

Correspondence

# Sentinel node navigation to treat early gastric cancer after non-curative endoscopic submucosal dissection: A case series



Dear Editor:

Gastric cancer is a leading cause of cancer-related death. With the development and popularization of endoscopic techniques, early gastric cancer (EGC) is being diagnosed more frequently. EGC is a carcinoma that invades the submucosa regardless of the lymph node status.<sup>1</sup> Endoscopic submucosal dissection (ESD) has been accepted as an optimal treatment for patients with EGC due to its low invasiveness and functional preservation. Guidelines indicate the curability of EGC after ESD based on the curative criteria.<sup>2,3</sup> ESD is considered a curative resection of EGC when all the following conditions are met: en bloc resection, during histopathology negative horizontal and vertical margin as well as no lymphovascular invasion, and within the expanded criteria for ESD. Gastrectomy with lymphadenectomy is recommended for EGC after non-curative ESD. Currently, however, the follow-up treatment of patients with EGC after non-curative ESD is controversial. A large-scale study indicated that additional surgery resulted in a better long-term outcome.<sup>4</sup> A retrospective study on EGC after non-curative ESD demonstrated that the difference in cancer-specific survival between patients who underwent additional radical surgery and the follow-up group was not statistically significant.<sup>5</sup> Additional radical surgery after ESD may have serious implications on the quality of life of patients due to late-phase complications including dumping syndrome, weight

reduction, and malnutrition.<sup>6,7</sup> Moreover, an additional surgery may lead to high health-care costs.

The sentinel lymph node navigation concept is based on the principle that the first regional lymph node to receive drainage from the primary lesion is the earliest site of metastasis. This has already been confirmed in breast cancer and melanoma.<sup>8,9</sup> Previous studies demonstrated the effectiveness of the sentinel node concept in the treatment of EGC.<sup>6,10,11</sup> The prognosis of EGC is mainly associated with lymph node metastases (LNM) and remnant cancer. The presence of positive resected margins, specifically positive vertical margins, during histology is significantly correlated with remnant cancer. In this case series, we presented five cases that demonstrate the utility of sentinel node navigation in the treatment of non-curative ESD but margins-negative EGC. Radionuclide gastric emptying imaging is considered as the ideal method for the assessment of gastric emptying function among the commonly used methods. We, subsequently, estimated the function of the stomach after ESD with sentinel lymph nodes dissection using radionuclide gastric emptying imaging.

Five patients, who complained of EGC after non-curative ESD, were admitted to the department of general surgery in the Beijing Friendship Hospital. The patient in Case 1 did not meet the expanded indication for ESD because the tumor size was bigger than 3 cm and it was ulcerated. He met the beyond expanded indication according to the criteria used in some studies. Su et al<sup>12</sup> reported that compared to the natural course of EGC, ESD resulted in a better long-term outcome in patients who meet the beyond expanded indication. The patient was 64 years old and had several underlying diseases such as hypertension and coronary heart disease. Finally, he underwent ESD. The four other patients met the expanded indication for ESD. The median age of

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patients was 64 years old, and 3/5 of patients were men. In three cases, the tumors were located in the middle third of the stomach, while in the other two cases, the tumors were in the distal third of the stomach. The mean size of the tumor was 36.4 mm. One of the tumors was ulcerated. After ESD, histology revealed that the tumor in Case 4 was confined to the mucosal layer, those in Cases 1 and 2 infiltrated submucosal depths less than 500  $\mu\text{m}$  (SM1), while those in Cases 3 and 5 infiltrated submucosal depths between 500  $\mu\text{m}$  and 1000  $\mu\text{m}$  (SM2). Among the five tumors, four were well-differentiated, while one was poorly differentiated. In Cases 2 and 3, cancer cells invaded the lymphovascular space. The clinical and pathologic characteristics of the five patients are described in Table 1.

All the five patients underwent sentinel node navigation after eliminating the contraindications. First, endoscopy examination was conducted to identify the location of the scar after ESD. Subsequently, indocyanine green was used for sentinel node navigation in four quadrants around the scar. Within 10 minutes after the indocyanine green injection, stained sentinel nodes were observed in the peritoneal serosa and around the adipose tissue. Stained lymph nodes were observed at stations no.1, no.3, and no.7 in Case 1; no.3, no.5, and no.6 in Case 2; no.6, no.4sb, and no.4d in Case 3; no.6, no.4sb, no.4sa, and no.4d in Case 4; and no.1, no.3, and no.7 in Case 5. According to the results, all sentinel nodes under suspicion were removed by laparoscopy. A total of 8, 2, 8, and 39 lymph nodes were obtained respectively in Cases 1, 2, 3, and 4. However, in Case 5, suspected indocyanine green-stained lymph nodes were displayed as vascular adipose tissue. The mean total number of lymph nodes obtained was 11.4. No metastatic lymph nodes (0/57) were detected following sentinel lymph node dissection. After discharge, a radionuclide gastric emptying

examination was conducted in four patients at the outpatient department. The patient in Case 4 refused to complete the radionuclide gastric emptying examination because he lived far away from hospital and didn't feel uncomfortable. First, the patients ate a test meal made of solid food mixed with an imaging agent that is not absorbed by the gastric mucosa. Subsequently, computer region of interest technology was applied to calculate the time needed to discharge half of the radioactive food in the stomach. In principle, the half gastric emptying time of solid food is between 76 and 108 minutes. The half gastric emptying time was 477 minutes for Case 1, 60 minutes for Case 2, 64 minutes for Case 3, and 5636 minutes for Case 5. According to the results, the patients in Cases 1 and 5 suffered from delayed gastric emptying. However, only the patient in Case 5 had symptoms such as abdominal distention, belching, and acid reflux. Table 2 shows the lymph node status and gastric function of the patients. Five patients underwent follow-up endoscopic examination with or without biopsy after 3, 6, and 12 months. One year after the lymphadenectomy, the endoscopic examination was carried out annually. The median follow-up duration was 31 months (range: 19–48 months). There was no gastric cancer recurrence in any of the patients who underwent lymph node dissection after non-curative ESD.

No metastatic lymph nodes (0/57) were detected following sentinel lymph node dissection in patients after non-curative ESD for EGC. Hatta et al.<sup>5</sup> found that LNM occurred in 8.4% (89/1064) of patients who underwent non-curative ESD. Another study indicated that the prevalence of LNM was 6.7% (18/267).<sup>13</sup> This study also revealed that venous invasion, SM2 invasion, and antral tumor location are predictors for LNM. A large-scale retrospective study developed a risk-scoring system for LNM after non-curative ESD. They found that lymphatic invasion was the most

Table 1  
Clinical and pathologic data of patients.

	Sex	Age (mm)	Size (mm)	Location	morphology	ESD pathologic results			
						Ulcer	Differentiation	Depth	Ly
1	M	64	35	Angle	I1c	Y	D	SM1	N
2	F	72	36	Antrum	I1a + I1c	N	D	SM1	Y
3	M	56	20	Antrum	I1a + I1c	N	D	SM2	Y
4	M	55	55	Antrum	I1a + I1c	N	PD	MM	N
5	F	73	36	Body	I1a + I1c	N	D	SM2	N

ESD: endoscopic submucosal dissection; SM1: submucosal depth < 500  $\mu\text{m}$ ; SM2: submucosal depth < 1000  $\mu\text{m}$ ; MM: muscularis mucosa; Ly: lymphovascular; D: differentiated; PD: poorly differentiated.

Table 2  
Lymph node status and stomach function of patients.

	LN station	LN total numbers	LN metastases	Stomach function
2	no.3, 5, and 6	2	N	Normal
3	no.6, 4d, and 4sb	8	N	Normal
4	no.6, 4d, 4sa, and 4sb	39	N	/
5	no.1, 3, and 7	0*	N	Abnormal

LN: lymph node; \*: Vascular adipose tissue; /: There was no result because that the patient 4 did not complete the radioactive gastric emptying test.

important factor, and that a tumor size greater than 30 mm, a positive vertical margin, a venous invasion, and a submucosal invasion greater than 500  $\mu\text{m}$  are risk factors for LNM.<sup>8</sup> In our study, cancer cells were observed in the lymphovascular space in Cases 2 and 3. Additionally, in Case 3 and 5, the submucosa was invaded by tumors at depths greater than 500  $\mu\text{m}$ . However, no local metastatic lymph nodes were detected in the aforementioned cases. Several studies found no statistical differences in cancer-specific survival between patients who underwent additional radical surgery and the follow-up group.<sup>13–16</sup> Currently, however, a large-scale study conducted in Korea showed that additional surgery resulted in a better long-term outcome.<sup>4</sup> In addition, some studies suggested that lymphatic invasion has a significant influence on prognosis.<sup>13,17</sup> All patients in our studies underwent follow-up endoscopic examination with or without biopsy after 3, 6, 12, and 24 months. Even though cancer cells invaded the lymphovascular space in Cases 2 and 3, there was no gastric cancer recurrence in any of the patients. According to the results, delayed gastric emptying occurred in the patients in Cases 1 and 5. Gastric emptying function in the other patients was normal. Only the patient in Case 5 had symptoms. Thus, sentinel lymph node dissection may be a desirable choice for some patients who suffer from EGC after non-curative ESD. Normal gastric motility occurs due to interaction between the nerves and hormones, leading to the regular stimulation of the stomach muscle. Mechanical obstruction was not observed in any patient using endoscopic examination. We believe that delayed gastric emptying mostly occurs when the vagus nerve is damaged. Stations no.1, no.3, and no.5 corresponded to lymph nodes along the lesser curvature, while stations no.2, no.4, and no.6 corresponded to lymph nodes along the greater curvature.<sup>1</sup> The vagus nerve can be divided into the anterior branch of the stomach, the hepatic branch, the posterior branch of the stomach, and the abdominal branch. The anterior and posterior branches of the stomach travel along the lesser curvature. The two patients with delayed gastric emptying underwent lymph node dissection at stations no.1 and no.3, which are located along the lesser curvature. This might have resulted in the vagus nerve being damaged.

Sentinel node navigation may be a feasible option for EGC with negative resected margins after non-curative ESD.

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## Conflicts of interest

None.

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Dong-Ya Hu

Jing-Wei Wu

Peng Li\*

Shu-Tian Zhang\*\*

*Department of Gastroenterology, Beijing Friendship Hospital, Capital Medical University, National Clinical Research Center for Digestive Diseases, Beijing Digestive Disease Center, Beijing Key Laboratory for Precancerous Lesion of Digestive Diseases, Beijing 100050, China*

\*Corresponding author. 95 Yong'an Road, Xicheng District, Beijing 100050, China.

\*\*Corresponding author.

*E-mail addresses:* [lipeng@ccmu.edu.cn](mailto:lipeng@ccmu.edu.cn) (P. Li), [zhangshutian@ccmu.edu.cn](mailto:zhangshutian@ccmu.edu.cn) (S.-T. Zhang)

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