



Possibility of limited gastrectomy for early gastric cancer located in the upper third of the stomach, based on the distribution of sentinel node basins

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Abstract

Purpose Several recent studies have evaluated the feasibility of the sentinel node (SN) concept for gastric cancer. The aim of our study was to investigate limited gastrectomy with SN basin dissection in SN navigation surgery (SNNS) for patients with early-gastric cancer located in the upper-third of the stomach.

Methods 147 patients received SNNS for early-gastric cancer at our institution. Of these, 26 patients diagnosed with early-gastric cancer < 4 cm in size and located in the upper-third of the stomach were retrospectively analyzed for the distribution of SN and SN basins.

Results In three of the 26 patients, lymph node metastasis was limited to the left gastric artery (LGA) basin. The breakdown of the basins were as follows: A single LGA basin, 19 cases; a non-single LGA basin, seven cases. A non-single LGA basin was significantly associated with the clinicopathological factors, such as tumor spread to the middle-third of the stomach, tumor location at the center of the greater curvature, and undifferentiated adenocarcinoma, compared to the single LGA basin group.

Conclusions Our data revealed that the distribution of the SN basins in early-gastric cancer measuring less than 4 cm in size and located in the upper-third of the stomach was significantly correlated with tumor spread, tumor location, and the pathological findings.

Keywords Gastric cancer · Limited gastrectomy · Sentinel node

Introduction

The sentinel lymph nodes (SN) are defined as the first lymph nodes that directly drain lymphatic flow from a primary tumor [1]. Thus, the SN concept identifies the SN as the first place where lymph node metastasis emerges. If the SN are negative for metastasis, then metastasis to other lymph nodes is assumed to be negative. The SN concept has been clinically applied to both melanoma and breast cancer, leading to

a reduction in the extent of surgical intervention and limited lymph node dissection [1, 2]. The clinical application of SN navigation surgery (SNNS) for early gastric cancer has long been debated due to the complicated lymphatic flow around the stomach, and SNNS has not been widely accepted for the treatment of gastric cancer. However, recent studies have demonstrated the feasibility of SNNS in early gastric cancer [3–6]. Kitagawa Y et al. [5] recommended that evaluating lymph node metastasis in the SN basins rather than in SN themselves is important for achieving SNNS success in gastric cancer patients with cT1N0M0 and lesions measuring less than 4 cm in diameter.

Although total gastrectomy is standard for the treatment of early gastric cancer located in the upper third of the stomach, the patient's postoperative nutritional status often suffers. Proximal gastrectomy is recommended for early gastric cancer located in the upper third of the stomach because it reduces surgical stress, maintains the physiological function

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of the remaining stomach, and improves the postoperative late-phase function compared with total gastrectomy [7–9]. Partial gastrectomy, including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), is confined solely to sites where the gastric cancer is present and omits lymph node dissection. Therefore, this procedure preserves the stomach volume, minimizes functional impairment, maintains the physiological function of the remaining stomach, and decreases any reflux of gastric acid and bile [10, 11].

However, adopting limited gastrectomy without lymph node dissection as the standard of care remains controversial from the stand-point of oncological safety [12]. Limited gastrectomy combined with SN basin dissection based on SNNS has the potential to better maintain the balance between quality of life (QOL) and curability for patients with early gastric cancer.

We herein analyzed the distribution of the SN and SN basins through SNNS and evaluated the possibility of performing function-preserving surgery with SN basin dissection for patients with early-stage gastric cancer located in the upper third of the stomach.

Methods

Patients

Between February 2001 and August 2009, SNNS was performed in 147 patients with cT1-2 and cN0 gastric cancer at the Department of Gastrointestinal and Pediatric Surgery of Mie University Graduate School of Medicine. Of these 147 patients, we retrospectively analyzed 26 patients with early gastric cancer located in the upper third of the stomach (Table 1). We excluded any patients with multiple lesions, cT2, and lesions greater than 4 cm in diameter, according to the findings of a previous report [5]. All patients underwent computed tomography, endoscopy, barium swallow, endoscopic ultrasonography, and abdominal ultrasound to diagnose the preoperative stage. Informed consent was obtained from all patients based on a document approved by the Ethics Committee of our hospital.

In 17 patients, the tumors were located in the upper third of the stomach (U), while in nine, the tumors spread from the upper third to the middle third (UM). Eleven patients underwent laparoscopic proximal gastrectomy, four underwent laparoscopic pylorus-preserving gastrectomy, and ten underwent laparoscopic total gastrectomy (Table 1).

Lymphatic mapping technique

The dual tracer method using 99 m-Tc-Technetium-Tin colloid and blue dye was performed as previously described [13].

Briefly, 1 day before surgery, 99 m-Tc-Technetium-Tin colloid was endoscopically injected. Intraoperatively, the stomach was mobilized by dissecting through the gastrocolic ligament without disrupting the gastroepiploic vessels. Then, 1% isosulfan blue dye was endoscopically injected in exactly the same manner as the preoperative injection of the radioactive tracer. Within 15 min, the lymphatic vessels and lymph nodes were dyed blue and imaged. Simultaneously, a handheld gamma probe (Tyco Healthcare, Ltd., Tokyo Japan) was used to locate the radioactive SN. Lymph nodes with radioactivity ten-fold greater than the background activity were defined as “hot” nodes. Hot and/or blue nodes were identified as the SN. The detected lymphatic basin, including the SN, was resected laparoscopically and recorded according to the lymph node station numbers as described in The Japanese Classification of Gastric Carcinoma [14]. Suspected SN underwent intraoperative frozen section histologic examination with hematoxylin and eosin staining. Laparoscopic gastrectomy with lymphadenectomy was performed in all patients according to the therapeutic guidelines recommended by The Japan Gastric Cancer Association [15].

Definition of lymphatic basins

The gastric lymphatic basins were divided into five directions along the main arteries according to the classification of gastric cancer location based on the physiological lymphatic flow as described by Kinami et al. [6]: the left gastric artery area, right gastric artery area, left gastroepiploic artery area, right gastroepiploic artery area, and posterior gastric artery area.

Statistical analysis

Continuous variables are shown as the median with standard deviation (SD). All statistical calculations were performed using the JMP software program, version 10 (SAS Institute, Cary, NC, USA). Clinicopathological variables were analyzed using Pearson’s Chi-squared test. Parameters with a value of $p < 0.05$ were considered to be statistically significant.

Results

Patients and surgical characteristics

The study group comprised 13 males and 13 females and the median age was 69 years old (SD:9.5). The median tumor size was 24 mm (SD:11.6). The characteristics of the study population are shown in Table 1. According to the Japanese Classification of Gastric Cancer (10th Ed.) [15], the tumor locations included U (17 patients, 65.4%), UM (9 patients,

Table 1 Patients and surgical characteristics ($n = 26$)

Variables	Number (rate)	Median \pm SD
Gender		
Male	13 (50%)	
Female	13 (50%)	
Age (years)		69 \pm 9.5
Tumor size (mm)		24 \pm 11.6
Tumor location		
U	17 (65.4%)	
UM	9 (34.6%)	
Lesser curvature	12 (46.2%)	
Anterior wall	2 (7.7%)	
Greater curvature	6 (23.1%)	
Posterior wall	6 (23.1%)	
Depth of tumor invasion		
T1a	3 (11.5%)	
T1b1	5 (19.2%)	
T1b2	15 (57.7%)	
T2	1 (3.8%)	
T3	2 (7.7%)	
Pathological type		
Differentiated	17 (65.4%)	
Undifferentiated	9 (34.6%)	
Operative procedure		
Laparoscopic partial gastrectomy	0 (0%)	
Laparoscopic proximal gastrectomy	12 (44%)	
Laparoscopic pylorus-preserving gastrectomy	4 (16%)	
Laparoscopic total gastrectomy	10 (39%)	
Extent of lymph node dissection		
D0	0 (0%)	
D1	0 (0%)	
D1+	24 (92.3%)	
D2	2 (7.7%)	
Estimated blood loss (g)		232 \pm 643
Duration of operation (min)		326 \pm 142
Complications		
Anastomotic leakage	0 (0%)	
Intra-abdominal abscess	1 (3.8%)	
Small bowel obstruction	1 (3.8%)	
Delayed gastric emptying	0 (0%)	
Postoperative hospital stay (days)		10.5 \pm 10.7

34.6%), lesser curvature (12 patients, 46.2%), anterior wall (2 patients, 7.7%), greater curvature (6 patients, 23.1%), and posterior wall (6 patients, 23.1%). Pathological depth of tumor invasion included T1a (3 patients, 11.5%), T1b1 (5 patients, 19.2%), T1b2 (15 patients, 57.7%), T2 (1 patient, 3.8%), and T3 (2 patients, 7.7%), respectively. The pathological types included differentiated (17 patients, 65.4%) and undifferentiated (9 patients, 34.6%). The median estimated blood loss was 232 g and the median duration of the operation was 326 min. Among the 26 patients investigated in this

study, 1 (3.8%) developed intra-abdominal abscess and 1 (3.8%) developed small bowel obstruction (Table 1).

Result of lymph node metastasis and SNNS

The results of the lymph node analysis and SNNS are shown in Table 2. The SN detection rate determined by the dual tracer method was 100% (26 of 26). The mean numbers of identified SN and SN basins were 3.54 and 1.27, respectively. Lymph node metastasis was diagnosed in 3 (11.5%) of

Table 2 Results of lymph node metastasis and SNNS

Variables	Number (rate)	Mean
Number of resected lymph nodes		22.5
Lymph node metastasis		
Positive	3/26 (11.5%)	
Negative	23/26 (88.5%)	
Identification of SN		
Detected	26/26 (100%)	
Undetected	0/26 (0%)	
Number of identified SN		3.54
Number of identified SN basin		1.27
Lymph node metastasis in SN		
Positive	2/3 (66.7%)	
Negative	1/3 (33.3%)	
Lymph node metastasis in the SN basin		
Positive	3/3 (100%)	
Negative	0/3 (0%)	
Lymph node metastasis in non SN		
Positive	1/23 (4.3%)	
Negative	22/23 (95.7%)	
Lymph node metastasis in the non SN basin		
Positive	0/23 (0%)	
Negative	23/23 (100%)	
Sensitivity	66.7%	
Specificity	100%	
Accuracy	96.2%	
Distribution of the SN basin		
LGA basin	25/26 (96.2%)	
LGEA basin	7/26 (26.9%)	
RGA basin	0/26 (0%)	
RGEA basin	1/26 (3.8%)	
PGA basin	0/26 (0%)	
No 2	1/26 (3.8%)	
No 9	2/26 (7.7%)	
No11d	0/26 (0%)	
No 10	0/26 (0%)	
Single LGA basin	19/26 (73.1%)	
No single LGA basin	7/26 (26.9%)	

SNNS sentinel node navigation surgery, SN sentinel node, LGA Left gastric artery, LGEA Left gastroepiploic artery, RGA Right gastric artery, RGEA Right gastroepiploic artery, PGA Posterior gastric artery

26 patients, and 3 of 26 patients had lymph node metastasis limited to the left gastric artery (LGA) basin. Two of three patients had lymph node metastasis in SN and the other had lymph node metastasis limited to the same SN basin. One false-negative case occurred in a patient with pathological T2, and our findings suggest that a complete obstruction of the lymphatic vessel to SN due to a tumor emboli had thus occurred in this case. The sensitivity of the method was 66.7% (2 of 3), the specificity was 100% (23 of 23), and the

accuracy of the metastatic status based on the SN evaluation was 96.2% (25 of 26).

Long-term outcomes

Among all 26 patients, one patient with pathological T3 and metastasis in SN died due to peritoneal metastasis 4 years after surgery, and the two patients who were diagnosed as pathological T1N0 died due to the other diseases. One patient with pathological T1N0 developed peritoneal metastasis 4 years after surgery, and is currently surviving while receiving chemotherapy. In contrast, the remaining 22 patients all survived without any recurrence to date.

Distribution of SN basins based on primary tumor characteristics

The primary tumor and SN basin characteristics of the study population are shown in Fig. 1. The pattern of the basins was as follows: Single LGA basin, 19 cases (Fig. 1a); LGA basin plus left gastroepiploic artery (LEGA) basin, five cases (Fig. 1b); single REGA basin, one case (Fig. 1c); LGA basin plus LEGA basin plus right gastroepiploic artery (RGEA) basin, one case (Fig. 1d). We divided the study population into two groups, including the single LGA basin group and the non-single LGA basin group, and investigated the association between the SN basin group and clinicopathological factors. Almost all tumors in the single LGA basin group were present in the lesser curvature, anterior wall, or posterior wall without any spread to the middle third of the stomach. The non-single LGA basin group was significantly associated with clinicopathological factors, such as tumor spread to the middle third of the stomach ($p=0.001$), tumor center at the greater curvature ($p=0.012$), and undifferentiated adenocarcinoma ($p=0.017$), compared to the single LGA basin group (Table 3). However, no significant associations were observed between the two groups according to the other clinicopathological factors, such as the depth of invasion and the diameter of the tumor (Table 3).

Discussion

In the present study, we evaluated the relationship between the SN basin and the characteristics of gastric cancer located in the upper third of the stomach. Our data suggest that careful consideration of the operative method, including partial resection, segmental gastrectomy, pylorus-preserving gastrectomy, and proximal gastrectomy, based on SNNS is important for patients with early gastric cancer measuring less than 4 cm in diameter located in the upper third of the stomach, particularly when tumors have characteristics such as spread to the middle third of the stomach, the center of

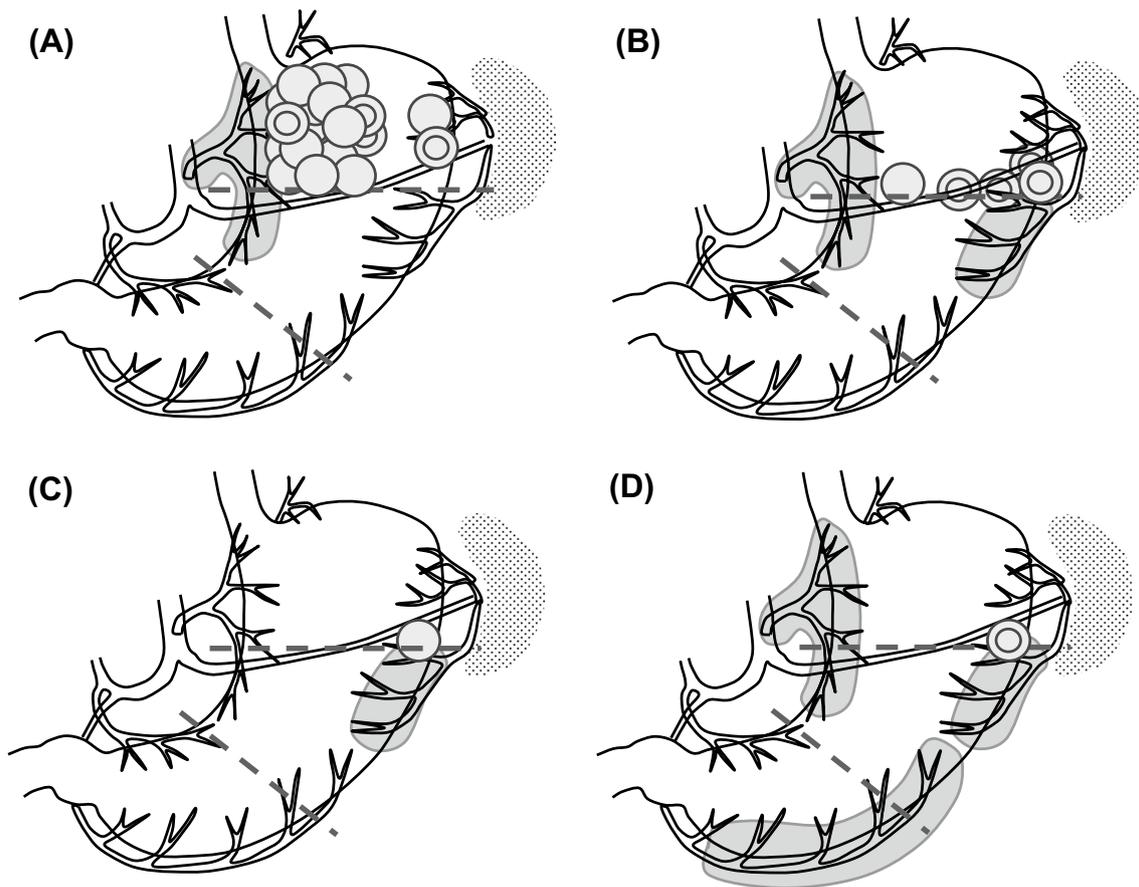


Fig. 1 Distribution of primary tumors and SN basins in the study participants. Round region, primary tumor of differentiated type; Double circle region, primary tumor of undifferentiated type; Irregular region along the blood vessel, sentinel node basins. **a** A single LGA basin was observed in 19 cases. In 16 of these cases, tumors were present in the lesser curvature, anterior wall, or posterior wall of the stomach, and in two cases tumors spread to the middle third of the stomach. **b** The LGA basin plus left gastroepiploic artery (LEGA) basin

was observed in five cases. In four of these cases, tumors spread to the middle third of the stomach, and in three cases tumor was present near the greater curvature. **c** A single REGA basin was observed in one case. The tumor was located at the greater curvature of the stomach and spread to the middle third. **d** The LGA basin plus LEGA basin plus right gastroepiploic artery (RGEA) basin was observed in one case. The tumor was located at the greater curvature of the stomach and spread to the middle third

the tumor is located in the greater curvature, and the tumor consists of undifferentiated adenocarcinoma. In contrast, partial gastrectomy with LGA basin dissection may be possible when tumors do not have any of these characteristics. Takeuchi H et al. [16] reported the SN distributions based on the cross-sectional location of the primary tumor in 489 patients with early gastric cancer. The study showed that the lymphatic flow tended to be scattered in various SN basins when lesions of the greater curvature were located in the upper third of the stomach. On the other hand, more than 90% of SN basins were distributed in the LGA region when the tumors were located at the lesser curvature, anterior wall, and posterior wall.

Limited gastrectomy is only adopted for gastric patients without lymph node metastasis in the detected SN basin. Although the choice of function-preserving surgery for early gastric cancers consisting of U or UM lesions is sometimes

difficult, a preserved vascular supply after lymph node dissection based on the one SN basin concept may provide individually determined indications for limited gastrectomy, including partial gastrectomy, segmental gastrectomy, pylorus-preserving gastrectomy and proximal gastrectomy in gastric cancer located in the upper third of the stomach. We propose the individual function-preserving surgeries as follows: (1) Partial gastrectomy is intended when the SN basin is limited to either the lesser or greater curvature, because the blood flow of resection line is maintained by blood supply from within the gastric wall [17]. (2) Segmental gastrectomy or pylorus-preserving gastrectomy is recommended when the SN basins are distributed along both the lesser and greater curvature including the left gastric artery area and right gastroepiploic artery area. (3) Proximal gastrectomy is recommended when the SN basins are distributed along both the lesser and greater curvature including the

Table 3 Comparison of the distribution of the SN basin based on the characteristics of the primary tumor

Variables	Single LGA basin group (n=19)	Non-single LGA basin group (n=7)	p value
Tumor size			
≤ 30 mm	13	3	0.2347
> 30 mm	6	4	
Tumor spread			
U	16	1	0.001
UM	3	6	
Tumor center			
Not greater curvature	17	3	0.012
Greater curvature	2	4	
Depth of tumor invasion			
T1a, T1b1	5	3	0.4176
T1b2, T2, T3	14	4	
Pathological type			
Differentiated	15	2	0.017
Undifferentiated	4	5	

SN sentinel node, LGA Left gastric artery

Significant associations are shown in bold ($p < 0.05$)

left gastric artery area and left gastroepiploic artery area or posterior gastric artery area. Theoretically, if SN are pathologically negative for cancer metastasis, then EMR or ESD may be sufficient for curative resection of early gastric cancer beyond the EMR criteria [18]. However, it is still not clear whether SN mapping is feasible after endoscopic resection. If this concept is proved to be feasible, then EMR or ESD with SN basin resection may be possible in patients with early gastric cancer and who are contraindicated for endoscopic treatment.

Although the standard methods of local stomach excision have not yet been established, laparoscopic endoscopic cooperating surgery (LECS) for gastrointestinal stromal tumors (GIST) has been reported to achieve partial gastrectomy with the satisfactory preservation of the stomach volume [19]. However, in the case of cancer surgery, a strict non-exposure technique is required to prevent the transfer of malignant cells into the abdominal cavity. To prevent the risk of seeding cancer cells during open gastrectomy, several non-exposure techniques have been developed, such as the crown method of LECS [20], non-exposed endoscopic wall-inversion surgery (NEWS) [21], and the combination of laparoscopic and endoscopic approaches to neoplasia with the non-exposure technique (CLEAN-NET) [22]. We believe that partial gastrectomy combined with SNNS may contribute to both oncological safety and an improved QOL in patients with gastric cancer.

There are several limitations associated with this study, including the relatively small number of patients and its

observational and retrospective design. To overcome these limitations, larger prospective trials should be performed to confirm the results obtained from our study. In addition, we did not investigate improvements in QOL in patients receiving function-preserving surgery for gastric cancer. We will address these issues in a multicenter prospective trial, which will evaluate both the long-term survival and patient QOL after function-preserving gastrectomy with SN mapping (UMIN 000014401).

In conclusion, we herein demonstrated that the careful evaluation of SN basin distribution is important for selecting the optimal surgical procedure for function-preserving limited gastrectomy, particularly for patients with early undifferentiated gastric cancer located at the greater curvature of the UM stomach.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest and received no financial support for this study.

Ethical statement All procedures and subsequent analyses were performed with the approval of the Institutional Review Boards of Mie University Hospital in Japan (No. 2004–445). The study was conducted in accordance with the guidelines of the 1975 Declaration of Helsinki.

Informed consent Written informed consent was obtained from all study participants.

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