Prognostic factors of survival in patients with gastric cancer: a retrospective study in the Aktobe region for 2010-2024.

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ABSTRACT

Relevance

Gastric cancer (GC) remains a leading cause of cancer mortality, with survival rates heavily dependent on early detection. Most cases are diagnosed at advanced stages, resulting in poor prognoses and low 5-year survival rates. Accurate survival estimates are essential for assessing treatment effectiveness and guiding healthcare strategies. However, data collection delays hinder timely analysis. Model-based period analysis addresses this issue, enabling real-time survival estimates and forecasting trends to improve patient outcomes and cancer management.

Aims

To evaluate the prognostic factors influencing survival in patients with gastric cancer, considering demographic, clinical, and histopathological characteristics in the Aktobe region from 2010 to 2024.

Methods

A retrospective study was conducted using data from 1859 GC patients registered in the Aktobe Cancer Registry. Survival analysis was performed using Kaplan-Meier estimation, log-rank tests, and Cox proportional hazards models. Factors such as age, sex, tumor stage, histological subtype, tumor location, and ethnicity were analyzed for their impact on survival.

Results

The overall five-year survival rate was 21.5%. Advanced tumor stage was the most significant prognostic factor, with stage IV patients having significantly worse survival than stage I ($p = 0.0124$). Ethnicity was associated with survival differences, with non-Kazakh patients showing a higher risk of mortality ($p = 0.0334$). However, age, sex, tumor location, and Lauren classification did not show a statistically significant impact on survival. Patients with localized GC had significantly better survival outcomes compared to those with advanced disease ($p < 0.001$).

Conclusion

Tumor stage and ethnicity were identified as key prognostic factors affecting GC survival, while other clinical variables had less predictive value. These findings highlight the need for improved early detection strategies and targeted interventions to enhance patient outcomes. Further research incorporating molecular profiling may improve individualized treatment approaches.

Keywords

Gastric cancer, prognostic factors, five-year survival, lauren classification, Kaplan-Meier.

INTRODUCTION

Gastric cancer (GC) remains a significant global health burden, ranking among the leading causes of cancer-related mortality worldwide. The number of new cases and deaths continues to rise due to population growth and aging[1]. Globally, GC is the fifth most common malignancy and the fourth leading cause of cancer-related deaths. Despite declining incidence rates, the global burden of this malignancy is projected to increase by 62% by 2040[2].

GC has particularly high incidence and mortality rates in East Asia, Eastern Europe, and South America[3]. The cumulative risk of GC is significantly higher in East Asia (2.64%)

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compared to the lowest rates in Southern Africa (0.42%)[4]. In 2022, approximately 20 million new cancer cases and 9.7 million cancer-related deaths were recorded worldwide. About one in five men and women develop cancer during their lifetime, with one in nine men and one in twelve women dying from the disease[5].

According to GLOBOCAN 2022 data, GC ranks fourth in cancer incidence (8.5% of all cases) and second in cancer-related mortality (10.1%) in Kazakhstan. Globally, the incidence of GC is 9.2 per 100,000 population, with a mortality rate of 6.1 per 100,000. In Kazakhstan, these figures are higher, with an incidence rate of 13.7 per 100,000 and a mortality rate of 9.3 per 100,000, placing the country among the 36 nations with the highest GC incidence rates[6].

The burden of GC morbidity and mortality is rapidly increasing worldwide, reflecting population aging, growth, and changes in the prevalence and distribution of key risk factors, some of which are associated with socioeconomic development. The incidence of GC is influenced by multiple factors, including genetic predisposition, dietary habits, Helicobacter pylori infection, and chronic gastric conditions such as gastritis and ulcers[7-9].

GC is a heterogeneous disease, encompassing various histological and molecular subtypes. Despite advancements in diagnostic and therapeutic approaches, GC remains a major global health challenge, necessitating further research into its various aspects, including the impact of age and histological classification on survival outcomes[10,11]. Clinicopathological factors, including the stage of lymph node metastasis, histological subtype, and genetic factors, play a crucial role in patient survival[12].

The Lauren classification, a widely used system, categorizes gastric adenocarcinomas into intestinal, diffuse, and mixed types[10,13]. The intestinal type is characterized by glandular structures and is often associated with chronic atrophic gastritis and intestinal metaplasia. The diffuse type exhibits infiltrative growth and poor differentiation, leading to a more aggressive course and poorer prognosis. Mixed-type adenocarcinomas display features of both intestinal and diffuse types, representing a combination of glandular and poorly cohesive growth patterns[14,15].

In recent years, increasing attention has been given to gastric microbiota dysbiosis and its role in gastric carcinogenesis. Studies have shown that the gastric microbiome consists of key bacterial species, including Firmicutes, Actinobacteria, Bacteroidetes, and Proteobacteria, which may contribute to tumor transformation[16].

Beyond histological characteristics, the molecular profiles of GC play a crucial role in prognosis and treatment selection. Recent studies have identified various biomarkers associated with disease progression[10]. The Cancer Genome Atlas (TCGA) classifies GC into four molecular subtypes: Epstein-Barr virus-positive tumors, microsatellite instability-high tumors, genomically stable tumors, and chromosomally unstable tumors. These molecular subtypes have distinct therapeutic approaches and survival outcomes. Tumor location and growth patterns have also been frequently described as critical pathological parameters in GC, highlighting their clinical significance[12]. The evaluation of early invasive GC detected in biopsy specimens remains essential[13]. Consequently, the histological and molecular characteristics of GC significantly impact its clinical course and patient survival.

Patient survival in GC is closely linked to the stage at diagnosis. The five-year survival rate remains relatively low; however, early detection significantly improves prognosis. Ten-year survival rates also vary but are influenced by patient age, disease stage, tumor type, and access to high-quality treatment[17,18].

Key factors affecting GC survival include early diagnosis, surgical intervention, chemotherapy, and targeted therapy. Additionally, overall patient health, comorbidities, and access to advanced medical technologies play a crucial role. The disease outcome is also influenced by both modifiable factors (H. pylori infection, obesity, dietary habits) and non-modifiable factors (genetic predisposition, age, sex). Socioeconomic status further impacts timely access to treatment and supportive care[3]. Other prognostic factors include tumor type, disease stage at diagnosis, race, and lifestyle habits[19,20].

Demographic projections indicate that the number of new cancer cases will reach 35 million by 2050. Investments in cancer prevention, including strategies targeting key risk factors such as smoking, obesity, and infections, could prevent millions of future cancer diagnoses and save lives globally, yielding substantial economic and social benefits in the coming decades[5].

GC significantly contributes to global cancer mortality, posing serious clinical challenges, particularly in advanced stages where treatment options are limited and prognosis is poor[21].

The complex interplay of modifiable and non-modifiable risk factors in GC epidemiology highlights the need for improved screening and comprehensive treatment strategies. Novel targeted therapies and immunotherapies have shown promising results, enhancing the precision of GC treatment. A comprehensive approach that integrates prevention, early detection, and innovative therapies is essential for improving survival rates and quality of life in GC patients[3].

Due to the complexity and variety of treatments for GC, as well as the high mortality rate from it, additional research is needed to understand what factors influence the development of the disease. Our work is aimed at studying the molecular and clinical lesions of the stomach in order to improve diagnostic and treatment methods.

MATERIALS AND METHODS

Study design. A retrospective cohort studies.

Study place. The research was carried out in the region of West Kazakhstan, which includes the territories of West Kazakhstan Province. The study was specifically conducted at the West Kazakhstan Marat Ospanov Medical University and affiliated healthcare institutions.

Sample Size. The study involved a cohort of 1859 patients diagnosed with gastric cancer in West Kazakhstan. Study setting This retrospective database research was approved by the University's IREC (Protocol No. 10, 27.10.2023) and performed following the Helsinki Declaration principles. Informed consent was not required as the individually identifiable data of patients were not involved.

Study population. Data on the province's total adult population (≥18) from 2010 to 2024, including males/females, and by age groups were requested from the Aktobe Statistical Committee. All incident first diagnosed GC cases (C16.0-C.16.9, The WHO ICD-10 Version: 2022) from 2010 to 2024 in adults aged 18 years and older were obtained from the Cancer Registry of the Aktobe Regional Oncologic Center. The disease clinical stage (The 8th edition of the UICC TNM classification, 2016: gastric carcinoma, adenocarcinoma). Stages were presented as local (St I; St II,St IIA, St IIB – T1-4a; N0-3, M0) and advantage (St III; St IIIa, St IIIb, St IIIc and St IV (T4b, any T; any N: M1a-M1b). By morphological type the following categories were used: diffuse, intestinal and mixed. By ethnicity all patients were dichotomized into Kazakh and others.

By location, the cancers were dichotomized into cardio and other parts of the gastric cancer (noncardio). What is considered the most favorable category was selected as the reference group.

We used data from all patients with gastric cancer in the Aktobe region, registered in the electronic register of cancer patients for the period from 2010 to 2024. All the research was obtained from the cancer registry at the West Kazakhstan Medical University named after Marat Ospanov.

The inclusion criteria were as follows. 1) diagnosis of gastric carcinoma according to the World Health Organization International Classification of Diseases (WHO - ICD 16) and 2) registry date at EROB between January 2010 and November 2024.

The exclusion criteria were 1) gastric carcinoma diagnosis before 2010 or after 2024; 2) Post-mortem patients with gastric cancer (identified at autopsy).

For the purpose of this paper we extracted information on date of birth, date of diagnosis of gastric cancer, date of death or censoring, ethnic background, morphological type of tumor by Lauren and prevalence stage of cancer.

Statistical analysis

In this study, we conducted a survival analysis of patients with gastric cancer, taking into aclinical and demographic factors. Standard statistical methods were employed to asses Kaplan-Meier analysis, the log-rank test, and the Cox proportional hazards model.

The Kaplan-Meier method wasprobability of survival at different time points, providing inone-year and five-year survival rates. Thione-year and five-year survival rates), 95% confidence intervals (CIs) were calculated to ensure the statistical precision of the obtained results. Additionally, the median survival time was determined along with its corresponding confidence intervals, allowing for an evaluation of the time at which 50% of patients in a given group remain alive.

To compare survival curves across different groups, the log-rank test was applied. This statistical test, used within the Kaplan-Meier framework, evaluates whether there is a statistically significant difference in survival between study groups[22]. Furthermore, to assess the impact of multiple factors on survival, we employed the Cox proportional hazards model, which was conducted in both univariate and multivariate approaches. This enabled us to account for the effects of various clinical and demographic factors on the survival of patients with gastric cancer[23]. All statistical analyses were performed using R software (v. 4.1.0, Vienna, Austria) (https://www.r-project.org/). The R environment provides a robust platform for conducting comprehensive survival analyses, including the application of Kaplan-Meier estimators, log-rank tests, and Cox proportional hazards models[24].

RESULTS

The main characteristics of the study are presented in Table 1. In the Aktobe Cancer Registry, a total of 1859 records of patients who were first diagnosed with GC over the 2010-2024 period were found. Median follow-up period was estimated as 7 (range, 6.2 to7.7) months including the last follow-up period. At the end of the follow-up period, 1646 (88.5%) patients exited. Young patients under 50 years of age accounted for 11%, while those over 89%. Patients under 50 years of age (11.1% of the cohort) had a one-year survival rate of 39%, compared to 34.1% for those over 50 (88.9% of the cohort). The five-year survival rate was higher in younger patients (28.9%) than in older patients (21.5%). Median survival was 8 months for patients under 50 and 7 months for those over 50, with no statistically significant difference between these two age groups (p=0.06).

Deceased cases consisted of 1229 male and 630 women patients with a male/female ratio of 1.94. Male patients (66.1% of the cohort) had a slightly higher one-year survival rate (36.3%) compared to females (33.9% of the cohort, 31.1% survival). However, five-year survival rates were similar between genders (21.9% for males and 23.2% for females).

Patients with localized disease (53.8% of the cohort) had a one-year survival rate of 44%, compared to 23.1% for those with advanced disease (46.2% of the cohort). Five-year survival rates were 29.1% for localized disease and 14.8% for advanced disease. Median survival was 10 months for localized disease and 4 months for advanced disease. Tumor stage was a significant predictor of survival ($p < 0.001$).

The location of the tumors was assessed based on endoscopic examinations and computed tomography results. Tumors located in the cardia and fundus (45.7% of the cohort) had a one-year survival rate of 31.7%, compared to 37.0% for non-cardia tumors (54.3% of the cohort). Five-year survival rates were 20.88% for cardia/fundus tumors and 23.6% for non-cardia tumors. Tumor location was a significant predictor of survival ($p < 0.001$).

Histological classification significantly impacted survival rate ($p = 0.009$).

Intestinal-type tumors (72.5% of the cohort) had a one-year survival rate of 36%, compared to 32.9% for diffuse-type tumors (21.0% of the cohort). Mixed-type tumors (6.5% of the cohort) had the lowest one-year survival rate (24%).

Histopathological grades of the patients were reported as well (n=4), moderately (n=51) and poorly (n=1293), undifferentiated (n=298), ring-shaped cell carcinoma (n=93) and other (n=120). Well-moderately differentiated tumors (0.2% of the cohort) had the highest one-year survival rate (38.9%), while poorly differentiated tumors (16.0% of the cohort) had a one-year survival rate of 33.6%. Five-year survival rates ranged from 32.6% for well-moderately differentiated tumors to 18.4% for poorly differentiated tumors (p=0.051).

Kazakh patients (84.7% of the cohort) had a one-year survival rate of 34%, compared to 35.4% for patients of other nationalities (15.3% of the cohort). Five-year survival rates were 22.7% for Kazakh patients and 21.3% for others (Fig 1).

Table 2 displays the results of both univariable and multivariable Cox proportional hazards regression analyses. The univariable analysis assesses the individual effect of each variable on the hazard ratio (HR), while the multivariable analysis adjusts for potential confounding factors by including all variables

simultaneously. The hazard ratios (HR) are presented with their corresponding 95% confidence intervals (95% CI) and p-values, which indicate the statistical significance of each variable. The research results included the following:

Age: Both univariable and multivariable analyses indicated that age (stratified as >50 years vs. <50 years) did not significantly affect the hazard ratio (HR ≈ 1.005 and HR ≈ 0.994, respectively; $p > 0.9$). This suggests that age is not a significant predictor of outcomes in this study.

Gender: Gender (female vs. male) also revealed no significant association with the outcome in either analysis (HR ≈ 1.0449 and HR ≈ 1.0429; $p>0.39$), indicating that gender does not significantly influence hazard ratios.

Nation: Nationality emerged as a significant predictor in the multivariable analysis (HR ≈ 1.1117; $p = 0.0334$), suggesting that individuals of non-Kazakh nationality have a slightly higher hazard compared to Kazakh individuals.

pTNM Stage: pTNM stage was significant in both analyses (HR ≈ 1.13087 and HR ≈ 1.1292; $p < 0.015$), indicating that advanced stages of gastric cancer (IIIA, IIIB, IIIC) correlate with a higher hazard compared to localized stages (I, IIA, IIB).

Tumor Location: The location of the tumor (cardia vs. non-cardia) showed no significant association with outcomes in either analysis (HR ≈ 1.021 and HR ≈ 1.0231; $p > 0.13$), suggesting its limited influence on hazard ratios.

Lauren Classification: Histological subtype, as classified by the Lauren classification (diffuse, intestinal, mixed), did not significantly affect hazard ratios ($p > 0.46$), indicating its non-critical role in predicting outcomes.

Differentiation Grade: Differentiation grade exhibited mixed results, with "other" differentiation types showing significance in both analyses (HR ≈ 1.263 and HR ≈ 0.7985; $p < 0.015$). This indicates that certain differentiation grades may influence hazard, though the effect's direction varies.

Stage: The analysis showed a significant association for Stage IV in both univariable (HR ≈ 1.18; $p = 0.017$) and multivariable analyses (HR ≈ 1.1936; $p = 0.0124$), indicating that Stage IV disease correlates with a higher hazard compared to Stage I.

The findings indicate that the most significant predictors of gastric cancer outcomes are nationality, pTNM stage, and overall stage of disease. Variables such as age, gender, tumor location, and Lauren classification did not demonstrate significant influence, suggesting they may not be critical in predicting outcomes in this context. The implication is a greater need for patient stratification based on disease stage and nationality, which could enhance treatment planning and prognostic assessment.

DISCUSSION

Survival outcomes in gastric cancer (GC) are influenced by multiple factors, including the disease stage at diagnosis, histological subtype, treatment modalities, and patient-specific characteristics[25].

The emphasis on personalized medicine and improved screening methods is crucial for enhancing early diagnosis, treatment efficacy, and overall survival rates in GC management. Effective treatment is complicated by late diagnosis and disease heterogeneity, with current therapeutic strategies including surgery, chemotherapy, radiotherapy, and targeted therapy[3].

Despite advances in diagnostics and treatment, the overall prognosis for GC remains poor due to late-stage detection and the aggressive nature of the disease. Most patients are diagnosed at advanced stages, limiting treatment options and necessitating palliative care[26]. Improved diagnostic technologies and screening initiatives, particularly in high-risk regions, can enhance early detection rates and clinical outcomes. A notable example is Japan's national screening program, which utilizes radiographic examination[7].

The development of novel therapeutic strategies, including targeted therapy and immunotherapy, offers hope for improving survival rates in patients with advanced GC. However, GC remains the second leading cause of cancer-related deaths worldwide, highlighting the need for a deeper understanding of key carcinogenic processes for early detection[12].

Survival Trends Based on Age. In our study, age did not show a statistically significant impact on prognosis. The findings of Zhang H. et al. indicate that the five-year relative survival rate at Nanfang Hospital of Southern Medical University from 2018 to 2022 was 71.4%. During this period, the five-year survival rates for patients aged <40, 40–54, 55–69, and ≥70 years were 67.5%, 73.5%, 72.0%, and 67.1%, respectively[27].

Gastric cancer in younger patients (under 45–50 years)

presents unique diagnostic and therapeutic challenges. This population is more likely to have aggressive tumor subtypes, particularly diffuse-type gastric cancer and signet-ring cell carcinoma[28]. These tumors exhibit rapid growth, early metastasis, and resistance to conventional chemotherapy. Additionally, younger patients are often diagnosed at advanced stages due to symptom underestimation by both patients and physicians[29].

Due to the high prevalence of undifferentiated tumors and disease progression, the prognosis in this group remains poor. Radical surgery is the only curative option, yet many cases present with locally advanced disease or peritoneal carcinomatosis, limiting therapeutic possibilities[28]. Younger patients frequently delay seeking medical attention, further complicating diagnosis and treatment[29].

Older patients with GC often present with comorbidities and reduced physiological reserves, impacting treatment decisions and outcomes. Chemotherapy and radical surgical interventions are less well tolerated, with a higher risk of postoperative complications and mortality, requiring a balanced approach to treatment[30]. However, appropriate therapy, including surgery, chemotherapy, and radiotherapy, can still improve survival outcomes in elderly patients. Individualized treatment strategies that balance treatment intensity with potential risks are essential.

Gastrectomy remains the main method of treating stomach cancer, however, about 60% of patients already have a locally advanced or metastatic process by the time of surgery, which reduces the effectiveness of surgical intervention[31].

Survival Trends Based on Sex. GC is more common in men, likely due to biological and behavioral factors. Over the past decade, men were 2.5 times more likely to develop GC than women, with the highest incidence observed between the ages of 60 and 64[32]. Demographic changes and population aging also influence disease trends and healthcare needs. Some countries with a high prevalence of GC have implemented screening programs that have improved early detection and survival rates[33,34].

Women tend to have longer survival durations, as demonstrated in EUROCARE-4 data Sex is an important variable influencing immune responses and cancer prognosis[35-37]. Clinicians should consider differences in toxicity, dosage responses, and therapeutic effects between men and women, as well as between younger and older patients.

Sex-specific physiological differences and molecular tumor characteristics may contribute to survival disparities between men and women. Further research is needed to refine treatment strategies and improve clinical outcomes for GC patients[7]. In our study, sex did not have a statistically significant impact on prognosis.

Survival Trends Based on Ethnicity. Our findings suggest that ethnicity influences survival outcomes, with non-Kazakh patients exhibiting an increased risk of mortality ($p = 0.0334$). The incidence of GC varies significantly across racial and ethnic groups, emphasizing the interplay of genetic predisposition and environmental factors in disease etiology[38,39].

Survival Trends Based on Tumor Stage and Progression. In our study, tumor stage was the most significant prognostic factor for survival. Patients with stage IV disease had a significantly worse prognosis compared to those with stage I ($p = 0.0124$). Signet-ring cell carcinoma and poorly differentiated tumors showed a tendency toward poorer prognosis, although the differences did not reach statistical significance ($p > 0.05$). The study by Zhang H. et al. reported that for stage IV patients, the five-year relative survival rate was 29% from 2018 to 2022. For patients with stage I–III disease, the five-year survival rate was 89.7% during the same period[40].

Patients with early-stage GC, confined to the mucosa or submucosa, have excellent prognoses after surgical treatment. Endoscopic resection methods (endoscopic mucosal resection, submucosal dissection) can be curative for carefully selected patients. The five-year survival rate for early GC reaches 75%[41].

Early stages of gastric cancer, limited to the mucous membrane or submucosa, have significantly higher survival rates compared to the common stages of the disease[42]. The five-year survival rate for early gastric cancer can exceed 90% with timely surgical intervention and adjuvant therapy. However, the prognosis for advanced gastric cancer remains unfavorable, with a five-year survival rate in the range of 20-40%[27].

Late diagnosis remains a major barrier in GC treatment, significantly affecting patient outcomes. Existing

screening methods, despite their invasiveness, cost, and accessibility issues, often fail to detect precancerous lesions. Addressing these challenges requires innovative screening approaches to improve early detection rates. The integration of molecular, clinical, and radiological data holds promise for enhancing screening effectiveness[43,44]. Early detection significantly improves survival rates and allows for the implementation of more effective treatment strategies.

The problem of gastric cancer heterogeneity complicates the prediction of treatment responses and the implementation of personalized medicine approaches. Multi-omics data integration holds promise for identifying molecular signatures and biomarkers associated with treatment responses and prognosis. Advances in high-throughput technologies provide unique opportunities to uncover the complexity of gastric cancer heterogeneity[45,46].

Gastric cancer is often associated with poor prognosis due to late diagnosis and the lack of effective screening protocols. Five-year survival rates are particularly low for metastatic cases, emphasizing the need for advanced therapeutic strategies and early detection methods. The heterogeneity of gastric cancer complicates the development of universal treatment protocols, highlighting the importance of personalized medical approaches[47-49].

Cancer-related stigma can lead to psychological stress and a reduced quality of life, underscoring the need for psychosocial support for patients and their families[50,51]. Advances in early detection methods present promising opportunities in the fight against gastric cancer. Five-year survival rates for early-stage detection can reach 95–99%, compared to less than 30% for late-stage diagnoses. Transforming knowledge about risk factors into actionable diagnostic algorithms for public health is essential[52,53].

Advanced Gastric Cancer. A recent study found that the majority of gastric cancer patients had the diffuse type (62.2%) and were diagnosed at late stages (89.8%), with 61.2% of patients having metastatic cancer[54]. Five-year relative survival rates vary significantly across different stages of gastric cancer: for localized gastric cancer, survival is approximately 75%; for regional gastric cancer, survival drops to around 35%; and for metastatic gastric cancer, survival is only 7%[55]. In the United States, the overall five-year survival rate for gastric cancer is 31%. Most cases are diagnosed at the metastatic stage, leading to lower survival rates. However, if diagnosed at the premetastatic stage, the five-year survival rate increases to 67%[56].

Factors contributing to poor survival in advanced gastric cancer include distant metastases, peritoneal carcinomatosis, and chemotherapy resistance. The Lauren classification also has prognostic significance, with diffuse-type gastric cancer generally associated with worse outcomes compared to the intestinal type. This may be attributed to its more aggressive growth pattern and higher tendency for peritoneal dissemination. Additionally, the presence of signet-ring cell tumors, characteristic of the diffuse type, has been linked to worse survival outcomes in some studies. The five-year survival rate for advanced gastric cancer is less than 20%[27,57].

Patients with metastatic gastric cancer have an extremely low chance of long-term survival—less than 5%. Systemic chemotherapy, often combined with targeted therapy or immunotherapy, remains the primary treatment approach. However, even for clinically resectable tumors, recurrence rates range from 40% to 65%[58].

Survival Trends Based on Treatment Approach. A multimodal approach combining surgery, chemotherapy, radiotherapy, and targeted therapies is the standard of care for most gastric cancer patients. Perioperative chemotherapy (administered before and after surgery) has been shown to improve survival in patients with resectable tumors[30].

Postoperative chemoradiation is recommended for locally advanced gastric cancer following surgical resection. Targeted therapy also plays a significant role. For example, in the ToGA study, trastuzumab (an anti-HER2 monoclonal antibody) combined with 5-fluorouracil, capecitabine, and cisplatin reduced the risk of death by 26% in HER2-positive gastric cancer patients[59]. The five-year relative survival rate for patients undergoing laparoscopic surgery at Nanfang Hospital increased from 50.3% in 2008–2012 to 71.4% in 2018–2022[40].

Surgical resection remains the cornerstone for localized

gastric cancer treatment. It provides an 80% five-year survival rate for early-stage gastric cancer; however, 60% of patients are diagnosed at advanced stages[60,61]. The global five-year survival rate for gastric cancer ranges from 28% to 51%, indicating a persistently high mortality rate[62]. For metastatic gastric cancer (mGC), systemic chemotherapy typically achieves a median progression-free survival (PFS) of approximately six months. For example, in the CheckMate-649 study, nivolumab plus chemotherapy showed a median PFS of 7.7 months compared to 6.0 months with chemotherapy alone (HR 0.68; $p < 0.0001$) in patients with PD-L1 CPS ≥ 5[63].

Immunotherapy has shown promising results in certain patient subgroups. The CheckMate-649 study demonstrated a median overall survival of 14.4 months with nivolumab plus chemotherapy compared to 11.1 months with chemotherapy alone in patients with PD-L1 CPS ≥ 5 (HR 0.70; $p < 0.0001$)[64].

HER2-targeted therapy, such as trastuzumab combined with chemotherapy, improves overall survival in HER2-positive patients. The ToGA study reported a median overall survival of 13.8 months with trastuzumab plus chemotherapy compared to 11.1 months with chemotherapy alone (HR 0.74; $p = 0.0046$)[65]. Systemic chemotherapy remains the mainstay for metastatic gastric cancer, with a median overall survival of approximately 12 months[66].

Gastric cancer exhibits significant intra- and intertumoral heterogeneity, contributing to its poor prognosis. Histological classifications alone are insufficient for effective patient stratification and improving clinical outcomes. Therefore, advanced diagnostic methods and molecular profiling are crucial for identifying potential therapeutic targets.

For localized gastric cancer, radical surgery remains the primary treatment, while perioperative chemotherapy, adjuvant chemotherapy, and adjuvant chemoradiation have been established to reduce recurrence risk and improve long-term survival[67,68]. Approximately 5–10% of gastric or gastroesophageal junction cancer patients exhibit EGFR amplification or overexpression, which is associated with poor prognosis [69]. However, major randomized clinical trials have not demonstrated significant survival benefits with EGFR-targeted therapies[70,71]. Primary or acquired resistance complicates HER2-targeted therapy in metastatic gastric cancer. The underlying mechanisms are not fully understood, but several potential resistance pathways have been identified, necessitating further research to improve treatment outcomes.

Despite these challenges, advances in biomarker research and targeted therapies offer hope for better disease management and improved patient outcomes. However, effectively addressing the complexities of gastric cancer requires coordinated efforts from researchers, clinicians, and policymakers to translate these scientific advancements into clinical practice.

CONCLUSION

Gastric cancer is a heterogeneous disease characterized by significant variations in incidence, clinical manifestations, and prognosis depending on age, sex, histological subtype, and disease stage. The tumor stage is the most significant prognostic factor for survival, with patients at stage IV having a significantly worse prognosis compared to those at stage I ($p=0.0124$). Ethnicity influences survival outcomes, with non-Kazakh patients demonstrating an increased risk of mortality ($p=0.0334$). Age, sex, tumor location, morphological type, and differentiation grade did not show statistically significant effects on prognosis. However, other studies have reported that younger patients are more likely to have aggressive forms of gastric cancer with poorer outcomes[12]. Men are more susceptible to gastric cancer, and differences in the distribution of Lauren subtypes may play a role in disease prognosis[10,12]. Signet-ring cell carcinoma and poorly differentiated tumors tended to have worse prognoses, although the differences did not reach statistical significance ($p>0.05$). Further research with larger patient cohorts and more detailed analyses of tumor biological markers is necessary to refine the role of morphological characteristics in predicting gastric cancer survival.

Despite declining incidence and mortality rates in some countries, gastric cancer remains a global public health challenge[72]. Continued research into the mechanisms of carcinogenesis and the development of effective therapeutic strategies are essential to improving patient outcomes[73]. This study highlights the urgent need for enhanced screening programs and early detection strategies for gastric cancer, which could improve treatment effectiveness and overall prognosis.

Table 1. One-and five-years survival of gastric cancer patients in 2010-2024 in the Aktobe region (WesternKazakhstan) with 95% confidence intervals.

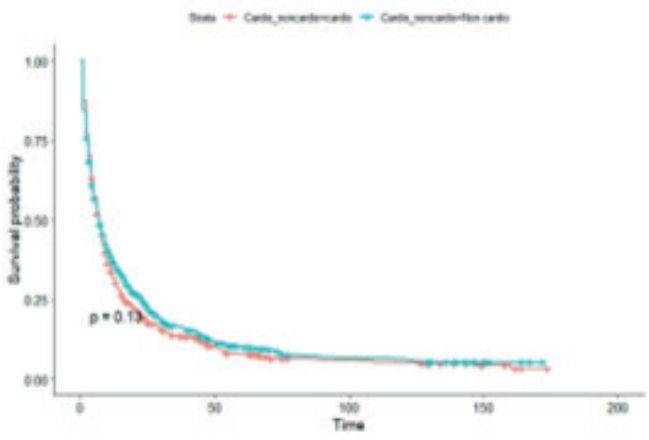
Variable	N of cases%	N of deaths%	One-year survival	St. error	95% CI	Five-year survival	95% CI	Median survival. months	P*long rang
Age years									0.06
<50	206(11.1%)	175	0.39	0.03	0.36:0.42	28.92%	21.54:36.31	8(6.49:9.51)	
>50	1653(88.9%)	1471	0.341	0.012	0.32:0.35	21.50%	19.42:23.58	7(6.42:7.58)	
Gender									0.604
Female	630(33.9%)	558	0.311	0.019	0.29:0.33	23.24%	19.47:24.33	6(5.261-6.739)	
Male	1229(66.1%)	1088	0.363	0.014	0.34:0.37	21.90%	19.47:24.33	7(6.292: 7.708)	
Stage									0.000
Local	1000(53.8%)	842	0.44	0.016	0.42:0.45	29.05%	25.84:32.27	10(8.88:11.11)	
Advanced	859(46.2%)	804	0.231	0.014	0.21:0.24	14.79%	12.55:17.03	4(3.49:4.50)	
Tumorlocation									0.134
Cardia	850(45.7%)	769	0.317	0.016	0.30:0.33	20.88%	18.04:23.73	7(6.29:7.70)	
Non cardia	1009(54.3%)	877	0.370	0.015	0.35:0.38	23.64%	20.75:26.53	7(6.13:7.86)	
Loren classification									0.009
Diffuse	391(21.0%)	366	0.329	0.024	0.30:0.35	18.44%	14.94:21.93	7(5.77:8.22)	
Intestinal	1348(72.5%)	1168	0.36	0.013	0.34:0.37	24.26%	21.68:26.85	7(6.32:7.67)	
Mixed	120(6.5%)	112	0.24	0.039	0.20:0.27	14.431	9.45:19.40	6(4.39:7.60)	
Differentiation grade									0.051
1Well moderate adenocarcinoma	4(0.2%)	4	0.389	0.069	0.32:0.45	32.61%	17.84:47.38	8(4.90:11.09)	
2 Moderately differentiated adenocarcinoma	51(2.7%)	41	0.25	0.013	0.23:0.26	25.5%	0.0:66.41	6(0.12:11.88)	
3 Poorly differentiated adenocarcinoma	1293(69.6%)	1123	0.359	0.013	0.34:0.37	23.78%	21.18:26.37	7(6.29:7.70)	
4 Undifferentiated adenocarcinoma	298(16.0%)	283	0.336	0.027	0.30:0.36	18.42%	14.59:22.25	7(5.66:8.33)	
Ring-shaped cell carcinoma	93(5%)	83	0.305	0.048	0.25:0.35	18.56	11.39:25.73	6(3.53:8.466)	

Variable	N of cases%	N of deaths%	One-year survival	St. error	95% CI	Five-year survival	95% CI	Median survival. months	P*long rang
Other	120(6.5%)	112	0.241	0.039	0.20:0.28	14.43%	9.45:19.40	6(4.39:7.60)	
Stage									0.000
I	90(4.8%)	56	0.77	0.044	0.72:0.81	63.384%	48.66:78.10	30(14.48:45.51)	
II	911(49.0%)	786	0.41	0.016	0.39:0.42	25.879%	16.04:34.05	9(7.968:10.03)	
III	653(35.2%)	603	0.27	0.018	0.25:0.28	17.433%	10.42:21.15	6(5.145:6.855)	
IV	205(11.0%)	201	0.09	0.021	0.06:0.11	5.368%	8.11:14.69	3(2.56:3.43)	
Nation									0.818
Kazakh	1574(84.7%)	1383	0.34	0.012	0.32:0.35	22.66%	20.38:24.94	7(6.41:7.58)	
Other	285(15.3%)	263	0.354	0.028	0.33:0.38	21.3%	16.73:25.80	7(5.51:8.48)	
Total	1859(100%)	1646	0.345	0.011	0.34:0.36	22.45%	20.40:24.50	7(6.45:7.54)	

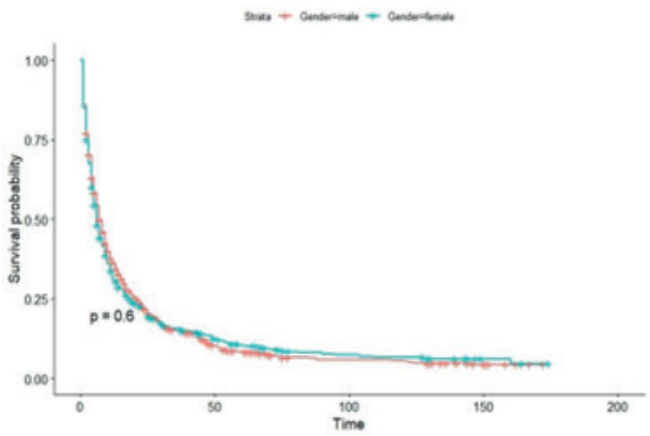
Table 2. Hazard COX proportional Univariable and Multivariable regression

Variable	Univariable analysis		Multivariable analysis	
	HR (95%Cl)	p	HR (95%Cl)	p
Age years				
<50	1(reference)		1(reference)	
>50	1.005 (0.9028:1.096)	0.9	0.994 (0.9014:1.0962)	0.9048
Gender				
Male	1(reference)		1(reference)	
Female	1.04490 (0.9486:1.151)	0.4	1.0429 (0.9459:1.1498)	0.3989
Nation				0.0334*
Kazakh	1(reference		1(reference	
Another	1.106 (1.004: 1.218)		1.1117(1.0083:1.2256)	
pTNM stage		0.013*		0.0147*
Local GC(I.IIA.IIB)	1(reference)		1(reference)	
AdvantageGC(IIIA.IIIB.IIIC)	1.13087 (1.026:1.246)		1.1292 (1.0242:1.2450)	
Tumor location		0.7		0.6458
Cardia	1(reference)		1(reference)	
Non Cardia	1.021 (0.92:1.12)		1.0231 (0.9283:1.1275)	0.139
Loren classification		0.7		

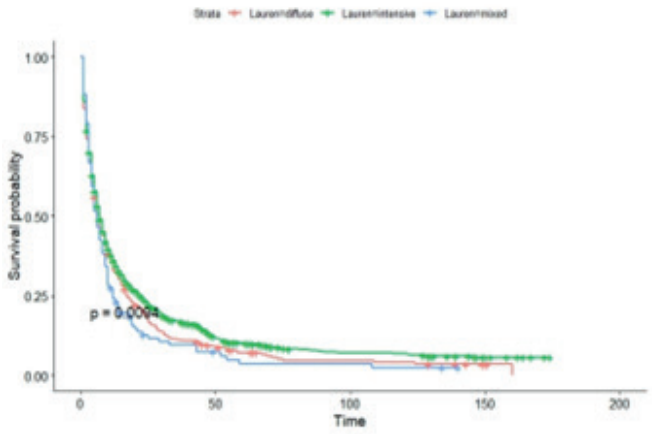
Variable	Univariable analysis		Multivariable analysis	
	HR (95%Cl)	p	HR (95%Cl)	p
Difusse	1(reference)		1(reference)	
Interstinal	1.025(0.9128:1.152)		1.0352 (0.9201:1.1648)	0.462
Mixed	0.97666(0.8673: 1.100)		0.9717(0.8619:1.0955)	
Differentiation grade				
Well moderate adenocarcinoma	1(reference)		1(reference)	
Moderately differentiated adenocarcinoma	1.095 (0.7620: 1.0939	0.0537	0.9019 (0.7522:1.0814)	0.2649
Poorly differentiated adenocarcinoma	1.115 (0.7509: 1.0714)		0.8919(0.7456: 1.0669)	0.2108
Undifferentiated adenocarcinoma	1.040(0.8041: 1.1488)		0.9549(0.7983:1.1423)	0.6138
Ring-shaped cell carcinoma	1.194 (0.6997: 1.0028)		0.8378(0.6992:1.0040)	0.0552
Other	1.263(0.6624: 0.9467)	0.0104*	0.7985(0.6673:0.9554)	0.0140*
Stage		0.02		
StageI	1(reference)		1(reference)	
StageII	0.98 (0.85:1.12)		0.9872 (0.8603:1.1328)	0.8539
StageIII	1.11 (0.9689:1.274)		1.1046 (0.9618:1.2687)	0.1589
StageIY	1.18 (1.03:1.35)	0.017*	1.1936 (1.0390:1.3713)	0.0124*



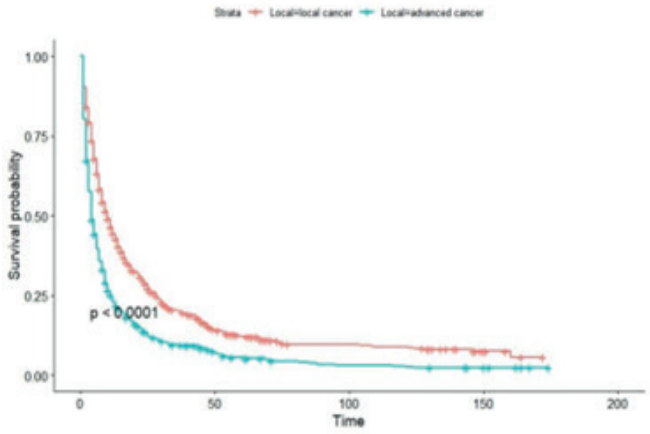
A. Five-Year Survival Respect to Tumor Subsites



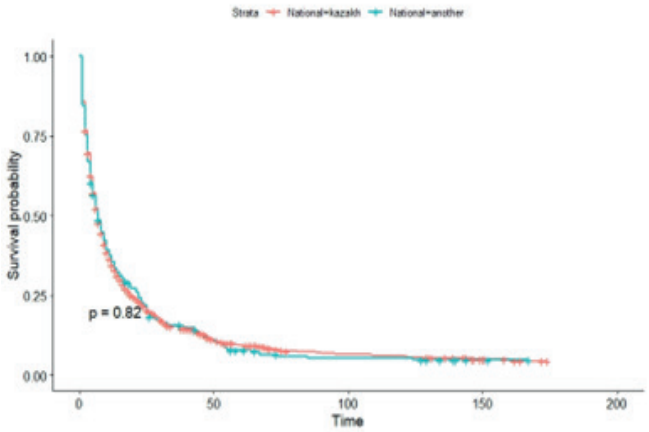
B. Five-Year Survival Across Different Age Groups



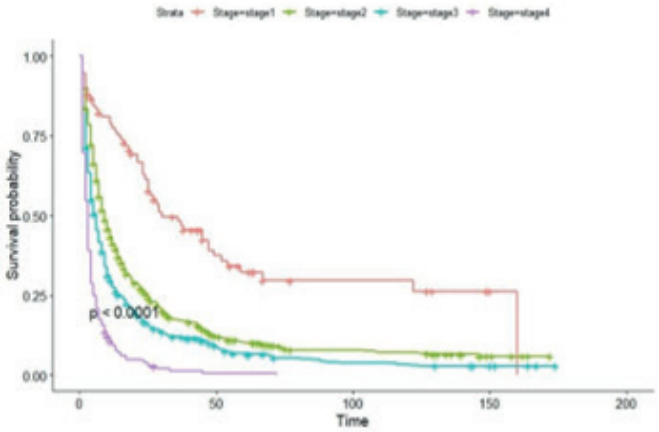
C. Five-Year Survival with Respect to Tumor Morphology



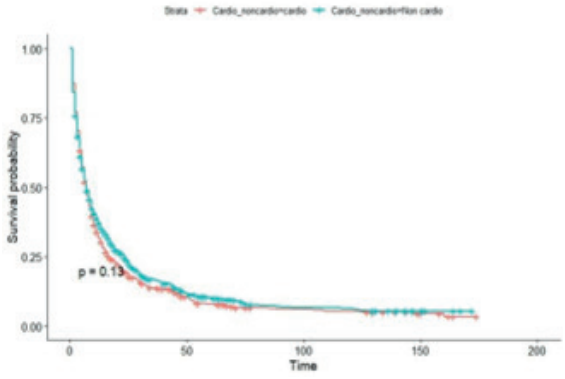
D. Five-Year Survival Across local and advantage disease



E. Five-Year Survival Across Different National Groups



F. Five-Year Survival Across Different Stage Groups



G. Five-Year Survival Across Different Localis Groups

Fingure 1. Five-Year Survival Analysis Across Various Factors

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