium, and alcohol abuse compared with expired individuals ($P>0.05$). The level of physical activity, history of *H. pylori* infection, familial history of GC, and gastric surgery were not different between the groups ($P>0.05$) (Table 2).

Discussion

GC is known as a multifactorial disease,[6] hence we have evaluated the relationship between selected risk factors of GC and the 1-year and 5-year survival rates in newly diagnosed patients in Isfahan city in 2016. The significant variables in our study were sociodemographic. Overall, older patients with GC had a lower survival chance than younger survivors. This was true for both 1- and 5-year survival. Getting aged is associated with exposure chance to risk factors during the lifespan. For example, exposure to hazardous chemicals and their byproducts, toxic metals,[35] *H. pylori* infection, stress,[36] processed nutrition,[37] poor oral hygiene,[38] and so forth increase the risk of GC. Accordingly, certain cancers, such as GC, are frequently

Table 1. Comparison of investigated variables between alive and dead persons after 1-year of GC diagnosis

		Alive	Dead	*P* value	HR (95% CI to HR)
Age		62.02±12.69	67.96±14.07	<0.001	1.014 (0.997-1.030)
Body mass index		25.66±4.69	25.33±4.33	0.624	
Gender	Male	108 (68.8%)	76 (65.5%)	0.569	
	Female	49 (31.2%)	40 (34.5%)		
Education level	Pre-high school education	104 (66.2%)	99 (85.3%)	0.012	1.887 (1.046-3.406)
	High school diploma or bachelor's degree	49 (31.2%)	17 (14.7%)		1
	Master or PhD	4 (2.5%)	0 (0%)		Not computable
Marital status	Married	155 (98.7%)	113 (97.4%)	0.425	
	Single	2 (1.3%)	3 (2.6%)		
Salt consumption (g/d)	<5	40 (25.5%)	41 (35.3%)	0.787	
	5-10	87 (55.4%)	60 (51.7%)		
	>10	30 (19.1%)	15 (12.9%)		
Fruit and vegetable consumption (g/d)	<100	36 (22.9%)	34 (29.3%)	0.334	
	100-500	73 (46.5%)	56 (48.3%)		
	>500	48 (30.6%)	26 (22.4%)		
Red meat consumption (g/d)	<50	23 (14.6%)	20 (17.2%)	0.459	
	50-150	100 (63.7%)	68 (58.6%)		
	>150	34 (21.7%)	28 (24.1%)		
Tobacco smoking	No smoking	113 (72.0%)	83 (71.6%)	0.789	
	Past smoker	15 (9.6%)	15 (12.9%)		
	Current smoker	29 (18.5%)	18 (15.5%)		
Opium consumption	No drug using	139 (88.5%)	109 (94.0%)	0.210	
	Past drug user	6 (3.8%)	1 (0.9%)		
	Current drug user	12 (7.6%)	6 (5.2%)		
Alcohol consumption	No alcohol consumption	153 (97.5%)	115 (99.1%)	0.367	
	Past alcohol consumption	1 (0.6%)	0 (0.0%)		
	Current alcohol consumption	3 (1.9%)	1 (0.9%)		
Job	Self-employed	34 (21.7%)	22 (19.0%)	0.509	0.699 (0.388-1.257)
	Unemployed	58 (36.9%)	44 (36.2%)		0.956 (0.575-1.588)
	Labor	18 (11.5%)	20 (17.2%)		1.060 (0.578-1.944)
	Employee	26 (16.6%)	8 (6.9%)		0.770 (0.325-1.821)
	Farmer	21 (13.4%)	24 (20.7%)		1
Level of physical activity	No physical activity	110 (70.1%)	90 (77.6%)	0.976	
	Once in the last 3 months	1 (0.6%)	2 (1.7%)		
	1 to 3 times a month	1 (0.6%)	0 (0.0%)		
	1 to 2 times a week	14 (8.9%)	9 (7.8%)		
	3 to 4 times a week	15 (9.5%)	2 (1.7%)		
	5 or more than 5 times a week	16 (10.2%)	13 (11.2%)		
History of *H. pylori* infection	Yes	15 (9.6%)	12 (10.3%)	0.829	
	No	142 (90.4)	104 (89.7%)		
Family history of GC	Yes	39 (24.8%)	19 (16.4%)	0.092	1.714 (1.023-2.870)
	No	118 (75.2%)	97 (83.6%)		
History of gastric surgery	Yes	1 (0.6%)	1 (0.9%)	0.830	
	No	156 (99.4%)	115 (99.1%)		

GC, gastric cancer; HZ, hazard ratio.

Table 2. Comparison of investigated variables between alive and dead persons after 5 years of GC diagnosis

		Alive	Dead	*P* value	HR (95% CI to HR)
Age		58.82±12.62	66.15±13.44	<0.001	1.005 (0.994-1.017)
Body mass index		25.75±4.89	25.46±4.43	0.695	
Gender	Male	32 (53.3%)	152 (71.4%)	0.009	1.009 (0.593-1.717)
	Female	28 (46.7%)	61 (28.6%)		
Education level	Pre-high school education	34 (56.7%)	169 (79.3%)	0.007	1.482 (0.987-2.223)
	High school diploma or bachelor's degree	24 (40.0%)	42 (19.7%)		1
	Master or PhD	2 (3.3%)	2 (0.9%)		0.757 (0.179-3.197)
Marital status	Married	59 (98.3%)	209 (98.1%)	0.914	
	Single	1 (1.7%)	4 (1.9%)		
Salt consumption (g/d)	<5	17 (28.3%)	64 (30.0%)	0.507	
	5-10	31 (51.7%)	116 (54.5%)		
	>10g/d	12 (20.0%)	33 (15.5%)		
Fruit and vegetable consumption (g/d)	<100	12 (20.0%)	58 (27.2%)	0.739	
	100-500	31 (51.7%)	98 (46.0%)		
	>500	17 (28.3%)	57 (26.8%)		
Red meat consumption (g/d)	<50	12 (20.0%)	31 (14.6%)	0902	
	50-150	36 (60%)	132 (62.0%)		
	>150	12 (20.0%)	50 (23.5%)		
Tobacco smoking	No smoking	45 (75.0%)	151 (70.9%)	0.669	
	Past smoker	5 (8.3%)	25 (11.7%)		
	Current smoker	10 (16.7%)	37 (17.4%)		
Opium consumption	No drug using	53 (88.3%)	195 (91.5%)	0.660	
	Past drug user	3 (5.0%)	4 (1.9%)		
	Current drug user	4 (6.7%)	14 (6.6%)		
Alcohol consumption	No alcohol consumption	60 (100.0%)	208 (97.7%)	0.243	
	Past alcohol consumption	0 (0%)	1 (0.5%)		
	Current alcohol consumption	0 (0%)	4 (1.9%)		
Job	Self-employed	12 (20.0%)	44 (20.7%)	0.021	0.706 (0.461-1.079)
	Unemployed	31 (51.7%)	69 (32.4%)		0.856 (0.481-1.522)
	Labor	4 (6.7%)	34 (16.0%)		0.895 (0.565-1.419)
	Employee	12 (20.0%)	22 (10.3%)		1.041 (0.588-1.842)
	Farmer	1 (1.7%)	44 (20.7%)		1
Level of physical activity	No physical activity	40 (66.7%)	160 (75.1%)	0.506	
	Once in the last 3 months	1 (1.7%)	2 (0.9%)		
	1 to 3 times a month	0 (0.0%)	1 (0.5%)		
	1 to 2 times a week	6 (10.0%)	17 (8.0%)		
	3 to 4 times a week	7 (11.7%)	10 (4.7%)		
	5 or more than 5 times a week	6 (10.0%)	23 (10.8%)		
History of *H. pylori* infection	Yes	8 (13.3%)	19 (8.9%)	0.313	
	No	52 (86.7%)	194 (91.1%)		
Family history of GC	Yes	16 (26.7%)	19 (16.4%)	0.246	
	No	42 (19.7%)	171 (80.3%)		
History of gastric surgery	Yes	0 (0.0%)	2 (0.7%)	0.452	

GC, gastric cancer; HZ, hazard ratio.

evident in older persons. As the older patients had a lower survival chance than younger participants, early diagnosis of GC promotes the patients' survival and probably better response to the treatment. Sex is a determinative risk for GC survival. Li and colleagues evaluated 96 501 patients with GC; of them, 34,862 (36.2%) were women. They reported that women had higher survival, and the female sex was associated with a lower hazard ratio than the male population.[39] Male patients had lower 5-year survival than women, but sex was not a determinative variable for 1-year survival. Anyhow, both sexes had a similar hazard risk of death for five years after GC onset. Androgen receptor overexpression induces tumorigenesis and metastasis in GC.[40] In the current study, after 1 year and 5 years of GC diagnosis, 65.5% and 71.4% of dead patients were male, respectively. However, 34.5% (1-year) and 28.6% (5-year) of expired patients were women. This finding confirms the effect of sex and hormonal status on the decreased survival chance of the male population compared with females with GC. Women have higher levels of estrogenic hormones than men. Therefore, we can conclude that the interaction between biological, hormonal, and sociodemographic factors could be important determinants in the patients' survival. In addition, male-specific hormones can probably play a role in gene-regulation and reprogramming of the cell cycle for GC development or prevention.

Lagergren and co-workers have shown that divorce, widowhood, living alone, low educational attainment, and low income increase the risk of esophageal and GC.[41] In our work, marital status was not a risk for a decrease in survival rate. However, lower educational levels were associated with a higher hazard risk of decreased 1- or 5-year survival. We think that the impact of higher education in the prevention of GC or postponing death relates to the hesitation from the risk factors or risky lifestyle. We suggest that peoples with higher education make better self-care, experience lower stressful situations due to more self-confidence, and, therefore, are involved with lower risk factors of GC. The patient's job was another risk factor for 5-year survival. After 5 years, most death events occurred among unemployed individuals. Patient's job was only an important risk factor for 5-years survival. After 5 years, most death events occurred among unemployed individuals. This finding is challenging as employment increases the exposure rate to hazardous circumstances. For instance, chemical toxicants, physical radiations, and biohazardous materials are potential risks in the working area. We suggest that unemployment evokes those psychological factors affecting physiological changes at the molecular level. The demonstration of this statement is complicated as we can explore the molecular, cellular, pathophysiological, and clinical changes in separate models to have repeatable results. Such a multifaceted system makes the investigation of cancer too complicated without a definitive or applicable outcome. What is the solution except continuing current works and going ahead with tinny findings? We suggest that investigators clarify the psychology and physiology relationship in cancer development for future studies.

In our study, salt, fruit, vegetables, red meat, alcohol intake, BMI, and marital status were not risk factors for a lower survival rate. Investigators have noted that diet and dietary habits could be notable risk factors for GC. In addition, salty diets have been mentioned to be a risk factor for GC.[6,42,43] Anyhow, in our study, salt and dietary habits, such as vegetable and fruit usage, were not significant risk factors or preventive agents for GC. An umbrella review of 72 meta-analyses, including 20 studies about red meat and 19 surveys about processed meat, has stated that red meat consumption is associated with cancer mortality, including gastric malignancy. Red meat (100 g/d) and processed meat (50 g/d) increase the risk of mortality by around 11-51% and 8-72%, respectively, according to the dose-response analysis.[42] Despite this finding, we did not have an increased risk of GC with red mead-enriched dietary habits. The reason behind this discrepancy could be the types of cancers. We have evaluated only patients with GC, whereas the mentioned review has evaluated several types of cancers. The genetics and ethnicity of the studied population are critical for cancer development after exposure to any risk factors such as salt, red meat, and alcohol consumption. Saumoy et al have shown endoscopic non-cardia GC screening for high-risk races and ethnicities is cost-effective in the United States.[44] Therefore, we suppose that racial and ethnic differences change the cancer development behavior in the patients exposed to the same risk factor

with similar circumstances and severity.

Yusefi et al have systematically reviewed the GC risk factors. They have cited articles reporting that higher BMI is present in patients with GC, whereas other studies show a protective impact of higher BMIs.[6] In our study, BMI was not a significant hazardous factor for 1- or 5-year survival. We think inconsistent results for BMI indicate this variable has no role in gastric tissue malignancy. Further, the role of BMI as a risk factor for GC should be clarified using a large sample size or multicenter studies, not systematic reviews. The meta-analysis also may not help denote the role of BMI, as it is under the effect of both patient's genetics and lifestyle, and published original studies are from different ethnic populations.[45] In approximately all cited studies reported by Yusefi and colleagues, alcohol consumption has been a serious risk factor for GC.[6] We have not seen any difference between alive and dead patients' frequencies for alcohol consumption considering 1- or 5-year survival. We have divided the alcohol drinkers into "No Alcohol Consumption, Past Alcohol Consumption, and Current Alcohol Consumption categories". However, less than five people existed in groups marked as the past consumers and current alcohol consumers groups; in fact, our results were not valid for this variable. Islam religion forbids alcohol consumption. In addition, most people in Iran are Shia Muslims. Therefore, alcohol consumption is considered a crime legally, and drinkers will be accused in court. Hence, compared with many countries worldwide, and considering the population of Iran, alcohol consumption is not frequent or at least has no clear statistics. Thus, evaluating alcohol consumption as a gastric risk factor is associated with bias and improper results.

Tobacco smoking, opium abuse, level of physical activity, history of *H. pylori* infection, family history of GC, or surgery did not affect the survival chance of investigated population. Tobacco smoking and opium abuse are frequent solely in Iranian men and not women. Most Iranian women disregard any addiction type, especially cigarette and tobacco smoking. The reason behind this is the Iranian women's point of view about the effect of smoking on their health, children, beauty, social status, and women's pride. In addition, according to the directions mentioned in the Holy Quran, a person is not permitted to make damage himself and herself. Regarding this direction, smoking and alcohol drinking are regarded as damaging behavior that should be hesitated from a person's life. In our study, there were 89 women, and hence we think this affects the frequency of smoking and drinking rates and made our results unreliable for risk estimation.

Level of physical activity and familial history are the other risk factors for GC.[46] But we have not seen a significant effect of these variables on the 1- and 5-year survival in patients with GC.

Helicobacter pylori evokes gastrointestinal tract cancers. It is prevalent worldwide and too contagious.[47,48] We have explored the dependence of patients' survival on the history of *H. pylori* infection. But there was no difference between the frequency of alive and dead patients after 1 and 5 years. This finding could be due to the early diagnosis of *H. pylori* infection and the prescription of proper treatments during the last years in Iran. Today, *H. pylori* infection is diagnosed with different paraclinical facilities and evaluations such as stool antigen, IgG, IgM, IgA antibodies, urea breath test, gastric biopsy, and stool polymerase chain reaction (PCR) test. Hence, rapid diagnosis and continuous monitoring seem to be helpful in infection control and subsequent inflammation that promotes GC.

Marital status and history of gastric surgery showed insignificant results. Overall, we think that non-significant results for 1- and 5-year survival of GC patients are because of the type of our study compared with other investigations. Most published studies have explored the GC risk factors using case-control studies, whereas we have surveyed the association between risk factors and patient survival. We have evaluated only patients with GC, whereas most studies have compared these patients with non-cancerous populations. Thus, we attribute the discrepancies between our study and the other research to the population types, methodology, and objects. It is probable that a risk factor promotes the initiation step of the GC but may not have a role in its survival. This fact is probably correct that after diagnosis of GC, most patients leave risky behaviors, habits, and lifestyles. Possibly, they improve their physical activity, health monitoring schedule, and *H. pylori* evaluation or treatment. They revise their dietary habits, leave stressful situations, make attention

to medical advice and enhance their lifestyle. Hence, after diagnosis of GC, the type of risk factors for survival differs from those inducing the initiation of the malignancy. We suggest that our study's discrepancies with the other research are related to the risk type change after the primary diagnosis of GC.

Overall, from sociodemographic factors, age, sex, educational level, and job were determinative in our study. But their effects seem to be time-dependent because the sex and job were significantly different between survived and dead individuals after 5 years and not 1 year. We hypothesize the risk factors exposure frequency is increased over time. Repeated exposures potentiate the chance of cancer development. The genetic and racial factors predispose a person to malignancy involvement or prevention. Therefore, we should consider each risk factor specifically for a population or even an individual. Personalized medicine seems to be the choice in the prevention, diagnosis, treatment, and monitoring of GC.

One of the limitations of our study was the stage of the disease, as we used only the patients in stage 3. Unfortunately, data of the patients with other stages were not available in the database.

Conclusion

In addition to the genomic changes, GC development depends on various environmental factors and lifestyle status. In our work, age, sex, education, and job were meaningful variables for 1-year or 5-year or both survivals in patients with GC. Anyhow, other studied variables were not accountable as the risk factors for GC, despite case-control studies. Hence, we suggest that sociodemographic risk factors of GC development could be different from those that affect malignancy survival. Hereupon, we suggest studies targeting sociodemographics and their effects on the physiopathology of GC. We need such evidence to promote and enhance GC patients' survival.

Conflict of Interest

The authors declare no conflict of interest related to this work.

Ethical Approval

Study proposal evaluation and legal permission to access the blinded data were under Isfahan Health Center's ethical committee license. It was registered in the Iranian Registry of Clinical Trials (identifier: IR.MUI.MED.REC.1399.142.).

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