

ORIGINAL RESEARCH

Retrospective Analysis of Diagnosis and Treatment of Gastric Cancer at Huzhou Central Hospital

Yu Xiang, MM; Lidi Yao, BM

ABSTRACT

Objective • To explore the results of lymph node metastasis in patients with gastric cancer in a real-world setting.

Methods • Patients ($n = 272$) who underwent radical gastrectomy with lymph node dissection for gastric cancer from November 2017 to August 2019 at Huzhou Central Hospital, China. The main outcome was the lymph node metastasis rate. The chi-square test was used to compare categorical variables. Binary logistic regression analysis was used to examine the relationship between risk factors and lymph node metastasis in gastric cancer and early gastric cancer. In multivariate analysis, OR and 95% CI were calculated to evaluate the risk. Statistical significance was defined as $P < .05$. Statistical analysis was performed using SPSS software version 26.0 (SPSS Inc.) and GraphPad PRISM 9.0.

Results • Among the 272 patients who underwent surgery, 143 (52.6%) had lymph node metastasis. The proportion of female patients was higher in those under 40 years of age. The incidence of gastric cancer was highest in the lesser curvature of the gastric antrum. The lymph node metastasis rates were 5.3%, 25%, 39%, 78.1%, and 76.8%

for invasion to the mucosal layer, submucosal layer, muscular layer, serosal layer, and beyond the serosal layer, respectively. There was a statistically significant difference in lymph node metastasis between invasion to the mucosal layer and the other four layers ($P < .05$), while there was no statistically significant difference between invasion to the submucosal and muscular layers ($P > .05$) and between invasion to the serosal layer and beyond ($P > .05$). Well-differentiated gastric cancer had almost no lymph node metastasis (0%), while moderately differentiated gastric cancer had a lower rate of lymph node metastasis (32%), and there was no statistically significant difference between the two. The lymph node metastasis rates were higher for poorly differentiated adenocarcinoma (66.7%), mucinous adenocarcinoma (63.6%), and signet ring cell carcinoma (57.1%), and there was no statistically significant difference between the three.

Conclusion • Lymph node metastasis in gastric cancer is related to the depth of invasion and pathological subtype, and is not related to age, sex, or tumor location. (*Altern Ther Health Med.* 2023;29(8):302-309).

Yu Xiang, MM, Attending Doctor, Department of Gastroenterology, Huzhou Central Hospital, Huzhou, China.
Lidi Yao, BM, Senior Technologist, Department of Radiology, Huzhou Central Hospital, Huzhou, China.

Corresponding author: Lidi Yao, BM
E-mail: xyu@hzhospital.com

INTRODUCTION

Gastric cancer is a malignant tumor that originates from the epithelium of the gastric mucosa, and is the fifth most common cancer and the third leading cause of cancer death globally.¹ In 2020, the number of new cases of this disease exceeded one million worldwide, with nearly 800 000 deaths.² Gastric cancer may be related to *Helicobacter pylori* infection, diet, smoking, alcohol consumption, and other unhealthy

lifestyles. Thanks to the development of *H. pylori* treatment and gastric endoscopy technology, the incidence of gastric cancer has slightly decreased in recent years.³ Currently, the main treatments for gastric cancer include surgical treatment, chemotherapy, and radiotherapy. For early-stage gastric cancer, endoscopic mucosal dissection (ESD) can be performed as a radical treatment. Compared with traditional surgical treatment, endoscopic treatment is easier to preserve the patient's organ function and improve their postoperative quality of life. However, compared with surgical treatment, endoscopic surgery cannot perform lymph node dissection, which may affect the survival period of some patients undergoing endoscopic treatment. Some studies have shown that there is still a risk of lymph node metastasis in early-stage gastric cancer, ranging from 10% to 17.1%.^{3,4} Preoperative enhanced computed tomography (CT) examination still has low resolution in distinguishing lymph node metastasis in

gastric cancer. This article aims to explore the risk of lymph node metastasis in gastric cancer and early gastric cancer, as well as the detection rate of preoperative abdominal enhanced CT examination for lymph node metastasis.

In recent years, there are many studies on early gastric cancer, but few studies on gastric cancer. At present, we know that metastasis will lead to the bad outcome of cancer. The traditional view on the definition of early gastric cancer is that the cancer is confined to the mucosa or submucosa, regardless of lymph node metastasis. There is still a certain probability of lymph node metastasis upon infiltration of gastric cancer into the submucosa. Compared with non-early gastric cancer, whether there is a clear statistical difference in the risk of lymph node metastasis in submucosal gastric cancer is worth discussing again.

MATERIALS AND METHODS

Study design and population

The study retrieved all patients who underwent radical surgery for gastric cancer from November 1, 2017 to August 31, 2019 in the medical records system of Huzhou Central Hospital. Inclusion criteria: All patients treated through radical gastrectomy, with pathological confirmation of cancer after operation. Among them, patients who received chemotherapy before operation, patients with multiple metastases, and patients with incomplete clinical information were excluded from this study. Variables included age, gender, site of gastric cancer, pathological classification, postoperative lymph node metastasis, tumor infiltration depth, presence of distant metastasis, and whether preoperative enhanced CT indicated lymph node metastasis. Data extraction was conducted in December 2022. Patient data were identified, and two researchers independently reviewed the data.

Statistical analyses

The main outcome was the lymph node metastasis rate. The chi-square test was used to compare categorical variables. Binary logistic regression analysis was used to examine the relationship between risk factors and lymph node metastasis in gastric cancer and early gastric cancer. In multivariate analysis, OR and 95% CI were calculated to evaluate the risk. Statistical significance was defined as $P < .05$. Statistical analysis was performed using SPSS software version 26.0 (SPSS Inc.) and GraphPad PRISM 9.0.

RESULTS

From November 1, 2017 to August 31, 2019, a total of 303 patients underwent radical gastrectomy with abdominal lymph node dissection in our hospital, of which 272 patients were included in the current analysis (see Figure 1 for the flowchart).

Baseline characteristics

Baseline demographic and clinical characteristics are shown in Table 1.

Figure 1. Flowchart

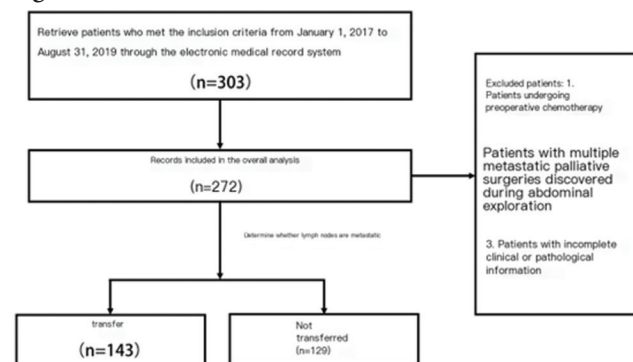
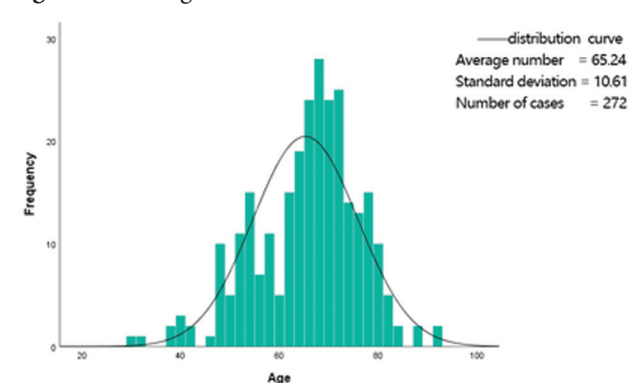


Table 1. Baseline Characteristics

Feature	n (%)
All cases	272
Age (years), median (years)	(30-91), 67
Gender	
Male	206 (75.7)
Female	66 (24.3)
Primary site,	
Cardia	51 (18.8)
Fundus	6 (2.2)
Body	34 (12.5)
Angle	18 (6.6)
Pylorus	152 (55.9)
Involvement of 2 or more sites	5 (1.8)
Synchronous cancers	6 (2.2)
Histological differentiation	
Well-differentiated adenocarcinoma	9 (3.3)
Moderately differentiated adenocarcinoma	75 (27.6)
Poorly differentiated adenocarcinoma	126 (46.3)
Mucinous adenocarcinoma	11 (4.0)
Signet ring cell carcinoma	49 (18.0)
Squamous cell carcinoma	2 (0.7)
Depth of invasion	
Mucosa	38 (14.0)
Submucosa	47 (17.3)
Muscularis propria	41 (15.1)
Serosa	64 (23.5)
Beyond serosa	82 (30.1)
Lymph node metastasis	
Metastasis	143 (52.6)
No metastasis	129 (47.4)
Distant metastasis	
Metastasis	13 (4.8)
No metastasis	259 (95.2)

Figure 2. The Age Distribution of the Patients



Analysis of patient age

Figure 2 shows the age distribution of the patients. The median age of all patients was 67 years, and the mean age was 65.24 years. The age distribution demonstrated a lower proportion of young and elderly patients and a higher proportion of middle-aged and older patients.

Figure 3. The Age Distribution of Patients with Different Pathological Subtypes of Gastric Adenocarcinoma

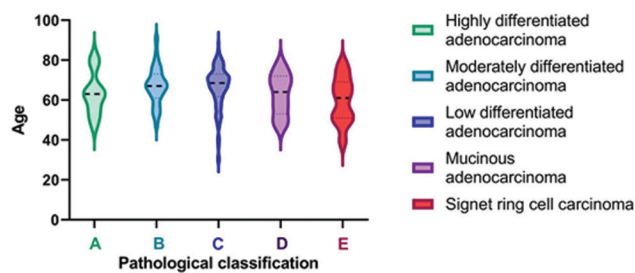


Figure 5. The Age Distribution of Patients of Different Genders

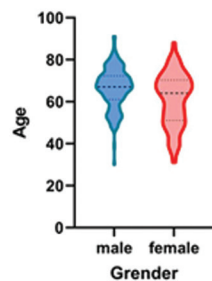


Figure 4. The Lymph Node Metastasis Rates of Patients in Different Age Groups

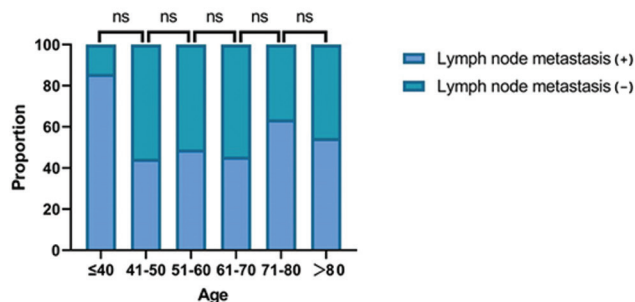


Figure 6. The Lymph Node Metastasis Rates of Patients with Gastric Cancer in Different Genders

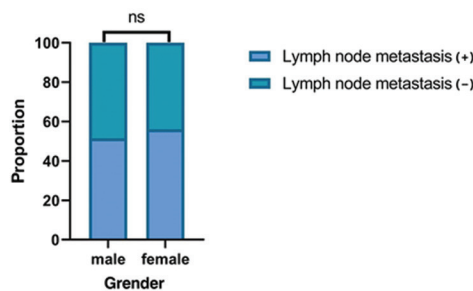


Figure 3 shows the age distribution of patients with different pathological subtypes of gastric adenocarcinoma, including well-differentiated adenocarcinoma, moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet ring cell carcinoma (2 cases of esophageal squamous cell carcinoma were not included in the statistics). The age distribution of patients with different pathological subtypes of gastric adenocarcinoma was similar, but younger patients seemed to be more prone to developing poorly differentiated adenocarcinoma and signet ring cell carcinoma.

Figure 4 shows the lymph node metastasis rates of patients in different age groups. The lymph node metastasis rates of patients aged ≤ 40 , 41-50, 51-60, 61-70, 71-80, and >80 years were 85.7%, 44.4%, 49%, 45.5%, 63.6%, and 54.5%, respectively ($P > .05$). The lymph node metastasis rates of patients in each age group were different, with a higher rate in younger patients aged ≤ 40 years. However, statistical analysis showed no difference in the lymph node metastasis rates among patients in different age groups.

Analysis of patient gender

Figure 5 shows the age distribution of patients of different genders, with a higher proportion of female patients (71.4%) in the younger age group (age ≤ 40 years).

Figure 6 shows the lymph node metastasis rates of patients with gastric cancer in different genders. The lymph node metastasis rates for male and female patients were 51.5% and 56.1%, respectively ($P > .05$), indicating no significant difference in lymph node metastasis between different genders.

Figure 7. The Pathological Classification of Gastric Adenocarcinoma in Different Genders

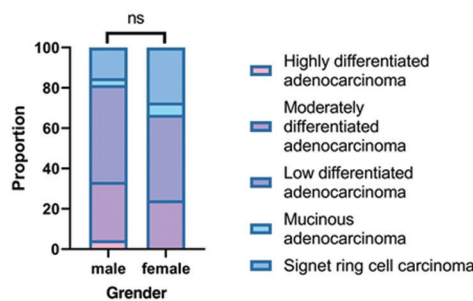


Figure 8. The Lymph Node Metastasis of Patients with Different Gastric Cancer Sites

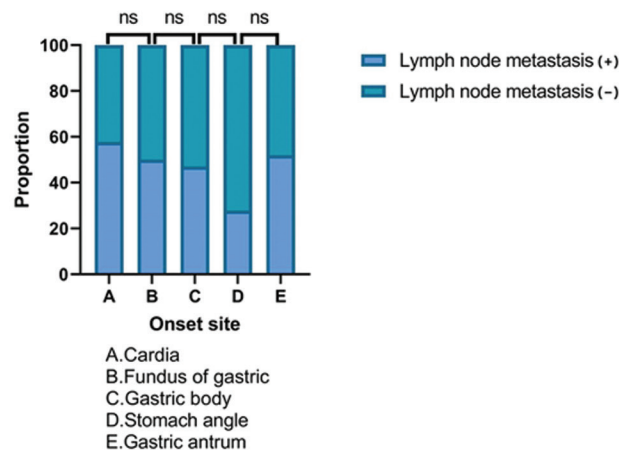


Figure 9. The Pathological Classification of Patients with Different Gastric Cancer Sites

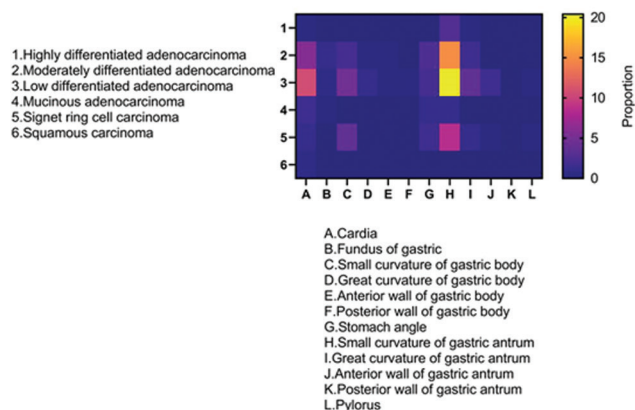


Figure 10. The Relationship Between Invasion Depth and Lymph Node Metastasis

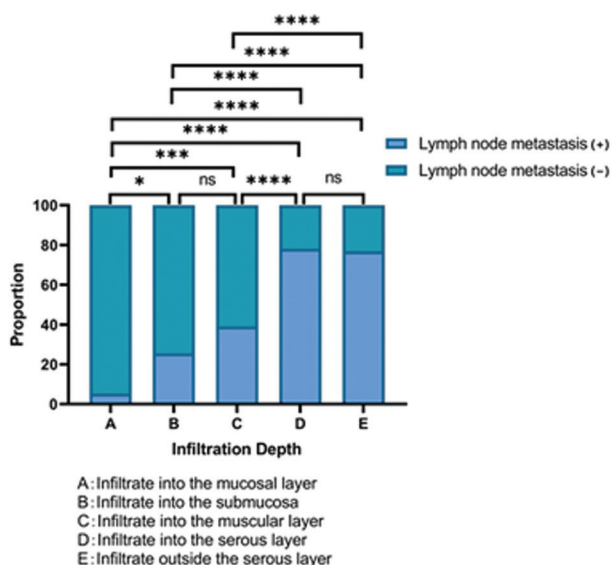


Figure 7 shows the pathological classification of gastric adenocarcinoma in different genders. In male patients, the proportions of well-differentiated adenocarcinoma, moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet ring cell carcinoma were approximately 4.4%, 28.6%, 47.6%, 3.4%, and 15%, respectively. In female patients, the proportions of moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet ring cell carcinoma were approximately 24.2%, 42.4%, 6.1%, and 27.3%, respectively ($P > .05$). These results indicate no significant statistical difference in pathological classification between male and female patients with gastric cancer.

Analysis of Gastric Cancer Site

Figure 8 shows the lymph node metastasis of patients with different gastric cancer sites (5 patients with infiltration into more than 2 sites, and 6 patients with simultaneous

cancer, none of which were included in the statistics). The lymph node metastasis rate of cardia cancer was 57.7%, that of gastric fundus cancer was 50%, that of gastric body cancer was 47.1%, that of gastric angle cancer was 27.2%, and that of gastric antrum cancer was 52% ($P > .05$), indicating no statistical difference in lymph node metastasis of different sites of gastric cancer.

Figure 9 shows the pathological classification of patients with different gastric cancer sites (5 patients with infiltration into more than 2 sites, and 6 patients with simultaneous cancer, none of which were included in the statistics). The sites of gastric cancer include cardia, gastric fundus, lesser curvature of the gastric body, greater curvature of the gastric body, anterior wall of the gastric body, posterior wall of the gastric body, gastric angle, lesser curvature of the gastric antrum, greater curvature of the gastric antrum, anterior wall of the gastric antrum, posterior wall of the gastric antrum, and pylorus. The pathological classification includes well-differentiated adenocarcinoma, moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet ring cell carcinoma. The proportion of patients with different sites and pathological types was calculated. The results showed that squamous cell carcinoma only occurred in the cardia of the stomach; in cardia cancer, the incidence of poorly differentiated adenocarcinoma was higher; in cancer of the lesser curvature of the gastric body, the incidence of poorly differentiated adenocarcinoma was higher. At the same time, the analysis showed that the proportion of gastric cancer occurring in the lesser curvature of the gastric antrum was the highest, and in cancer of the lesser curvature of the gastric antrum, the incidence of moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, and signet ring cell carcinoma was higher.

Analysis of Invasion Depth of Gastric Cancer

Figure 10 shows the relationship between invasion depth and lymph node metastasis. The lymph node metastasis rate was 5.3% for patients with invasion limited to the mucosal layer, 25% for patients with invasion into the submucosal layer, 39% for patients with invasion into the muscular layer, 78.1% for patients with invasion into the serosal layer, and 76.8% for patients with invasion beyond the serosal layer. There was a significant difference in lymph node metastasis between patients with invasion limited to the mucosal layer and those with invasion into the submucosal layer ($P < .05$), and also between patients with invasion limited to the mucosal layer and those with invasion into the muscular layer ($P < .05$). However, no significant difference in lymph node metastasis was found between patients with invasion into the submucosal layer and those with invasion into the muscular layer ($P > .05$), and between patients with invasion into the serosal layer and those with invasion beyond the serosal layer ($P > .05$). The results suggest that lymph node metastasis in patients with gastric cancer varies with invasion depth and patients with invasion limited to the mucosal layer had the lowest lymph node metastasis rate.

Figure 11. The Relationship Between Infiltration Depth and Pathological Types of Gastric Cancer

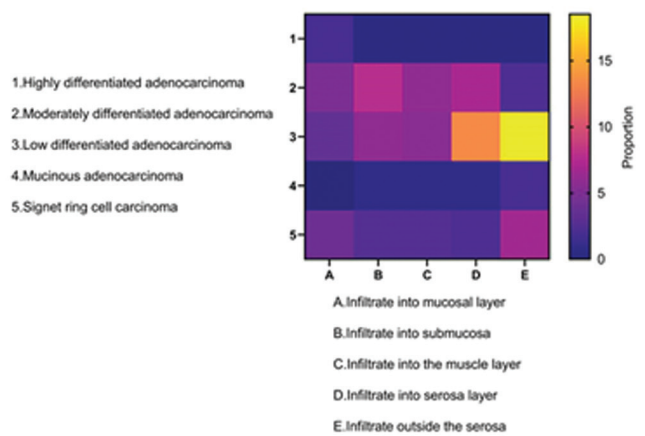


Figure 11 shows the relationship between infiltration depth and pathological types of gastric cancer. Infiltration depth includes infiltration into the mucosal layer, submucosal layer, muscular layer, serosal layer, and beyond. Pathological types of gastric cancer include well-differentiated adenocarcinoma, moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma. The proportions of patients with different infiltration depths and pathological types of gastric cancer were calculated. The results indicate that the proportion of infiltration into the mucosal layer is the highest in well-differentiated adenocarcinoma; infiltration depth is roughly equivalent in moderately differentiated adenocarcinoma; infiltration into the serosal layer and beyond is the highest in poorly differentiated adenocarcinoma, mucinous adenocarcinoma and signet-ring cell carcinoma. This suggests that with the increase in the degree of malignancy of gastric cancer, the tumor cells become more invasive.

Pathological Analysis of Gastric Cancer

Figure 12 shows the relationship between pathological types of gastric cancer and lymph node metastasis. Lymph node metastasis is almost absent in well-differentiated gastric cancer (0%), and the incidence of lymph node metastasis is relatively low in moderately differentiated gastric cancer (32%). However, there is no statistical difference between the two. The rates of lymph node metastasis are high in poorly differentiated adenocarcinoma (66.7%), mucinous adenocarcinoma (63.6%), and signet-ring cell carcinoma (57.1%). However, there is no significant difference among the three. This indicates that higher the degree of malignancy of tumor cells, the greater the risk of lymph node metastasis. The probability of lymph node metastasis is lowest in well-differentiated adenocarcinoma, followed by moderately differentiated adenocarcinoma, while the rates of lymph node metastasis are high but not significantly different in poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma.

Figure 12. The Relationship Between Pathological Types of Gastric Cancer and Lymph Node Metastasis

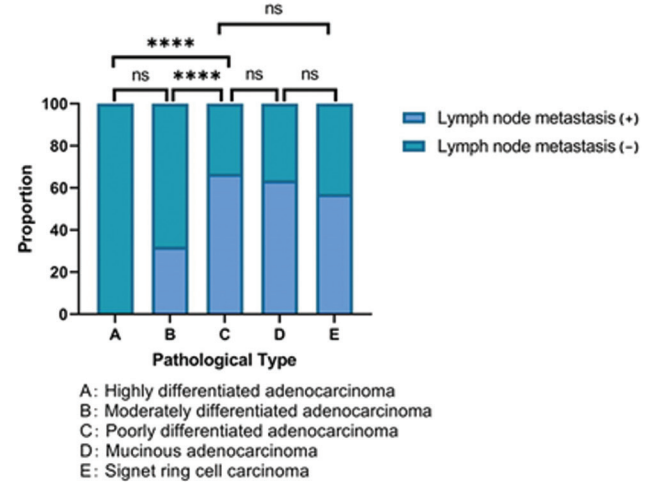


Table 2. Univariate and Multivariate Logistics Regression Analysis of Risk Factors for Lymph Node Metastasis in Gastric Cancer

Feature	n	Univariate Analysis		Multivariate Analysis	
		OR (95% CI)	P value	OR (95% CI)	P value
Gender					
Male	196	1.00	-	1.00	-
Female	64	0.829 (0.470-1.460)	.515	1.24 (0.530-2.386)	.761
Primary site					
Cardia	50	1.00	-	1.00	-
Fundus	6	1.386 (0.724-2.653)	.324	0.875 (0.372-2.057)	.760
Body	34	0.924 (0.181-4.724)	.924	0.531 (0.083-3.387)	.503
Angle	18	0.821 (0.390-1.730)	.605	0.422 (0.163-1.096)	.077
Pylorus	152	0.355 (0.121-1.046)	.060	0.362 (0.087-1.495)	.160
Histological differentiation					
Well-differentiated adenocarcinoma	9	1.00	-	1.00	-
Moderately differentiated adenocarcinoma	75	0.000 (0.000)	.999	0.000 (0.000)	.999
Poorly differentiated adenocarcinoma	132	0.430 (0.200-0.923)	.030	0.321 (0.116-0.887)	.028
Signet ring cell carcinoma	44	1.707 (0.855-3.408)	.130	0.849 (0.346-2.082)	.720
Depth of invasion					
Mucosa	38	1.00	-	1.00	-
Submucosa	47	0.016 (0.003-0.073)	.000	0.020 (0.004-0.096)	.000
Muscularis propria	40	0.099 (0.042-0.231)	.000	0.113 (0.044-0.289)	.000
Serosa	59	0.173 (0.075-0.399)	.000	0.187 (0.075-0.466)	.000
Beyond serosa	76	0.926 (0.413-2.075)	.852	1.160 (0.462-2.915)	.752

Among them, a total of 260 cases were included in the statistical analysis, and gastric cancer spreading to multiple sites, simultaneous multiple primary cancers, and squamous cell carcinoma were not included.

Univariate and multivariate logistic regression analysis of risk factors for lymph node metastasis in gastric cancer

We used logistic regression models to explore the factors predicting lymph node metastasis in gastric cancer (Table 2). Multivariate analysis showed that invasion depth and pathological type were associated with lymph node metastasis, while tumor location and gender were not.

Figure 13 is a forest plot of the multivariable logistic regression analysis of risk factors for lymph node metastasis in gastric cancer.

Univariate and multivariate logistic regression analysis of risk factors for lymph node metastasis in early gastric cancer

We found that invasion depth was significantly associated with lymph node metastasis in our analysis of risk factors for

Figure 13. The Forest Plot of the Multivariable Logistic Regression Analysis of Risk Factors for Lymph Node Metastasis in Gastric Cancer

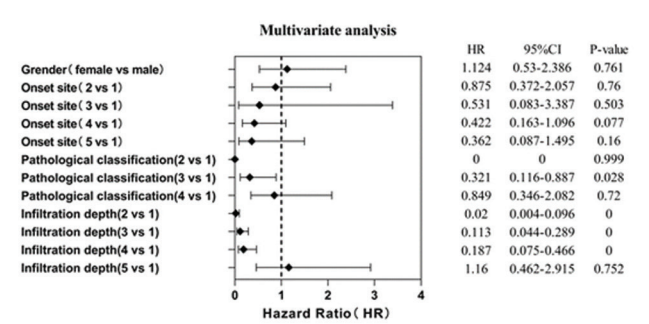
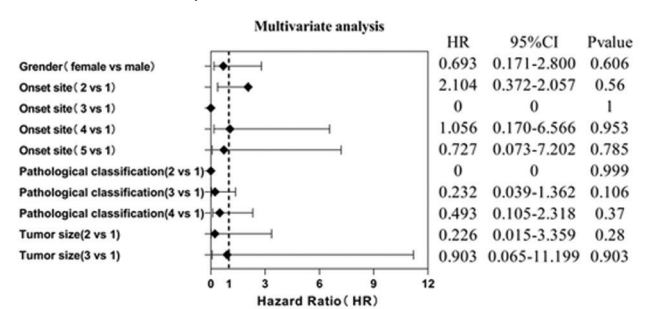


Table 3. Univariate and Multivariate Logistic Regression Analyses of Risk Factors for Lymph Node Metastasis in Early Gastric Cancer

Feature	n	Univariate Analysis		Multivariate Analysis	
		OR (95% CI)	P value	OR (95% CI)	P value
Gender					
Male	64	1.00	-	1.0	-
Female	21	0.524 (0.154-1.786)	.301	0.693 (0.171-2.800)	.606
Primary site					
Cardia	7	1.00	-		
Fundus	1	0.767 (0.083-7.092)	.815	2.104 (0.172-25.700)	.560
Body	12	0.000 (0.000)	1.000	0.000 (0.000)	1.000
Angle	9	0.920 (0.174-4.863)	.922	1.056 (0.170-6.566)	.953
Pylorus	56	0.575 (0.064-5.130)	.620	0.727 (0.073-7.202)	.785
Histological differentiation					
Well-differentiated adenocarcinoma	6	1.00	-	1.0	-
Moderately differentiated adenocarcinoma	34	0.000 (0.000)	.999	0.000 (0.000)	.999
Poorly differentiated adenocarcinoma	27	0.194 (0.042-0.901)	.036	0.232 (0.039-1.362)	.106
Signet ring cell carcinoma	18	0.455 (0.114-1.806)	.263	0.493 (0.105-2.318)	.370
Age group					
≤40	2	1.00	-		
41-50	6	1615473897.542 (0.000)	.999		
51-60	21	323094779.508 (0.000)	.999		
61-70	36	504835592.982 (0.000)	.999		
71-80	17	146861263.413 (0.000)	.999		
>80	3	497068891.551 (0.000)	.999		
Tumor size					
≤2	49	1.00	-	1.0	-
>2 & ≤4	31	0.356 (0.032-3.991)	.402	0.226 (0.015-3.359)	.280
>4	5	1.636 (0.160-16.726)	.687	0.903 (0.065-11.199)	.903

Figure 14. The Forest Plot of the Multivariable Logistic Regression Analysis of Risk Factors for Lymph Node Metastasis in Early Gastric Cancer



gastric cancer. Early gastric cancer refers to tumors in which cancer cells invade only the mucosal layer or submucosal layer. We used logistic regression models to explore the factors predicting lymph node metastasis in early gastric cancer (Table 3). Univariate analysis showed that pathological type might be associated with lymph node metastasis in early

gastric cancer, while gender, tumor location, age, and tumor size were not. However, in multivariate analysis, none of these variables were significantly associated with lymph node metastasis.

Figure 14 is a forest plot of the multivariable logistic regression analysis of risk factors for lymph node metastasis in early gastric cancer.

Mucosal Adenocarcinoma

In this study, there were a total of 38 cases of mucosal adenocarcinoma, among which 2 cases (5.3%) had lymph node metastasis. The pathological classification of both cases with lymph node metastasis was signet-ring cell carcinoma.

Detection Rate of Abdominal Enhanced CT for Lymph Node Metastasis in Gastric Cancer

In this study, among the 143 patients with lymph node metastasis, 36 cases were detected by abdominal enhanced CT, with a detection rate of approximately 25.17%.

Synchronous Cancer

There was a total of 6 cases of synchronous cancer in this study, all of which had lymph node metastasis. Five cases were male patients and one case was a female patient. The age of the patients ranged from 37 to 77 years old, with the youngest patient being a 37-year-old female. This patient had two signet-ring cell carcinomas, approximately 1.2 cm and 1.0 cm in diameter respectively, in the anterior and posterior walls of the gastric body. The lesion in the anterior wall infiltrated the serosal layer, while the lesion in the posterior wall infiltrated the submucosal layer.

DISCUSSION

In this retrospective study, we analyzed 272 patients who underwent radical gastrectomy and lymph node dissection at Huzhou Central Hospital. Our study showed that the incidence of gastric cancer in male patients was significantly higher than in female patients, possibly due to long-term alcohol and tobacco consumption in the local area. Studies have shown that drinking white wine and beer significantly increases the risk of gastric cancer.⁶ Meanwhile, a survey found that the drinking rate among Chinese males aged 18 and above was 64.5%, significantly higher than that of females.⁷ Smoking may also increase the incidence of gastric cancer.⁹ Our study found that the incidence of gastric cancer was higher in the gastric antrum, especially in the lesser curvature. The gastric antrum lacks parietal cells, making it more susceptible to gastric cancer. At the same time, atrophy and intestinal metaplasia associated with intestinal-type gastric cancer often occur in the lesser curvature.⁹ Intestinal-type gastric cancer is closely related to *H. pylori* infection, which has a high prevalence in most countries. The prevalence in Asia is usually more than 50%, while about one-third of adults in Nordic and North American populations are infected.¹⁰ In our sample of 272 cases, 2 cases of squamous cell carcinoma occurred in the cardia.

Our study showed that young patients (≤ 40 years old) had a higher proportion of females (71.4%), and a higher proportion of poorly differentiated adenocarcinoma and signet ring cell carcinoma, which is similar to other studies.¹¹⁻¹³ Similar to other studies,^{5,7,14} our study found that lymph node metastasis in gastric cancer was not related to gender, age, or tumor location.

Our research indicates that lymph node metastasis in gastric cancer is related to invasion depth, a higher risk of lymph node metastasis is associated with deeper invasion. The accepted definition of early gastric cancer is that cancer tissue is limited to the mucosal layer or submucosal layer of the stomach, regardless of the size or presence of lymph node metastasis.^{15,16} However, our study found that although gastric cancer infiltrating the submucosal layer has a lower lymph node metastasis rate than gastric cancer infiltrating the muscular layer, there was no statistically significant difference between the two. In other words, once cancer cells infiltrate the submucosal layer, the risk of lymph node metastasis is similar to that of cancer cells infiltrating the muscular layer. The Japanese gastric cancer treatment guidelines state that the absolute indication for endoscopic submucosal dissection (ESD) in early gastric cancer requires cancer cells infiltration to the T1a stage. This is similar to our research results, as ESD can eradicate lesions within the gastric cavity while fully preserving the patient's natural organ structure. However, endoscopic treatment cannot perform lymph node dissection. In addition to being related to the tumor cell typing of the patient, the invasion depth of gastric cancer is also related to the length of the patient's disease course. Many patients have clinical symptoms when they undergo endoscopic examinations. We should advocate for gastroscopy examinations in high-risk populations while also increasing the proficiency of endoscopists. Japan and South Korea's endoscopic screening of healthy populations has reduced the risk of gastric cancer by 20% compared to non-participating populations. Some studies¹⁷ have indicated that endoscopic ultrasonography can improve the accuracy of clinical staging of gastric cancer, so pre-treatment endoscopic ultrasonography can evaluate the invasion depth of gastric cancer cells.

Our research shows that lymph node metastasis in gastric cancer is related to the pathological classification of gastric cancer. For pathological classification, the lymph node metastasis rate of poorly differentiated adenocarcinoma and signet ring cell carcinoma, which have a higher degree of malignancy, is higher than that of well-differentiated adenocarcinoma and moderately differentiated adenocarcinoma, which have a lower degree of malignancy. Many studies have shown that the type of histology is related to lymph node metastasis.^{4,5}

We also conducted a regression analysis on 83 early gastric cancer patients out of 272 cases. In the multiple factor regression analysis, we found that there was no significant correlation between pathology and lymph node metastasis, which contradicts our previous conclusion for early gastric cancer. One possible reason for this is that the sample size of

early gastric cancer patients was small, making the statistical results less objective. However, some studies have also suggested that in individuals over 70 years of age, the risk of lymph node metastasis in early gastric cancer is unrelated to tumor pathology type. Our study also found that there was no significant relationship between the risk of lymph node metastasis and tumor size in early gastric cancer, which is similar to the results of Feng Sun's study,¹⁴ but Fenglin Cai and Yoon Jung Oh's studies have proposed the opposite view.^{4,5} Therefore, further research is needed to clarify this situation.

In 38 cases of mucosal carcinoma, two cases had lymph node metastasis, and the pathological type of both was signet ring cell carcinoma. A meta-analysis indicated that the frequency of distant metastasis in gastric signet ring cell carcinoma is higher than that in non-signet ring cell carcinoma.¹⁸

In this study, the detection rate of lymph node metastasis in gastric cancer by abdominal enhanced CT was 25.17%. Currently, some studies have suggested that CT-based imaging group models have higher advantages in detecting lymph node metastasis in early gastric cancer compared to traditional enhanced CT.¹⁹ Improving the detection rate of lymph node metastasis in gastric cancer is of great help for treatment.

The innovation of this study is that we studied patients with gastric cancer rather than just patients with early gastric cancer. In this study, we found that there was no statistical difference in the risk of lymph node metastasis between gastric cancer infiltrating into submucosa and gastric cancer infiltrating into muscularis. Hence, is it necessary to redefine early gastric cancer? At the same time, our study pointed out that the detection rate of preoperative enhanced CT for lymph node metastasis of gastric cancer is low. This provokes thought on whether preoperative enhanced CT examination is necessary and whether there are new methods to better evaluate preoperative patients. These problems are worthy of further consideration and study.

We acknowledge that this study has certain limitations. It is a single-center retrospective study, and as a result, the dataset and data sources are limited, which reduces its generalizability. As a retrospective study, missing data is inevitable. At the same time, our study only included surgical cases, while neglecting patients treated with endoscopic submucosal dissection (ESD) and also those with distant metastasis who cannot undergo surgery, which may result in selection bias. In this study, the pathological reports of gastric cancer came from multiple pathologists, making it difficult to ensure that the pathological results were completely standardized. In addition, this study requires a large sample size to conduct further research.

CONCLUSIONS

The risk factors for lymph node metastasis in gastric cancer are mainly related to tumor infiltration depth and pathological classification, and are not related to gender, age, or tumor location.

FUNDING

This study did not receive any funding in any form.

AUTHOR DISCLOSURE STATEMENT

The authors have no potential conflicts of interest to report relevant to this article.

ACKNOWLEDGEMENT

YX and LY designed the study and performed the experiments, YX collected the data, LY analyzed the data, YX and LY prepared the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Zhao X, Li K, Chen M, Liu L. Metabolic codependencies in the tumor microenvironment and gastric cancer: difficulties and opportunities. *Biomed Pharmacother.* 2023;162:114601. doi:10.1016/j.biopha.2023.114601
2. Norwood DA, Montalvan-Sanchez E, Dominguez RL, Morgan DR. Gastric Cancer: Emerging Trends in Prevention, Diagnosis, and Treatment. *Gastroenterol Clin North Am.* 2022;51(3):501-518. doi:10.1016/j.gtc.2022.05.001
3. Joshi SS, Badgwell BD. Current treatment and recent progress in gastric cancer. *CA Cancer J Clin.* 2021;71(3):264-279. doi:10.3322/caac.21657
4. Cai F, Dong Y, Wang P, et al. Risk assessment of lymph node metastasis in early gastric cancer: establishment and validation of a Seven-point scoring model. *Surgery.* 2022;171(5):1273-1280. doi:10.1016/j.surg.2021.10.049
5. Oh YJ, Kim DH, Han WH, et al. Risk factors for lymph node metastasis in early gastric cancer without lymphatic invasion after endoscopic submucosal dissection. *Eur J Surg Oncol.* 2021;47(12):3059-3063. doi:10.1016/j.ejso.2021.04.029
6. Fang X, Wei J, He X, et al. Landscape of dietary factors associated with risk of gastric cancer: A systematic review and dose-response meta-analysis of prospective cohort studies. *Eur J Cancer.* 2015;51(18):2820-2832. doi:10.1016/j.ejca.2015.09.010
7. Qian F, Ogundiran T, Hou N, et al. Alcohol consumption and breast cancer risk among women in three sub-Saharan African countries. *PLoS One.* 2014;9(9):e106908. doi:10.1371/journal.pone.0106908
8. López MJ, Carbajal J, Alfaro AL, et al. Characteristics of gastric cancer around the world. *Crit Rev Oncol Hematol.* 2023;181:103841. doi:10.1016/j.critrevonc.2022.103841
9. Lai S. A human mode of intestinal type gastric carcinoma. *Med Hypotheses.* 2019;123:27-29. doi:10.1016/j.mehy.2018.12.009
10. Smith S, Fowora M, Pellicano R. Infections with *Helicobacter pylori* and challenges encountered in Africa. *World J Gastroenterol.* 2019;25(25):3183-3195. doi:10.3748/wjg.v25.i25.3183
11. Li J, Kuang XH, Zhang Y, Hu DM, Liu K. Global burden of gastric cancer in adolescents and young adults: estimates from GLOBOCAN 2020. *Public Health.* 2022;210:58-64. doi:10.1016/j.puhe.2022.06.010
12. Mehdi M, Kong AL, Frebault J, Huang S, Huang CC, Cortina CS. Prognostic Outcomes of Signet Ring Cell Carcinoma of the Breast. *J Surg Res.* 2021;264:138-148. doi:10.1016/j.jss.2021.02.020
13. Cormedi MCV, Katayama MLH, Guindalini RSC, Faraj SF, Folgueira MAAK. Survival and prognosis of young adults with gastric cancer. *Clinics (São Paulo).* 2018;73(suppl 1):e651s. doi:10.6061/clinics/2018/e651s
14. Sun F, Zhang S, Wang X, et al. Mixed Histologic Type is a Risk Factor for Lymph Node Metastasis in Submucosal Invasive Early Gastric Cancer. *J Surg Res.* 2023;282:160-167. doi:10.1016/j.jss.2022.09.013
15. Japanese gastric cancer treatment guidelines 2018 (5th edition). *Gastric Cancer.* 2021;24(1):1-21. doi:10.1007/s10120-020-01042-y
16. Hamashima C; Systematic Review Group and Guideline Development Group for Gastric Cancer Screening Guidelines. Update version of the Japanese Guidelines for Gastric Cancer Screening. *Jpn J Clin Oncol.* 2018;48(7):673-683. doi:10.1093/jcco/hyy077
17. Lee KG, Shin CI, Kim SG, et al. Can endoscopic ultrasonography (EUS) improve the accuracy of clinical T staging by computed tomography (CT) for gastric cancer? *Eur J Surg Oncol.* 2021;47(8):1969-1975. doi:10.1016/j.ejso.2021.02.031
18. Li Y, Zhu Z, Ma F, Xue L, Tian Y. Gastric Signet Ring Cell Carcinoma: Current Management and Future Challenges. *Cancer Manag Res.* 2020;12:7973-7981. doi:10.2147/CMAR.S268032
19. Gao X, Ma T, Cui J, et al. A CT-based Radiomics Model for Prediction of Lymph Node Metastasis in Early Stage Gastric Cancer. *Acad Radiol.* 2021;28(6):e155-e164. doi:10.1016/j.acra.2020.03.045