Clinical Implications Prognostic Role of Lymphatic Vessel Invasion in

the Early Gastric Cancer: A Retrospective Study of 188

Patients Cases

Running title: Lymphatic vessel invasion in early gastric cancer

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Message to the author:

Dear Dr. Lxx,

- 1. I changed the title;
- 2. I re-arranged the order of the Discussion;
- 3. Please complete the tables as I did.
- 4. Please check the original articles and cite them appropriately, especially regarding lymphatic vessel invasion.

Best regards,

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Abstract

Purpose: To investigate the clinical implications determine the prognostic role of lymphatic vessel invasion in the early gastric cancers, especially those confined to gastric mucosa, according to the nodal status, and lay a foundation for the improvement of category of lymphoid metastasis.

Methods: Clinicopathological characteristics and prognostic outcomes of 188 patients early gastric cancer patients—who received a gastrectomy for early gastric cancer between 1980 and 2003 were retrospectively evaluated based on the subclassification of pN category. A multivariate analysis was performed by using the Cox regression model, where lymphatic vessel invasion and other potential prognostic factors (i.e. age, gender, location of tumor, the number of tumor, maximum tumor diameter, histological type, infiltrated depth, and pN category) were included.

Results: Of the 188 easespatients, 158 patients had T1N0M0 cancers and 30 had T1N1M0 cancers, and In patients with the survival rate of the cases with or without lymphatic vessel invasion were significantly different (χ^2 =4.025, P=0.045). However, for in the patients with T1N1M0 easescancers, the survival the cases with or without lymphatic vessel invasion did not have significantly different survival (χ^2 =0.253, P=0.615). The evaluation of multivariate analysis lymphatic vessel invasion with other prognostic factors (sex, age, location of tumor, the number of tumor, maximum tumor diameter, histological type, infiltrated depth, and pN category were determined by Cox regression, and it was identified that overall, age (P=0.033) and lymph node metastasis (P=0.019) were as independent prognostic factors for all the early gastric

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cancers (P=0.033; 0.019).; Hhowever, for the IA early gastric cancers, age (P=0.042), tumor location (P=0.032); and lymphatic vessel invasion (P=0.010) were the independent prognostic factors for T1N0M0 cancers, whereas XXX (). (P=0.042; 0.032; 0.010).

Conclusions: For the IA early gastric cancers, ILymphatic vessel invasion along with age, tumor location was an independent prognostic factor for T1N0M0 early gastric cancers, and thus would be a prominent factor that should be included infor the category of lymphoid metastasis in patients with early gastric cancer.

Introduction

In recent years, it has the tendency to advocate Lless invasive surgeriesy for early gastric cancer have been increasingly advocated over the past decade... The tendency hasre are two considerations for ldifferent ess invasive surgeriesaspects: one is a reduction in theed scope of lymphadenectomy, and the other is a reduction ined the resected sizeion of the stomach [1-4]. Therefore, surgeries such as So-EMR(eEndoscopic mucosal resection (EMR), partial gastrectomy, or laser surgery under gastroscopy and reduced gastrectomy, all-have emerged appeared[5-7]. Early gastric cancer is defined as a gastric carcinoma lesion of the stomach confined to the mucosa and/or submucosa, regardless of lymph node metastatic status [8]. Previous authors-studies have reported that lymph node metastasis was is one of the most important factors in determining the prognosis of patients with early gastric cancerand the incidence of lymph node metastasis was 5.7% to 20% [9, 10]. The incidence of lymph node metastasis in early gastric cancer ranges from 5.7% to 20%, with The the incidences-rate being 0-5% and 10-20% in cancers withof lymph node metastasis in intraomucosal invasion gastric cancer and in-submucosal invasion, gastire cancer were 0.5% and 10-20%, respectively [210]. However, based on a retrospective study of the 266 cases of early gastric cancer, Yokota et al believes lymphatic invasion to be more important than nodal metastasis [11].

At present, most of the studies on therapeutic strategies <u>have focused on related to</u> submucosal gastiric cancer^[12-14], however, reports on the association between both-clinicopathological and surgical prognostic factors, especially (lymphatic invasion).

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BACKGROUND: Early gastric cancer is defined as a gastric carcinoma confined to the mucosa or submucosa regardless of lymph node status, and it has an excellent prognosis with a 5-year survival rate of more than 90%. From 1985 to 1995, we encountered 266 cases of early gastric cancer in our hospital. METHODS: A retrospective analysis of the 266 cases of early gastric cancer was performed to evaluate the prognostic significance of clinicopathological features (age, gender, tumor size, tumor location, depth of invasion, lymph node metastasis, histological type, lymphatic invasion, vascular invasion, histological growth pattern, cancer-stromal relationship and type of operation). RESULTS: The overall survival rate of all the patients with early gastric cancer was 95.7%. In univariate analysis, the statistical significant prognostic factors were regional lymph node metastasis (P = 0.0004), lymphatic invasion (P = 0.0053) and cancer-stromal relationship (P = 0.0016). Absence of lymph node metastasis and lymphatic invasion, and a medullary-type histopathology were associated with improved survival. In multivariate analysis, the statistically significant prognostic factors were lymph node metastasis and cancer-stromal relationship. CONCLUSIONS: Presence of lymph node involvement and a scirrhous type of gastric cancer are associated with poor prognosis. Lymph node dissection with gastric resection is necessary for patients with early gastric cancer who have a high risk of lymph node metastasis. Postoperative chemotherapy is recommended for a

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scirrhous type of early gastric cancer.

and especially) associated with prognosis of intranucosal gastric cancer the T1N0M0

(I A)patients are still sparse. (venous invasion including lymphatic invasion and blood vessel invasion, lymphatic invasion is more important for the survival of the gastric cancer than blood vessel invasion.)

Therefore, we carriedy out this study to especially investigatedetermine both clinicopathological and surgical prognostic factors. (lymphatic invasion especially) of T1N0M0 patients in order to improve the classification and therapeutic strategies of for early gastric cancers, especially those confined to in chinese patients gastric mucosa.

Patients and methods

Patient's information

The inclusion criteria for this retrospective were as follows: 1), the gastric tumor invasion was limited in intramucosal or submucosal; 2) no less than D1 lymph node dissection (i.e. D1+ lymph nodes along the left gastric artery, D1+ lymph nodes along the common hepatic artery, D2, or D3) was performed; 3) the patient medical records were complete and available.

A total of 188 cases—patients with early gastric cancer were treated at the Department of Oncology, First Affiliated Hospital of China Medical University, between 1980 and 2003. In Of the 188 cases, 7-seven had been performed underwent a D1 lymph node dissection, 29 had a D1 + No.7, 8-eight lymph node dissection, 107 had a D2 lymph node dissection, and 45 had a more than D2 lymph node dissection.

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The criteria used for inclusion was as follows: 1) the tumor invasion limited in introducosal or submucosal; 2) no less than D1 lymph node dissections(D1+ lymph nodes along the left gastric artery, D1+ lymph nodes along the common hepatic artery, D2, D3) had been performed; 3) the patient medical records was complete.

Lymph nodes were dissected from enbloc speciments, and the classification of the dissected lymph nodes was verified by surgeons reviewing the excised specimens after surgery based on the Japanese Classification of Gastric Carcinoma (JCGC) [14]. The resected enbloc speciments and lymph nodes retrieved were stained with hematoxylin and eosin and examined by specialized pathologists—who used light microscopy. Clinical-findings, surgical findingsand, pathological findings and eachall follow-up information were collected and recorded in the database, and 5-year survival rate was calculated. In the present study, the pathological information was mainly based on simple reading of the "histopathological reports" for initial screening. Then, one of the authors (XXXX) and another pathologist (YYYY) re-examined all the slides to confirm the subclassification of pT1 gastric cancers (i.e. early gastric cancer) and the status of the lymphatic vessalvessel for all the cases.

The study protocol was approved by the Ethics Committee of China Medical University.

Classification of lymphadenectomy

The definitions for lymphadenectomy were based on the J<u>CGC</u> apanese

Classification of Gastric Carcinoma [8]: D1, : Dissection dissection of all nodes in the

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批注 [x11]: Who? Should you include the pathologists in the authorship, or in the acknowledgement? You better add the initials of the author and pathologist who re-examined the slides here.

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According to JCGC, Group 1 consists of the perigastric lymph nodes, Group 2 consists of the lymph nodes along the left gastric artery, the common hepatic artery, and the splenic artery and around the celiac axis; hHowever, when the tumor is located in the lower third stomach, the lymph nodes along the splenic artery are classified as being in Group 3. Group 3 also—consists of lymph nodes in the hepatoduodenal ligament, at the posterior aspect of the head of the pancreas, and at the root of the mesentery. [18]

The location of tumors <u>also</u> referred to the <u>classification of JCGC apanese</u> Classification of Gastrie Carcinoma^[8]. The histological type (i.e. differentiated and <u>undifferentiated types</u>) and pN category includinges pN0-3 according to <u>UICC5th</u> Edition, (i.e. PpN0th, 0-no involved-node involved; PN1pN1th, 1-6 node involved; PN2pN2: 7-15 node involved; and, PN3pN3, the classification (5th Edition) of the International Union Against Cancer (UICC) [15]. The histological types include differentiated and undifferentiated types. Histological growth patterns includinge expanding and infiltrative types was defined according to Ming [16]. In addition, the presence or absence of

lymphatic vessel invasion was observed. (本后切除标本连续切片,观察淋巴管内有无癌枠)

Statistical Methods methods

All the data were analyzed with SPSS 13.0 statistics software (Chicago, IL, USA). Chi-square and independent t-tests where appropriate were used to compare the

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Results

Clinicopathological characteristics of the early gastric cancers

The male-to-female ratio among the 188 patients enrolled was 3.372:1 and the mean age was 53.90 years (range, 26 to 80 years). From 188 cases, a total of 2752 lymph nodes were picked up and examined (mean 14.638). Of the study grouppatients, 158 (84.04%) patients had T1N0M0_(IA)_cancers, 27 (14.36%) had_T1N1M0 (IB) cancers, 2_two_(1.06%) had_T1N2M0_cancers, and 4_one_(0.53%) had_T1N3M0 cancers.

Table-1 includes shows the clinico-pathological informationcharacteristics in relation to lymphatic vessel invasion.

Survival outcomes

Of the 188 casesOverall, the 5-year survival rate of the patients with lymphatic invasion waswas—not significantly different 80% between patients with and those without lymphatic invasion 80% vs 88.24%, y²=0.493, P=0.482), and the cases without lymphatic invasion was 88.24%. The two groups have significantly different

survival ($\chi^2 = 0.493$, P = 0.482). However, In the 158 patients had with T1N0M0 (IA)

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cancers, the 5-year survival rate was significantly lower in of the cases with or without lymphatic vessel invasion (were significantly different (the 5-year survival rate: 71.43% vs 88.51%, χ^2 =4.025, P=0.045) (Figure 1a). However, for In patients with the T1N1M0 (IB) cases, the 5-year survival rate was similar between the cases with or those without lymphatic vessel invasion did not have significantly different survival (χ^2 vs χ^2 =0.253, χ^2 =0.615) (Figure 1b). The two patients with T1N2M0 cancers survived for χ^2 and χ^2 vears, and the only patient with T1N3M0 survived for χ^2 years. (Table 2)

In addition. After investigating there was no significant difference in the 5-year survival between the T1N0M0 (IA) cases with lymphatic vessel invasion and T1N1M0 (-IB-) cases without lymphatic vessel invasion, no significant difference was observed ($\frac{3}{2}$ vs $\frac{3}{2}$, $\frac{3}{2}$ =2.539, $\frac{3}{2}$ =0.111) (Figure 2).

Multivariate analysis of prognostic factors

The multivariate analysis by using the Cox regression model, where tThe evaluation presence of lymphatic vessel invasion along with other potential prognostic factors (such assex, age, gender, tumor location of tumor, the number of tumor, maximum tumor diameter, histological type, infiltrated depth, and pN category were included, determined by Cox regression, It demonstrated identified age (P = 0.033) and lymph node metastasis (P = 0.019) as independent prognostic factors for all the early gastric cancers (P = 0.033; 0.019) (Table 2.23; Hhowever, for the T1N0M0 (IA) early gastric cancers, age (P = 0.042), tumor location (P = 0.032), and lymphatic vessel

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invasion (P = 0.010) were identified to be independent prognostic factors (P = 0.042; 0.032; 0.010) (Table .43).

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Discussion

Gastric cancer remains a major cause of cancer death₂₇ and the 5 year Saurvival rate inof patients with gastric cancer is still poor although the 5-year survival rate despite has been improved survival due to early detection, rational lymphadenectomy and several modified therapeutic modalities [1,17]. Most of the studies reported is generally accepted that lymph node metastasis is considered one of the most important prognostic factors [18-20]₂₅ howeverRecently, some presumed studies have demonstrated that lymphatic vessal vessel invasion is also ann more important prognostic factor [21,22]. So Therefore, accurate evaluation of lymph node and lymphatic vessal vessel status, or optimization of pN category is fundamentally critical for decision making of the subsequent therapies after initial surgery for early gastric cancer. Thus, the rational categorization of lymphoid metastasis will help further improve therapeutic efficacy.

The former_TNM classification proposed by IUAC in 1997_defined the pT2 designation for primary tumors that invade the muscularis propria or subserosa_[15]. In 2002, the American Joint Committee on Cancer (AJCC) further divided pT2 gastric adenocarcinomas into type pT2a (invasion of the muscularis propria) and type pT2b (invasion of the subserosa) [23] due to the significantly different survival. RThe recent studies has have been confirmed that the current upgrated upgraded stage grouping is

better to represent the prognosis for pT2 gastric cancers; i.e. pT2a cancers are associated with improved survival comaperd with pT2b cancers, indicating that, subclassification of pT2 cancers and would be helps further improve therapeutic efficacy_[24,25]. Whether this is the case for pT1 gastric cancers However, there are rare studies on PT1 gastric cancer is unknown. In the present study, we investigated the potential prognostic factors including age, gender, tumor location, number, maximum diameter, histological type, infiltrated depth, and currently recommended pN category for survival of patients with early gsatric gastric cancers. Overall, age (P=0.033) and lymph node metastasis (P=0.019) were identified as independent prognostic factors. in different lymphatic vessal invasion status were significently different. However, in patients without lymph node metastasis To be interested, patients with (i.e. T1N0M0 eancerscases, current IA), age, tumor location, and lymphatic invasion were independent prognostic factors. Moreover, without the 5-year survival rate was significantly higher in cases without lymphatic vessel invasion than in those with lymphatic vessel invasion. (current stage IA) showed the best survival, It was noticed that the 5-year survival rate was similar between while patents without lymph node metastasis (i.e.-_T1N0M0 cases, current IA), with but with lymphatic vessel invasion (current stage IA) and those with lymph node metastasis (i.e. T1N1M0 cases, current stage IB), but without lymphatic vessel invasion-(current stage IB) had similar survival rate. Thus, the current stage grouping system for pN category does not adequately reflect early gastric cancer patient-the prognosis for patients with early gastric cancer.

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Based on the resluts results obtained in the present study, we proposed that the current

cancer stage grouping system should be modified, taking lymphatic vessel invasion into the account. For example, for the equivalence of T1N0M0 cases with lymphatic vessel invasion and T1N1M0 cases without lymphatic vessel invasion with respect to prognosis, and that T1N0M0 cases with lymphatic vessel invasion and T1N1M0 cases without lymphatic vessel invasion be allocated to the same stage. The current stage IA may be classified to the subgroups of T1N0M0 cases with lymphatic vessel invasion and without lymphatic vessel invasion. However, the modification of the current gastric cancer grouping system should be very cautious, and more studies should be performed to confirm the above phenomenon.

The 2004 Japanese Geastric Ceancer Tereatment Geuideline reported—[26].

recommended that Ffor lymph node-negative intramucosal gastric cancer fi.e.

TINOMO cases, currently IA), EMR should be performed for cases with well—
differentiated, depressed type without ulceration, cases—and D1+No.7

lymphadenectomy for all other the cases excluding the above mentioned. For lymph node-negative submucosal gastric cancer (i.e. T1NOMO cases, currently IA), D1+No.7

lymphadenectomy should be received performed for cases with well—differentiated, focus diameter <1.5 cm. cases—and D1+No.7—8a—9 lymphadenectomy for the all other cases excluding the above mentioned cases. Shimoyama 8—et al [27]reported suggested that the scope of lymphadenectomy can be reduced to a modified D1 for intractinically mucosal, node-negative, nonpalpable gastric cancer, or for clinically submucosal, node-negative gastric cancer ≤1.5 cm for intestinal type, or ≤ 1.0 cm for diffuse type. Otherwise, a modified D2 lymphadenectomy is sufficient. It has been

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How about: IA1=T1N0M0 without lymphatic vessel invasion; IA2=

T1N0M0 with lymphatic vessel invasion;

IB1= T1N1M0 without lymphatic vessel invasion; and IB2= T1N1M0 with lymphatic vessel invasion? This keeps the current pN

category, and adds new sub-grouping to show the prognosis.

You have to consider the all staging system for your proposal, and try to make your proposal acceptable by others..

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clearly demonstrated that the depth of invasion and lymph node status are important prognostic factors for early gastric cancer.

The the former previous guidelines and reports studies did not take lymphatic vessel invasion as a prognostich factor for chemotherapy [28-30]₂₅ Furthermore, the 2007 guideline of NCCN(2007) did not introduce chemotherapy treatment for the patients with T1N0M0 gastric cancer who receive an curative operation because XXXX [31]₂... Studies have indicated that Tthe T1N0M0 cases with lymphatic vessel invasion may gotare associated with a more higher risk for recurrence than those without lymphatic vessel invasion, and thus should be receive appropriate treated therapies after the initial surgeryespecially [21,22]. Theoretically, For lymphatic invasion, because the lymphatic are a route to lymph nodes, it would be reasonable to conclude postulate that lymphatic vessel invasion is one of the predictors of lymph node recurrence since the lymphatic vessels are an essential route for lymph node metastasis.

In recent years, minimal less invasive surgical procedures such as endoscopic techniques and laparoscopic resection have been developed to treat early gastric cancer. Hhowever, there remains a serious problem concern of ignoring the status of regional lymph nodes in such treatment. When we encounter lymphatic vessel invasion at the primary site by microscopic –examination– of early gastric cancer. So, we need to must consider the possibility of the regional lymph node metastasis and the subsequent lymph node recurrence.

In the present study, we investigated the potential prognostic factors including age,

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gender, tumor location, number, maximum diameter, histological type, infiltrated depth, and currently recommended pN category for early gastric cancers. Overall, age (P=0.033) and lymph node metastasis (P=0.019) were identified as independent prognostic factors. However, in patients without lymph node metastasis (i.e. T1N0M0 cases, current IA), age, tumor location, and lymphatic invasion were independent prognostic factors. Moreover, the 5-year survival rate was significantly higher in cases without lymphatic vessel invasion than in those with lymphatic vessel invasion. It was noticed that the 5-year survival rate was similar between patents without lymph node metastasis (i.e. T1N0M0 cases, current IA), but with lymphatic vessel invasion and those with lymph node metastasis (i.e. T1N1M0 cases, current stage IB), but without lymphatic vessel invasion. These findings indicate that lymphatic vessel invasion is indeed an important factors influencing the survival, and thus, the current stage grouping system for pN category appears not adequately reflect the prognosis for patients with early gastric cancer.

Based on the results obtained in the present study, we propose that the current cancer stage grouping system should be modified, taking lymphatic vessel invasion into the account. For example, for the equivalence of T1N0M0 cases with lymphatic vessel invasion and T1N1M0 cases without lymphatic vessel invasion with respect to prognosis, and that T1N0M0 cases with lymphatic vessel invasion and T1N1M0 cases without lymphatic vessel invasion be allocated to the same stage. The current stage IA may be classified to the subgroups of T1N0M0 cases with lymphatic vessel invasion and without lymphatic vessel invasion. However, the modification of the current

批注 [x29]: Or category of lymphoid metastasis? I think staging grouping system is based on TNM categories. Please clarify this.

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gastric cancer grouping system should be very cautious, and more studies should be performed to confirm the above phenomenon.

In our study, multivariate analysis of those prognostic factors demonstrated that age and lymph node metastasis were independent prognostic factors for all the early gastric cancers. These findings confirm the previous reports that the lymph node status (pN stage) are accepted as important prognostic factors for patients with early gastric cancers. However, for the IA early gastric cancers without lymph node metastasis, age, tumor location, and lymphatic invasion were independent prognostic factors. Based on the data, lymphatic invasion was an important factors influencing the survival, meanwhile, it also provided an directions for the clinical mangement for the IA early gastric cancers.

Conclusions

Lymphatic vessel invasion along with age, tumor location was an independent prognostic factor for T1N0M0 early gastric cancers,, and thus would be a prominent factor that should be included in the category of lymphoid metastasis in patients with early gastric cancer.

For the IA early gastric cancers, lymphatic vessel invasion was independent prognostic factor, and would be a prominent factor for the category of lymphoid metastasis.

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How about: IA1=T1N0M0 without lymphatic vessel invasion; IA2=T1N0M0 with lymphatic vessel invasion;

IB1=T1N1M0 without lymphatic vessel invasion; and IB2=

T1N1M0 with lymphatic vessel invasion? This keeps the current pN category, and adds new sub-grouping to show the prognosis.

You have to consider the all staging system for your proposal, and try to make your proposal acceptable by others...

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This work was supported in part by the Ggastric Ceancer Lłaboratory of Chinese Medical University, Shenyang, China.

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Figure legends

Figure 1e. Cumulative survival of patients with T1N0M0 (IA) gastric cancers (A)

(IA), and those with T1N1M0 cases (IB) (B) according to the presence of

批注 [x36]: I think the color can be changed in to black and white

to avoid color printing charge.

lymphatic vessel status.

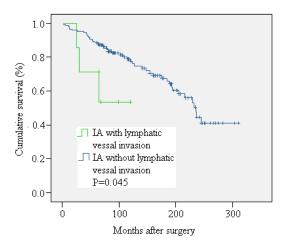


Figure 1Ab. Cumulative survival of patients with T1N1M0 cases (IB), according to the lymphatic vessel status.

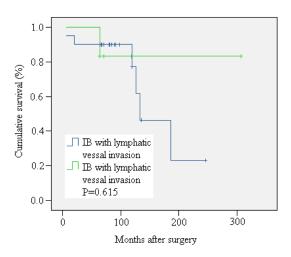


Figure 1B

Figure 2. Cumulative survival of the T1N0M0(IA)cases with lymphatic vessel invasion compared with T1N1M0(IB) cases without lymphatic vessel invasion

批注 [x37]: This is a repetition of figure 1 (a and b). Suggest replacement by a table (see my comment in the Results).

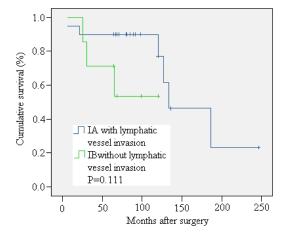


Table.1 Clinicopathological Characteristics of 188 early gastric cancers in relation to lymphatic

vessel invasion

Variable	Lymphatic vessel invasion		P value
	Present (n=15)	Absent (n=173)	
Mean age (years)	48.60	54.36	0.584
Gender ratio (n (%))			0.100
Male (n=145)	9 (6.21)	136 (93.79)	
Female (n=43)	6 (13.95)	37 (86.05)	
Mean (rang) number of tLN	14.27	18.93	0.827
Tumor focus number(n (%))			0.530
Single (n=181)	14(7.73)	167(92.27)	
Multiple (n=7)	1(14.29)	6(85.71)	
Tumor location (n (%))			0.319
Upper stomach (n=9)	0(0.00)	9(100.00)	
Middle stomach (n=32)	1(3.125)	31(30.16)	
Lower stomach (n=147)	14(9.52)	133(90.48)	
Maximum cancer diameter (cm)	3.18	2.78	0.452
Depth of invasion (n (%))			0.008
Mucosal (n=87)	2 (2.30)	85(97.70)	
Submucosal (n=101)	13(12.87)	88(87.13)	
Histological type (n (%))			0.295
Differentiated(n=87)	5(5.75)	82(94.25)	
Undifferentiated(n=101)	10(9.90)	91(90.10)	
Pathological lymph node status (n			0.000
(%))			
pN0 (n=158)	6 (3.80)	152 (96.20)	
pN1 (n=27)	7 (25.93)	20 (74.07)	
pN2 (n=2)	1(50.00)	1 (50.00)	
pN3 (n=1)	1 (100.00)	0 (0.00)	

Table 2. The 5-year survival rate in relation to TNM category and the presence of lymphatic vessel invasion

Table 23. Multivariate analysis of the prognostic characters for the all 188 patients with early

批注 [x38]: please complete the table.

gastric cancer (n=188)

Characteristics — Hazard ratio P value

Hazard ratio 95% confidence (95% confidence interval)

interval P value

Gender

Male vs. Female 1.069 (0.511-2.235) 0.860 带格式表格

Gender

Male

1.069 0.511-2.235 0.860 old) (years Age 1.929 1.056-3.522 0.033 Number of tumors 0.000 0.000-6E + 270 0.969 Tumor location 0.977-2.165 1.455 0.065 Maximum tumor size (cm) 0.874-1.257 1.048 0.613 Histologic grade

Differentiated vs. Undifferentiated

vs.

0.758

0.109

mucosal

Infiltrated depth

0.540-1.063

submucos al

Female

0.928 0.511-1.685

0.806

 $Lymphatic \ \underline{vessel}\ invasion$

Present vs. Absent

1.783 0.588-5.404

0.307

pN category

1.191 1.029-1.379

0.019

Characterist	ics		Hazard ratio	<u>P value</u>
Hazard rat	io 959	% confidence	(95% confidence interval)	
interval I	² value			
<u>Gender</u>				
Male vs. F	<u>emale</u>		1.209 (0.572-2.552)	0.619
Gender				
Male	VS.	Female		
1.209		0.572-2.552		
0.619				
Age	(years	old)		
1.934		1.025-3.649		
0.042				
Number	of	tumors		
0.000	0	.000-2E + 273		
0.972				
Tumor		location		
1.569		1.039-2.369		
0.032				
Maximum	tumor	size (cm)		
1.030		0.849-1.250		

Table 4.3 Multivariate analysis of the prognostic characters for the T1N0M0 patients with

批注 [x39]: please complete the table.

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0.762

Histologic grade

Differentiated vs. Undifferentiated

0.790 0.553-1.128

0.195

Infiltrated depth

mucosal vs. submucosal

1.099 0.592-2.039

0.764

Lymphatic invasion

Present vs. Absent

4.524 1.433-14.288

0.010