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Research Article

A retrospective analysis of Gastric Cancer Lymph Nodes Based on Groups, Regions, and Stages

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ARTICLE INFO	A B S T R A C T				
<i>Keywords:</i> Gastric cancer Gastrectomy Lymph node metastasis Prognosis Diagnose	 Objective: The consistency between clinical and pathological staging of lymph nodes (LNs) in gastric cancer (GC) remains suboptimal, and there is currently no standardized imaging criterion for diagnosing lymph node metastasis (LNM). This study aimed to elucidate the differences in LNs among various groups, regions, and stages, utilizing imaging and histopathology as the foundational basis. <i>Methods</i>: We retrospectively analyzed the clinical data of 100 GC patients who underwent surgical treatment at Zhongnan Hospital of Wuhan University between January 2022 and May 2023. Patient characteristics, along with pathological and radiological data of LNs, were collected and compared across different groups, regions, and stages. <i>Results</i>: Pathologically, 3566 LNs were collected, with a median of 35 (range: 17–72). Radiologically, 2233 LNs were collected, with a median of 22 (range: 3–47). Significant differences were observed in the long-axis diameter (LAD), short-axis diameter (SAD), ratios of long to short axis (RLSA), and product of long and short axis (PLSA) between negative and positive LNs. However, only within group 3 did the RLSA show statistical significance upon grouping analysis. The areas under the curve (AUC) for LAD, SAD, PLSA, and their combination index (CI) in diagnosing LNM were 0.817, 0.817, 0.828, and 0.827, respectively. Diverse groups, regions, and stages exerted a more pronounced influence on LN groups 1–6, while having a comparatively lesser impact on LN groups 7–16. <i>Conclusion</i>: LAD, SAD, and PLSA exhibited significant diagnostic value for LNM and could serve as diagnostic criteria; however, RLSA demonstrated limited diagnostic utility. The formulation of diagnostic criteria should consider the impact of groups, regions, and stages to enhance sensitivity and specificity. 				

According to global cancer statistics, gastric cancer (GC) accounted for 1.089 million new cases and 0.768 million deaths in 2020, ranking as the fifth most common malignancy and the third leading cause of cancer-related deaths worldwide[1]. Due to the absence of typical early symptoms, patients often present at advanced stages. The role of neoadjuvant chemotherapy in managing advanced GC has gained prominence, as evidenced by the MAGIC trial[2], which demonstrated that a regimen of epirubicin, cisplatin, and infused fluorouracil (ECF) improves both disease-free survival (DFS) and overall survival (OS). Subsequent regimens such as SOX (S-1 and oxaliplatin) and DOS (docetaxel, oxaliplatin, and S-1) have also proven effective[3,4]. Current consensus recommends neoadjuvant treatment for patients with LNM and stage T3 or higher. Accurate LN staging, which relies on the number of LNM, is crucial for determining the final treatment strategy. Multi-detector computed tomography (MDCT) is a fundamental diagnostic tool for GC and plays a significant role in LN assessment, although its accuracy in LN staging is relatively lower compared to tumor and distant metastasis staging.

The size, morphology, and CT enhancement of LNs are commonly used imaging criteria for diagnosing LNM, with LN size being particularly significant. In 1995, Fukuya et al.[5]. reported that the average diameter of positive LNs was (7.3 \pm 4.1) mm, compared to (4.1 \pm 2.7)

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Abbreviations: LN, lymph node; GC, gastric cancer; LNM, lymph node metastasis; LAD, long-axis diameter; SAD, short-axis diameter; RLSA, ratios of long to short axis; PLSA, product of long and short axis; AUC, area under the curve; CI, combination index; ROC, receiver operating characteristic curve.

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mm for negative LNs. However, Chai et al.[6]. found no significant difference in LAD between positive and negative LNs, while significant differences were observed in SAD and RLSA. Despite these findings, a unified diagnostic standard remains elusive. Increasing the threshold for positive LNs enhances specificity but reduces sensitivity, potentially leading to missed diagnoses. Conversely, lowering the threshold may result in unnecessary treatments.

This study aimed to investigate the correlation between LNs and different groups, regions, and stages by comprehensively analyzing pathological and radiological data from GC patients, with the goal of improving LN staging accuracy and diagnostic precision.

Materials and methods

Patients and indices

The study included patients who underwent radical gastrectomy with D2 LN dissection at Zhongnan Hospital of Wuhan University between January 2022 and May 2023. Inclusion criteria were: age \geq 18 years, localized GC without metastatic disease, and undergoing radical gastrectomy. Exclusion criteria included inability to tolerate surgery, additional malignancies, Siewert type 1 or 2 gastroesophageal junction adenocarcinoma, preoperative complications related to GC, and known HIV, HBV, or HCV infection.

Data collected included gender, age, body mass index (BMI), primary tumor location, surgical approach, type of resection, TNM staging, tumor size, pathological category, differentiation degree, Lauren subtype, and radiological and pathological LN data.

Grouping of LNs around the stomach

LN grouping was based on the "Japanese Gastric Cancer Treatment Guidelines (6th Edition)"[7], categorizing perigastric LNs into 16 groups across three stations.

Staging of gastric cancer

Staging followed the 8th edition of the American Joint Committee on Cancer (AJCC) TNM staging system.

Diagnostic criteria for LNM

Lymph node metastasis (LNM) was radiologically defined as meeting at least two of the following three criteria: LAD \geq 10 mm; SAD \geq 6 mm; abnormal enhancement. Additionally, the fusion of LNs was also considered indicative of metastasis.

Mode of surgical approach

All patients underwent standard radical gastrectomy for GC, including D2 LN dissection. Distal gastrectomy included dissection of groups 1, 3–9, 11, and 12a, while total gastrectomy included dissection of groups 1–11 and 12a.

Quality control

Specimens were resected in their entirety, followed by the surgeon's separation and classification of LNs. The pathological report described the size range for each LN group. The cisterna chyli adjacent to the abdominal aorta was excluded from imaging. Final results were determined by MDCT and pathology, with discrepancies resolved through group discussion.

Statistical analysis

Data were managed using Microsoft Excel and analyzed with SPSS

26.0. Quantitative data were expressed as means or medians, and comparisons were made using *t*-tests, SNK tests, or rank sum tests. Count data were represented as frequencies or percentages, with chi-square tests used for comparisons. The Kappa consistency test assessed agreement between CT imaging and pathological diagnoses of LNM. Diagnostic performance was evaluated using AUC, with cut-off values determined by ROC curves and Youden's index (J = sensitivity + specificity - 1).

Results

Clinical characteristics

This study included 100 patients with a median age of 64 years, comprising 71 males and 29 females. Distal gastrectomy was performed in 60 patients, while total gastrectomy was performed in the remaining 40. Surgical approaches included open surgery in 26 patients and laparoscopic surgery in 74. Clinical characteristics of the patients are summarized in Table 1.

Pathological analysis identified a total of 3566 LNs, with a median of 35 (range: 17–72) per patient. Imaging analysis identified 2233 LNs, with a median of 22 (range: 3–47) per patient. For groups 1–12 in imaging, a total of 1557 LNs (including groups 2 and 10 in distal gastrectomy) were identified, with a median of 15 (range: 3–38). The overall LN detection rate was 40.89 %, with a positive LN detection rate of 38.89 %. Among these, LN groups 2 and 3 exhibited the highest positive rates at 18.37 % and 17.24 %, respectively. In terms of detection rates, LN

Table 1

The o	characteristics	of	patients.
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Characteristics	N = 100
Age (years)	
Median (range)	64 (31–84)
Gender (n)	. ,
Male	71 (71 %)
Female	29 (29 %)
BMI (kg/m2)	
Mean	23.44 ± 3.02
Preoperative comorbidities (n)	
Diabetes mellitus	3
Hypertension	31
coronary heart disease	10
Course (months)	
Median (range)	1 (0.2–24)
Mode of surgical approach (n)	
Laparoscopic	74 (74 %)
Open	26 (26 %)
Type of resection (n)	
Distal gastrectomy	60 (60 %)
Total gastrectomy	40 (40 %)
T stage 1/2/3/4	24/15/32/
	29
N stage 0/1/2/3	47/18/12/
	23
pTNM stage I/II/III *	32/32/36
Tumor site (In accordance with the direction of lymphatic drainage)	
Inferior gastric subpyloric	15 (15 %)
Pancreaticolienal	2 (2 %)
Superior gastric	62 (62 %)
Suprapyloric	21 (21 %)
Tumor maximum diameter	
Median (range)	3 (0.4–13)
Pathological category	
Adenocarcinoma	72 (72 %)
Signet-ring cell carcinoma	13 (13 %)
Combination type	15 (15 %)
Differentiation degree High/Median/Low	7/31/62
Lauren subtype Intestinal/Diffuse/Mixed	37/42/21
Her2 \pm	2 (2.02 %)
dMMR \pm	4 (4.04 %)

^{*} TNM staging were according to the Union for International Cancer Control (UICC) TNM classification (7th edition).

groups 3 and 10 showed relatively higher values at 56.66 % and 57.75 %, respectively. Notably, group 3 displayed the most remarkable positive LN detection rate, reaching 61.39 %.

Comparison between negative LNs and positive LNs

The imaging parameters of GC LNs (LAD, SAD, and PLSA) showed significant differences between metastatic and non-metastatic groups. The median values of metastatic LNs (LAD 8.45 mm, SAD 5.62 mm, PLSA 46.00 mm²) were significantly higher than those of non-metastatic LNs (LAD 4.62 mm, SAD 3.39 mm, PLSA 16.12 mm²). Notably, group 8 LNs in the non-metastatic group already exhibited relatively large dimensions (LAD 7.11 mm, SAD 4.31 mm), while group 3 metastatic LNs demonstrated particularly prominent PLSA values (66.59 mm²). Further analysis revealed that RLSA showed statistically significant differences (p < 0.05) only in specific groups (e.g., group 3), suggesting its limited clinical diagnostic value. In contrast, LAD, SAD, and PLSA exhibited significant differences (p < 0.05) across all groups except group 12.

Comparison between different T stages

From T1 to T4 stages, LAD, SAD, and PLSA of LNs exhibited an increasing trend. When analyzing negative and positive LNs separately, only T1 stage showed significant differences among negative LNs, while only T2 stage demonstrated notable differences among positive LNs. Group-based analysis revealed differences in all first-station groups, group 10 in the second station, and groups 14, 15, and 16 in the third station.

Comparison between different N stages

From N0 to N2 stages, LAD, SAD, and PLSA of LNs showed an increasing trend, with no significant differences observed between N2 and N3 stages. In negative LNs, only N3 stage exhibited significant differences compared to other stages, while in positive LNs, differences were noted only between N2 and N3 stages. Group-based analysis revealed differences in groups 2 and 6 at the first station, groups 7, 8, 10, and 12 at the second station, and group 13 at the third station.

Comparison between different regions

Based on lymphatic drainage, the stomach was divided into four regions: inferior gastric subpyloric, pancreaticolienal, superior gastric, and suprapyloric. Due to only two cases in the pancreaticolienal region, analysis was limited to the remaining three regions. No statistically significant differences were observed among the three regions. Group-based analysis revealed differences in groups 2, 5, and 6 at the first station, groups 8 and 10 at the second station, and groups 13, 15, and 16 at the third station. Superior gastric LNs were larger compared to those in the suprapyloric and inferior gastric subpyloric regions.

Consistency analysis

The Kappa value for N-stage consistency was 0.369. The Kappa value for concordance between imaging and pathology in total LNs was 0.50, with a sensitivity of 45.4 % and specificity of 96.8 %. Group-based analysis showed Kappa values ranging from 0.21 (group 11) to 0.78 (group 10), sensitivity ranging from 13.3 % (group 11) to 59.5 % (group 3), and specificity ranging from 91.4 % (group 8) to 100 %.

The diagnostic value in LNs

The AUCs for LAD, SAD, PLSA, and CI in diagnosing LNM were 0.817, 0.817, 0.828, and 0.827, respectively. No significant differences were observed between LAD and SAD or between PLSA and CI. The critical values for LAD, SAD, and PLSA were 6.35 mm, 4.28 mm, and

27.07 mm², respectively. AUCs and critical values for each group are detailed in Table 2, and AUCs for each group are illustrated in Fig. 1.

Discussion

The diagnosis of LNM in GC continues to present significant clinical challenges. While treatment guidelines from both the Chinese Society of Clinical Oncology (CSCO) and the National Comprehensive Cancer Network (NCCN) provide diagnostic frameworks, neither has established comprehensive criteria for LNM detection. With the increasing adoption of neoadjuvant chemotherapy, accurate LNM diagnosis and staging have become critical for treatment decision-making. Our multidimensional analysis of LN characteristics offers new insights for developing more reliable diagnostic indicators.

In clinical practice, LNM diagnosis primarily relies on measurements of long-axis diameter (LAD) and short-axis diameter (SAD), with conventional diagnostic thresholds set at 8/10/14 mm for LAD and 6/8 mm for SAD. Notably, our study confirmed that while significant differences exist in LAD, SAD and PLSA between metastatic and non-metastatic LNs, RLSA demonstrated limited diagnostic utility (AUC=0.564), likely attributable to the inherent morphological diversity of LNs. In contrast,

Table 2		
The AUCs and critical	values of each	group

-	AUC	critical values (mm/ mm ²)	Sensitivity (%)	specificity(%)
Group 1				
LAD	0.847	6.15	83.3	85.7
SAD	0.859	4.41	77.8	84.3
PLSA	0.876	27.1	83.3	87.1
Group 2				
LAD	0.935	7.87	88.9	90.2
SAD	0.952	4.58	88.9	90.2
PLSA	0.961	36.58	88.9	94.1
Group 3				
LAD	0.864	7.19	77.2	81.4
SAD	0.872	4.28	92.4	68.0
PLSA	0.878	33.22	82.3	79.4
CI	0.876	_	81.0	82.2
Group 4				
LAD	0.880	5.78	85.2	82.7
SAD	0.866	4.06	81.5	79.9
PLSA	0.883	26.16	85.2	86.3
Group 5				
LAD	0.851	5.91	66.7	88.2
SAD	0.831	3.44	86.7	66.7
PLSA	0.851	21.52	80.0	78.4
CI	0.855	_	80.0	78.4
Group 6				
LAD	0.675	4.49	42.9	86.6
SAD	0.667	3.83	82.1	46.3
PLSA	0.672	27.65	39.3	87.8
Group 7				
LAD	0.796	6.54	74.3	73.4
SAD	0.776	4.51	71.4	72.2
PLSA	0.800	32.12	68.6	77.8
Group 8				
LAD	0.793	7.73	89.5	58.6
SAD	0.783	5.37	63.2	82.8
PLSA	0.830	37.47	94.7	63.8
Group 9				
LAD	0.722	6.64	75.0	71.4
SAD	0.782	4.65	75.0	75.0
PLSA	0.777	36.62	75.0	84.5
Group 11				
LAD	0.712	5.04	86.7	57.6
SAD	0.728	4.46	53.3	88.9
PLSA	0.742	25.92	60.0	82.8
Total				
LAD	0.817	6.35	73.1	76.3
SAD	0.817	4.28	76.8	74.0
PLSA	0.828	27.07	73.1	78.7
CI	0.827	—	78.2	74.3



Fig. 1. The AUCs of each group.

the PLSA showed superior diagnostic value, with AUC values exceeding those of individual parameters and comparable to CI, while maintaining consistent diagnostic performance across all LN groups.

To address the current limitations in diagnostic sensitivity, we propose a multifaceted approach:

From an imaging technology perspective, multimodal imaging integration shows significant promise. Combining MDCT with diffusionweighted MRI or PET/CT can substantially improve detection rates for micrometastases[8] For instance, high-resolution MRI with targeted contrast agents has demonstrated excellent potential[9]. Concurrently, dynamic threshold adjustment strategies warrant attention - implementing group-specific diagnostic thresholds (e.g., LAD 6.35 mm for Group 1 vs 7.87 mm for Group 2) may optimize sensitivity without compromising specificity, highlighting the need to develop intelligent clinical decision support systems.

Artificial intelligence-assisted diagnosis represents another crucial direction. Deep learning-based LN analysis systems, trained on largescale annotated datasets, have shown unique advantages in detecting small and intermediate-sized LNs. Recent studies demonstrate that AIassisted analysis can improve the diagnostic accuracy for metastatic LNs by 20–30 % [10]. Additionally, advances in intraoperative navigation technologies, particularly novel tracers like carbon nanoparticles and indocyanine green[11], provide new methods for real-time identification of suspicious LNs during surgery.

Our study revealed a 61.11 % missed diagnosis rate for micrometastases, underscoring the necessity for standardized imagingpathology correlation protocols. Establishing uniform LN sampling and mapping methods could significantly reduce false-negative rates. For diagnostically challenging "intermediate-status LNs," we recommend combined diagnostic strategies incorporating PLSA with CT texture analysis[12].

At the technological development level, emerging imaging modalities like spectral CT and dual-energy CT may bring breakthroughs[13]. These technologies can provide not only morphological information but also functional parameters, offering multidimensional criteria for LNM diagnosis. We anticipate future prospective studies to validate the clinical value of these innovative approaches.

The morphological characteristics of both positive and negative LNs are influenced by multiple factors, including tumor grouping, anatomical location, and disease stage. Recent evidence suggests that tumor differentiation status may also significantly impact LN dimensions^[14]. Consequently, variations in sample characteristics across studies inevitably lead to divergent data outcomes. A persistent controversy in surgical oncology revolves around the necessity of group 10 LN dissection, particularly given its frequent association with splenectomy. Current surgical practice, whether robotic or laparoscopic, typically excludes routine group 10 LN dissection [15], with splenectomy specifically for LN clearance being exceptionally uncommon. The landmark JCOG0110 trial[16] from Japan demonstrated that combined splenectomy and gastrectomy not only failed to provide survival benefits but also increased complication rates and perioperative mortality. This evidence has led to the exclusion of group 10 lymphadenectomy from standard D2 lymphadenectomy in the Japanese gastric cancer treatment guidelines [17]. However, our study's finding of a 12.5 % metastasis rate in group 10 LNs suggests that their clinical significance should not be overlooked. Recent advancements in minimally invasive surgical techniques, particularly laparoscopic and robotic approaches, have enabled spleen-preserving LN clearance[18], offering substantial improvements in both disease-free and overall survival outcomes [19,20]. Nevertheless, some researchers caution that the relatively limited patient populations in Western countries may hinder the widespread adoption of these techniques[21].

Limitations

This study has several limitations that need to be addressed. First, as a retrospective study, potential selection bias and information bias may exist, particularly due to incomplete matching between imaging and pathological results in some LNs. Second, numerous anatomically small LNs (especially those <2 mm in diameter) remain undetectable with current imaging techniques. Although the multidetector computed tomography (MDCT) used in this study achieved 1-mm thin-section scanning, 59.11 % of overall LNs and 61.11 % of metastatic LNs were still unidentified. Third, the limited sample size of positive LNs in certain subgroups (e.g., greater curvature, n = 2) constrained the statistical power. Additionally, this study did not incorporate Hounsfield unit (HU) value analysis from contrast-enhanced CT, thus failing to provide reference data for this parameter. Future research should adopt prospective designs and integrate higher-resolution imaging technologies with molecular imaging approaches to enable more comprehensive evaluation of LNM status.

Conclusion

In summary, this study demonstrates that LAD, SAD and PLSA serve as valuable imaging parameters for diagnosing LNM in GC, with PLSA showing particular promise as a comprehensive diagnostic indicator. However, the suboptimal sensitivity highlights the need for integrating advanced imaging techniques and AI-assisted analysis to improve detection of micrometastases, while the significant variations observed across different nodal groups and tumor stages underscore the importance of developing context-specific diagnostic criteria. These findings contribute to the evolving paradigm of precision staging in GC management, though further prospective multicenter studies are needed to validate and refine these diagnostic approaches for clinical implementation.

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary files. The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University (Reference Number: 202,304,796). As all collected data were anonymized and de-identified, the requirement for informed consent was waived by the institutional review board.

Consent for publication

Not applicable.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) used DeepSeek-V3, an AI-powered language polishing tool, in order to improve the clarity and fluency of the manuscript. After using this tool, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the publication.

The imaging and histopathological data of lymph nodes

	Histopathologic Examination		CT Examination		Detection rates		
LN groups	No. of LNs	No. of positive LNs	No. of LNs	No. of positiveLNs	Rates of total LNs	Rates of positive LNs	
1	241 (6.76)	30 (7.25)	88 (6.04)	9 (5.59)	36.51	30.00	
2*	98 (2.75)	18 (4.35)	34 (2.33)	5 (3.11)	34.69	27.78	
3	586 (16.43)	101 (24.40)	332 (22.77)	62 (38.51)	56.66	61.39	
4	555 (15.56)	55 (13.29)	166 (11.39)	20 (12.42)	29.91	36.36	
5	243 (6.81)	25 (6.04)	66 (4.53)	6 (3.73)	27.16	24.00	
6	391 (10.96)	36 (8.70)	192 (13.17)	9 (5.59)	49.10	25.00	
7	360 (10.09)	44 (10.63)	193 (13.24)	21 (13.04)	53.61	47.73	
8	268 (7.52)	31 (7.49)	77 (5.28)	15 (9.32)	28.73	48.39	
9	259 (7.26)	20 (4.83)	96 (6.58)	5 (3.11)	37.07	25.00	
10*	71 (19.91)	10 (2.42)	41 (2.81)	2 (1.24)	57.75	20.00	
11	247 (6.93)	22 (5.31)	114 (7.82)	2 (1.24)	46.15	9.09	
12	247 (6.93)	22 (5.31)	59 (4.05)	5 (3.11)	23.89	22.73	
13	_	_ ` `	68	_	_	_	
14	_	_	109	_	_	_	
15	_	_	124	_	_	_	
16	_	_	375	_	_	_	
Total	3566	414	$1458^{\#}$	161	40.89	38.89	

* Patients with distal gastrectomy were excluded. # The lymph nodes from groups 13–16 were excluded.

The characteristics of each LN group

LNs Characteristics	No.	LAD	P value	SAD	P value	RLSA	P value	PLSA	P value
group 1	88								
Negative	70	4.56 (1.79–10.74)	< 0.001	3.29 (1.62-7.00)	< 0.001	1.31 (1.00-2.37)	0.58	16.17 (2.90-70.76)	< 0.001
Positive	18	7.53 (3.44–14.63)		5.59 (3.13-11.60)		1.27 (1.02-2.13)		43.64 (10.77-162.98)	
Group 2*	60								
Negative	51	4.86 (1.54-10.02)	$< 0.001^{\#}$	3.30 (1.45-5.77)	$< 0.001^{\#}$	1.42 (1.00-2.70)	0.35	14.68 (2.23–54.43)	< 0.001
Positive	9	10.04 (5.27-13.50)		6.38 (3.93-8.32)		1.57 (1.00-2.37)		64.06 (24.77-98.69)	
Group 3	332								
Negative	253	4.86 (1.41-17.16)	< 0.001	3.59 (1.17-12.70)	< 0.001	1.31 (1.00-3.26)	< 0.05	18.22 (1.65–199.40)	< 0.001
Positive	79	10.48 (3.59-39.24)		6.72 (2.99-22.69)		1.41 (1.00-2.50)		66.59 (10.73-890.36)	
Group 4	166								
Negative	139	3.54 (1.66-10.21)	< 0.001	2.91 (1.32-8.42)	< 0.001	1.25 (1.00-2.43)	0.086	10.36 (2.36–78.98)	< 0.001
Positive	27	9.51 (2.19-13.48)		5.80 (2.18-11.56)		1.37 (1.00-2.51)		60.77 (4.77-155.83)	
Group 5	66								
Negative	51	3.92 (1.97-17.22)	< 0.001	3.01 (1.33-11.78)	< 0.001	1.21 (1.00-2.73)	0.057	10.86 (2.87-202.85)	< 0.001
Positive	15	6.77 (3.72–14.65)		5.03 (2.82-10.18)		1.49 (1.03–1.99)		34.05 (12.39–149.14)	
Group 6	192			. ,					
Negative	164	4.06 (1.84–10.46)	0.003	2.96 (1.48-8.80)	0.005	1.30(1.00-2.45)	0.588	11.55 (2.83-92.05)	0.004
Positive	28	4.91 (2.65-23.51)		3.56 (1.89-18.48)		1.34 (1.00-1.98)		17.19 (5.97-434.46)	
Group 7	193			. ,					
Negative	158	5.03 (1.96-18.38)	< 0.001	3.68 (1.20-9.20)	< 0.001	1.30 (1.00-3.88)	0.169	18.37 (2.35–119.60)	< 0.001
Positive	35	8.57 (3.20-17.11)		5.60 (1.95-10.40)		1.40 (1.04-3.37)		46.63 (6.24-141.79)	
Group 8	77			,		,			
Negative	58	7.11 (2.94–14.87)	< 0.001	4.31 (1.83-11.68)	< 0.001	1.58 (1.04-3.99)	0.632	30.89 (6.29–157.80)	< 0.001
Positive	19	10.39 (5.74–18.55)		5.71 (3.49-12.06)		1.64 (1.01-3.67)		56.27 (32.78-192.96)	
Group 9	96								
Negative	84	5.62 (2.47-15.97)	0.013	3.98 (1.66-6.72)	0.001#	1.45 (1.01-3.04)	0.723	22.29 (4.1-83.84)	0.002
Positive	12	8.17 (2.24–18.68)		5.26 (1.76-7.49)		1.43 (1.00-2.49)		41.61 (3.94–139.91)	
Group 10*	114	,		,					
Negative	111	3.66 (1.64-9.06)	_	2.97 (1.50-7.31)	_	1.27(1.00-2.02)	_	10.67 (2.64-63.52)	_
Positive	3	7.18 (4.34–10.54)		6.73 (3.75-8.12)		1.16 (1.07–1.30)		48.32 (16.28-85.58)	
Group 11	114								
Negative	99	4.65 (1.83-12.54)	0.008	3.18 (1.12-6.13)	0.005	1.49 (1.00-3.63)	0.913	15.61 (2.13-58.48)	0.003
Positive	15	5.85 (2.71-17.55)		4.47 (2.40-8.51)		1.41 (1.04–3.28)		26.62 (6.50–149.35)	
Group 12	59			(
Negative	48	6.33 (2.55-15.81)	0.599	4 47 (1 63-11 53)	0.340	1.41(1.00-2.88)	0.559	30 48 (4 16-167 76)	0 484
Positive	11	6.23(4.60-17.21)	01033	4 41 (2.65-8.19)	01010	1.44(1.07-2.44)	01003	27.23 (12.19–121.16)	01101
Total	1557								
Negative	1286	4 62 (1 41-18 38)	< 0.001	3 39 (1 12-12 70)	< 0.001	1 33 (1 00_3 00)	0.001	16 12 (1 65-202 85)	< 0.001
Positive	271	8.45 (2.19–39.24)	0.001	5.62 (1.76-22.69)	0.001	1.41 (1.00–3.67)	5.001	46.00 (3.94–890.36)	~0.001

The distribution of data was normal, *t*-test was used.

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CRediT authorship contribution statement

Si-kai Song: Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. Jiang Zhu: Formal analysis, Data curation. Hai-min Feng: Data curation. An-she Ma: Data curation. Chao-gang Yang: Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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