

# Infrapyloric lymph node metastasis pattern in middle/lower gastric cancer: an exploratory analysis of a multicenter prospective observational study (IPA-ORIGIN)

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*To the Editor:* Gastric cancer is one of the most common cancers in China. It is mainly found in the middle/lower part of the stomach,<sup>[1]</sup> where it commonly metastasizes from the infrapyloric lymph node (No. 6). Previous studies reported that the risk of No. 6 lymph node metastasis was different based on tumor locations. In lower gastric cancer patients, the metastatic rate of No. 6 lymph node can reach up to 18.7%, and in upper gastric cancer, the rate is merely 1.9%.<sup>[2]</sup> The distance between the primary tumor and the pylorus was proved to be related to No. 6 lymph node metastasis. However, most of the studies were retrospective and their lymph nodes dissection's quality control was controversial.

The infrapyloric artery (IPA)-Origin study was a prospective multicenter observational study that aimed at clarifying the origin of infrapyloric artery (ClinicalTrials.gov, NCT03071237).<sup>[3]</sup> In this study, the surgical quality control was strict, and photos or videos of the No. 6 lymph node area were recorded in all patients. Our study is an exploratory analysis based on the IPA-Origin study and that explores the pattern and risk factors of No. 6 lymph node metastasis, which may provide bases for future clinical diagnoses and treatments. The IPA-Origin study contained 34 gastrointestinal surgery centers in China and a total of 429 patients were enrolled. In this study, 424 cases were successfully collected, and 39 cases were excluded due to post-operative pathological non-malignant diagnosis or inappropriate gastrectomy. Among the

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385 cases included, distal resection margin (DRM) and No. 6 lymph node grouping data were available in 181 cases (distal gastrectomy: 120 cases; total gastrectomy: 61 cases). The study protocol was approved by the Institutional Review Board of Medical Ethics Committee of Peking University Cancer Hospital and by the review boards of each study center before the initiation of patients enrollment (No. 2017YJZ07). The authors certify that they have obtained all appropriate patient consent forms.

Among the 120 patients who underwent distal gastrectomy and who had No. 6 lymph node grouping and DRM data, the median number of retrieved total lymph nodes and No. 6 lymph nodes were 32.9 and 3.5, respectively. The No. 6 lymph node metastatic rate was 22.5% (27/120) with metastatic rates of 12.7% (7/55) in T1 and 30.8% (20/65) in T2–T4a [Table 1]. Univariate analysis indicated that tumors maximum diameter of  $\geq 2$  cm (relative risk [RR]: 9.043, 95% confidence interval [CI]: 1.164–70.291,  $P = 0.035$ ), neural infiltration (RR: 2.632, 95% CI: 1.094–6.332,  $P = 0.031$ ), vascular infiltration (RR: 3.056, 95% CI: 1.266–7.376,  $P = 0.013$ ), advanced stage (RR: 3.048, 95% CI: 1.176–7.896,  $P = 0.022$ ) and DRM of  $\leq 3$  cm (RR: 4.121, 95% CI: 1.630–10.421,  $P = 0.003$ ), were risk factors of No. 6 lymph node metastasis. Multivariate analysis showed that tumors

maximum diameter of  $\geq 2$  cm (RR: 8.079, 95% CI: 1.016–64.227,  $P = 0.048$ ) and DRM of  $\leq 3$  cm (RR: 3.831, 95% CI: 1.485–9.884,  $P = 0.006$ ), were independent risk factors of No. 6 lymph node metastasis.

Our study shows that tumor size and its location have an influence on No. 6 lymph node metastasis in gastric cancer patients. A DRM of  $\leq 3$  cm and tumors maximum diameter of  $\geq 2$  cm are independent risk factors for No. 6 lymph node metastasis. Lymphatic metastasis is the most common metastasis of gastric cancer and is an important factor affecting patients' treatment and prognosis. A standardized lymph node dissection is extremely important for patient prognosis. It is generally considered that the lymph node metastatic direction is different based on tumor location, and that the rate of No. 6 lymph node metastasis in the lower/middle part of the stomach is higher than that of the upper part. Univariate analysis showed that DRM, tumor size, T2–T4 stage, neural infiltration, and vascular infiltration, were risk factors for No. 6 lymph node metastasis, and that differentiation was not a risk factor. Multivariate analysis showed that a DRM of  $\leq 3$  cm and a maximum tumor diameter of  $\geq 2$  cm were independent risk factors for No. 6 lymph node metastasis. Wang *et al*<sup>[4]</sup> reported that the maximum diameter of a

**Table 1: Clinical pathological characteristics and No. 6 lymph node metastasis analyses of 120 distal radical gastrectomy cases.**

Characteristics	<i>n</i>	Number of cases with No. 6 lymph node metastasis, <i>n</i> (%)	$\chi^2$	<i>P</i>
Sex			0.022	0.882
Male	77	17 (22.1)		
Female	43	10 (23.3)		
Age			0.329	0.566
$\geq 60$ years	68	14 (20.6)		
$< 60$ years	52	13 (25.0)		
Maximum tumor diameter			6.198	0.008
$\geq 2$ cm	95	26 (27.4)		
$< 2$ cm	25	1 (4.0)		
T stage			5.561	0.015
T1	55	7 (12.7)		
T2–4a	65	20 (30.8)		
Neural infiltration			4.844	0.026
Positive	41	14 (34.1)		
Negative	79	13 (16.5)		
Vascular infiltration			6.471	0.011
Positive	42	15 (35.7)		
Negative	78	12 (15.4)		
Histological type			1.653	0.148
Differentiated type	86	22 (25.6)		
Undifferentiated type	34	5 (14.7)		
DRM			23.030	0.001
DRM $\leq 1$ cm	11	8 (72.7)		
1 cm $<$ DRM $\leq 2$ cm	18	5 (27.8)		
2 cm $<$ DRM $\leq 3$ cm	24	6 (25.0)		
3 cm $<$ DRM $\leq 4$ cm	25	3 (12.0)		
4 cm $<$ DRM $\leq 5$ cm	17	4 (23.5)		
5 cm $<$ DRM $\leq 6$ cm	12	1 (8.33)		
DRM $> 6$ cm	13	0		

DRM: Distal resection margin.

tumor had a significant effect on lymph node metastasis. The No. 6 lymph node metastasis rate was 27.4% when a maximum tumor diameter of gastric cancer was  $\geq 2$  cm (RR: 9.043, 95% CI:1.164–70.291,  $P = 0.035$ ), and was 4.0% when it was  $< 2$  cm, which has a certain meaning for guiding the elimination of No. 6 lymph nodes. According to the safe resection margin distance, Kong *et al*<sup>[5]</sup> divided the tumor DRM into DRM  $\geq 6$  cm and DRM  $< 6$  cm groups and the No. 6 lymph node metastatic rate was 15.2% in the DRM  $< 6$  cm group. In our study, the No. 6 lymph node metastatic rate of the DRM  $\leq 6$  cm group was 25.2% (27/107). The difference may be due to the fewer advanced stage gastric cancers in Kong *et al*'s study. For the middle/lower early gastric cancer, there were seven cases with No. 6 lymph node metastasis and the average diameter was 3 cm, which suggest that if a lesion is large in the middle/lower early gastric cancer and close to the pylorus, there is still a possibility of No. 6 lymph node metastasis. For such cases, pylorus-preserving gastrectomy should not be performed, and the No. 6 lymph node should be completely dissected.

In conclusion, DRM of  $\leq 3$  cm and tumors maximum diameter of  $\geq 2$  cm are independent risk factors for No. 6 lymph node metastases. In clinical practice, regardless of early or locally advanced stage, if a tumor is large and close to the pylorus, the No. 6 lymph node should be completely dissected.

### Conflicts of interest

None.

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