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Association Between Metastatic Patterns and Overall Survival in Metastatic Gastric Cancer: A Single-Centre Real-World Study

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Abstract:

Objective: Objective: Metastatic gastric cancer is a biologically heterogeneous disease with a poor prognosis. Although the presence of distant metastasis defines advanced disease, the prognostic impact of specific metastatic patterns remains unclear. This study aimed to evaluate the association between metastatic patterns and overall survival in patients with metastatic gastric cancer.

Methods: In this retrospective single-centre study, 292 patients with histopathologically confirmed metastatic gastric cancer were included. Metastatic sites were evaluated using computed tomography, magnetic resonance imaging, and/or positron emission tomography. Overall survival (OS) was analysed using the Kaplan–Meier method and compared using the log-rank test. Prognostic factors were assessed through univariate and multivariate Cox proportional hazards regression models.

Results: The median OS for the entire cohort was 10 months (95% CI, 9.3–12.0). The most common sites of metastasis were non-regional lymph nodes (78.8%), liver (49.7%), and peritoneum (30.8%). Peritoneal metastasis was associated with significantly worse survival in unadjusted Kaplan–Meier analysis (9.5 vs 11 months, P<0.001), whereas other metastatic sites were not significantly associated with OS. No significant difference in OS was observed between patients with single-site and multiple-site metastases (P=0.31). In multivariate analysis, Eastern Cooperative Oncology Group performance status (ECOG) and prior gastrectomy were identified as independent prognostic factors, while the impact of metastatic site did not remain statistically significant.

Conclusion: Metastatic gastric cancer exhibits substantial heterogeneity in survival outcomes according to the distribution of metastatic sites. Peritoneal involvement was associated with worse survival in unadjusted analyses and may represent a clinically relevant marker of adverse prognosis. Including site-specific metastatic information in prognostic assessments may contribute to improved risk stratification in addition to the conventional staging system.

Keywords: Metastatic Gastric Cancer, Metastasis Pattern, Peritoneal Metastasis, Prognosis, Overall Survival

Gastric cancer remains a major global health burden, being both a common malignancy and a significant cause of cancer-related deaths [1]. The absence of specific early symptoms often leads to delayed diagnosis, and patients commonly present with advanced disease, which limits treatment options

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and is associated with a poorer prognosis [2]. While both incidence and mortality, when adjusted for age, have declined over time, improvements in survival have lagged behind those seen in other gastrointestinal cancers [3, 4].

At diagnosis, more than 40% of patients present with metastatic disease, for whom prognosis is a key determinant of treatment strategy. Despite advances in systemic therapies, five-year survival rates for metastatic gastric cancer remain poor [5-7].

Reliable risk stratification in advanced gastric cancer is essential for treatment decision-making and overall patient management. The TNM (Tumor, Node, Metastasis) classification system developed by the American Joint Committee on Cancer (AJCC) remains the cornerstone of prognostic assessment [8].

Prognosis is influenced by multiple clinical factors beyond TNM stage, including both patient-related characteristics and disease-specific features such as treatment history and metastatic spread. Therefore, prognostic stratification in advanced disease remains challenging [9].

In this context, metastatic gastric cancer exhibits significant biological and clinical heterogeneity. The pattern of metastases is a key indicator of this heterogeneity and may serve as a phenotypic marker of the tumour's underlying biology [10, 11].

Gastric cancer commonly metastasises to distant lymph nodes, liver, peritoneum, lungs, bones, and other organs. However, studies evaluating the distribution of metastatic sites are limited, and considerable heterogeneity exists across reports from different populations. Moreover, most available data are derived from population-based registries, whereas single-centre real-world studies remain scarce. Reported liver metastasis frequencies vary significantly across populations and study designs. A registry study from Sweden reported liver metastasis in 48% of patients, whereas a Surveillance, Epidemiology, and End Results (SEER) - based analysis from the United States found a rate of 44%. Conversely, a Japanese autopsy study reported liver involvement in up to 78% of patients with gastric adenocarcinoma [12].

A better understanding of the relationship between metastatic patterns and survival may improve risk stratification and support treatment planning in metastatic gastric cancer. Real-world datasets are particularly valuable for evaluating the prognostic relevance of these patterns. In this study, we aimed to evaluate the association between metastatic patterns and overall survival in patients with metastatic gastric cancer using real-world data from a single centre, highlighting the need for institutional-level evidence.

Most previous studies investigating metastatic patterns in gastric cancer have primarily relied on population-based registries, whereas detailed single-centre real-world studies remain limited. Therefore, our study provides complementary real-world evidence regarding metastatic patterns and their prognostic significance.

METHODS

A retrospective cohort was established using data from patients treated at the Medical Oncology Clinic of Kartal Dr Lütfi Kırdar City Hospital from January 2015 to August 2025. Inclusion criteria comprised patients aged ≥18 years with histologically verified gastric adenocarcinoma and stage IV disease, as defined by the AJCC 8th edition, along with imaging-confirmed distant metastases. Imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and/or positron emission tomography (PET-CT) were used to determine metastatic involvement. Patients lacking survival or follow-up data, those with previous malignancies, or those missing information on metastatic sites were excluded. All procedures were conducted in accordance with the principles of the Declaration of Helsinki. Approval for the study was granted by the Scientific Research Ethics Committee of Kartal Dr Lütfi Kırdar City Hospital (27 January 2026; Decision No: 2026/010.99/24/53). Considering the study's retrospective design and reliance on anonymised data, the ethics committee approved a waiver of informed consent.

Statistical Analysis

The primary outcome measure was overall survival (OS), defined as the time from diagnosis of metastatic disease to death from any cause or to the last follow-up. The distribution of categorical

variables is presented in counts and percentages. Summary statistics for continuous variables included median values, with variability expressed using ranges or interquartile ranges (IQR). Survival estimates were derived using Kaplan–Meier analysis, and group differences were assessed with the log-rank test. Median follow-up time was estimated using the reverse Kaplan–Meier method. Cox proportional hazards regression was applied in both univariable and multivariable models to assess factors associated with prognosis. The findings are presented as hazard ratios (HRs) with 95% confidence intervals (CIs). Variables considered clinically relevant, along with those achieving statistical significance (P<0.05) in univariable analyses, were included in the multivariable model. Variables considered clinically relevant based on previous literature, including Human Epidermal Growth Factor Receptor 2 (HER2) status, signet ring cell histology, linitis plastica, and treatment-related factors, were initially evaluated in univariable analyses. To avoid model overfitting, only clinically relevant variables and/or variables demonstrating statistical significance were retained in the final multivariable model. The validity of the proportional hazards assumption was assessed by analysing Schoenfeld residuals. Statistical significance was defined as a two-sided P-value < 0.05. Statistical analyses were performed using R software (version 4.4.2; R Foundation for Statistical Computing, Vienna, Austria), including the survival, survminer, and rstatix packages.

TABLE 1. Baseline Characteristics of Patients with Metastatic Gastric Cancer (n=292)

Characteristic	n (%)
Age <65/ ≥65 years	161 (55)/ 131 (45)
ECOG PS (0/ 1/ ≥2)	100 (34)/ 157 (54)/ 35 (12)
Male/ female	200 (68)/ 92 (32)
Drinking history (yes/ no)	49 (17)/ 243 (83)
Primary tumor location (proximal/ distal/total)	114 (39)/ 94 (32)/ 84 (29)
Histologic grade (well/ moderate/ poor)	143 (49)/ 149 (51)
Histologic subtype (adenocarcinomaNOS/ Signet ring/ mucinous)	227 (78)/ 48 (16)/ 17 (6)
Lauren type (intestinal/diffuse/ mixed/ unclassified)	34 (12)/ 19 (7)/ 9 (3)/ 230 (79)
HER2 negative / positive	214 (73)/ 78 (27)
Prior gastrectomy (yes/ no)	111 (38)/ 181 (62)
Linitis plastica (yes/ no)	37 (13)/ 255 (87)
Chemotherapy received (yes/ no)	280 (96)/ 12 (4)
Systemic treatment exposure*	
First-line therapy	280 (96)
Second-line therapy	248 (85)
Best supportive care	12 (4)
Chemotherapy regimen (oxaliplatin/ irinotecan/ other/ BSC)	136 (47)/ 20 (7)/ 124 (42)/ 12 (4)
Number of metastatic sites (1/ ≥2/ missing)	75 (26)/ 211 (72)/ 6 (2)
Metastatic sites (liver/ peritoneum/ non-regional lymph nodes/ lung/ bone/ ovary)†	145 (50)/ 90 (31)/ 230 (79)/ 58 (20)/ 40 (14)/ 15 (5)

BSC, best supportive care; ECOG PS, Eastern cooperative oncology group performance status; HER2, human epidermal growth factor receptor 2; NOS, not otherwise specified.

*Line-of-therapy categories represent treatment exposure throughout the disease course; therefore, percentages may exceed 100%, and patients may be included in more than one category. †Patients may have more than one metastatic site.

RESULTS

Patient Characteristics

The study included 292 patients with metastatic gastric cancer. The median age at diagnosis was 63 years (range: 22–90), with 161 patients (55%) aged ≤65 years. Most patients were male (n=200, 68%), and the majority had a good performance status (ECOG 0–1; n=257, 88%).

Regarding tumour characteristics, 149 (51%) tumours were poorly differentiated, and 48 (16%) patients had signet ring cell histology. HER2 positivity was observed in 78 (27%) patients. Among treatment-related variables, 111 (38%) patients underwent gastrectomy, and 280 (96%) patients received systemic chemotherapy. Oxaliplatin-based regimens were the most commonly used (47%). Detailed baseline characteristics are presented in Table 1.

Distribution of Metastasis

Regarding metastatic burden, 211 (74%) patients had metastases involving multiple sites, whereas 75 (26%) patients had a single metastatic site. Data on the number of metastatic sites were missing for 6 patients. The most common metastatic sites were non-regional lymph nodes (78.8%), liver (49.7%), peritoneum (30.8%), lung (19.9%), and bone (13.7%). Ovarian metastases were observed in 15 patients, accounting for 5.1% of the overall cohort and 16.3% of female patients. The distribution of metastatic sites in the study population is shown in Figure 1.

Overall Survival Analysis

For the entire cohort, the median follow-up duration was 10.35 months (IQR: 5.61–19.49), while it was 11.23 months (IQR: 3.90–20.49) among patients who remained alive. Overall survival for the cohort was 10 months (95% CI: 9.3–12.0). The estimated OS rates at 6, 12, and 24 months were 74%, 44%, and 18%, respectively (Table 2 and 3). In the univariate analyses, several clinical variables were significantly associated with overall survival (Table 2 and 3). Median overall survival was longer in patients younger than 65 years (13 months) compared to those aged ≥65 years (7.9 months; P=0.003). Lower ECOG performance status was also associated with better survival (P=0.041). Although median OS values were similar between the ECOG 1 and ECOG ≥2 groups, differences in the overall survival distributions across ECOG categories remained statistically significant. A marked difference in overall survival was observed by gastrectomy status, with a median survival of 18 months in patients who had undergone gastrectomy and 7.9 months in those who had not (P<0.001). In univariate analyses, age, ECOG performance status,

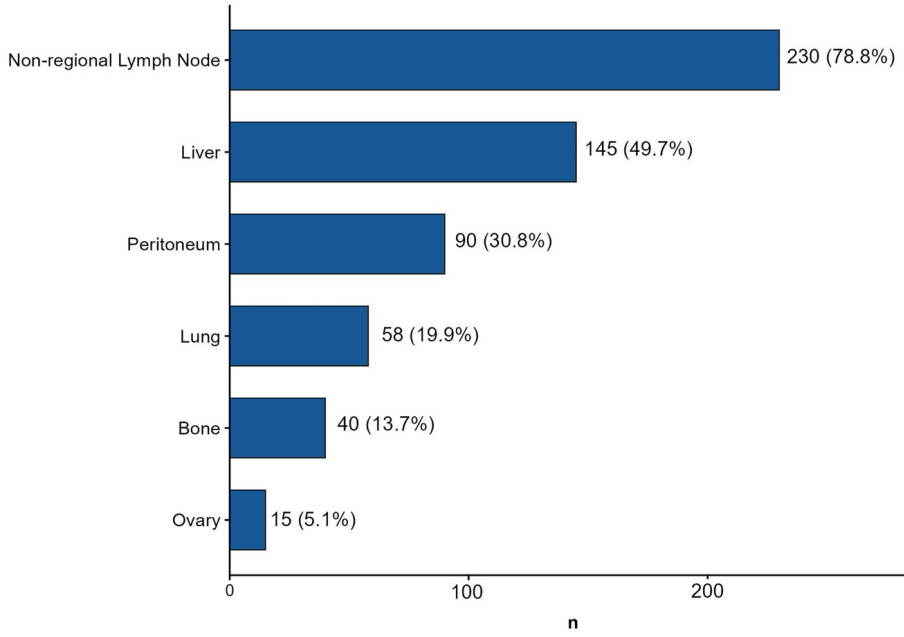

FIGURE 1. Distribution of metastatic sites in patients with metastatic gastric cancer.

TABLE 2. Median Overall Survival According to Baseline Characteristics

Characteristic	Median OS (months) (95% CI)	P-value
Overall	10 (9.3–12)	–
Age (years)		
<65	13 (11–16)	**0.003**
≥65	7.9 (7.2–10)	
ECOG PS		
0	18 (11–25)	**0.041**
1	10 (8.1–14)	
≥2	10 (8.1–13)	
Sex		
Female	10 (7.9–12)	0.20
Male	11 (9–14)	
Drinking history		
Yes	12 (8–18)	>0.9
No	10 (8.9–12)	
Primary tumour location		
Proximal	11 (9–15)	0.60
Distal	12 (9.5–16)	
Total	8.8 (7.8–11)	
Histologic grade		
Well/moderately differentiated	12 (8.1–18)	0.60
Poorly differentiated	12 (10–16)	
Histologic subtype		
Signet ring cell	12 (9.5–18)	0.70
Adenocarcinoma, NOS	10 (8.4–12)	
Mucinous adenocarcinoma	13 (8.1–20)	
Lauren type		
Intestinal	17 (9.9–20)	0.15
Diffuse	15 (10–31)	
Mixed	16 (11–22)	
Unclassified	9.7 (8.3–11)	
HER2 status		
Negative	10 (9–12)	0.80
Positive	10 (8.1–16)	
Prior gastrectomy		
Yes	18 (17–20)	**<0.001**
No	7.9 (7.2–9.6)	

TABLE 2 CONTUNIED. Median Overall Survival According to Baseline Characteristics

Characteristic	Median OS (months) (95% CI)	P-value
Chemotherapy regimen		
Oxaliplatin-based	9.5 (7.9–11)	**0.024**
Irinotecan-based	19 (16–29)	
Others	10 (8.4–14)	
Number of metastatic sites		
1 site	12 (8.1–18)	0.30
≥2 sites	10 (8.8–12)	
Metastatic sites		
Liver metastasis: Yes	9.6 (7.9–11)	0.30
Liver metastasis: No	12 (10–15)	
Peritoneal metastasis: Yes	9.5 (7.2–11)	**<0.001**
Peritoneal metastasis: No	11 (9.7–16)	
Non-regional lymph node metastasis: Yes	10 (8.8–12)	0.50
Non-regional lymph node metastasis: No	11 (9–17)	
Lung metastasis: Yes	11 (7.9–18)	0.30
Lung metastasis: No	10 (8.9–12)	
Bone metastasis: Yes	10 (7.3–19)	0.40
Bone metastasis: No	10 (9.3–12)	

ECOG PS, Eastern cooperative oncology group performance status; HER2, human epidermal growth factor Receptor 2; NOS, not otherwise specified; OS, overall survival.
Statistically significant P-values are shown in bold.

prior gastrectomy, chemotherapy regimen, and peritoneal metastasis were significantly associated with OS. The apparent benefit in the irinotecan-based group may be influenced by the small number of patients included in this subgroup.

Consistent with the univariate analyses, peritoneal metastasis was associated with shorter OS (9.5 vs 11 months, P<0.001). In contrast, metastases to specific sites, including the liver, lung, bone, and non-regional lymph nodes, were not significantly associated with overall survival (Figure 2).

Single-site versus Multi-site Metastasis

When stratified by metastatic burden, overall survival was similar between patients with single-site and multiple-site disease (12 versus 10 months; P=0.31). Kaplan–Meier curves are shown in Figure 3.

Prognostic Factors for Survival

Independent prognostic factors for overall survival were assessed using univariable and multivariable Cox proportional hazards models (Table 4). Older age, poorer ECOG performance status, absence of prior gastrectomy, and peritoneal metastasis were associated with worse survival in univariable Cox analysis. ECOG performance status and prior gastrectomy remained independent predictors of survival in the multivariable model. Certain chemotherapy regimens were associated with OS in univariate analyses; however, these associations did not persist after multivariable adjustment. Mortality risk increased with worsening ECOG performance status: compared to ECOG PS 0, hazard ratios are 1.70 (95% CI: 1.02–2.85; P=0.043) for ECOG PS 1 and 1.95 (95% CI: 1.12–3.40; P=0.019) for ECOG PS ≥2. Patients with

TABLE 3. Long-Term Overall Survival Rates According to Baseline Characteristics

Characteristic	6-month OS % (95% CI)	12-month OS % (95% CI)	24-month OS % (95% CI)	36-month OS % (95% CI)
Overall	74 (69–80)	44 (39–50)	18 (14–23)	7 (4.4–11)
Age <65	78 (72–85)	51 (43–59)	22 (17–30)	8.6 (5.1–14)
Age ≥65	70 (62–79)	36 (28–45)	11 (7–19)	4.7 (2–11)
ECOG 0	94 (86–100)	58 (43–78)	29 (17–50)	19 (9–40)
ECOG 1	70 (63–78)	43 (36–52)	17 (12–24)	7.7 (4.4–14)
ECOG ≥2	74 (66–84)	41 (32–52)	15 (9.2–24)	2.1 (0.5–8.3)
Female	69 (60–79)	39 (30–51)	12 (7.1–22)	5.6 (2.4–13)
Male	77 (71–83)	46 (40–54)	20 (15–27)	7.5 (4.5–13)

CI, confidence interval; ECOG, Eastern cooperative oncology group; OS, overall survival.

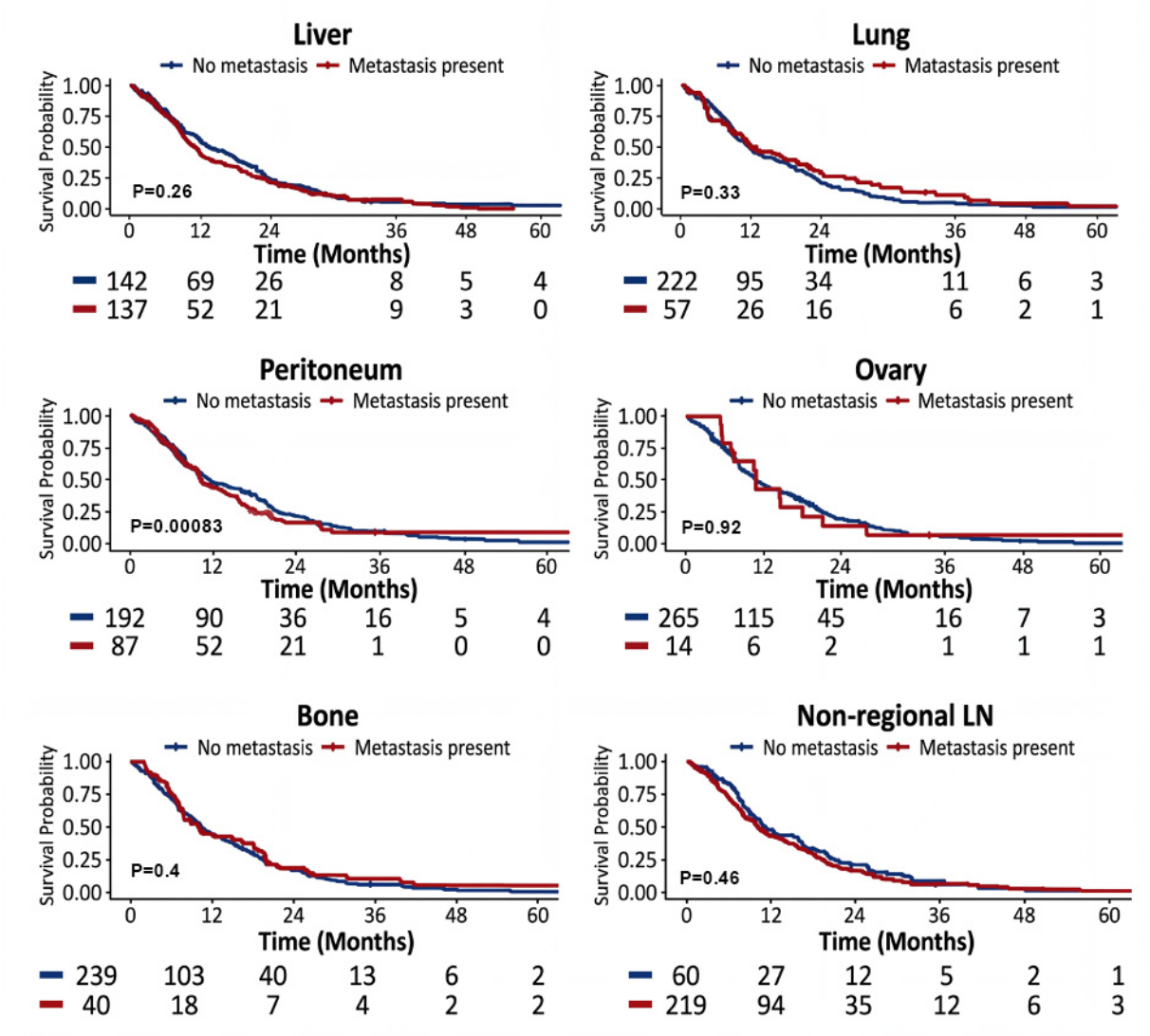

FIGURE 2. Kaplan-Meier survial curves according to metastatic site. Survival comparisons were performed using the log-rank test.

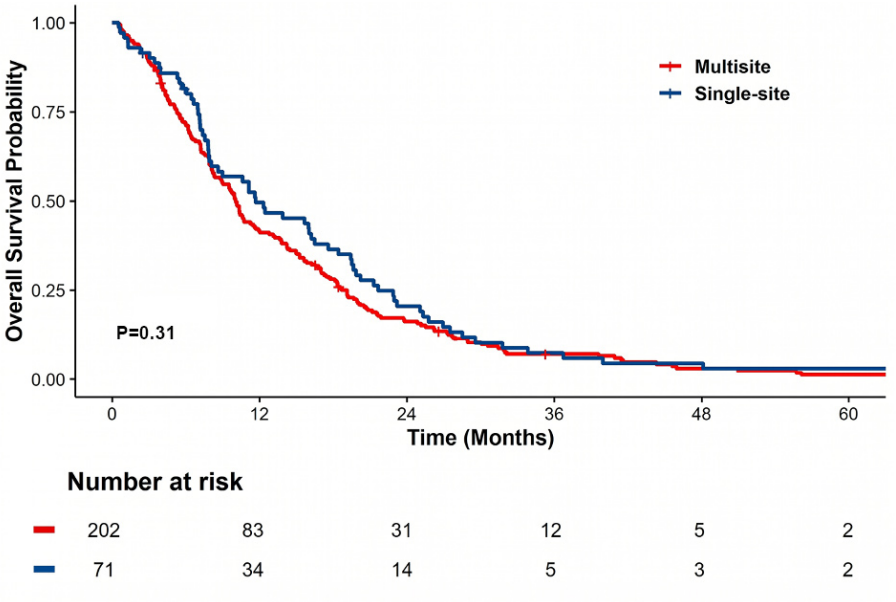

FIGURE 3. Kaplan-Meier survial curves comparing single-site and multisite metastases.

a history of gastrectomy had a lower risk of mortality (HR = 0.49, 95% CI: 0.34–0.70; P<0.001). Compared with patients receiving active chemotherapy, those receiving only best supportive care had a significantly higher risk of death (HR = 3.17, 95% CI, 1.58–6.35, P=0.001). The association between peritoneal metastasis and survival observed in univariable analysis did not persist after adjustment in the multivariable model (HR = 1.35, 95% CI: 0.95–1.91; P=0.092). Peritoneal involvement was associated with poorer survival in unadjusted analyses; however, this association did not remain statistically significant after multivariable adjustment.

DISCUSSION

The principal finding of this study is that survival in metastatic gastric cancer varies according to the distribution of metastatic sites, with patients exhibiting peritoneal involvement experiencing poorer survival outcomes in unadjusted analyses. However, this association did not remain statistically significant after multivariable adjustment, suggesting that the adverse prognostic effect of peritoneal metastasis may be influenced by other clinicopathological factors.

Gastric cancer is a malignancy associated with high mortality, particularly in the metastatic setting [13]. Prognosis in gastric cancer is stage-dependent, with five-year survival rates declining from approximately 30% overall to 5% in metastatic disease [7, 14]. These findings underscore the need to better characterise clinicopathological features and organ-specific metastatic behaviour [15].

In this single-centre cohort, we examined the association between metastatic patterns and survival in metastatic gastric cancer. Our findings indicated that non-regional lymph nodes, the liver, and the peritoneum were the most common sites of metastasis. Kaplan–Meier analysis showed poorer survival in patients with peritoneal metastasis, while survival was comparable across other metastatic sites. Overall survival was similar regardless of metastatic burden (single-site versus multiple-site involvement). In the multivariate analysis, performance status and prior gastrectomy were identified as independent prognostic factors.

Reported frequencies of liver metastasis vary substantially across studies, depending on study design, patient selection, and stage distribution [16, 17]. In our study, the most frequently involved metastatic sites were non-regional lymph nodes (78.8%), followed by the liver (49.7%) and the peritoneum (30.8%). The liver was reported as the predominant metastatic site in a Swedish study. In contrast, peritoneal involvement was more common in a Korean retrospective cohort [18, 19].

TABLE 4. Univariable and Multivariable Cox Proportional Hazards Regression Analysis for Overall Survival

Variable	Univariable HR (95% CI)	P-value	Multivariable HR (95% CI)	P-value
Age at diagnosis	1.01 (1.00–1.02)	**0.039**	1.01 (0.99–1.02)	0.50
ECOG PS				
1 vs 0	1.51 (1.02–2.25)	**0.040**	1.70 (1.02–2.85)	**0.043**
≥2 vs 0	1.71 (1.12–2.59)	**0.012**	1.95 (1.12–3.40)	**0.019**
Drinking history (yes vs no)	0.99 (0.72–1.35)	>0.90	—	—
Primary tumor location				
Proximal vs distal	0.89 (0.67–1.18)	0.40	—	—
Total vs distal	1.00 (0.75–1.35)	>0.90	—	—
Lauren type				
Diffuse vs intestinal	0.95 (0.52–1.72)	0.90	—	—
Mixed vs intestinal	0.75 (0.33–1.71)	0.50	—	—
Unclassified vs intestinal	1.32 (0.90–1.94)	0.20	—	—
HER2 positive vs negative	0.96 (0.73–1.27)	0.80	—	—
Linitis plastica (yes vs no)	1.22 (0.85–1.75)	0.30	—	—
Signet ring cell histology (yes vs no)	0.78 (0.61–1.01)	0.060	—	—
Prior gastrectomy (yes vs no)	0.48 (0.37–0.62)	**<0.001**	0.49 (0.34–0.70)	**<0.001**
Number of metastatic sites (≥2 vs 1)	1.15 (0.88–1.52)	0.30	0.92 (0.62–1.37)	0.70
Liver metastasis (yes vs no)	1.15 (0.90–1.46)	0.30	—	—
Lung metastasis (yes vs no)	0.86 (0.64–1.16)	0.30	—	—
Bone metastasis (yes vs no)	0.86 (0.61–1.22)	0.40	—	—
Peritoneal metastasis (yes vs no)	1.56 (1.20–2.03)	**<0.001**	1.35 (0.95–1.91)	0.092
Non-regional lymph node metastasis (yes vs no)	1.12 (0.83–1.50)	0.50	—	—
Chemotherapy (yes vs no)	0.58 (0.32–1.04)	0.069	—	—
Chemotherapy regimen				
Oxaliplatin-based vs others	0.53 (0.31–0.89)	**0.016**	0.74 (0.41–1.36)	0.30
Irinotecan-based vs others	0.88 (0.68–1.13)	0.30	0.98 (0.71–1.37)	>0.90
Best supportive care vs others	1.53 (0.84–2.79)	0.20	3.17 (1.58–6.35)	**0.001**

CI, confidence interval; ECOG PS, Eastern cooperative oncology group performance status; HER2, human epidermal growth factor receptor 2; HR, hazard ratio.

Reference categories were ECOG PS 0, proximal tumor location, intestinal Lauren type, HER2-negative status, no prior gastrectomy, one metastatic site, absence of metastasis, and best supportive care.

Statistically significant P-values are shown in bold.

The relatively high incidence of non-regional lymph node metastases in our cohort likely reflects differences in patient selection, imaging, and staging practices. This distribution differs somewhat from large population-based analyses, such as SEER analyses, which report liver metastasis as the most common site. However, our findings are consistent with real-world clinical cohorts and support the notion that lymphatic spread is an important route of metastasis in gastric cancer.

Approximately one-third of patients develop peritoneal metastasis, which aligns with previous reports describing the peritoneum as a common site of spread in gastric cancer. Importantly, peritoneal dissemination is associated with a more aggressive biological phenotype and poorer clinical outcomes [20].

There is considerable heterogeneity in survival rates among patients with metastatic gastric cancer [12, 21]. Kaplan–Meier curves demonstrated worse survival in patients with peritoneal metastasis ($P<0.001$). In contrast, metastases to the liver, lungs, bones, and non-regional lymph nodes did not significantly affect overall survival. These findings suggest that not all metastatic sites confer equal prognostic significance in metastatic gastric cancer. Although previous studies have reported heterogeneous results, our findings further support the clinically relevant association between peritoneal metastasis and poorer survival outcomes.

Several mechanisms may underlie the adverse prognostic impact of peritoneal metastasis. Limited penetration of systemic chemotherapeutic agents into the peritoneal cavity can reduce treatment efficacy and hinder disease control. Additionally, peritoneal spread is often associated with diffuse type or signet ring cell histology in previous reports; these subtypes are characterised by more aggressive tumour biology. Furthermore, peritoneal metastasis generally progresses with a higher tumour burden and rapid disease progression [22]. Clinically, complications such as ascites development, bowel obstruction, and malnutrition can deteriorate patients' overall condition, negatively affecting survival.

Although peritoneal metastasis was significant in univariate analyses, this association did not remain significant after multivariable adjustment. This finding suggests that the prognostic impact of peritoneal metastasis may be partially mediated by performance status and treatment-related factors rather than acting as an independent determinant. Previous studies have evaluated heterogeneity in metastatic gastric cancer based on the number of metastatic organs, with multiple-site involvement associated with poorer survival [23-25]. However, our findings suggest that biological behaviour and the site of metastasis may be more relevant than metastatic burden.

Contrary to previous reports, overall survival did not differ between patients with solitary and multiple organ metastases ($P=0.31$). This finding further supports the idea that the prognostic impact of metastatic disease may rely more on biological behaviour and organ involvement than merely on the number of metastatic sites.

In a study by Chau *et al*. [26], involving 1,080 patients with metastatic gastric cancer undergoing various chemotherapy regimens, performance status at diagnosis was identified as an independent predictor of overall survival, with poorer outcomes seen in patients with ECOG PS ≥ 2.

Prior gastrectomy was associated with improved survival in our cohort; however, this finding should be interpreted with caution due to potential selection bias, as patients undergoing surgery are more likely to have better performance status and lower tumour burden. Therefore, the role of gastrectomy in metastatic gastric cancer remains controversial and requires further prospective evaluation [27, 28].

Patients selected for gastrectomy may represent a highly selected subgroup with lower tumour burden and more favourable disease characteristics. Our findings suggest that metastatic gastric cancer is biologically heterogeneous and that site-specific metastatic patterns, including peritoneal involvement, may have prognostic relevance. However, prospective studies are needed to validate these findings before such information can be incorporated into prognostic models or staging systems.

Strengths and Limitations

This study has several important strengths. First, it represents a well-characterised real-world cohort of patients with metastatic gastric cancer treated at a single tertiary referral centre over a 10-year study period. Second, the single-centre setting ensured relatively homogeneous diagnostic, treatment, and follow-up practices, thereby reducing institutional variability. Third, the study comprehensively evaluated the distribution of metastatic sites, including non-regional lymph nodes, liver, peritoneum, lung, bone, and ovarian metastases. Fourth, robust survival methodology was applied, including Kaplan–Meier analysis, reverse Kaplan–Meier estimation of follow-up time, and both univariable and multivariable Cox proportional hazards models. Fifth, the proportional hazards assumption was formally assessed using

Schoenfeld residuals, supporting the validity of the Cox regression models. Sixth, clinically relevant prognostic variables, including HER2 status, signet ring cell histology, linitis plastica, ECOG performance status, prior gastrectomy, and treatment-related factors, were systematically evaluated. Finally, the study distinguished between unadjusted and adjusted survival analyses, allowing a balanced interpretation of prognostic factors and reducing the risk of overinterpreting univariable associations. To our knowledge, this is one of the few single-centre real-world studies that comprehensively evaluate the prognostic significance of individual metastatic sites in patients with metastatic gastric cancer.

Several limitations should be considered. First, the retrospective, single-centre design may have introduced selection bias and limited the generalisability of the findings. Second, the relatively short follow-up duration, which was close to the median overall survival, may have limited the maturity of the survival data. Additionally, a limited number of events for some subgroup analyses may have reduced statistical power and affected the robustness of the results. Third, heterogeneity in treatment approaches, including different chemotherapy regimens, treatment lines, and surgical procedures, may have influenced survival outcomes. Fourth, the absence of data on key prognostic and predictive biomarkers, such as molecular subtype, microsatellite instability (MSI) status, and PD-L1 expression, limited the scope of the analyses. Furthermore, metastatic patterns were assessed only at the time of diagnosis based on imaging findings; therefore, changes in disease distribution and newly developed metastatic sites during follow-up could not be evaluated. Lastly, the apparent survival benefit associated with prior gastrectomy should be interpreted with caution, as patients undergoing surgery may have represented a more favourable subgroup. Therefore, residual confounding and selection bias cannot be completely excluded despite multivariable adjustment.

In addition, treatment standards for metastatic gastric cancer evolved during the 10-year study period with the introduction of new systemic therapies, including immune checkpoint inhibitors and HER2-targeted agents. Therefore, temporal changes in treatment strategies (era effect) may have influenced survival outcomes. Finally, the study evaluated overall survival only; cancer-specific survival and cause-specific mortality could not be assessed because reliable information on the cause of death was unavailable.

Future multicentre prospective studies incorporating comprehensive molecular profiling, infectious factors (including Helicobacter pylori and Epstein–Barr virus status), and contemporary treatment strategies are needed to validate these findings and further refine prognostic models in metastatic gastric cancer.

CONCLUSION

Survival in metastatic gastric cancer appears to vary according to the distribution of metastatic sites. Peritoneal involvement was associated with poorer survival in unadjusted analyses, although this association did not remain statistically significant after multivariable adjustment, while metastatic burden alone did not significantly influence outcomes. These findings suggest that site-specific metastatic patterns may have prognostic relevance in metastatic gastric cancer. However, prospective multicentre studies incorporating molecular profiling and more standardised treatment data are needed to validate these observations before their incorporation into prognostic models or staging systems.

Ethics Approval and Consent to Participate

This study was approved by the University of Health Sciences Turkey, Kartal Dr Lütfi Kırdar City Hospital Scientific Research Ethics Committee (Decision No: 2026/010.99/24/53; Date: 27.01.2026). All procedures were conducted in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki Declaration and its later amendments. Due to its retrospective design, the ethics committee waived the requirement for informed patient consent.

Clinical Trial Registration

Not Available.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' Contribution

Study Conception: SO, HB; Study Design: SO, HB; Supervision: SO, SY, MA; Funding: N/A; Materials: SO, MA, SY; Data Collection and/or Processing: SO, SY, MA, ET; Statistical Analysis and/or Data Interpretation: SO, HB; Literature Review: SO, UDG, HO; Manuscript Preparation: UDG, HO, NT; Critical Review: UDG, NT.

Conflict of Interest Statement

All authors have completed the ICMJE uniform disclosure form and declare that no potential conflicts of interest, financial or otherwise, exist regarding the research, authorship, or publication of this manuscript.

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Generative Artificial Intelligence Statement

The authors declare that no artificial intelligence-based tools or applications were used during the preparation process of this manuscript. All content of the study was produced by the authors in accordance with scientific research methods and academic ethical principles.

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