

Lymphadenectomy along the infrapyloric artery may be dispensable when performing pylorus-preserving gastrectomy for early middle-third gastric cancer

Aya Mizuno¹ · Hisashi Shinohara^{1,2}  · Shusuke Haruta¹ · Shigeru Tsunoda² · Yasunori Kurahashi³ · Yu Ohkura¹ · Harushi Udagawa¹ · Yoshiharu Sakai²

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Abstract This study investigated the incidence of gastric cancer metastasis to the lymph nodes along the infrapyloric artery (IPA), namely no. 6i, by reviewing our medical records of 348 patients who underwent complete no. 6 dissection. Metastasis to these nodes was observed in 11 (3.2 %) patients. In these patients, one huge tumor was located in the middle third and ten including two early tumors were located in the lower third; the metastasis rate in early lower-third tumors was 2.1 % and reached 19.5 % in advanced tumors. In contrast, no early middle-third gastric cancers had no. 6i metastasis. The median diameter of 6i-positive tumors was 62 (range 18–115) mm, and the distance from the distal tumor border to the pyloric ring was no more than 44 mm. Lymphadenectomy along the IPA is important for treating gastric cancer invading the antrum, but may be dispensable when performing pylorus-preserving gastrectomy for early middle-third cancer.

Keywords Infrapyloric artery · Infrapyloric lymph nodes · Pylorus-preserving gastrectomy · Lymphadenectomy · Gastric cancer

Introduction

The no. 6 infrapyloric lymph nodes (LNs) are important perigastric nodes that drain the lymphatic flow from the greater curvature of the stomach [1, 2]. The Japanese Gastric Cancer Association (JGCA) has defined this nodal station as the area including the “afferent” LNs along the proximal part of the right gastroepiploic artery (RGEA) and the “efferent” LNs along the right gastroepiploic vein (RGEV) [3]. This definition is sensible because most lymphatic channels are accompanied by blood vessels. The infrapyloric artery (IPA) is the main nutrient vessel supplying the pylorus, including the area 3–5 cm proximal to the greater curvature to the duodenal bulb [4, 5]. Our recent study revealed that the IPA diverges independently with RGEA in 76.9 % patients and is closely associated with a certain number of LNs, namely no. 6i [6]. These LNs may be assigned to other afferent lymphatic channels draining the antrum. However, to date, there is limited knowledge about the frequency of metastases to these LNs in gastric cancer. If metastasis to no. 6i LNs is associated with cancer located in the antrum only, lymphadenectomy along the IPA does not contribute significantly to a cure when performing pylorus-preserving gastrectomy (PPG). The aim of this study was to analyze the incidence of metastasis at no. 6i LNs depending on the tumor location and depth of invasion and to discuss the significance of lymphadenectomy in gastric cancer surgery.

Patients and methods

Patients

This study included 348 gastric cancer patients who underwent total or distal radical gastrectomy with complete

Aya Mizuno and Hisashi Shinohara contributed equally to this work.

✉ Hisashi Shinohara
shinosug@kuhp.kyoto-u.ac.jp

¹ Department of Gastroenterological Surgery, Toranomon Hospital, Tokyo, Japan

² Department of Surgery, Kyoto University Graduate School of Medicine, 54 Shogoin Kawara-cho, Sakyo-ku, Kyoto 606-8507, Japan

³ Department of Surgery, Hyogo Prefectural Amagasaki General Medical Center, Hyogo, Japan

no. 6 lymphadenectomy from December 2011 through June 2015 at Toranomon Hospital, Tokyo, Japan. Tumor stage was classified according to the 7th edition of the TNM classification [7], and macroscopic type was classified by the Japanese classification [3].

Preparation for LN examination

Surgical procedures for no. 6 lymphadenectomy were described in detail elsewhere [6, 8, 9]. After surgery, all regional LNs were individually retrieved from the adipose tissue of the surgical specimen. The no. 6 nodes were divided into three substations as per our previous report: 6a is adjacent to the RGEA from its first gastric branch to its root; 6v is adjacent to the RGEV, between the root of the RGEA and the confluence of the anterior superior pancreaticoduodenal vein, and 6i is located along the IPA [6, 8]. Figure 1 shows a representative surgical specimen, demonstrating the infrapyloric lymph station divided into three sections. Section 6i was distinguished from section 6a along the avascular area between the proximal branch of the IPA and the RGEA.

Statistics

Statistical analysis was performed using the Pearson's chi-squared test. A P value < 0.05 was regarded as statistically significant.

Results

Patient background

The background clinicopathological characteristics of 348 patients (234 males and 114 females) are given in

Table 1. The most frequent location of the primary tumor was in the middle stomach (M) ($n = 164$, 47.1 %), followed by the lower stomach (L) ($n = 136$, 39.1 %) and upper stomach (U) ($n = 48$, 13.8 %). The proportion of early gastric cancer was 67.8 %. Overall, 89 (25.6 %) patients had nodal metastasis. Distal gastrectomy and total gastrectomy were performed in 266 and 82 patients, respectively.

Metastasis at no. 6 lymph nodes

The median numbers of four (interquartile range 3–6), two (1–4), and two (0–3) LNs were retrieved at nos. 6a, 6v, and 6i substations, respectively. Metastases to no. 6 LNs were observed in 31 (8.9 %) patients. The number of patients and metastasis rates at each no. 6 substation according to the tumor location and depth of invasion are summarized in Table 2. No patients with tumors located in U had nodal metastasis to any no. 6 substations, whereas 31 out of 300 (10.3 %) distal two-third gastric cancers had no. 6 metastasis. The rate of metastasis from advanced lower-third tumors of 45.3 % was significantly ($P < 0.01$) higher than that from middle-third tumors (8.5 %). Number 6a was the most frequent substation for metastasis ($n = 19$, 5.5 %), followed by no. 6v ($n = 15$, 4.3 %) and 6i ($n = 11$, 3.2 %), including ten double metastases (nos. 6a + 6v in 5, nos. 6a + 6i in 4, and nos. 6v + 6i in 1) and two triple metastases. Metastasis to no. 6i LNs was observed in 11 patients. The majority (10 out of 11) of tumors including two early tumors were located in L. The no. 6i metastasis rates in early and advanced lower-third tumors were 2.1 and 19.5 %, respectively. Notably, none of 117 early middle-third gastric cancers had no. 6i or 6v metastasis.

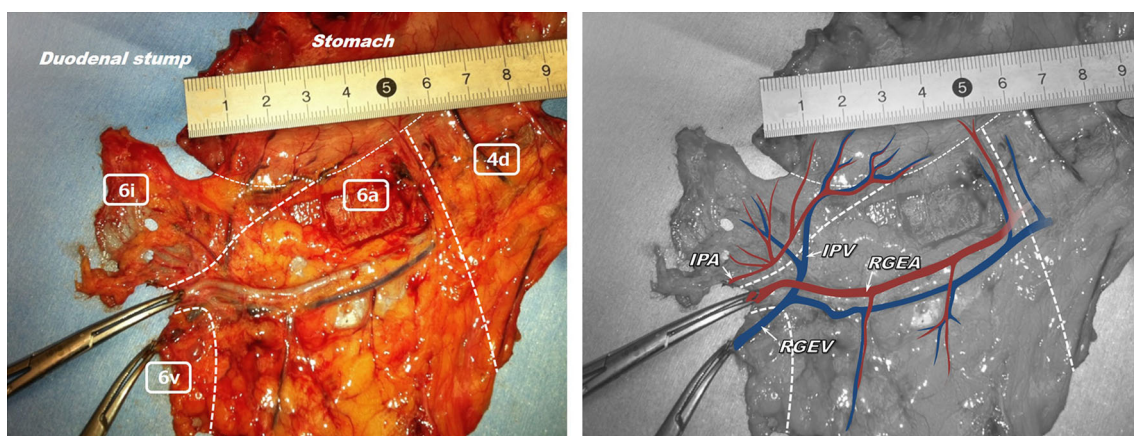


Fig. 1 Representative surgical specimen demonstrating the infrapyloric lymph station divided into three sections. In the right panel, the right gastroepiploic artery (RGEA), right gastroepiploic vein

(RGEV), infrapyloric artery (IPA), and infrapyloric vein (IPV) are enhanced by red or blue colors

Table 1 Characteristics of the 348 patients who underwent gastrectomy

Variables	N (%)
Sex	
Male	234 (67.2)
Female	114 (32.8)
Tumor location	
U	48 (13.8)
M	164 (47.1)
L	136 (39.1)
Macroscopic types	
0	241 (69.2)
1	10 (2.8)
2	29 (8.3)
3	59 (19.5)
4	9 (2.5)
Histological type	
Differentiated	133 (38.2)
Undifferentiated	210 (60.3)
Others	5 (1.4)
Depth of tumor invasion	
T1	236 (67.8)
T2	37 (10.6)
T3	37 (10.6)
T4	38 (10.9)
Nodal involvement	
N0	259 (74.4)
N1	34 (9.8)
N2	32 (9.2)
N3	23 (6.6)
Gastrectomy	
Distal	266 (76.4)
Total	82 (23.6)

Characteristics of no. 6i-positive tumors

Clinicopathological features of 11 tumors with no. 6i metastasis are shown in Fig. 2. Except one huge tumor whose diameter was 115 mm (case 11), ten were located in L. The depth of tumor invasion was defined as T1b in two patients, T3 in two, and T4a in seven. Macroscopic types included two 0-IIc cases, three type 2, five type 3, and one type 4 cases. The median tumor diameter was 62 (range 18–115) mm, and the median distance from the distal tumor border to the pyloric ring was 14 (range 0–44) mm. The distances in two early tumors (cases 1, 2) were very close to the pylorus (20, 0 mm). Histological examination did not show any notable characteristics in no. 6i-positive tumors (differentiated type in 4 and undifferentiated type in 7); this histological ratio was similar to the overall ratio in 348 cases as shown in Table 1. All advanced tumors had LN metastases to plural stations, although both of the T1 tumors with no. 6i metastasis had no other metastatic LN stations.

Discussion

The no. 6 infrapyloric LN station is considered an important confluence of lymphatic channels draining the distal two-thirds of the stomach [1, 8]. The dissection of the no. 6 station is an important surgical step because several studies demonstrated that metastasis to the no. 6 nodes is very common [2, 10]. Our present results showing that nearly 10 % of distal two-third gastric cancers had no. 6 metastasis were compatible with their results. However, after subdividing the no. 6 station into three substations,

Table 2 Number of patients and metastasis rates at no. 6 lymph node substations according to the location and T stage

	Any no. 6 ^a N (%)	No. 6a N (%)	No. 6v N (%)	No. 6i N (%)
U				
T1 (N = 24)	0	0	0	0
>T2 (N = 24)	0	0	0	0
M				
T1 (N = 117)	3 (2.6)	3 (2.6)	0	0
>T2 (N = 47)	4 (8.5)	3 (6.4)	1 (2.1)	1 (2.1)
L				
T1 (N = 95)	5 (5.3)	3 (3.2)	2 (2.1)	2 (2.1)
>T2 (N = 41)	19 (45.3)*	10 (24.4)*	12 (29.3)*	8 (19.5)*
Total (N = 348)	31 (8.9)	19 (5.5)	15 (4.3)	11 (3.2)

* $P < 0.01$ as compared with M

^a The number does not add up because of metastases at plural substations

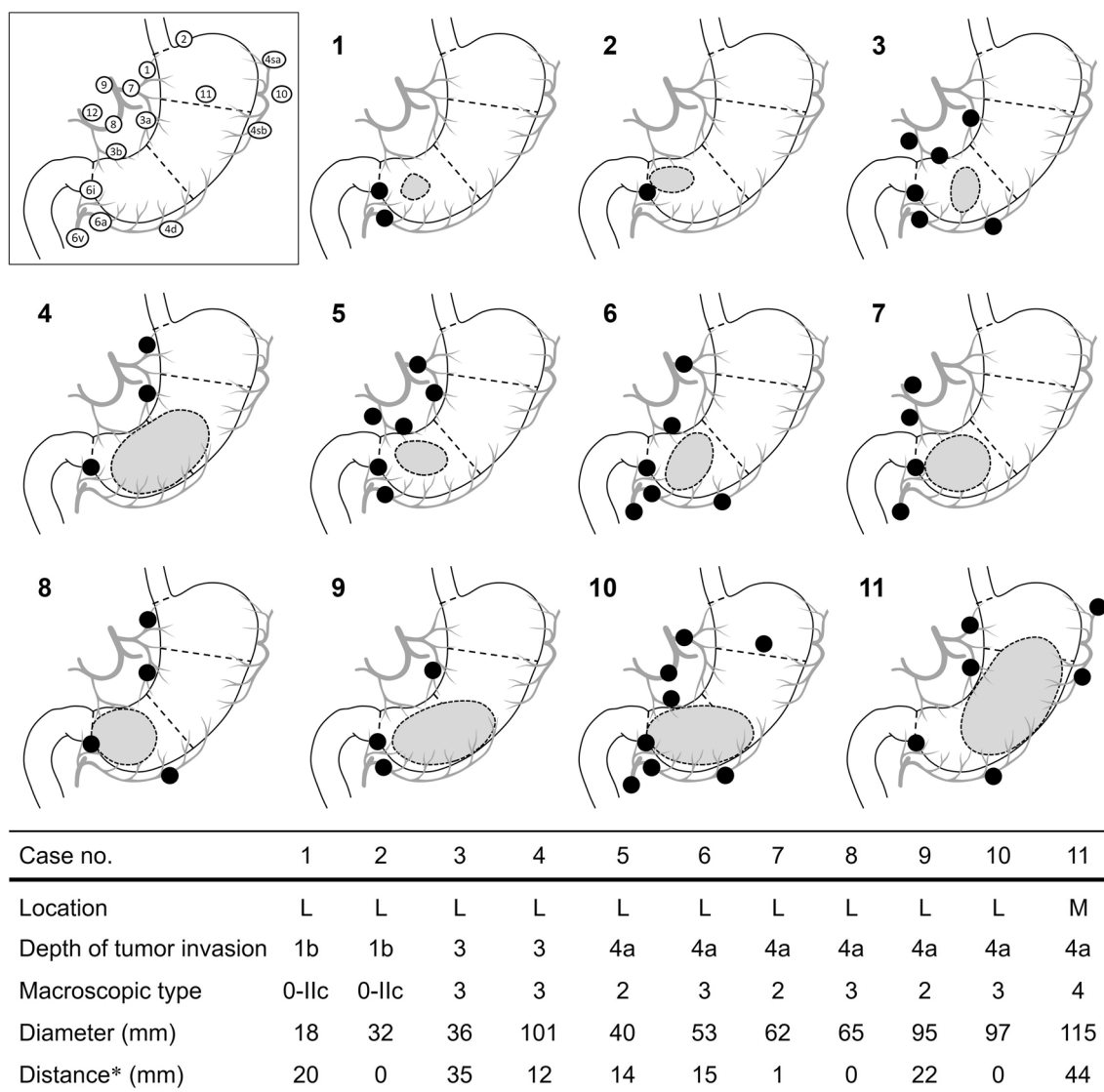


Fig. 2 Characteristics of 11 gastric cancers with nodal metastasis along the infrapyloric artery. The gray oval in each figure roughly indicates the location and diameter of the tumor. Black circles

indicate metastasis-positive lymph node stations, which were depicted in the upper left panel. Asterisk indicates the distance from the distal tumor border to the pyloric ring

metastasis to the no. 6i LNs was observed in only 11 tumors. The majority of these tumors, including two early tumors, were located in L, and the distance from the distal tumor border to the pyloric ring was no more than 44 mm. The no. 6i metastasis rate of early lower-third tumors was 2.1 %, and the rate reached 19.5 % in advanced tumors. These results are consistent with the anatomy of the IPA, which supplies the pyloric antrum for a length of 3–5 cm [4, 5], and indicate that lymphadenectomy along the IPA is an important part in no. 6 LN dissection for treating gastric cancer invading the antrum. Further studies using dye imaging [11] would visualize the lymphatic stream in the infrapyloric region.

Clinically, T1N0 gastric cancer whose distal border is at least 4 cm proximal to the pylorus is a good indication for

PPG [12]. This operation has an advantage over conventional distal gastrectomy, with a lower incidence of dumping syndrome, bile reflux gastritis, and nutritional deficit [13–16]. These advantages are attributable to preservation of the pyloric branch of the vagus nerve and the nutrient vessels supplying the antrum [17–20]. Since the rate of metastasis to nodes along the right gastric artery (no. 5 LNs) from early middle-third gastric cancer is known to be extremely rare [18, 21], omission of the suprapyloric LN dissection in PPG has been agreed upon by surgeons [12]. In contrast, the infrapyloric LN dissection has involved skeletonization of the IPA and the vein [20] while meticulously removing the soft tissue since no data about metastatic frequency at LNs along the vessels were available [19]. In the present study, there was no early

middle-third gastric cancer patients with no. 6i metastasis, implying that lymphadenectomy along the IPA may be dispensable in PPG. Our results also showed that the incidence of no. 6v metastasis is as low as that of no. 6i in early middle-third gastric cancer. The therapeutic benefit of dissection of the no. 6 LNs in these cases is not negligible since the metastasis rate reached 2.6 %; the value is consistent with a report by Kong et al. [18]. However, considering that all metastases were localized in the no. 6a substation, lymphadenectomy along the RGEV below the level of the root of the RGEA may not be so essential when performing PPG.

In conclusion, in gastric cancer invading the antrum, lymphadenectomy along the IPA is important in radical surgery since metastasis to no. 6i LNs was frequent. In contrast, metastasis was not observed in early middle-third gastric cancer, suggesting that lymphadenectomy along the IPA may be dispensable when performing PPG. Further prospective studies are required to validate our hypothesis.

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Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval and patient consent All patients gave their informed consent before the procedures were performed, and the study protocol was approved by the Ethics Committee of Toranomon Hospital (no. 1164).

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