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Retrospective Study

Risk factors for lymph node metastasis and invasion depth in early gastric cancer:

Analysis of 210 Cases

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Risk Factors for Lymph Node Metastasis and Invasion Depth in Early Gastric Cancer

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Abstract

BACKGROUND

Gastric cancer is a leading cause of cancer deaths worldwide. Early gastric cancer (EGC) often presents with a risk of lymph node metastasis, which influences treatment decisions. Despite the use of enhanced CT, predicting lymph node involvement remains challenging.

AIM

This study aims to investigate the risk factors for lymph node metastasis and the risk factors for invasion depth in patients with early gastric cancer.

METHODS

A total of 210 patients with pathologically diagnosed early gastric cancer were included. Univariate and multivariate statistical analyses were used to predict the risk factors for lymph node metastasis and invasion depth in patients with early gastric cancer.

RESULTS

Among the 210 patients, 27 cases (12.9%) had lymph node metastasis. Of the 117 patients with submucosal gastric cancer, 24 cases (20.5%) had lymph node metastasis. Both univariate and multivariate analyses indicated that the depth of invasion in early gastric cancer is a risk factor for lymph node metastasis in these patients. Additionally, pathological type was identified as a risk factor for cancer cell invasion in patients with early gastric cancer.

CONCLUSION

The risk factors for ³ lymph node metastasis in early gastric cancer are related to the depth of cancer invasion and are not related to pathological type, tumor size, age, gender, or site of onset. The risk factors for cancer cell invasion in early gastric cancer

are associated with pathological type and are not related to tumor size, age, gender, or site of onset.

Key Words: Early Gastric Cancer (EGC); Lymph Node Metastasis; Invasion Depth; Risk Factors; Submucosal Invasion; Pathological Type

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Core Tip: This study investigates the risk factors for lymph node metastasis and invasion depth in early gastric cancer (EGC) by analyzing 210 cases from Huzhou Central Hospital. Our findings highlight that invasion depth and pathological type are significant predictors of lymph node metastasis in EGC, while other factors such as tumor size, age, gender, and tumor location are not. The study underscores the importance of assessing invasion depth and pathological type in EGC diagnosis and treatment planning, offering valuable insights for improving patient outcomes.

INTRODUCTION

Gastric cancer is the fifth most common cancer type worldwide and ranks third in global cancer-related deaths. In China, gastric cancer has an incidence rate of 20.6 per 100,000, ranking fifth globally[1]. Early gastric cancer refers to tumors confined to the mucosal layer or submucosal layer, regardless of the tumor size or the presence of lymph node metastasis. This concept was first proposed by the Japanese scholar T. Murakami. The primary responsibility of gastroenterological endoscopists is the timely diagnosis of early gastric cancer and the correct classification of lesions to choose appropriate treatment options, such as surgical treatment or endoscopic therapy. The choice of treatment mainly depends on the risk of lymph node involvement[2]. However, it is currently believed that imaging examinations have low sensitivity and specificity for the detection of lymph node metastasis in early gastric cancer[3]. Most

studies agree that invasion depth and tumor size are related to lymph node metastasis in early gastric cancer[4–8]. Some studies[4–6] suggest that histological type of the tumor is related to lymph node metastasis in early gastric cancer, but this view is not universally accepted[7,8]. There are also studies suggesting that the location of the tumor may be related to lymph node metastasis in early gastric cancer[6].

The significance of this study is to provide a deeper understanding of the factors influencing lymph node metastasis in early gastric cancer, which is crucial for optimizing treatment strategies and improving patient outcomes. By exploring not only the commonly accepted risk factors such as invasion depth and tumor size but also less universally agreed factors like histological type and tumor location, this study aims to contribute to a more comprehensive approach to assessing lymph node metastasis risk. Additionally, the investigation into the diagnostic value of the 'lymph node presentation' observed in enhanced CT scans could potentially offer new insights into improving the accuracy of lymph node metastasis prediction in early gastric cancer, further guiding clinical decisions.

This article primarily discusses the risk factors for lymph node metastasis in early gastric cancer. Most studies agree that invasion depth is a risk factor for lymph node metastasis in early gastric cancer, therefore, this article will also discuss the risk factors for invasion depth in early gastric cancer.

It is well known that the success rate of enhanced CT scans in predicting lymph node metastasis in early gastric cancer patients is currently low, despite numerous studies dedicated to improving the detection rate of lymph node metastasis in early gastric cancer through CT scans[9–11]. We have found that when radiologists observe enlarged lymph nodes but cannot definitively determine whether there is metastasis, they often make a diagnosis of 'lymph node presentation'. This article will also discuss whether the diagnosis of 'lymph node presentation' has any indicative significance for lymph node metastasis in early gastric cancer.

MATERIALS AND METHODS

Study Design and Subjects

This study retrieved data from the medical record system of Huzhou Central Hospital for all patients who underwent radical gastrectomy and were pathologically diagnosed with early gastric cancer from December 1, 2017, to August 31, 2021.

Inclusion criteria: All patients underwent radical gastrectomy and were pathologically confirmed as early gastric cancer. Patients who received preoperative chemotherapy, patients with multiple metastatic tumors, and those with incomplete clinical data were excluded from this study. Variables included age, gender, location of gastric cancer, pathological classification, postoperative lymph node metastasis, tumor invasion depth, tumor size, and preoperative enhanced CT indicating lymph node metastasis. Data extraction was carried out in February 2023. After determining the patient data, two researchers independently reviewed the data.

Statistical Analysis

The primary dependent variables are lymph node metastasis and invasion depth. The χ^2 test was used to compare categorical variables. Binary logistic regression analysis was employed to explore the relationship between lymph node metastasis and invasion depth in early gastric cancer. In both univariate and multivariate analyses, the odds ratio (OR) and 95% confidence interval (CI) were calculated to assess risk. Statistical significance was defined as $P < 0.05$. Statistical analyses were conducted using SPSS software version 27.0 and GraphPad PRISM 9.5.

RESULTS

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Results

Baseline Data Analysis

Among the 210 patients, their ages ranged from 31 to 91 years, with a median age of 66. There were 156 males (74.3%) and 54 females (25.7%). Tumors were located in the cardia in 18 cases (8.6%), the fundus in 2 cases (1.0%), the body of the stomach in 41 cases (19.5%), the angular incisure in 21 cases (10.0%), and the antrum in 128 cases (60.9%). Pathological types included highly differentiated adenocarcinoma in 14 cases (6.7%), moderately differentiated adenocarcinoma in 84 cases (40.0%), poorly differentiated adenocarcinoma in 66 cases (31.4%), mucinous adenocarcinoma in 3 cases (1.4%), signet ring cell carcinoma in 41 cases (19.5%), papillary adenocarcinoma in 1 case (0.5%), and lymphoepithelioma-like carcinoma in 1 case (0.5%). Invasion reached the mucosal layer in 93 cases (44.3%), and the submucosal layer in 117 cases (55.7%).

There were 27 cases (12.9%) with lymph node metastasis and 183 cases (87.1%) without lymph node metastasis (Table 1).

Age Distribution Analysis

Among all patients, the number of males was significantly higher than that of females. The median age of female patients (60 years) was lower than that of male patients (66 years). In younger patients (aged 45 or below), the proportion of females was higher (7 persons, 100%). (Figure 1)

The median age of patients with highly differentiated adenocarcinoma was 64 years, with moderately differentiated adenocarcinoma it was 67.5 years, with poorly differentiated adenocarcinoma it was 65 years, and with signet ring cell carcinoma it was 55 years. Among younger patients (aged 45 or below), the proportion was higher for poorly differentiated adenocarcinoma (2 persons, 28.6%) and signet ring cell carcinoma (5 persons, 71.4%) (Figure 2).

In patients with highly differentiated and moderately differentiated adenocarcinoma, 100% were older than 45 years, and 0% were younger than 45 years. In contrast, among patients with poorly differentiated adenocarcinoma and signet ring cell carcinoma, 93.5% were older than 45 years, and 6.5% were younger than 45 years, $P < 0.05$ (Figure 3).

The median age of patients with gastric cancer invading the mucosal layer was 62 years, and for those with invasion to the submucosal layer, it was 66 years (Figure

Analysis of the Site of Onset

In cardia cancer, 38.9% of cases had invasion to the mucosal layer, and 61.1% to the submucosal layer; 77.8% had no lymph node metastasis, and 22.2% had lymph node metastasis. In fundus cancer, 0% of cases had invasion to the mucosal layer, and 100% to the submucosal layer; 100% had no lymph node metastasis, and 0% had lymph node metastasis. In gastric body cancer, 51.2% of cases had invasion to the mucosal layer, and 48.8% to the submucosal layer; 87.8% had no lymph node metastasis, and 12.2% had

lymph node metastasis. In angular incisure cancer, 61.9% of cases had invasion to the mucosal layer, and 38.1% to the submucosal layer; 95.2% had no lymph node metastasis, and 4.8% had lymph node metastasis. In antral cancer, 40.6% of cases had invasion to the mucosal layer, and 59.4% to the submucosal layer; 86.7% had no lymph node metastasis, and 13.3% had lymph node metastasis; $P > 0.05$ (Figure 5).

Analysis of Invasion Depth

In gastric cancers with invasion to the mucosal layer, 96.8% had no lymph node metastasis, and 3.2% had lymph node metastasis. In gastric cancers with invasion to the submucosal layer, 79.5% had no lymph node metastasis, and 20.5% had lymph node metastasis, $P < 0.05$ (Figure 6).

In highly differentiated adenocarcinoma, 85.7% of cases had invasion to the mucosal layer and 14.3% to the submucosal layer. In moderately differentiated adenocarcinoma, 44% had invasion to the mucosal layer and 56% to the submucosal layer. In poorly differentiated adenocarcinoma, 30.3% had invasion to the mucosal layer and 69.7% to the submucosal layer. In signet ring cell carcinoma, 30.3% had invasion to the mucosal layer and 69.7% to the submucosal layer. There was a significant difference between highly differentiated adenocarcinoma and moderately differentiated adenocarcinoma, $P < 0.05$. There was no significant difference between moderately differentiated adenocarcinoma and poorly differentiated adenocarcinoma, $P > 0.05$. There was no significant difference between poorly differentiated adenocarcinoma and signet ring cell carcinoma, $P > 0.05$ (Figure 7).

Tumor Size Analysis

In patients without lymph node metastasis, the median tumor size was 2cm; in patients with lymph node metastasis, the median tumor size was 2.2cm(Figure 8).

In patients with invasion to the mucosal layer, the median tumor size was 2cm; in patients with invasion to the submucosal layer, the median tumor size was also 2cm(Figure 9).

In tumors smaller than 2cm, 58.19% had no lymph node metastasis and 40.74% had lymph node metastasis. In tumors larger than 2cm, 41.81% had no lymph node metastasis and 59.26% had lymph node metastasis, $P > 0.05$. In tumors smaller than 2cm, 62.92% had no lymph node metastasis and 37.08% had lymph node metastasis. In tumors larger than 2cm, 50.43% had no lymph node metastasis and 49.57% had lymph node metastasis, $P > 0.05$ (Figure 10).

Analysis of Preoperative Abdominal Enhanced CT Results

In patients with negative lymph nodes postoperatively, 100% had no indication of metastasis in preoperative enhanced CT, and 0% had an indication of metastasis. In patients with positive lymph node dissection postoperatively, 96.3% had no indication of metastasis in preoperative enhanced CT, and 3.7% had an indication of metastasis, $P > 0.05$. In patients with negative lymph nodes postoperatively, 86.1% had no indication of metastasis in preoperative enhanced CT, and 13.9% had lymph node presentation indicated; in patients with positive lymph nodes postoperatively, 65.4% had no indication of metastasis in preoperative enhanced CT, and 34.6% had lymph node presentation indicated, $P < 0.05$ (Figure 11).

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Univariate and Multivariate Logistic Regression Analysis of the Risk of Lymph Node Metastasis in Early Gastric Cancer

We used logistic regression models to explore the risk factors predicting lymph node metastasis in early gastric cancer. Multivariate analysis showed that invasion depth is associated with adverse outcomes, while gender, age, pathological type, and tumor size are not associated with adverse outcomes(Table 2).

Univariate and Multivariate Logistic Regression Analysis of Invasion Risk in Early Gastric Cancer

We used logistic regression models to explore the risk factors predicting invasion in early gastric cancer. Multivariate analysis showed that pathological type is associated

with adverse outcomes, while gender, age, and tumor size are not associated with adverse outcomes(Table 3).

DISCUSSION

In this retrospective study of 210 patients who underwent radical gastrectomy for early gastric cancer (EGC), we found a significant gender disparity, with more male than female patients. This could be associated with unhealthy lifestyle habits among men, such as smoking and alcohol consumption. While gastric cancer predominantly affects middle-aged and elderly individuals, we observed that younger patients were more likely to present with poorly differentiated gastric cancers, including poorly differentiated adenocarcinoma and signet ring cell carcinoma. Consistent with previous studies, we found that the most common site for gastric cancer was the antrum, particularly the lesser curvature[12,13]. The lack of parietal cells in this region may render it more susceptible to cancer, as atrophy and intestinal metaplasia—conditions linked to intestinal-type gastric cancer—are more prevalent along the lesser curvature[14].

Our results suggest that lymph node metastasis in EGC is not associated with factors such as gender or age. However, we found that the risk of lymph node metastasis is closely related to invasion depth, consistent with prior research[4–8,15]. Moreover, our findings did not show a significant association between tumor size and lymph node metastasis[16]. Additionally, the location of the tumor did not appear to influence the likelihood of lymph node metastasis.

Tumors with poorer differentiation are known to be more aggressive and linked to worse prognoses. In our study, three cases of intramucosal cancer with lymph node metastasis were all identified as signet ring cell carcinoma. Nevertheless, our analysis suggests that the risk of lymph node metastasis in EGC is not significantly associated with tumor cell type, which contradicts existing literature[17]. Some studies have shown that signet ring cell carcinoma has a higher rate of distant metastasis compared to non-signet ring cell carcinoma[18]. This discrepancy may be due to our relatively

small sample size. Since invasion depth is a key factor in EGC, it is critical to understand what influences this invasion. Our data suggest that tumor differentiation plays a role: Poorly differentiated adenocarcinomas and signet ring cell carcinomas are more prone to invading the submucosal layer compared to well-differentiated adenocarcinomas. Thus, histopathology may have an indirect impact on lymph node metastasis, a relationship that warrants further exploration in larger datasets.

Regarding preoperative detection of lymph node metastasis, we found that enhanced abdominal CT scans did not provide reliable predictive value. While imaging can suggest lymph node involvement, its specificity remains low, meaning clinicians must still be cautious when deciding on treatment strategies. Our study indicates that enhanced CT could benefit from more sensitive contrast agents and higher resolution to improve the detection of small metastatic lymph nodes. Regular follow-up with gastroscopy and imaging remains critical in postoperative management, especially for patients undergoing ESD, to monitor potential lymph node metastasis.

The innovative aspect of our study lies in the investigation of both lymph node metastasis and invasion risk factors in EGC. We found no significant association between pathological type and lymph node metastasis risk, but did observe a strong correlation between pathological type and invasion risk. Furthermore, we highlighted the limitations of using preoperative CT for lymph node metastasis detection, suggesting that intermediate lymph nodes identified in imaging should not be overlooked.

Our study has certain limitations. Being a single-center retrospective analysis, the data is inherently limited in scope and generalizability. As with any retrospective study, there was some degree of data loss. Moreover, we excluded cases that underwent ESD or had distant metastases, which may have introduced selection bias. Pathology reports from multiple sources also posed challenges in standardizing tumor size measurements. Future studies should include a larger sample size and consider multi-center collaboration to validate these findings.

CONCLUSION

1. The risk of lymph node metastasis in gastric cancer is mainly related to the depth of tumor invasion, possibly indirectly related to pathological type, and not related to gender, age, tumor location, or tumor size.

2. Preoperative enhanced CT examination does not provide guidance in determining whether patients with early gastric cancer have lymph node metastasis. However, clinicians should pay attention to lymph nodes that are intermediate between metastatic and normal, as identified by radiologists.

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