

Original Article

Survival analysis of gastric cancer patients in El Salvador

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Análisis de supervivencia de pacientes con cáncer gástrico en El Salvador

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Abstract

Introduction. Gastric cancer is one of the most prevalent and deadly malignancies worldwide. The survival prognosis depends on clinical presentation, diagnostic evaluation, initiation of treatment, and several other influencing factors. The objective of this research was to analyze the four-year survival of gastric cancer patients in El Salvador. **Methodology.** A retrospective cohort study was conducted with patients diagnosed with gastric cancer from a national hospital. Patient characteristics were described, and overall survival rates at one year and four years was calculated using the Kaplan-Meier method. The Tarone-Ware test was used to assess statistical significance with a p-value < 0.05 and 95% confidence intervals. A Cox regression was performed to evaluate the association between independent and dependent variables. **Results.** Seventy-nine patients were analyzed. Overall survival rates at one year and four years were 46.84% and 31.65%, respectively. Chronic kidney disease was associated with a *hazard ratio* (HR) of 4.204, smoking with HR of 3.533, age with HR of 0.98, high blood pressure with HR of 0.654, and alcoholism with HR of 0.367, all with p < 0.05. **Conclusion.** The four-year survival rate is below 40 %. Smoking, chronic kidney disease, cancer stage, and adenocarcinoma decreased four-year survival in patients with gastric cancer.

Keywords

Catheters; Umbilical Veins, Infant, Newborn.

Resumen

Introducción. El cáncer gástrico es una de las neoplasias malignas más prevalentes y mortales a nivel global. El pronóstico de supervivencia depende de la presentación clínica, del estudio de diagnóstico, el inicio del tratamiento, así como una serie de factores que influyen en esta. Objetivo. Analizar la supervivencia a los cuatro años de los pacientes con cáncer gástrico de un centro hospitalario. Se hizo una caracterización de los pacientes incluidos en el estudio y se calculó la tasa de supervivencia global al año y a los cuatro años, se utilizó el estimador de Kaplan-Meier y aplicó la prueba de Tarone-Ware como prueba para evaluar la significancia estadística (p < 0,05 e intervalos de confianza al 95 %). Para comprobar la asociación entre las variables independientes y la dependiente, se realizó una regresión de Cox. Resultados. Se analizaron 79 pacientes. La supervivencia general al año fue del 46,84 % y a los cuatro años del 31,65 %. La enfermedad renal crónica presentó un hazard ratio de 4,204, el tabaquismo fue de 3,533, mientras que, la edad obtuvo un hazard ratio de 0,98, la hipertensión arterial un 0,654 y el alcoholismo un 0,367, todas con p < 0,05. Conclusión. La supervivencia a los cuatro años es menor al 40 %. El tabaquismo, la enfermedad renal crónica, el estadio del cáncer y el adenocarcinoma disminuyeron la supervivencia a los cuatro años en pacientes con cáncer gástrico.

Palabras clave

Catéteres, Venas Umbilicales, Recién Nacido.

Introduction

Gastric cancer (GC) is among the most prevalent and deadly malignant neoplasms worldwide. It is currently the fifth most common cancer and the third leading cause of cancer-related death globally.^{i,i} Each year,

it is estimated that approximately 980 000 new cases of GC are diagnosed and 660 000 GC-related deaths occur globally. These figures reflect the high mortality burden associated with GC, especially in regions where early diagnosis and effective treatment remain difficult to access.

Five-year overall survival in GC patients ranges from 20 % to 40 %. In general, younger patients have longer survival compared to older adults, with the risk increasing with advancing age6. However, these differences are determined by multiple factors, such as clinical presentation, stage at diagnosis, presence of comorbidities, substance use, and timely access to treatment. VII-IX

Despite advances in diagnosis and treatment, the survival of GC patients remains limited and varies significantly between individuals 10 due to clinical, biological, and demographic factors that influence prognosis and treatment efficacy. Identifying and understanding of these factors is essential to improve outcomes in patients with GC and to implement effective and targeted strategies for early detection of the disease. Vixiii

In El Salvador, the available information on GC is limited, highlighting the importance of conducting a survival analysis of patients diagnosed in a tertiary care hospital. This analysis aims to identify the variables that influencesurvival duration in patients with GC, providing valuable information on the factors associated with prognosis. In addition, it offers a comprehensive perspective on how different factors affect clinical outcomes, contributing to a better understanding of the elements that determine the evolution of the disease.

Methodology

A retrospective analytical cohort-type analytical study was conducted with patients registered in the gastric cancer patient database of a national tertiary care hospital in El Salvador in 2019. All patients over 18 years, diagnosed for the first time, and with a confirmatory histopathological diagnosis of GC were included. Patients with incomplete records, those who died within the first 24 hours of admission, those residing abroad or identified as foreign nationals, and those with duplicate records were excluded.

Initially, the database consisted of 81 records; however, after eliminating those that did not meet criteria, the number was reduced to 79. These individuals were followed up until death or until the end of the study, at which point censoring was considered.

Survival time was measured from the date the biopsy was taken until the date of patient death or the last recorded follow-up contact.

To collect the data, a structured questionnaire was designed in digital format using KoboToolbox, a tool for creating, collecting, and managing digital forms. The questionnaire included the variables age, sex, educational level, marital status, work activity, tobacco use, alcohol consumption, diagnoses of diabetes *mellitus*, dyslipidemia, arterial hypertension, and chronic kidney disease, as well as the stage of GC, date of biopsy, presence of *Helicobacter pylori*, pathological variant of cancer, date of death, basic cause of death and the patient's area of residence.

Statistical analysis

The normality of continuous variables was assessed using the Anderson-Darling test. When a p-value < 0.05 was obtained, the median and interquartile range were used. Statistical significance was set at p < 0.05, with 95 % confidence intervals. For comparison between two independent groups, the Mann-Whitney U test was used. Differences in proportions by area of origin, sex, and place of origin were analyzed using the Chi-square test.

To calculate the overall survival rate at one and four years, the Kaplan-Meier estimator was used. To test for differences among the groups, the Tarone-Ware test was used as a test of statistical significance with a p-value < 0.05 and 95 % confidence intervals.

A Cox proportional hazards model was constructed to evaluate the association between predictor variables and time to event. Prior to adjustment, the variables available in the database and the presence of missing data were identified. For variable selection, multicollinearity was assessed using the Variance Inflation Factor (VIF), and variables with a VIF \geq 5 were excluded. Missing data were handled using multiple imputations with the predictive mean matching method, as implemented in the mice package in RStudio. The model was fitted on each imputed dataset, and the results were combined by pooling, a process that integrates the results of the different analyses to obtain a final estimate that considers the variability caused by the missing data, thereby achieving a more reliable result.

The goodness of fit of the model was evaluated using the Likelihood Ratio test and Wald test, with p-values < 0.05 to be considered statistically significant. To evaluate the predictive capacity of the model, Harrell's concordance index (C-index) was used. To verify the assumption of proportionality of risks over time, the Schoenfeld residuals analysis was used. Data processing and analysis were conducted using RStudio version 4.3.2.

This study was conducted in accordance with the Declaration of Helsinki, the Nuremberg Code, the guidelines of the Council for International Organizations of Medical

Sciences (CIOMS), and other international ethical guidelines for health research. Good clinical practice was followed, and patient identity was protected through data coding. The study protocol was approved by the Ethics Committee of the Hospital Nacional Rosales, under act number 32/2024.

Results

Seventy-nine patients corresponding to those diagnosed with GC in 2019 in a tertiary care hospital were analyzed; of these, 54 died at the end of the study (68. 3 %). Fifty-nine percent of the participants were male. The median age was 66 years (RI: 58-73), with a minimum age of 36 years and a maximum of 94 years. No significant difference was observed between the medians by sex (p = 0.214). Fifty-six percent were from urban areas (p = 0.779), with the highest frequency in the department of San Salvador (39 %), followed by La Paz (14 %) and Chalatenango (10 %). However, there were patients from all departments of El Salvador.

According to the sociodemographic variables analyzed, 49 % of participants were married. In terms of educational level, 32 % had first to sixth-grade education, while 11 % had completed seventh to ninth grade. However, 29 % had no record of their education level. Regarding occupation, 34 % were farmers, followed by individuals engaged in domestic cleaning services, with 29 %.

Table 1 summarizes the clinical and pathological characteristics and comorbidities of the patients with GC. The presence of Helicobacter pylori was identified in 34 % of the cases, while in 48 %, this information could not be confirmed. Twentynine percent of the patients were smokers, and 26 % reported alcohol consumption. Regarding comorbidities, 10 % of the patients were diagnosed with diabetes *mellitus*, 21 % had arterial hypertension, and 6 % had chronic kidney disease.

Regarding the stage of GC at diagnosis, 34 % of patients were stage IV, followed by stages II and III, each accounting for approximately 9 % each. However, 47 % of the cases could not be staged. Regarding pathological classification, 86 % of the patients had adenocarcinoma.

Survival of patients with gastric cancer

Figure 1 shows the survival curve of GC patients. A steady decline over time is observed, with a sustained loss of patients,

especially pronounced during the first two years of follow-up.

In the first year, the survival rate was 46.84 % (95 % Cl: 37.03 % - 59.24 %). From the second year onwards, a stabilization of the curve is observed; however, as time goes by, the curve continues to decline, reaching a survival rate of 31.65 % (95 % Cl: 22.89 % - 43.76 %) at the end of the study, equivalent to 25 of the 79 patients who made up the initial cohort.

Figure 2. shows the survival curves of GC patients at four years, classified by sex, area of origin, smoking and alcohol consumption.

Regarding sex, the survival rate at one year was 50 % (35.36 % - 70.70 %) in women and 44.68 % (32.51 % - 61.42 %) in men. At four years, survival rates were 37.5 % (23.98 %-58.65 %) in women and 27.66 % (17.42 % - 43.92 %) in men. Although women showed a higher survival rate at both one and four years compared to men, this difference was not statistically significant (p > 0.05).

Regarding the area of origin, survival at one year was 50 % (37.21 % - 67.19 %) in rural areas and 42.86 % (29.23 % - 62.83 %) in urban areas. At four years, survival rates were 34.09 % (22.61 % - 51.41 %) in rural areas and 28.57 % (16.92 % - 48.24 %) in urban areas. People living in rural areas had a higher survival rate at one year; however, this difference was reduced at four years (p> 0.05).

Regarding smoking, non-smokers had a one-year survival rate of 57.5 % (44.05 % -75.05 %), while smokers had a survival rate of 39.13 % (23.50 % - 65.14 %). At four years, survival rates are 37.5 % (25.14 % - 55.95 %) for non-smokers and 30.43 % (16.41 % - 56.46 %) for smokers; however, the difference was not statistically significant (p > 0.05).

Concerning alcohol consumption, survival at one year was 53.49% (40.48% - 70.68%) for non-drinkers and 47.62% (30.41% - 74.58%) for drinkers. At four years, survival was 32.56% (21.18% - 50.06%) in non-drinkers and 38.1% (22.08% - 65.71%) in drinkers, with no significant differences (p > 0.05).

Figure 3 shows the 4-year survival curves for GC patients classified by arterial hypertension, diabetes *mellitus*, chronic kidney disease, and pathological variant.

For arterial hypertension, the one-year survival rate is 51.02 % (38.78 % - 67.13 %) in those without the diagnosis and 52.94 % (33.82 % - 82.88 %) in those with the diagnosis. At four years, survival is 32.65 % (21.84 % - 48.82 %) in those without hypertension and 41.18 % (23.33 % - 72.68 %) in those with hypertension (p > 0.05).

For diabetes *mellitus*, the one-year survival rate was 54.39 % (95 % Cl: 42.88 % - 68.98 %) in those without the diagnosis and 37.5 %

Table 1. Clinical characteristics of patients diagnosed with gastric cancer at the tertiary hospital in El Salvador in 2019

Variable		Survivors (n=25)	%	Deceased (n=54)	%	Total	%
	Yes	11	44,0	16	29,6	27	34,2
Helicobacter pylori	No	6	24,0	8	14,8	14	17,7
	No data	8	32,0	30	55,6	38	48,1
Smoker	Yes	7	28,0	16	29,6	23	29,1
	No	15	60,0	25	46,3	40	50,6
	No data	3	12,0	13	24,1	16	20,3
Alcohol	Yes	8	32,0	13	24,1	21	26,6
	No	14	56,0	29	53,7	43	54,4
	No data	3	12,0	12	22,2	15	19,0
Diabetes mellitus	Yes	3	12,0	5	9,3	8	10,1
	No	20	80,0	37	68,5	57	72,2
	No data	2	8,0	12	22,2	14	17,7
Dyslipidemia	Yes	0	0,0	1	1,9	1	1,3
	No	23	92,0	40	74,1	63	79,7
	No data	2	8,0	13	24,1	15	19,0
Arterial hypertension	Yes	7	28,0	10	18,5	17	21,5
	No	16	64,0	33	61,1	49	62,0
	No data	2	8,0	11	20,4	13	16,5
Chronic renal disease	Yes	1	4,0	4	7,4	5	6,3
	No	22	88,0	38	70,4	60	75,9
	No data	2	8,0	12	22,2	14	17,7
Cancer stage	Stage I	0	0,0	1	1,9	1	1,3
	Stage II	5	20,0	2	3,7	7	8,9
	Stage III	2	8,0	5	9,3	7	8,9
	Stage IV	9	36,0	18	33,3	27	34,2
	Not staged	9	36,0	28	51,9	37	46,8
Pathologic classification	Well-differentiated adenocarcinoma	17	68,0	47	87,0	64	81,0
	Poorly differentiated adenocarcinoma	1	4,0	3	5,6	4	5,1
	Gastric GIST* 2	2	8,0	1	1,9	3	3,8
	Non-Hodgkin's lymphoma	4	16,0	3	5,6	7	8,9
	Neuroendocrine tumor	1	4,0	0	0,0	1	1,3

^{*}GIST: gastrointestinal stromal tumor.

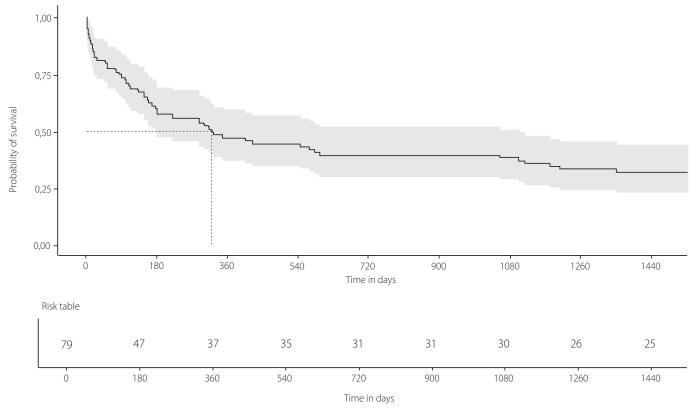


Figure 1. Cumulative survival of patients with gastric cancer at four years in a tertiary hospital in El Salvador, 2019 to 2023.

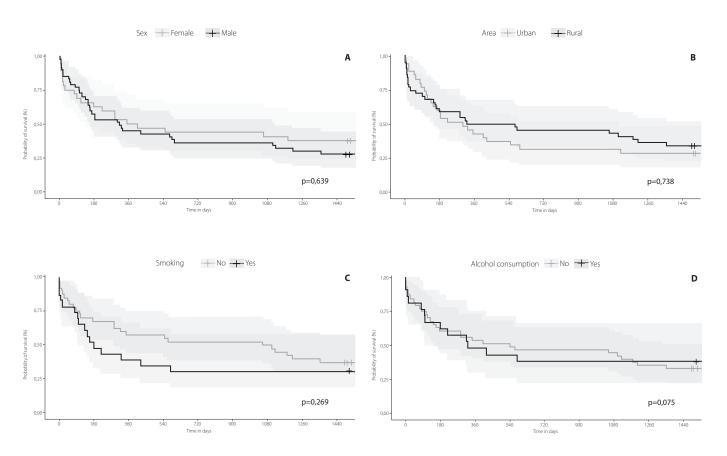


Figure 2. Four-year survival curve of gastric cancer patients by sex (Figure 2A), area of origin (Figure 2B), smoking (Figure 2C) and alcohol consumption (Figure 2D), 2019 to 2023.

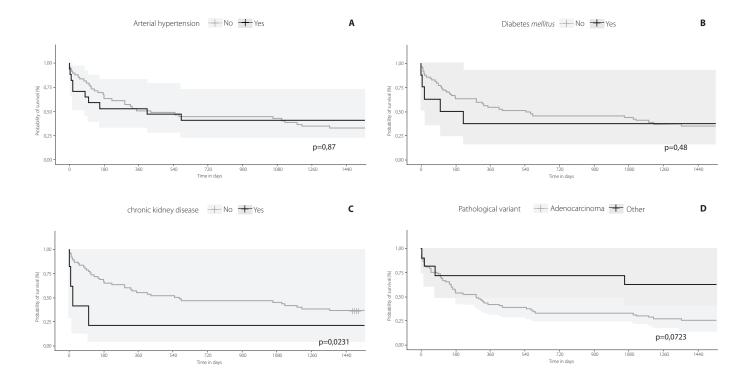


Figura 3. Four-year survival curve of patients with gastric cancer at four years of arterial hypertension (Figure 3A), diabetes *mellitus* (Figure 3B), chronic kidney disease (Figure 3C), pathological variant (Figure 3D), 2019 to 2023.

(95 % Cl: 15.33 % - 91.74 %) in those with the diagnosis. At four years, survival was 35.09 % (95 % Cl: 24.65 % - 49.95 %) in those without diabetes *mellitus* and 37.5 % (95 % Cl: 15.33 % - 91.74 %) in those with the diagnosis (p > 0.05).

As for CKD, survival at one year is 55 % (43.75 % - 69.15 %) in those without CKD and 20 % (3.46 % - 100 %) in those with CKD. At four years, survival is 36.67 % (26.29 % - 51.13 %) in those without a diagnosis of chronic kidney disease and 20 % (3.46 % - 100 %) in those with the diagnosis, with significant differences between the groups (p < 0.05).

When comparing survival between patients with adenocarcinoma and those with other pathological variants, it is observed that at one year, the survival rate of patients with adenocarcinoma was 42.65 % (32.37 % - 56.18 %), while those with other variants reached 72.73 % (50.64 % - 100 %). This trend was continued over four years, with survival rates of 26.47 % (17.81 % - 39.34 %) for patients with adenocarcinoma and 63.64 % (40.71 % - 99.47 %) for those with other variants; however, the differences were not significant (p \geq 0.05).

Table 2 summarizes the results of the multivariate Cox model analyzing the relationship between various clinical variables and the risk of death from GC. Smoking was associated with lower survival, with a hazard ratio (HR) of 3.53 (95 % Cl: 1.31-9.48; p= 0.0172). Similarly, chronic kidney disease was associated with a significant increa-

se, with an HR of 4.20 (95 % CI: 1.17-14.98; p = 0.0329). On the other hand, alcoholism showed a trend toward higher survival, although it did not reach statistical significance (HR = 0.37; 95 % CI: 0.12-1.04; p = 0.0710). Finally, neither high blood pressure nor age showed significant associations in this analysis (HR = 0.65, p = 0.3467 and HR = 0.99, p = 0.3540, respectively).

The Schoenfeld test of the proportionality of hazards tests indicate that there are no problems with the proportionality assumption for the variables included in the model (p > 0.05). The overall test also suggests that the model as a whole adequately meets this assumption (p > 0.05). In addition, the statistical tests showed that the model is significant, has a good fit, and provides an adequate explanation of the outcome from the included data (p < 0.01), showing moderate agreement (0.623).

Discussion

This study provides an overview of survival rates and variables associated with GC in patients diagnosed at a tertiary care hospital in El Salvador during 2019. The findings offer valuable insights into the prognosis and clinical characteristics of the disease within the Salvadoran context.

The Kaplan-Meier survival curve shows a steep decline during the first two years after diagnosis, followed by relative stabilization.

Table 2. Results of the multivariable Cox model for gastric cancer risk

Variable	Coefficient	Hazard Ratio (HR)	IC 95%	Standard error	z-statistic	p-value
Chronic kidney disease	1,436	4,204	1,17-14,98	0,648	2,215	0,0329
Smoking	1,262	3,533	1,31-9,48	0,504	2,504	0,0172
Age	-0,012	0,988	0,96-1,01	0,013	-0,938	0,3540
Arterial hypertension	-0,424	0,654	0,27-1,56	0,446	-0,952	0,3467
Alcoholism	-1,003	0,367	0,12-1,04	0,536	-1,871	0,0710

Harrell's average C-index: 0.623 Standard deviation of C-index: 0.019 Likelihood ratio test: p=0.01 Wald test: p=0.01 Test score (log rank): p=0.01

The one- and four-year survival rates reflect the aggressive nature of the disease and underscore the importance of early diagnosis and timely treatment.xii,xiii These results are consistent with previous studies that have reported similar survival rates in developing countries.xiv The observed survival rate could be related to various factors, such as diagnosis in advanced stages, limitations in access to specialized treatment, the presence of comorbidities, and administrative aspects of the health system, as reported by other studies in the region. XV,XVI It is important to consider that the hospital where the research was conducted is the main referral center in El Salvador; it usually treats more complex cases and in advanced stages, which could influence the survival rates observed.

Analysis using the Cox regression model determined that smoking is a factor associated with lower survival in gastric cancer. Current literature has established smoking as an important risk factor not only for gastric cancer but for multiple types of cancers. The mechanism by which smoking increases the risk of gastric cancer is multifactorial and includes exposure to carcinogens, induction of chronic inflammation, and alteration of the immune response. The marked difference in survival between smokers and non-smokers, mainly in the early years, shows the importance of public health interventions aimed at reducing tobacco use.

Lower survival rates was observed in patients with chronic kidney disease, a finding consistent with previous studies reporting worse outcomes in patients with cancer and chronic kidney disease20. This condition may make cancer management more difficult, limit treatment options, and

increase the risk of complications, which could explain the lower survival found in these patients.^{xxi}

Regarding demographic factors, a trend toward more prolonged survival was observed in women compared to men; however, this difference did not reach statistical significance. This finding differs from some previous studies, which have documented significant differences in survival according to sex, with a slight female predominance. The absence of statistical significance could be related to the sample size, the characteristics of the patients treated in the hospital, or to factors specific to the population of El Salvador.

Patients from rural areas had slightly longer survival compared to those from urban areas, although this difference was not statistically significant. This result contrasts with the trend observed in some studies, which have shown higher mortality rates in rural areas, mainly attributed to barriers to accessing health services.xxiii However, in the context of El Salvador, geographic barriers may not have a significant impact on survival. Instead, factors such as diet, exposure to environmental contaminants, the presence of comorbidities, and lifestyle differences between populations may explain this trend and have a more significant impact on survival. xxiv

Although no statistically significant association was found between alcohol consumption and GC survival, it is important to highlight that non-drinkers showed a more prolonged survival at 1-year follow-up. The relationship between alcohol consumption and GC is complex and has shown diverse results in different studies.xxxxxxi Factors such

as the type of alcoholic beverage, the amount consumed, and the interaction with other risk factors may influence this relationship.

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No significant difference in survival was observed between hypertensive and non-hypertensive patients, which contrasts with some studies that have suggested a possible protective effect of certain antihypertensive drugs on the development and progression of GC28. Other studies have related the occurrence of hypertension to the use of certain drugs to treat cancer or even to increased survival associated with more effective therapies.^{xxix}

Diabetic patients showed lower survival rates at one year, although this difference was not statistically significant; this trend was also maintained at four years. The relationship between diabetes and GC is complex and may be influenced by factors such as glycemic control, duration of diabetes, and antidiabetic treatment30. Recent studies indicate that new therapies and lifestyle changes have improved blood glucose control, which in turn contributes to a better quality of life and longer survival in cancer patients by reducing long-term complications. XXXI,XXXIII

Although in this study, it was not possible to accurately assess the association between dyslipidemia and gastric cancer mortality due to the small number of cases, some studies have suggested a possible relationship between lipid disorders and GC risk, possibly mediated by inflammatory mechanisms or alterations in cellular metabolism. **xxxiii,xxxxii**

The limitation in establishing an association between dyslipidemia and gastric cancer opens new lines of research in El Salvador, which could contribute to a deeper understanding of the pathogenesis of this disease. Currently, some studies have shown that dyslipidemia is associated with an increased risk of gastric cancer, even after adjusting for age, sex, and other factors. Further studies are needed to explore this relationship and assess whether managing dyslipidemia could impact the prevention or prognosis of GC.

Regarding pathological characteristics, the study found evidenced that patients with adenocarcinoma presented a higher risk of mortality compared to other histological variants; however, this difference did not reach statistical significance. This contrasts with the literature, which has established adenocarcinoma as the most common and generally more aggressive histologic type of GC. The shorter survival observed

in patients with adenocarcinoma highlights the importance of accurate histologic diagnosis for risk stratification and treatment planning. XOXVI Recent studies have identified molecular subtypes of gastric adenocarcinoma with different prognoses and responses to treatment. Future studies in this population could benefit from more detailed molecular characterization to improve risk stratification and guide personalized therapeutic decisions XXIII,XXXVIII

A significantly longer survival was observed in patients diagnosed at early stages of the disease. This finding highlights the importance of early diagnosis and early detection programs in the management of GC.xiii,xxxxiiiA significant proportion of cases may be diagnosed at advanced stages; this pattern of late presentation is common in many developing countries and highlights the need for improved early detection and GC awareness programs.xiii,xxxxxxii On the other hand, the marked decrease in survival during the first two years after diagnosis underscores the urgency of implementing and improving GC early detection programs.xviii,xix

The main limitations of this study include the relatively small sample size, which may reduce the statistical power to detect significant associations, especially in subgroup analyses. As a retrospective cohort, the study is subject to inherent biases such as the presence of missing or incomplete data in the medical records. Additionally, the lack of direct interviews with patients restricted the the collection of additional clinical or contextual variables that were not routinely documented, potentially affecting the completeness and interpretability of the results.

Despite these limitations, the study presents notablestrengths. It provides specific data on GC in El Salvador, addressing a significant gap in the national and regional literature. The use of Cox proportional hazards models, along with appropriate performance metrics allowed for a robust assessment of multiple prognostic factors simultaneously. Consideration of multiple comorbidities provides a more comprehensive view of factors influencing GC survival, and follow-up of up to four years provided valuable information on survival in this population.

Finally, this study provides an overview of survival and factors associated with GC survival in Salvadoran patients. The findings underscore the critical importance of early detection, management of comorbidities, and consideration of modifiable risk factors such as smoking.

The identification of smoking and chronic kidney disease as factors associated with survival opens up new lines of research that

could have important implications for the prevention and comprehensive management of CG. Further studies, preferably multicenter and prospective, are needed to confirm and extend these findings, as well as to evaluate specific interventions aimed at improving clinical outcomes in this population.

Conclusion

Survival of less than 40% at four years for GC patients reflects the severity of the disease and the complexity of its management from diagnosis onwards, highlighting the persistent challenge this condition poses particularly in achieving favorable long-term prognosis and ensuring adequate management.

The profile of patients diagnosed with GC, characterized by a predominance of older men, urban residency and a high rate of Helicobacter pylori infection, suggests deficiencies in the early detection of the disease, highlighting the need to strengthen prevention and improve early diagnosis strategies and the implementation of intervention programs on the risk factors identified in the study.

The factors most strongly associated with reduced survival of patients with gastric cancer were smoking, chronic kidney disease, and, more decisively, the clinical stage and histological type of tumor.

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