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Prognostic significance of lymphovascular invasion in pN0 stage gastric cancer: a propensity score matching analysis

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Abstract

Background To explore the potential impact of lymphovascular invasion (LVI) on overall survival (OS) of pN0 stage gastric cancer (GC) after curative resection.

Methods A total of 497 GC patients who underwent curative gastrectomy and postoperative pathology proved negative lymph node metastasis between January 2015 and December 2018 in our center were enrolled in this study. All patients were divided into two groups according to the status of LVI. Their clinical and pathological features were compared and potential prognostic factors were analyzed using the propensity score matching analysis (PSM).

Results Ninety-nine (19.9%) patients had LVI. The presence of LVI was associated with significantly worse survival outcomes in both the overall and PSM cohorts ($\chi2 = 19.635$, $p < 0.001$; $\chi2 = 9.367$, $p = 0.002$). After PSM, data of 99 pairs of patients were extracted. Multivariate analysis revealed that number of examined lymph nodes (LNs), and LVI were independent predictors of OS (all $p < 0.05$). Following stratified analysis, patients with LNs 11–25 and those without LVI tended to have better OS than those with LVI (LNs 11–15: $\chi2 = 5.019$, $p = 0.025$; LNs 16–25: $\chi2 = 11.876$, $p = 0.001$).

Conclusions pN0 stage GC patients with LVI have poor prognosis. More than 15 lymph nodes need to be dissected to reduce the influence of LVI on the prognosis of pN0 stage GC patients.

Keywords Gastric cancer, Node negative, Lymphovascular invasion, Prognosis

Background

The depth of tumor invasion and lymph node metastasis have been widely acknowledged as the two most crucial prognostic indicators for gastric cancer (GC) patients [1, 2]. Due to nonspecific clinical manifestations and signs, GC patients are often diagnosed at an advanced stage, resulting in a poor prognosis. Radical gastrectomy with adequate lymphadenectomy is considered the most effective approach for curing GC. Among GC patients who underwent radical surgery, approximately 38.1-68.6% were found to be lymph node negative based on postoperative pathological findings. These patients exhibited varying 5- and 10-year overall survival (OS) rates ranging from 72 to 92% and from 88 to 93%, respectively, which

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were significantly higher than those observed in patients with node-positive GC [3–5].However, even among the node-negative patients, certain subgroups had worse OS compared to others and remained at risk of recurrence and cancer-related mortality.

Recent studies have demonstrated that, in addition to the primary prognostic factor T stage, various clinicopathologic factors including tumor size [5, 6], lymphovascular invasion (LVI) [6, 7] and examined lymph nodes (LNs) [8, 9], have been independently validated as significant prognostic factors associated with survival in pN0 stage GC patients following curative resection. Among these indicators, LVI was considered an early event in the process of lymph node or hematogenous metastasis. However, current researches on the correlation between the presence of LVI and the prognosis of pN0 stage GC patients remained controversial [10, 11].

In retrospective studies, patient baseline characteristics between LVI status are not comparable. If LVI status was shown to have an effect on the OS, such an effect could then be due to other unbalanced factors. To overcome the lack of comparability of baseline characteristics in retrospective studies, the propensity matching analysis (PSM) method can be used to balance patient characteristics between LVI status groups. Thus, we retrospectively analyzed the outcomes of 497 pN0 stage GC patients using the method of PSM. We aimed to explore the potential impact of LVI on OS of pN0 stage GC patients.

Materials and methods

Patients and data

We reviewed and analyzed 1,508 GC patients between January 2015 and December 2018 at the Department of Gastrointestinal Surgery, Weifang People's Hospital. All patients underwent radical gastrectomy and lymph node dissection.

The eligibility criteria included: (1) pathologically confirmed adenocarcinoma; (2) patients received radical gastrectomy (R0) with D1 (early stage) or D2 (advanced stage) lymphadenectomy; this study also encompassed patients with LNs less than 15, aiming to investigate the correlation between LVI and LNs. (3) postoperative pathology confirmed no lymph node metastasis; (4) no history of neoadjuvant chemotherapy.

The exclusion criteria included: (1) patients with distant metastasis; (2) patients with lymph node metastasis; (3) patients lost to follow-up.

In accordance with the eligibility criteria described above, 497 patients were enrolled in this study. The percentage of pN0 stage GC patients was 32.9%. All patients were divided into two groups according to the status of LVI. LVI was defined as the infiltration of tumor cells into vessel walls and/or the presence of tumor emboli within an endothelial-lined space, without distinguishing between vascular and lymphatic vessels. The independent Ethics Committee of Weifang People's Hospital (Shandong, China) approved this study. Written informed consent was obtained from all the participants.

Surgical procedures and histopathological evaluations

Radical gastrectomy and systematic lymph node dissection were performed for all patients. The reconstruction method of digestive tract was determined by the surgeon according to the intraoperative situation. All surgical specimens were processed following standard pathological procedures and stained with hematoxylin and eosin. Subsequently, the primary tumor and regional lymph node staining slides were examined by at least two pathologists. The diagnosis of LVI was determined based on the TNM classification of malignant tumors eighth edition [12], as follows: L0, no lymphatic invasion; L1, lymphatic invasion is observed; V0, no venous invasion; V1, microscopic venous invasion is observed; V2, macroscopic venous invasion is observed. However, this classification method is subject to some degree of subjectivity and may exhibit inconsistency in evaluation among pathologists. Therefore, in the present study, L0 and V0 were defined as L(–) and V(–), respectively, and L1 and V1-2 were defined as L(+) and V(+), respectively. Furthermore, L(–) and V(–) were defined as LVI-negative [LVI(–)], and L(+) and/or V(+) was defined as LVI-positive [LVI(+)].

Clinicopathological data and survival

The patients' demographic data included gender, age, type of gastrectomy, tumor size, tumor location, Lauren's classification, depth of tumor invasion, number of examined lymph nodes, and adjuvant chemotherapy. We first compared the clinicopathological parameters between the two groups using PSM analysis. Survival analysis was then performed to identify prognostic risk factors affecting patients' outcomes. Tumor staging was conducted according to the 8th edition of UICC TNM classification system. Lymph node dissection was performed in accordance with Japanese gastric cancer treatment guidelines 2021 (6th edition) [2].

Follow-up

During the initial two-year postoperative period, patients underwent follow-up assessments every three months. Subsequently, between years two and five following gastrectomy, follow-up evaluations were conducted every six months. After five years, annual patient follow-ups were performed. Detailed records of each assessment were documented.

Propensity score matching

To overcome possible selection bias between the LVI (+) and LVI (-) groups, we performed one-to-one matching using PSM. The propensity score, defined as the conditional probability of patients being treated given the covariates, can be used to balance the covariates in two groups and therefore reduce such bias. It has also been reported that potential confounding variables that are unrelated to the exposure but related to the outcome should be included in the propensity score model, and that this will decrease the variance of an estimated exposure effect without increasing the bias. The propensity scores were estimated by using a nonparsimonious multiple logistic regression model. Accordingly, in our study, which aimed to obtain more reliable results, the following covariates were selected for the calculation of the propensity score: gender, age at surgery, tumor size, type of gastrectomy, tumor location, Lauren's classification, adjuvant chemotherapy, and depth of invasion. Nearest neighbor matching was performed in a 1:1 ratio without replacement and a caliper width with a 0.01 standard deviation was specified.

Statistical analysis

Categorical variables were compared using the Chi-square test, and *t*-tests were used for comparing continuous variables. OS were evaluated using the Kaplan–Meier method, and statistical differences between groups were evaluated using the log-rank test. Univariate and multivariate analyses were performed using the Cox proportional hazards regression model to identify the risk factors of mortality, which were expressed as hazard ratio (HR) with 95% confidence interval (CI). Proportional hazards assumption were tested and met in the Cox regression model. For all analyses, $p<0.05$ was considered statistically significant. All statistical analyses were performed using SPSS software version 24.0 (SPSS Inc, Chicago, IL USA).

Results

Patient characteristics

Among all the 497 pN0 stage GC patients, 99 patients (19.9%) exhibited LVI. The clinical characteristics of GC patients in the LVI(+) and LVI(-) groups are listed in Table 1. The tumor size was found to be significantly larger in patients with LVI compared to those without LVI (5.872±3.783 vs. 4.516±2.586, $p<0.001$). Furthermore, the LVI (+) group demonstrated a higher incidence of total gastrectomy than the LVI (-) group (29.3% vs. 13.3%, $p<0.001$). Additionally, patients with LVI were observed to have deeper tumor invasion when compared to their counterparts without LVI ($p<0.001$) (Table 1).

PSM analysis

After performing a 1:1 matching based on the propensity score, we successfully matched 99 patients without LVI to 99 patients with LVI. The basic covariates between the two groups in the matched data are listed in Table 1. After matching, all of the baseline characteristics became comparable between the two groups, except for T stage.

Survival analysis

Figure 1 presents the 5-years OS of all patients in the LVI(-) group was significantly superior to that of those in the LVI(+) group (70.7% vs. 49.0%, $p<0.001$) before PSM. Figure 2 illustrates the survival difference in patients with LVI post-PSM, showing a significant decrease in 5-year OS compared to LVI-negative patients (52.6% vs. 70.7%, $p=0.002$). Figure 3 presents the OS curves for all GC patients with or without LVI stratified by T stage, the 5-year OS of T1-T4 stage patients with LVI were significantly lower than those without LVI (all $p<0.05$). Figure 4 illustrates the OS curves for all GC patients with or without LVI stratified by LNs, the 5-year OS of patients with LVI was significantly lower than those without LVI in LNs 11–15 and 16–25 subgroups ($p<0.05$), while in LNs 1–3, 4–10, and 26- subgroups, there were no statistical differences between patients with and without LVI. The results of survival analysis are shown in Tables 2 and 3. Univariate analysis demonstrated that tumor size, tumor location, LNs, depth of invasion, and LVI were associated with prognosis among all GC patients in the entire study population. After matching, LNs, depth of invasion, and LVI remained significantly associated with prognosis in PSM cohort (Table 2). Multivariate analysis revealed that LNs, depth of invasion and LVI independently served as prognostic factors for GC patients in the entire study population. LNs and LVI emerged as independent prognostic factors for GC patients in propensity-score-matched pairs (Table 3).

Discussion

LVI is generally defined as the presence of tumor cells in the lumen covered by endothelial cells under an optical microscope, which can reflect tumor biological behavior. Initially infiltrating the microvessel and lymphatic vessel network to form micrometastases, tumor cells eventually progress to metastatic lesions. Consequently, LVI is considered a crucial initial step in tumor dissemination. In terms of prognostic significance, several malignancies such as colorectal cancer, breast cancer, and non-small cell lung cancer have demonstrated that the presence of LVI correlates with higher recurrence rates and poorer prognosis [13–16]. In GC, the importance of LVI primarily manifests in early GC undergoing endoscopic treatment. The identification of LVI in endoscopically resected specimens deems them non-curative due

Table 1 Comparison of clinicopathologic characteristics between patients with and without lymphovascular invasion

Variables	Whole study series			Propensity-score-matched pairs	
	LVI (+)	LVI (-)	*P*	LVI (-)	*P*
Gender			0.612		0.096
Male	75 (75.8)	290 (72.3)		85 (85.9)	
Female	24 (24.2)	108 (27.7)		14 (14.1)	
Age at surgery (years)	61.32 ± 11.382	59.87 ± 11.099	0.247	59.21 ± 11.535	0.201
Tumor size (cm)	5.872 ± 3.783	4.516 ± 2.586	**<0.001**	5.840 ± 2.680	0.446
Type of gastrectomy			**<0.001**		0.628
Distal	44 (43.4)	236 (59.3)		39 (39.4)	
Proximal	26 (26.3)	109 (27.4)		27 (27.3)	
Total	29 (29.3)	53 (13.3)		33 (33.3)	
Tumor location			0.514		0.280
Low	46 (46.5)	210 (52.8)		36 (36.4)	
Middle	8 (8.1)	39 (9.8)		14 (14.1)	
Upper	33 (33.3)	13 (4.4)		35 (35.4)	
Diffuse	12 (12.1)	36 (12.1)		14 (14.1)	
Lauren's classification			0.820		0.664
Intestinal	40 (40.4)	167 (42.0)		45 (45.5)	
Diffuse	59 (59.6)	231 (58.0)		54 (54.5)	
Depth of invasion			**0.014**		**<0.001**
T1	3 (3.0)	31 (7.8)		13 (13.1)	
T2	10 (10.1)	84 (21.1)		26 (26.3)	
T3	15 (15.2)	56 (18.8)		23 (23.2)	
T4	71 (71.7)	227 (57.0)		37 (37.4)	
LNs			0.166		0.618
1–3	17 (17.2)	43 (10.8)		16 (16.2)	
4–10	35 (35.4)	140 (35.2)		32 (32.3)	
11–15	12 (12.1)	84 (21.1)		20 (20.2)	
16–25	20 (20.2)	82 (20.6)		17 (17.2)	
≥ 26	15 (15.1)	49 (12.3)		14 (14.1)	
Adjuvant chemotherapy			0.817		0.147
No	13 (13.1)	108 (27.1)		37 (37.4)	
Yes	86 (86.9)	290 (72.9)		62 (62.6)	

LVI = lymphovascular invasion; LNs = Number of examined lymph nodes

to their high incidence of lymph node metastasis, thus gastrectomy with systematic lymphadenectomy should be subsequently performed according to the latest edition of Japanese GC treatment guidelines [2]. Concerning advanced GC cases, some studies have indicated a significant association between LVI and poor prognosis; however, others have shown no impact on prognostic outcomes for node-positive patients or those with early-stage disease [17, 18]. Nevertheless, uncertainty remains regarding the relationship between the presence of LVI and prognosis among node-negative GC patients.

In this study, the incidence of LVI in pN0 stage GC was 19.9%, consistents with previous reports [3, 9, 19, 20]. Furthermore, there was a positive correlation between LVI incidence and tumor diameter as well as invasion depth. The submucosa of the gastric wall is highly vascularized, containing abundant capillaries and lymphatics. Consequently, infiltration of tumor cells into the gastric submucosa increases the likelihood of their dissemination through the lymphovascular system. Additionally, our findings demonstrated a higher incidence of LVI in patients who underwent total gastrectomy compared to those who underwent partial gastrectomy due to larger tumor size and deeper invasion commonly observed in total gastrectomy cases, which aligns with the process of tumor development.

The prognosis of GC patients with negative lymph node metastasis is comparatively favorable compared to those with positive lymph node metastasis. However, approximately 17.0-24.2% of these patients still experience recurrence and metastasis within 5 years, resulting in a 5-years OS rate ranging from 53 to 72.6% [7, 20–22]. In order to further guide postoperative therapeutic strategies, predictive factors for tumor prognosis of pN0 stage GC patients have been investigated. The influence of LVI on the prognosis of patients with pN0 stage GC remains controversial. Chou et al. [22] indicated that LVI was not associated with tumor recurrence and outcome

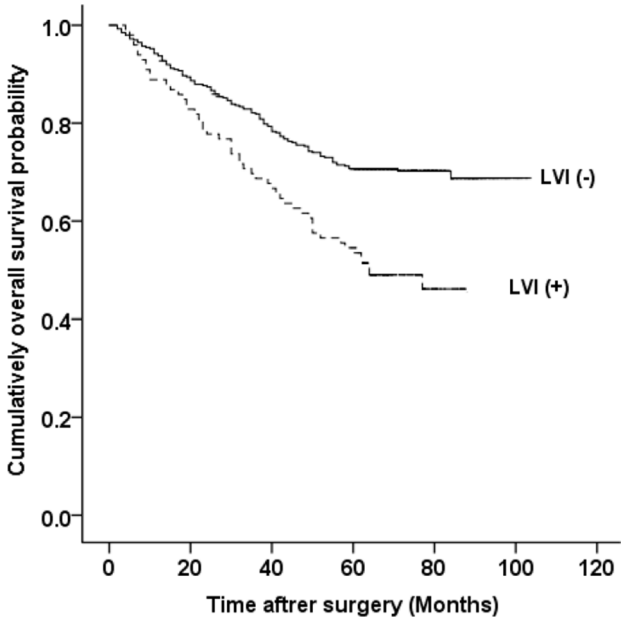

Fig. 1 Overall survival curves for all patients with or without lymphovascular invasion. ($\chi 2 = 19.635$ $p < 0.001$)

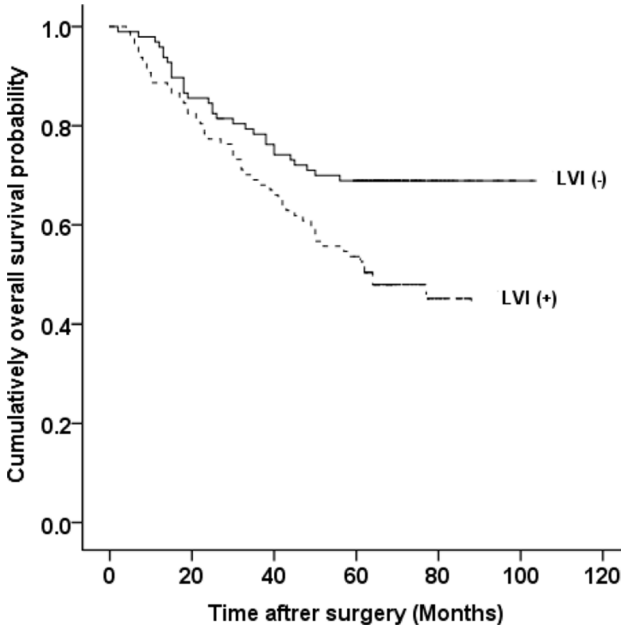

Fig. 2 Overall survival curves for all patients with or without lymphovascular invasion in the propensity score-matched cohort. ($\chi 2 = 9.367$ $p = 0.002$)

in 448 node-negative advanced GC patients. However, Jin et al. [7], by conducting an analysis of data from 314 pN0 stage GC patients from seven institutions affiliated with the US Gastric Cancer Collaborative, discovered that the presence of LVI, T-stage 3 or higher and signet ring histology were unfavorable prognostic indicators for pN0 stage GC. Similarly, Baiocchi et al. [21] performed an in-depth pathological analysis of 478 cases from four centers affiliated with the Italian Research Group for Gastric Cancer and revealed that lymphatic embolization and perineural infiltration were significant parameters associated with recurrence in pN0 GC. The eastern and western studies mentioned above yielded contrasting outcomes. To exclude confounding factors, we employed PSM analysis as a statistical method to identify risk factors affecting the prognosis of pN0 GC. We observed that prior to PSM, LVI, LNs, and T stage were significantly associated with the prognosis of pN0 GC patients in multivariate analysis; however, after PSM adjustment only LVI and LNs demonstrated a significant association with the prognosis.

The depth of tumor invasion is a crucial prognostic indicator for GC patients. Multiple studies have demonstrated that the depth of tumor invasion is an independent risk factor for both recurrence and survival in pN0 GC [9, 19, 20, 22]. Other studies have shown that LVI solely contributes to tumor recurrence as an independent risk factor [21, 23]. In view of the importance of T stage in evaluating prognosis, Lu et al. [19] revealed that the OS of N0 patients with LVI was similar to that of N1 patients. Therefore, N0 patients with LVI were upgraded to stage N1, while N0 patients without LVI remained in stage N0. Compared to the standalone AJCC staging system (8th edition), incorporating LVI into the system exhibited better linear trend $\chi 2$ statistics, likelihood ratio $\chi 2$ statistics, and AIC value. Surprisingly in our study, T stage emerged as a significant independent prognostic factor for the entire cohort but not in the PSM cohort due to limited sample size after PSM analysis and predominant influence of LNs and LVI on prognostic factors' weightage. Nevertheless, our study still found statistically significant effects of LVI on OS within each T stage subgroup.

The question of adequate lymph node dissection in patients deemed lymph node–negative has been extensively discussed. Large population studies on GC from various institutions and countries have consistently shown that adequate number of lymph node dissection and detection conveys a survival benefit, hence the latest TNM staging system recommend that at least 15 lymph nodes should be examined for the accurate N staging. Li et al. [24] suggested that node-negative GC patients should be classified as N1 stage when the number of LNs was inadequate. However, Jin et al. [7] did not find the rates of D2 dissection or having more than 15 nodes examined to differ significantly by recurrence status. Although understaging and stage migration are important concerns, we decided to analyze the effect of LVI on prognosis in this group regardless of the total number of examined nodes. In our study population, all patients with advanced disease received at least a D2 lymphadenectomy and 33.4% had more than 15 LNs.

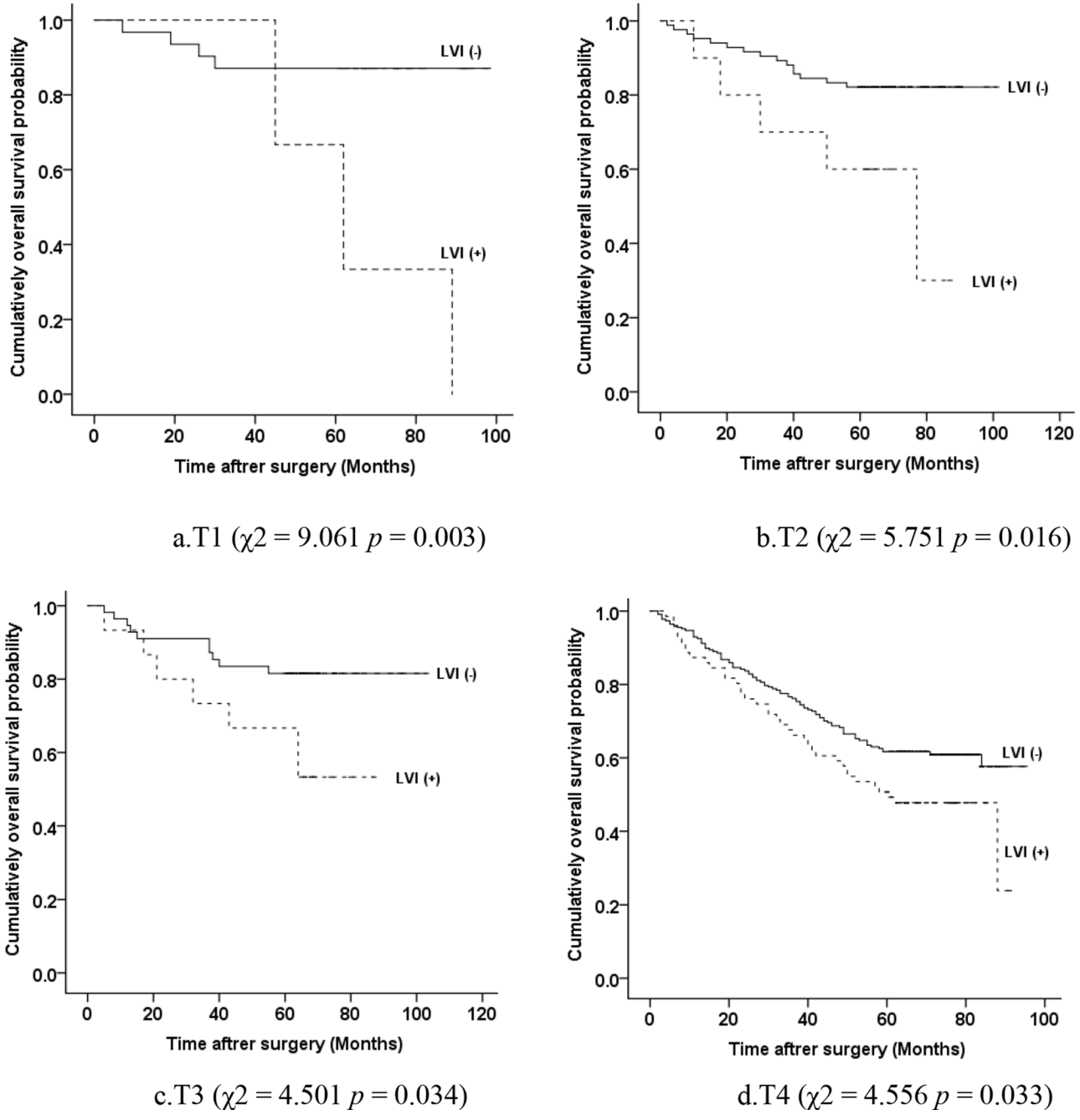

Fig. 3 Overall survival curves for all patients with or without lymphovascular invasion in terms of T stage. **a**: the 5-year OS of T1 stage patients with LVI were significantly lower than those without LVI ($\chi2 = 9.061$ $p = 0.003$); **b**: the 5-year OS of T2 stage patients with LVI were significantly lower than those without LVI ($\chi2 = 5.751$ $p = 0.016$); **c**: the 5-year OS of T3 stage patients with LVI were significantly lower than those without LVI ($\chi2 = 4.501$ $p = 0.034$); **d**: the 5-year OS of T3 stage patients with LVI were significantly lower than those without LVI ($\chi2 = 4.556$ $p = 0.033$)

Stratified analysis revealed that patients with LVI exhibited significantly poorer survival rates within the range of 11–25 LNs. N-stage migration may occur in patients with fewer than 10 LNs potentially indicating the presence of lymph node metastasis, thus diminishing the significance of LVI on prognosis. Patients presenting with more than 15 LNs constituted only 12.9% of the overall population. Multivariate analysis identified LNs as an independent prognostic risk factor both in the entire cohort and PSM cohort. In this study, the proportion of patients receiving adjuvant chemotherapy was relatively low due to economic constraints, personal willingness, comorbidities and compromised physical condition. Although a statistically significant association between adjuvant chemotherapy and improved survival was not observed, we still posit that pN0 GC patients with LVI and inadequate

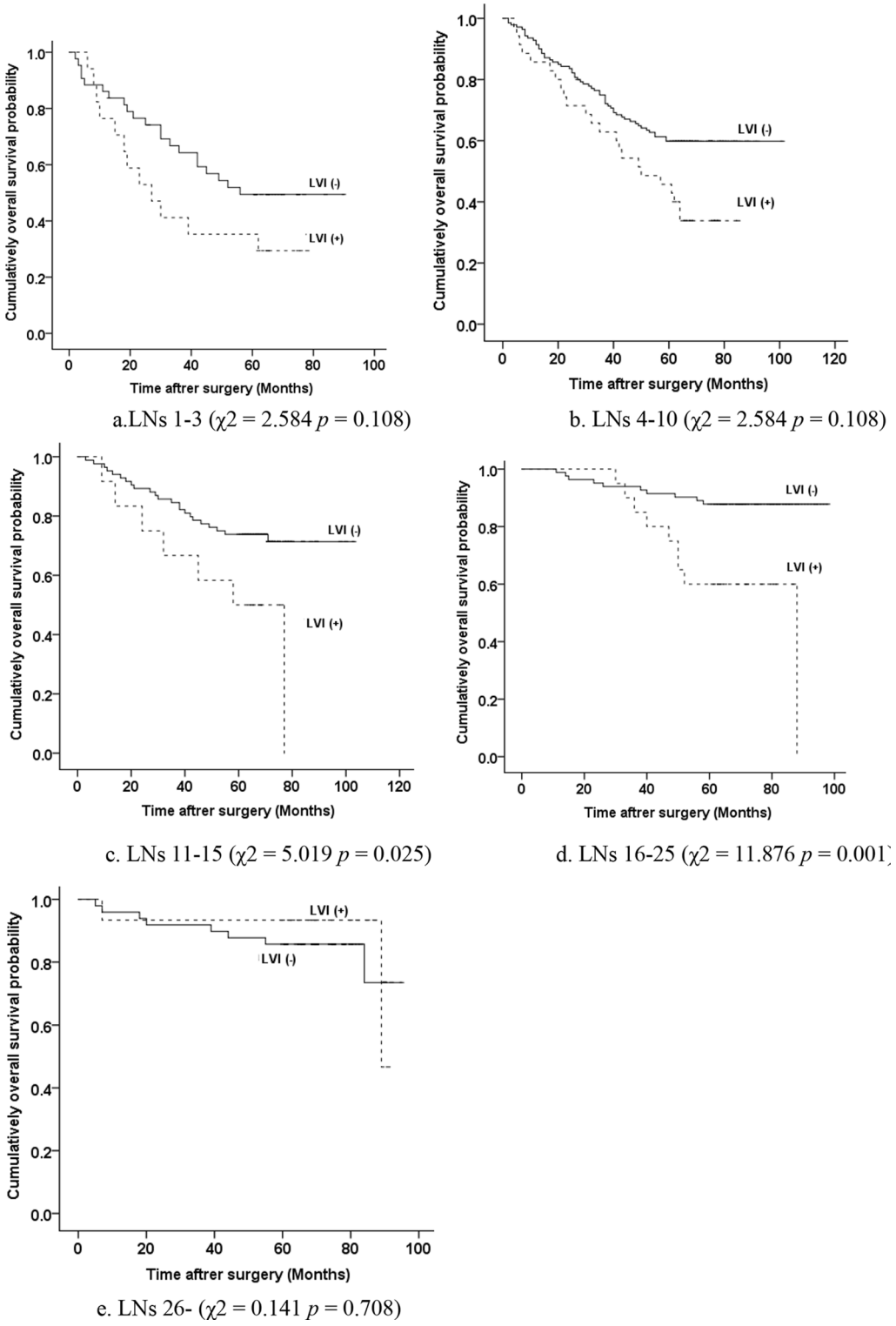

Fig. 4 Overall survival curves for all patients with or without lymphovascular invasion in terms of examined lymph nodes (LNs). **a**: there were no statistical differences between patients with and without LVI in LNs 1–3 subgroup ($\chi2 = 2.584$ $p = 0.108$); **b**: there were no statistical differences between patients with and without LVI in LNs 4–10 subgroup ($\chi2 = 2.584$ $p = 0.108$); **c**: the 5-year OS of patients with LVI was significantly lower than those without LVI in LNs 11–15 subgroup ($\chi2 = 5.019$ $p = 0.025$), **d**: the 5-year OS of patients with LVI was significantly lower than those without LVI in LNs 16–25 subgroup ($\chi2 = 11.876$ $p = 0.001$); **e**: there were no statistical differences between patients with and without LVI in LNs 26- subgroup ($\chi2 = 0.141$ $p = 0.708$)

Table 2 Univariate survival analysis of all gastric cancer patients in the whole study series and propensity score-matched pairs

Variables	Whole study series			Propensity-score-matched pairs.		
	5YSR	χ2	*p*	5YSR	χ2	*p*
Gender		0.827	0.363		0.010	0.921
Male	66.7			62.5		
Female	68.9			58.3		
Age at surgery(year)		1.698	0.193		0.002	0.961
<60	69.7			58.8		
≥60	64.8			57.8		
Tumor size (cm)		7.775	**0.005**		0.003	0.954
<5	72.5			60.1		
≥5	61.4			20.0		
Type of gastrectomy		4.337	0.114		0.066	0.967
Distal	79.1			61.1		
Proximal	64.3			54.3		
Total	62.2			58.9		
Tumor location		8.430	**0.038**		4.369	0.224
Low	69.4			53.6		
Middle	50.9			54.5		
Upper	69.0			69.3		
Diffuse	62.0			61.5		
Lauren's classification		0.072	0. 788		0.916	0.339
Intestinal	66.6			65.5		
Diffuse	67.4			56.9		
Adjuvant chemotherapy		2.700	0.100		1.827	0.176
No	33.6			55.9		
Yes	42.8			65.9		
LNs		50.318	**<0.001**		18.412	**0.001**
1–3	45.4			46.9		
4–10	57.0			51.1		
11–15	70.8			68.8		
16–25	82.4			66.7		
≥26	87.5 L			85.7		
LVI		19.635	**<0.001**		9.367	**0.002**
Absent	70.7			68.9		
Present	49.0			52.6		
Depth of invasion		21.951	**<0.001**		8.328	**0.040**
T1	85.3			81.3		
T2	79.8			69.4		
T3	74.8			65.7		
T4	59.1			50.4		

LVI = lymphovascular invasion; LNs = Number of examined lymph nodes

lymph node retrieval should derive a survival benefit from adjuvant chemotherapy. Patients receiving preoperative chemotherapy were not included in this study, while preoperative chemotherapy has become a novel issue in patients with locally advanced GC in recent years. To date, only a few studies have evaluated D2plus lymphadenectomy in patients with locally advanced or oligometastatic GC after preoperative therapy. A recent study revealed that high survival rates can be achieved in locally advanced or oligometastatic GC treated with neoadjuvant chemotherapy/conversion therapy and D2plus lymphadenectomy [25].

Lee CC et al. [26] found LVI and depth of cancer invasion were two independent survival predictors, but LVI and serosal invasion were also correlated. Jin et al. [7] reported that LVI was associated with decreased OS and was not associated with shorter time to recurrence. However, their study included a large number of patients receiving neoadjuvant chemotherapy and radiation. This may have an impact on the correlation between LVI and prognosis. While, Lee JH et al. [6] did not evaluate LVI as a prognostic factor. All of the above studies were retrospective single-center or multicenter studies, patient baseline characteristics between LVI status were not

Table 3 Multivariate survival analysis of all gastric cancer patients in the whole study series and propensity score-matched pairs

Variables	Whole study series		Propensity-score-matched pairs.	
	HR (95%CI)	*p*	HR (95%CI)	*p*
LNs		**<0.001**		**0.001**
1–3	1		1	
4–10	5.624 (2.762–11.452)	**<0.001**	5.702 (2.078–15.641)	**0.001**
11–15	3.939 (2.035–7.627)	**<0.001**	4.618 (1.788–11.930)	**0.002**
16–25	2.629 (1.280–5.401)	**0.009**	2.645 (0.909–7.697)	0.074
≥ 26	1.345 (0.625–2.896)	0.449	2.156 (0.766–6.066)	0.146
LVI		**<0.001**		**0.001**
Absent	1		1	
Present	1.870 (1.344–2.602)		1.452 (1.038–2.016)	
Depth of invasion		**0.001**		
T1	1			
T2	0.419 (0.195–0.903)	**0.026**		
T3	0.495 (0.307-0.800)	**0.004**		
T4	0.529 (0.318–0.879)	**0.014**		

LVI = lymphovascular invasion; LNs = Number of examined lymph nodes

comparable. PSM method can overcome the lack of comparability of baseline characteristics in retrospective studies. Therefore, the statistical method of PSM was employed in this study to ascertain the adverse impact of LVI on the prognosis of pN0 stage GC.

This study has several limitations. First, this was a retrospective and single-center study. The retrospective study design may result in a bias or could have an influence on the results of this study, although PSM analysis and multivariate analysis were performed to reduce the selection bias and possible confounding factors. The conclusion drawn from a single-center cannot fully represent the characteristics of other study centers and populations, limiting its generalizability. Second, the location, extent, and number of LVI were not accurately documented, thus precluding an exploration into the prognostic impact of quantified LVI. Third, The impact of adjuvant chemotherapy on the prognosis of pN0 GC patients could not be statistically determined in this study due to the limited sample size and absence of clinical data on adjuvant chemotherapy. Consequently, it remains uncertain which patients would derive benefits from adjuvant chemotherapy. Finally, The impact of lymph node micrometastasis on pN0 GC was not considered in this study. The proportion of patients with more than 15 LNs accounted for only 33.4% of all cases. For patients with fewer than 15 LNs, the presence of micrometastasis may potentially influence the accuracy of the study findings. Thus, there is a need for a multicenter clinical trial with a larger sample size to confirm our findings.

Conclusions

In conclusion, our findings suggest that pN0 GC patients with LVI exhibit a poor prognosis. More than 15 lymph nodes is recommended to mitigate the impact of LVI on the prognosis of pN0 GC patients. To further improve the survival of node-negative patients, these risk factors should be considered when selecting candidates for adjuvant chemotherapy and postoperative surveillance. Further studies should be conducted to investigate the benefit of adjuvant therapies for LVI-positive pN0 patients.

Abbreviations

LVI Lymphovascular invasion
OS Overall survival
GC Gastric cancer
PSM Propensity score matching analysis
LNs Number of examined lymph nodes

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Author contributions

Fu WH was responsible for the overall project progress, paper revision and submission; Jiao XG and Wang Y contributed to manuscript writing and editing and data collection; Fu H and Liu YN contributed to the data analysis; Qu JJ contributed to the conceptualization and supervision. All the authors read and approved the final manuscript.

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Data availability

The data that support the findings of this study are not openly available due to patient privacy concerns and are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The independent Ethics Committee of Weifang People's Hospital (Shandong, China) approved this study. Written informed consent was obtained from all the participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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