Prognostic Factors and Survival Analysis in Undifferentiated Gastric Carcinoma

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ABSTRACT

Objective: Gastric cancer, with notable regional variations in incidence rates, ranks as the third most prevalent cause of cancer-related deaths globally and the fifth most common cancer overall. The objective of this study is to examine the pathological, clinical, and demographic characteristics of patients diagnosed with undifferentiated gastric cancer (UGC) and to determine the major prognostic markers that impact survival and recurrence.

Materials and Methods: This retrospective analysis included patients who underwent surgery for gastric cancer at our center between March 2010 and February 2019. The inclusion criteria required a confirmed diagnosis of UGC and availability of pathological data. Data collected included demographic information, clinical parameters, pathological findings, surgical details, and survival outcomes. The primary outcomes were overall survival and local recurrence.

Results: Twenty-four patients were included, 66.7% of whom were male, with a mean age of 58.5 years. Local recurrence occurred in 50% of patients and was significantly associated with perineural and vascular invasion. Receiver operating characteristic (ROC) analysis identified a metastatic lymph node cutoff of 8.5, with an area under the curve (AUC) of 0.826, specificity of 100%, and sensitivity of 63.2%. Patients with fewer than 8.5 metastatic lymph nodes had a median survival of 16.0 months, compared to 7.0 months for those with more than 8.5 nodes (p=0.003).

Conclusion: Perineural and vascular invasion significantly affect local recurrence in UGC patients. A metastatic lymph node cutoff of 8.5 is a critical predictor of mortality. These findings underscore the importance of thorough pathological assessments and lymph node evaluations in guiding treatment decisions and improving outcomes. Further research is necessary to validate these results and explore additional prognostic markers.

Keywords: Gastric carcinoma, mortality, prognostic factors, survey, undifferentiated carcinoma.

INTRODUCTION

With notable regional variations in incidence rates, gastric cancer ranks as the third most prevalent cause of cancer-related deaths globally and the fifth most common cancer overall.[1] The prognosis for gastric cancer remains poor despite advancements in detection and therapy, especially for

individuals with undifferentiated gastric carcinoma (UGC), a highly aggressive subtype characterized by rapid disease progression and the absence of glandular differentiation.[2]

The aggressive nature of UGC leads to a poor prognosis, with five-year survival rates often below 30%, even in early-stage disease.[3] The lack of effective screening programs and the nonspecific nature of early symptoms contribute to late diagnoses and limited therapeutic options for these patients.[4]

Improving patient outcomes requires an understanding of the prognostic factors influencing survival and recurrence in UGC. Previous studies have identified several clinical and pathological variables, including tumor stage, lymph node involvement, and molecular characteristics, that impact the prognosis of gastric cancer.[5,6] However, there is limited data specifically focused on UGC, underscoring the need for more targeted research in this area.

This study aims to examine the demographic, clinical, and pathological features of patients with UGC and to determine the primary prognostic factors affecting survival and recurrence. By analyzing these factors, we aim to provide insights that can guide clinical decision-making and improve the management of UGC patients.

MATERIALS AND METHODS

Patient Selection and Study Design

The study received approval from the Erciyes University Ethic Committee (2024/39). It involved patients who underwent surgery for gastric cancer between March 2010 and February 2019. Our study was conducted by retrospectively reviewing the data from our center. The inclusion criteria were a confirmed diagnosis of undifferentiated gastric carcinoma based on histopathological examination and the availability of complete clinical and pathological data. Exclusion criteria included other histological types of gastric cancer and incomplete data.

Clinical and pathological data were collected from patient medical records, including demographic information (age, gender), clinical parameters (American Society of Anesthesiologists [ASA] score, tumor location), pathological findings (tumor characteristics, lymph node involvement), surgical details (type and date of surgery), and survival data (date of surgery, last follow-up, date of death, and survival status). The main outcomes of interest were overall survival and local recurrence. Overall survival was defined as the period from the date of surgery to the date of death or the last follow-up. Local recurrence was defined as the recurrence of cancer in the same location after initial treatment.

KEY MESSAGES

- Patients with a metastatic lymph node count below the cutoff of 9 exhibited significantly longer median survival times of 16.0 months.

- A metastatic lymph node count above the cutoff of 9 was associated with a markedly reduced median survival time of 7.0 months, with a log-rank test p-value of 0.003, indicating a higher risk of mortality with higher metastatic lymph node counts.

- The impacts of perineural invasion and vascular invasion on local recurrence have been objectively demonstrated.

Statistical Analysis

All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY). A p-value of <0.05 was considered statistically significant. Descriptive and inferential statistical methods were employed to analyze the data, ensuring a comprehensive understanding of the factors affecting patient outcomes. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables with normal distribution were presented as mean±standard deviation (SD), while numeric variables without normal distribution were presented as median (minimum–maximum), and categorical variables as frequencies and percentages. Receiver operating characteristic (ROC) analysis was conducted to determine the prognostic value of metastatic lymph nodes on mortality. The area under the curve (AUC) was calculated to assess the discriminatory power of the metastatic lymph node count. The optimal threshold value for metastatic lymph nodes was determined using Youden's index. Kaplan-Meier survival analysis was performed to assess overall survival, and the log-rank test was used to compare survival between groups.

RESULTS

A total of 24 patients were included in the study. Of these patients, 66.7% were male and 33.3% were female. The mean age of the patients was 58.5±13.2 years. The demographic data of the patients are presented in Table 1.

Local recurrence developed in 50% of the patients. The statistical analysis of patients with local recurrence is presented in Table 2.

We used the metastatic lymph node count to determine a cutoff for mortality using ROC-AUC analysis (Fig. 1). The Youden index indicated that a metastatic lymph node cutoff of 9 had an AUC of 0.826, with a specificity of 100%

Table 1. Demographic analysis of patients

Variables	n=24
Age (years)	58.5±13.2
Gender	
Male	16 (66.7%)
Female	8 (33.3%)
BMI (kg/m^2)	24.9±4.0
Tumor localization	
GOJ	3 (12.5%)
Lesser curvature	11 (45.8%)
Greater curvature	4 (16.7%)
Pylorus	6 (25.0%)
ASA score	
1	16 (66.7%)
2	5 (20.8%)
3	3 (12.5%)
WBC (10^3/µl)	8.1±2.7
Hgb (g/dL)	12.9±2.7
Albumin (g/dL)	3.7±0.7
CEA (ng/mL)	4.6±3.8

Quantitative data are presented as mean±standard deviation. BMI: Body mass index; GOJ: Gastroesophageal junction; ASA: American Society of Anesthesiologists; WBC: White blood cell count; Hgb: Hemoglobin; CEA: Carcinoembryonic antigen.

Figure 1. Analysis of metastatic lymph nodes and mortality.
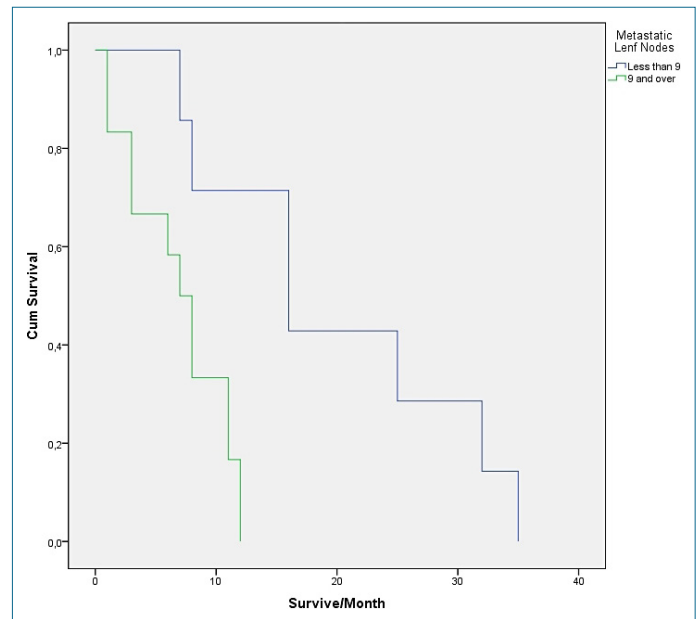
Figure 2. Kaplan-Meier Analysis of survival in patients with metastatic lymph nodes.

and a sensitivity of 63.2%. For the metastatic lymph node test, the positive predictive value is 100%. This means that if the test is positive, there is a 100% chance that the illness is present. The metastatic lymph node test has a 41.7% negative predictive value, meaning that if the test results are negative, there is a 41.7% chance that the illness is not present.

Patients with a metastatic lymph node count below the cutoff of 8.5 exhibited significantly longer median survival times of 16.0 months. In contrast, those with a metastatic lymph node count above the cutoff of 8.5 had a markedly reduced median survival time of 7.0 months. A log-rank test with a p-value of 0.003 indicated a higher risk of mortality associated with higher metastatic lymph node counts (Fig. 2).

DISCUSSION

In this study, we analyzed 24 patients with undifferentiated gastric carcinoma, of whom 66.7% were male and 33.3% were female, with a mean age of 58.5±13.2 years. The demographic and clinical characteristics of the patients are detailed in Table 1. Most t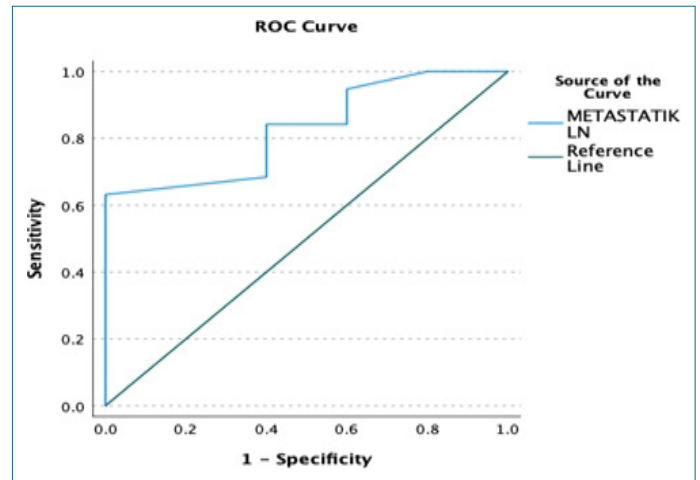umors were localized to the lesser curvature (45.8%), followed by the pylorus (25.0%), the greater curvature (16.7%), and the gastroesophageal junction (12.5%). The majority of patients had an ASA score of 1 (66.7%), indicating a relatively low surgical risk profile. These demographic findings are consistent with previous studies reporting a higher incidence of gastric carcinoma in males and a typical presentation in the sixth decade of life.[2,3]

Local recurrence was observed in 50% of the patients. A comparative analysis of patients with and without local recurrence revealed no significant differences in age,

Table 2. Comparative analysis of local recurrence

Variables	Local recurrence- (n=12)	Local recurrence + (n=12)	p
Age*	58.6±14.7	58.3±10.9	0.953
Gender			0.386
Male	7 (58.3%)	9 (75.0%)	
Female	5 (41.7%)	3 (25.0%)	
Localization			0.935
Gastroesophageal junction (GOJ)	2 (16.7%)		
Lesser curvature	5 (41.7%)	6 (50.0%)	
Greater curvature	2 (16.7%)	2 (16.7%)	
Pylorus	3 (25.0%)	3 (25.0%)	
Operation type			0.615
Subtotal gastrectomy	3 (25.0%)	2 (16.7%)	
Total gastrectomy	9 (75.0%)	10 (83.3%)	
Systemic metastasis	1 (8.3%)	5 (41.7%)	0.059
Perineural invasion	7 (58.3%)	12 (100%)	**0.012**
Vascular invasion	6 (50.0%)	11 (91.7%)	**0.025**
Total No. of lymph nodes#	25 (13–43)	23 (14–37)	0.685
No. of metastatic lymph nodes#	7 (0–30)	9 (1–35)	0.174
Tumor size#	5.5 (3.5–37.5)	5.0 (2.0–9.6)	0.291

*: Arithmetic mean and standard deviation. #: median and range (min–max). Variables in bold indicate statistical significance.

gender, or tumor localization (Table 2). However, perineural invasion and vascular invasion were significantly more prevalent in patients with local recurrence (p=0.012 and p=0.025, respectively). These findings suggest that certain pathological features may predispose patients to a higher risk of local recurrence, aligning with existing literature identifying perineural and vascular invasion as poor prognostic factors in gastric cancer.[7]

The prognostic significance of metastatic lymph node involvement was further explored using ROC-AUC analysis. We determined an optimal cutoff value of 9 metastatic lymph nodes for predicting mortality, with an AUC of 0.826, specificity of 100%, and sensitivity of 63.2% (Fig. 1). This is consistent with previous studies that emphasize the importance of lymph node metastasis in predicting survival outcomes in gastric cancer.[8] Kaplan-Meier survival analysis demonstrated that patients with fewer than 9 metastatic lymph nodes had a significantly longer median survival time of 16.0 months, compared to 7.0 months for those with more than 9 metastatic lymph nodes (log-rank test p=0.003), highlighting the critical impact of nodal metastasis on patient outcomes.

Deng et al.[9] found that perineural invasion is a significant prognostic factor in gastric cancer, associated with poor survival outcomes. Similarly, Zhao et al.[10] reported that perineural invasion dramatically reduces overall survival and increases the probability of recurrence in individuals with gastric cancer. Similar to these findings, we observed that perineural invasion was significantly more prevalent in patients with local recurrence, underscoring its role as a critical factor in disease progression and recurrence.

Li et al.[11] demonstrated that vascular invasion is another important prognostic indicator in gastric cancer, correlating with higher rates of recurrence and reduced survival. Similarly, a study by Li et al.[12] confirmed that the presence of vascular invasion is linked to poor prognosis and increased metastatic potential, even in stage 1 gastric cancer patients. Our results align with these studies, as we found a significant association between vascular invasion and local recurrence, emphasizing the necessity of assessing vascular invasion during patient evaluations. Fukuda et al.[13] identified the number of metastatic lymph nodes as a key determinant of survival in gastric cancer, with higher lymph node counts and metastatic lymph node ratio (MLR) correlating with worse outcomes.

This study has several limitations that should be considered. First, the sample size included only 24 patients, which may limit the broad applicability of our results. Additionally, the retrospective nature of the study may introduce selection bias and affect the accuracy of the recorded data. The finding of a 63.2% sensitivity in the mortality-related ROC analysis of metastatic lymph nodes indicates that while the study demonstrated high specificity, it had relatively lower sensitivity. Furthermore, we did not include molecular or genetic analyses, which could provide deeper insights into the mechanisms underlying local recurrence and survival in undifferentiated gastric carcinoma. Lastly, the fact that the study conducted at a single institution may limit the broader applicability of the findings.

CONCLUSION

In conclusion, our study highlights the significant impact of perineural and vascular invasion on local recurrence in patients with undifferentiated gastric carcinoma. We also identified a metastatic lymph node cutoff of 8.5 as a critical predictor of mortality, with higher counts associated with significantly reduced survival times. These findings underscore the importance of thorough pathological assessment and lymph node evaluation in guiding treatment decisions and improving patient outcomes. Further research involving larger, multicenter cohorts and molecular analyses is needed to validate these results and explore additional prognostic markers.

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