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Original Article

Potential Applicability of Local Resection With Prophylactic Left Gastric Artery Basin Dissection for Early-Stage Gastric Cancer in the Upper Third of the Stomach

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ABSTRACT

Purpose: Total or proximal gastrectomy of the upper-third early gastric cancer (u-EGC) often causes severe post-gastrectomy syndrome, suggesting that these procedures are extremely invasive for patients without pathologically positive lymph node (LN) metastasis. This study aimed to evaluate the clinical applicability of a stomach function-preserving surgery, local resection (LR), with prophylactic left gastric artery (LGA)-basin dissection (LGA-BD).
Materials and Methods: The data of patients with u-EGC (pathologically diagnosed as T1) were retrospectively analyzed. Total gastrectomy was performed in 30 patients, proximal gastrectomy in 45, and subtotal gastrectomy in 6; the LN status was evaluated assuming that the patients had already underwent LR + LGA-BD. This procedure was considered feasible in patients without LN metastases or in patients with cancer in the LGA basin. The reproducibility of the results was also evaluated using an external validation dataset.
Results: Of the 82 eligible patients, 79 (96.3%) were cured after undergoing LR + LGA-BD, 74 (90.2%) were pathologically negative for LN metastases, and 5 (6.1%) had LN metastases, but these findings were only observed in the LGA basin. Similarly, of the 406 eligible tumors in the validation dataset, 396 (97.5%) were potentially curative. Tumors in the lesser curvature, post-endoscopic resection status, and small tumors (<20 mm) were considered to be stronger indicators of LR + LGA-BD as all subpopulation cases met our feasibility criteria.
Conclusions: More than 95% of the patients with u-EGC might be eligible for LR + LGA-BD. This function-preserving procedure may contribute to the development of u-EGC without pathological LN metastases, especially for tumors located at the lesser curvature.

Keywords: Gastric cancer; Gastrectomy; Lymph node dissection; Minimally invasive surgical procedures

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INTRODUCTION

Early gastric cancer (EGC), which is not eligible for or not cured after endoscopic submucosal dissection (ESD), requires radical gastrectomy with D1/D1+ lymphadenectomy; however, the incidence of regional lymph node (LN) metastasis is only 20% or less [1,2]. Post-gastrectomy syndrome (PGS), which is associated with the surgical removal of the stomach, is an unavoidable drawback of radical gastrectomy, leading to permanently impaired living status and quality of life [3,4]. In particular, total gastrectomy (TG) or proximal gastrectomy (PG) for upper-third EGC (u-EGC) is associated with a higher loss (13.8%/10.9%) of body weight compared with that of distal gastrectomy [5]. If pathologically negative LN metastases are correctly diagnosed preoperatively, >80% of EGC patients may not require gastrectomy with LN dissection, thus preventing PGS.

Local resection (LR) with lymphatic basin dissection (BD) is a gastric function-preserving surgery [6] and may provide survival benefits for patients without LN metastases. This procedure was previously known as sentinel node (SN) navigation surgery [7,8]; BD, which involves dissection of the SN, is initially performed, followed by function-preserving radical gastrectomy according to the metastatic status of the SN. Patients with a single SN basin drainage are considered eligible for this procedure[6] and have an advantage in terms of quality of life after surgery [9]. Despite the ideal concept, this procedure is not widely applied in clinical situations because SN navigation requires the use of a dual tracer method including radioisotopes [10], thus limiting its application in experienced facilities [11].

In general, gastric regional LNs are divided into five SN basins along with the following main gastric arteries: the left gastric artery (LGA), right gastric artery (RGA), left gastroepiploic artery (LGEA), right gastroepiploic artery (RGEA), and posterior gastric artery (PGA) [12]. According to the results of a multicenter trial on SN navigation surgery, the SN distribution of upper-third gastric cancer was mostly (96%–100%) in the lymphatic basin along the LGA, with less than 11% in other basins, excluding the tumor located in the greater curvature [7]. Another study also revealed that the lymphatic stream in almost all areas of the upper third of the stomach was the LGA, and the area of the LGEA was limited [13]. In addition, the distal side, the RGA, or the RGEA had no lymphatic stream.

Based on the LGA-dominant lymphatic flow and limited flow to other lymphatic basins in the upper third of the stomach, we hypothesized that prophylactic BD of the LGA (LGA-BD, **Fig. 1A**) might have surgical outcomes similar to that of SN navigation surgery in patients with u-EGC. This hypothesis was validated in this study.

MATERIALS AND METHODS

Inclusion criteria and data collection

A prospectively collected gastric cancer data were retrospectively reviewed to identify patients who underwent gastrectomy at the University of Tsukuba Hospital between July 2006 and December 2020. Patients (1) diagnosed with primary gastric cancer, (2) with pathological tumor invasion limited to the mucosa or submucosa (pT1), and (3) with tumors in the upper third of the stomach, which is divided into three portions by the lines connecting the trisected points on the lesser and greater curvatures, which are located in the upper third, were included in this study [14]. Patients who had esophageal invasion, esophagogastric

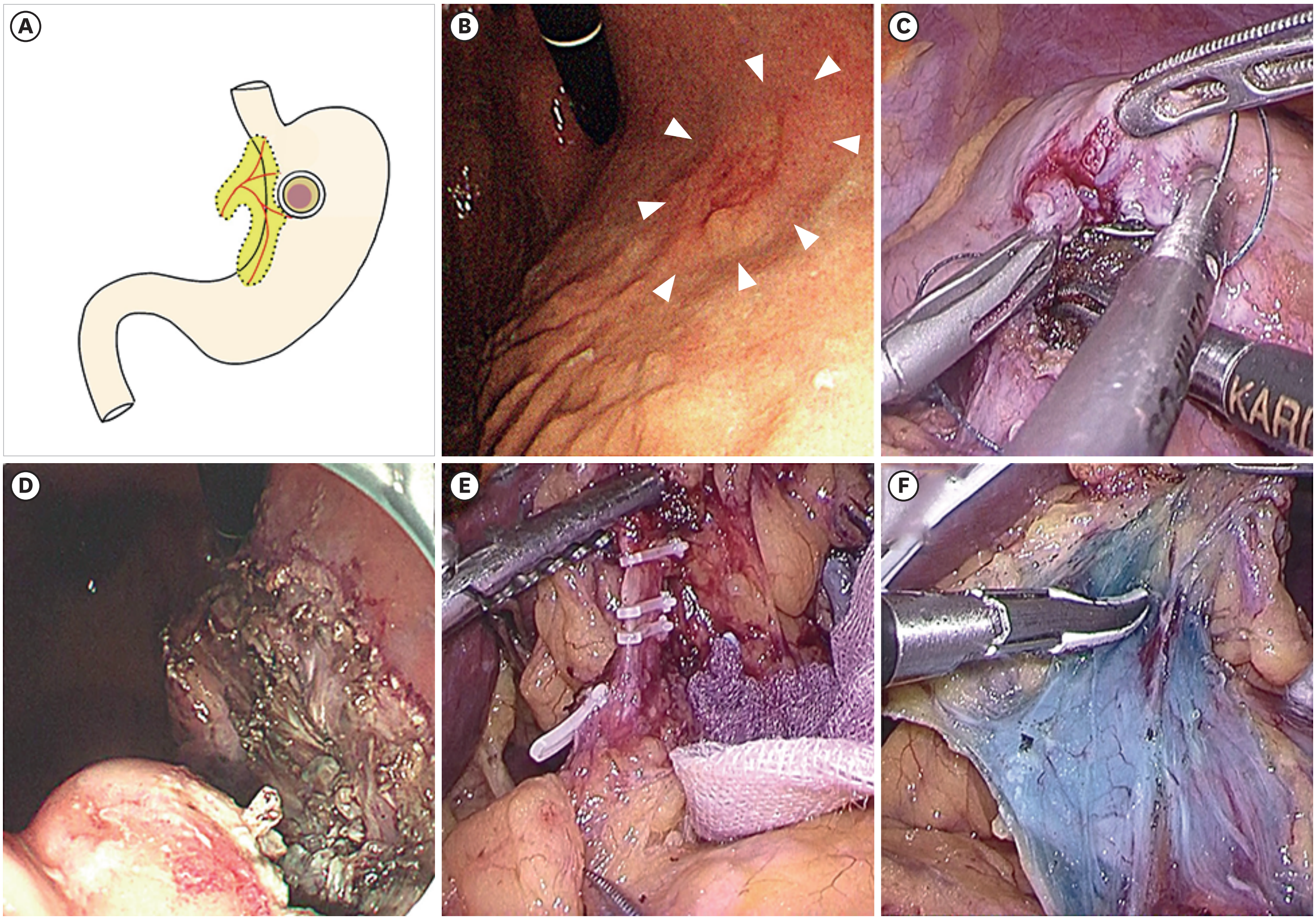

Fig. 1. Tumor findings and laparoscopic LR procedure (non-exposed endoscopic wall inversion surgery, NEWS) with LGA-BD. (A) Schema of LR + LGA-BD. The tumor (purple circle) was removed through LR, and the lymphatic basin along the left gastric artery (LGA, yellow area) was dissected. (B) Depressed-type early gastric cancer is located in the lesser curvature of the upper-third stomach before endoscopic submucosal dissection (arrowheads). (C) Seromuscular suture closure and spontaneous inversion of the dissected area. (D) Mucosubmucosal layer dissection using endoscopy and oral harvesting of the specimen. (E) LGA was cut at the root. (F) The entire lymphatic basin along the LGA was removed.
LR = local resection; LGA-BD = LGA basin dissection.

junction (EGJ) cancer, and tumors in the border area between the upper and middle third or those that extended to the middle third of the stomach were excluded.

The clinical characteristics (age, sex, surgical procedure, and recurrence) and pathological factors (tumor location, size, histological type, pathological T stage, N stage, number, and station of LN metastases) were evaluated. The LN stations were classified according to the Japanese Classification of Gastric Carcinoma [14].

Additional informed consent was obtained from all patients, and their information was identified. This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the Tsukuba Clinical Research and Development Organization (T-CReDO, R01-016).

Surgical procedure of LR + LGA-BD

LR + LGA-BD was performed in a patient with u-EGC, diagnosed as non-curative after ESD; the patient showed submucosal tumor invasion, lymphatic invasion, and vertical cutting

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margin. Although the metastasis risk was classified as high (5 points) according to the eCura system [15], the patient requested to preserve the stomach and refused to undergo TG at a previous hospital. The tumor was located in the lesser curvature of the upper third of the stomach (**Fig. 1B**). Therefore, this procedure was performed after obtaining informed consent from the patient.

LR was performed using a combination of laparoscopy and endoscopy, which is called the non-exposed endoscopic wall inversion surgery technique (NEWS [16], **Fig. 1C and D**), to avoid exposure of the remaining cancer cells to the abdominal cavity during laparoscopy. The LGA was cut at the root (**Fig. 1E**), and the whole lymphatic basin of the LGA was removed, including LN stations 1, 3a, and 7 (**Fig. 1F**). After harvesting, 9 LNs that were picked up from the LGA basin at the back table were confirmed to be pathologically negative for LN metastases through intraoperative frozen section biopsy. The hepatic and pyloric branches of the anterior vagal trunk were also preserved. The postoperative pathological diagnosis of this case revealed the absence of residual cancer in the primary lesion of the ESD scar and the absence of metastases in 14 LNs retrieved from the LGA basin. Without performing additional gastrectomy, the patient did not experience tumor recurrence in the follow-up period; PGS or body weight loss was not also observed.

Validation of surgical sufficiency

Theoretically, this procedure can switched to a radical surgery if the cancer cells exist, but only in the primary tumor location without any pathological LN metastases (pN0), or if LN metastases exist only in the LGA lymphatic basin ($pN+_{LGA}$). Therefore, the sufficiency of this procedure is measured based on the percentage of pN0 and $pN+_{LGA}$. The surgical sufficiency was also evaluated using the estimated contributing factor subgroups: presence or absence of preoperative ESD, tumor circumference location, tumor size, and histological type (differentiated or undifferentiated). Additionally, the correlation between LN metastases of the LGA and other basins (non-LGA) was evaluated.

External validation dataset

Since the number of patients who fulfilled the eligibility criteria was relatively small to verify the objective significance of this procedure, a commercially available open-source database [17] was used as an external validation dataset. This dataset included the clinicopathological data of 15,604 patients with gastric cancer who underwent radical surgery at the Cancer Institute Hospital. A total of 406 validation data were selected using the following two sorting algorithms: pathological tumor depth was indicated as “M” or “SM,” while the tumor location was indicated “U” (**Supplementary Fig. 1**). This dataset did not include all variables in all case records; therefore, the number of cases in the subgroup analysis was fewer than the total eligible cases due to the lack of categorical data.

Statistical analysis

The continuous and categorical data were expressed as median values with ranges and total counts with associated percentile values, respectively. The categorical data were analyzed using the chi-square test. Statistical significance was set at $P<0.05$. All statistical analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA).

Ethics statements

All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the 1964 Declaration

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of Helsinki and its later versions. Informed consent was obtained from all patients. This study was approved by the ethics committee of Tsukuba Clinical Research and Development Organization (T-CReDO, R01-016).

RESULTS

Patients' characteristics

During the study period, 921 patients underwent surgery for primary gastric cancer, and 436 (47.3%) had pT1 tumors. Eighty-two patients with u-EGC were included in this study (**Supplementary Fig. 1**). The patients' characteristics are summarized in **Table 1**. Eight patients (9.8%) were positive for LN metastases. Thirty (36.6%), 45 (54.9%), and 6 (7.3%) patients underwent TG, PG, and subtotal gastrectomy (sTG), respectively. Recurrence occurred in one patient (1.2%) with liver metastasis, but LN recurrence was not observed.

Risk factors and distribution of LN metastases

A comparison of the pathological factors between patients with LN metastases and those without LN metastases is shown in **Supplementary Table 1**. Positive lymphatic invasion was more strongly associated with LN metastasis compared with negative lymphatic invasion (28.0 vs. 1.8%, P=0.001). A tumor size of >20 mm (14.0 vs. 3.1%, P=0.141), submucosal tumor invasion (12.7 vs. 0%, P=0.188), and positive venous invasion (16.0 vs. 7.0%, P=0.239) also seemed to be positively correlated, but this finding was not considered significant.

Table 1. Clinicopathological characteristics of the patients

Variable	pT1, upper third (n=82)
Age, yr, median (range)	71 (49–85)
Sex	
Female	25 (30.5)
Male	57 (69.5)
Tumor size (mm)	
Median (range)	25 (7–80)
Invasive depth	
M	19 (23.2)
SM1	8 (9.8)
SM2	55 (67.0)
Histological type	
Differentiated	57 (69.5)
Undifferentiated	25 (30.5)
Lymph node metastasis	
Negative	74 (90.2)
Positive	8 (9.8)
Preoperative ESD	
Yes	15 (18.3)
No	67 (81.7)
Surgical procedure	
Total gastrectomy	30 (36.6)
Proximal gastrectomy	45 (54.9)
Subtotal gastrectomy	6 (7.3)
NEWS + LGA-BD	1 (1.2)
Recurrence	1 (1.2)
Liver	1 (1.2)
Lymph node	0

M = mucosa; SM = submucosa; ESD = endoscopic submucosal dissection; NEWS = non-exposed endoscopic wall-inversion surgery; LGA-BD = left gastric artery basin dissection.

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Table 2. Association between tumor circumferences and metastatic lymph node basin and station

Lymphatic basin	LN station	Tumor location (experimental dataset)				Tumor location (validation dataset)			
		Ant (n=12)	Post (n=19)	Less (n=47)	Gre (n=4)	Ant (n=45)	Post (n=130)	Less (n=138)	Gre (n=18)
pN+ (number of cases)		0	3 (15.8)	4 (8.5)	1 (25.0)	5 (11.1)	8 (6.2)	9 (6.5)	3 (16.7)
LGA	1	0	2 (10.5)	1 (2.1)	0	1 (2.2)	1 (0.7)	4 (2.9)	
	3a	0	1 (10.0)	3 (6.4)	1 (25.0)	4 (8.9)	5 (3.8)	6 (4.3)	
	7	0	1 (5.3)	1 (2.1)	0	2 (4.4)	0	3 (2.2)	
LGEA	4sa	0	0	0	0	0	0	0	1 (5.6)
	4sb	0	0	0	1 (25.0)	0	0	0	0
PGA	11p	0	0	0	0	0	0	0	0
	11d	0	1 (5.3)	0	0	0	0	0	0
LIPA	2	0	1 (5.3)	0	0	1 (2.2)	2 (1.5)	0	
Other	4d	0	0	0	0	0	0	0	1 (5.6)
	8a	0	0	0	0	1 (2.2)	0	1 (0.7)	
	9	0	0	0	0	2 (4.4)	1 (0.7)	2 (1.4)	1 (5.6)

LN = lymph node; Ant = anterior wall; Post = posterior wall; Less = lesser curvature; Gre = greater curvature; pN+ = pathologically positive lymph node metastasis; LGA = left gastric artery; LGEA = left gastroepiploic artery; PGA = posterior gastric artery; LIPA = left inferior phrenic artery.

The distribution of the LN metastases is shown in **Table 2**. The circumferential locations of the primary cancer with positive LN metastasis were in the lesser curvature in 4 (8.5%) out of 47 patients, in the posterior wall in 3 (15.8%) out of 19 patients, and in the greater curvature in 1 (25.0%) out of 4 patients. No LN metastases were observed in the tumors located in the anterior wall. The tumors located in the lesser curvature only metastasized to the LGA basin. By contrast, posterior wall tumors metastasized to the LGA, PGA, and left inferior phrenic artery. Greater curvature tumors metastasized to the LGA and LGEA basins.

In the validation dataset, pathologically positive LN metastases were observed in 25 (6.2%) of the 406 eligible patients. LN metastases of the lesser curvature tumor were dominant in the LGA basin; three patients had second-tier LN metastases, stations 8a and 9. LGEA basin metastasis was observed in only 1 (5.6%) of 18 patients with greater curvature tumor, but PGA basin metastases were not observed. One (2.2%) of the 45 patients with anterior wall tumors and 2 (1.5%) of the 130 patients with posterior wall tumors showed LN metastases at station 2 located along the cardiac branch of the left inferior phrenic artery. LN metastases in the RGA and RGEA basins were not observed in the validation datasets.

Probability of surgical sufficiency

The surgical sufficiency rates for LR + LGA-BD are summarized in **Table 3**. Pathologically negative LN metastases were found in 74 (90.2%) patients, while 5 (6.1%) patients were positive for LN metastases in the LGA basin ($pN+_{LGA}$); therefore, the surgical sufficiency rate was 96.3%. Positive LN metastases were detected outside the LGA basin in three patients (3.7%), but two (2.5%) of them were also positive for LN metastases in the LGA basin. In the validation dataset, 375 (92.4%) patients were pathologically negative for LN metastases, while 21 (5.2%) had $pN+_{LGA}$. Therefore, the surgical sufficiency rate was 97.5%.

To clarify the indications for this procedure, the factors influencing the LN metastasis status and location were compared. The surgical sufficiency rate was 100% in post-ESD patients, patients with tumors in the lesser curvature, and patients with a tumor size of <20 mm. In the validation dataset, the surgical sufficiency rates in patients with tumors located in the lesser curvature and tumor of <20 mm in size were 98.6% and 98.9%, respectively. The surgical sufficiency in post-ESD patients was not evaluated in the validation dataset owing to the lack of data. Based on the histological subtype, the surgical sufficiency rates in patients

Table 3. Surgical sufficiency of local resection with left gastric artery basin dissection

Variable	Experimental dataset (n=82)				Validation dataset (n=406)			
	n	pN0 (a)	$pN+_{LGA}$ (b)	Sufficiency (%) = (a) + (b)	n	pN0 (a)	$pN+_{LGA}$ (b)	Sufficiency (%) = (a) + (b)
Total	82	74	5	96.3	406	375	21	97.5
Preoperative ESD								
Yes	16	15	1	100	1	1	0	100
No	66	59	4	95.5	51	46	4	98.0
Circumference								
Ant	12	12	0	100	45	40	3	95.6
Post	19	16	1	89.5	130	122	5	97.7
Less	47	43	4	100	138	129	7	98.6
Gre	4	3	0	75.0	18	15	0	83.3
Tumor size, mm								
≤20	32	31	1	100	185	177	6	98.9
>20, ≤30	25	21	2	92.0	115	101	9	95.7
>30	25	22	2	96.0	107	98	6	97.2
Histological type								
Differentiated	57	52	3	96.5	253	240	9	98.4
Undifferentiated	25	22	2	96.0	152	134	12	96.1

pN0: pathologically negative lymph node metastasis, $pN+_{LGA}$: pathologically positive lymph node metastasis exists only in the left gastric artery lymphatic basin, ESD: endoscopic submucosal dissection, Ant: anterior wall, Post: posterior wall, Less: lesser curvature, Gre: greater curvature.

with differentiated and undifferentiated types of gastric cancer were 96.5% and 96.0% in the experimental dataset and 98.4% and 96.1% in the validation dataset, respectively.

Findings that should be excluded from the application of LR + LGA-BD

To clarify the appropriate target of LR + LGA-BD and to avoid inadequate treatment of patients who are potentially cured by conventional radical gastrectomy, the details of three patients with LN metastases outside the LGA basin were summarized (**Fig. 2**). Two (patients 2 and 3) of the three patients were preoperatively diagnosed with T2 advanced cancer; therefore, they could be excluded from the study prior to surgery. In addition, these patients had LN metastases in the LGA basin; thus, additional radical gastrectomy could be considered after confirming the presence of pathological metastases in the LGA basin. By contrast, one patient (patient 1) only had paracardial LN metastases (station 2) but not in the LGA basin. The LN metastasis status in the LGA and other basins was also compared (**Supplementary Table 2**). Seventy-four (98.7%) of 75 patients who were pathologically negative for LN metastases in the LGA basin did not have LN metastases in other basins, except in one patient (patient 1). On the contrary, two (28.6%) of the seven patients who were pathologically positive for LN metastases in the LGA basin also had LN metastases in other lymphatic basins.

DISCUSSION

This retrospective analysis revealed that more than 95% of patients with u-EGC might achieve complete cancer removal by LR with LGA-BD. An ideal eligible population for this procedure should be u-EGC patients who (1) previously received non-curative ESD treatment and required additional surgical resection, (2) developed tumors in the lesser curvature, and/or (3) had tumors of <20 mm in size. Additionally, if LN metastasis did not occur in the LGA lymphatic basin, 98.7% of patients did not also develop LN metastases in other lymphatic basins; therefore, additional radical gastrectomy might be avoided.

Currently, patients with u-EGC who are ineligible for ESD are recommended to undergo PG or TG [14]. Several studies have shown equivalent survival outcomes between PG and TG

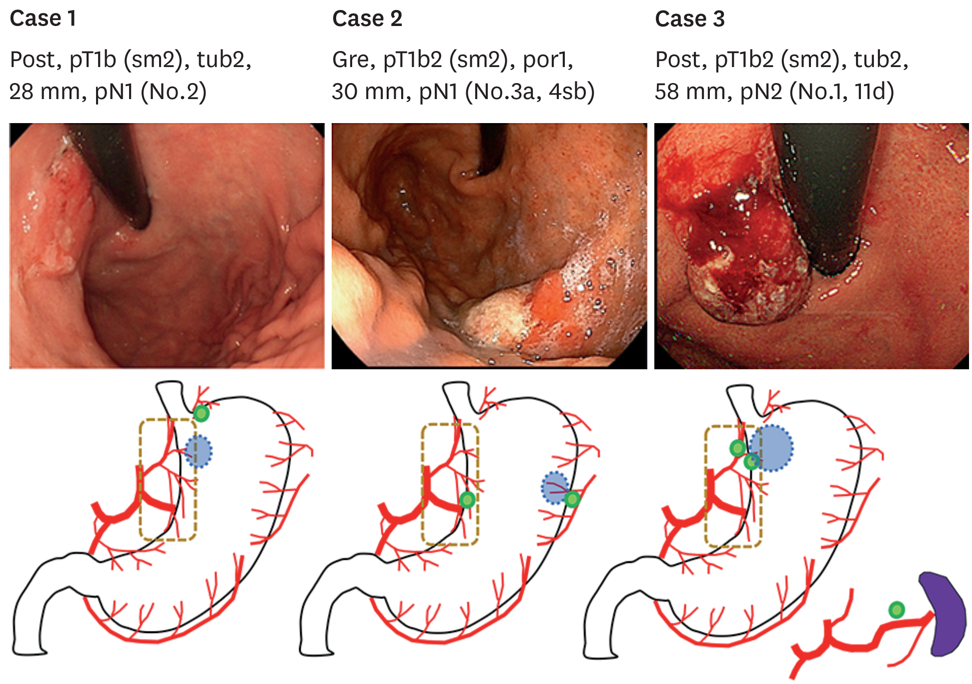

Fig. 2. Endoscopic findings and distribution of tumor and metastatic lymph node in three patients considered ineligible for local resection with left gastric artery basin dissection. The blue dotted circle indicates tumor location, while the green circle indicates metastatic lymph node. The gold dotted line indicates the area of lymphatic basin along the left gastric artery.
Post = posterior wall; Gre = greater curvature.

[18,19]. Additionally, patients with advanced gastric cancer of T2/T3 are also considered a candidate for PG because LN metastases along the RGA and RGEA rarely occur in tumors located in the upper third of the stomach [20]. Therefore, from the perspective of radical LN dissection, the lymphatic flow of the following three basins should be considered in patients with u-EGC: LGA, LGEA, and PGA. The main lymphatic and vascular flows of the stomach are the LGA and RGEA [13]; therefore, the main stream of lymphatic flow in the upper third of the stomach is the LGA. This has been verified by several studies using SN mapping. Kitagawa et al. [10] showed the distribution of SN in the upper third of the stomach. The rate of SN detection in LGA was highest (station 1: 51%, station 3: 79%, and station 7: 39%), whereas those in LGEA (station 4sb: 9%) and PGA (station 11p: 4%, station 11d: 4%) were relatively low. Kinami et al. [12] showed a slightly higher frequency of SN staining in the LGEA (25.6%) and PGA (23.1%), while the highest SN staining was also observed in the LGA (94.9%). This evidence forms the basis of the current study, and the theoretical achievement of radical surgery was acceptably high (96.3%).

Tumors limited to the lesser curvature are more appropriate targets for this procedure because they are adjacent to the LGA basin, and most of the patients with this type of tumors might undergo LR + LGA-BD. However, one patient (**Fig. 2**, patient 1), which was considered an inappropriate target of LGA-BD, showed a posterior wall tumor close to the lesser curvature. The patient had LN metastases outside of the LGA basin (LN station 2). Station 2 was defined as the left paracardial LN along the esophago-cardiac branch of the left inferior phrenic artery [11]. These LNs were completely removed through TG or PG, and the rate of LN metastasis was not low. Therefore, patients with tumors on the left side of the cardia or EGJ, which are adjacent to LN station 2, should not be indicated for LR + LGA-BD. On the

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contrary, the requirement for LN dissection at station 2 in patients with upper-third tumors, which are distant from the EGJ, remains controversial. Jiang et al. [21] proposed laparoscopy-assisted sTG for u-EGC patients to improve the surgical outcomes and quality of life than TG/PG by preserving the cardia [22]; however, this procedure did not include dissection of LN station 2. Therefore, patients with tumors eligible for sTG may undergo our procedure. To reduce the risk of missed LN metastases at station 2, near-infrared imaging with indocyanine green (ICG) staining may be useful for detecting LNs and sampling [23,24]. However, the submucosal injection of ICG dye is not currently approved by the Japanese medical insurance; hence, this method will only be used in clinical trials.

Patients with tumors in the greater curvature should not undergo LR + LGA-BD because they are adjacent to the LGEA lymphatic basin. However, u-EGC located in this area was less frequent; only four patients (3.6%) were included in this analysis, and 18 (4.4%) patients were included in the validation dataset. By contrast, tumors located in the posterior wall were more common (24.1%) and were distributed in various lymphatic basins. Therefore, they should also be excluded from the LR + LGA-BD.

In this study, the surgical sufficiency rate was 100% in post-ESD patients. These patients were considered to have a low risk of LN metastases despite the non-curative judgment after ESD; only one patient (6.3%) had LN metastases, which occurred in the LGA basin. The actual LN metastasis ratio of patients requiring additional gastrectomy after non-curative ESD were reported to be 10% [25]; therefore, more than 90% of u-EGC patients theoretically do not require radical gastrectomy. Additionally, tumors <20 mm in size showed a 100% surgical sufficiency rate. However, small tumors that are eligible for LGA-BD are limited, since this size criterion is same as the indication for ESD. The sufficiency rates of tumors >30 mm in size was as high as 96.0%. Because of the limited number of patients with larger tumors, the cut-off size of tumors could not be defined based on these study results alone. The criterion for SN navigation surgery was a tumor size of <40 mm as reported in several studies [8,10]; therefore, it might be an appropriate cut-off for LGA-BD. Accordingly, in cases where the tumor is located in the lesser curvature and is relatively small, LR + LGA-BD might help preserve the stomach function.

Adequate identification of patients requiring additional radical gastrectomy is also important. In our study, 98.7% of patients who had no LN metastases in the LGA basin did not have LN metastases in other basins. Although our procedure omitted the SN navigation, the extraction rate of pN0 or pN+ located in the LGA basin ($pN+_{LGA}$) was as high as the SN detection rate using the dual tracer method (reported as 97.5% [10]). Therefore, if the patient has no LN metastases in the LGA basin, an additional gastrectomy may not be required. However, the requirement for additional gastrectomy in patients with LN metastases in the LGA basin remains controversial. The risk of LN metastases in the lymphatic basins other than the LGA is 28.6%; therefore, additional gastrectomy is essentially recommended. However, the proportion of elderly patients with gastric cancer has increased, and the validity of radical gastrectomy for such older patients remains under debate. Gastrectomy, especially TG, may have limited oncological benefits in comparison to best supportive care and may worsen the quality of life of patients aged >85 years [26]. Thus, especially for older patients with severe comorbidities, additional gastrectomy must be avoided, even if the surgery is noncurative.

The present study has some limitations. First, it was a retrospective analysis with a small sample size. To overcome this limitation, a commercially available external validation dataset

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from high-volume hospitals were used, and consistent results were obtained for this dataset. Second, the indication for LR + LGA-BD was determined based on the circumferential location of the tumor, but the circumferential borders between the two areas were ambiguous and had no landmarks (**Fig. 3A**). In this study, the circumferential location was classified according to the database description, but the ambiguous borders might cause some problems for future research in this field. Hence, we have two proposals regarding this issue. First, a new quadrant classification is suggested, in which the border is rotated 45 degrees (**Fig. 3B**). In this classification, the midlines of the anterior and posterior walls, and the lesser and greater curvatures are identified as borders. The advantages of this new classification are as follows: 1) the borders between two areas are easily and clearly defined, and 2) axes of the borders are consistent with each lymphatic flow: LGA, LGEA, and PGA. Therefore, it may have better utility for studies on function-preserving surgery including SN navigation. Another proposal is the use of a clock-like classification (**Fig. 3C**). This classification is helpful in explaining the surgical indication, such as LGA-BD. Based on the results of this study, we identified the appropriate indications (green), possible indications (light green), and contraindications (red) (**Fig. 3C**). Finally, surgical sufficiency is defined in this study as the calculated rate and has not been established. Thus, it may just be a desk theory and requires prospective evaluation. However, the diagnostic accuracy of computed tomography for LN metastases is very limited and unreliable, especially in EGC [27], and retrospective evaluation using surgically resected specimens is the only reliable method to estimate the incidence of LN metastases; the

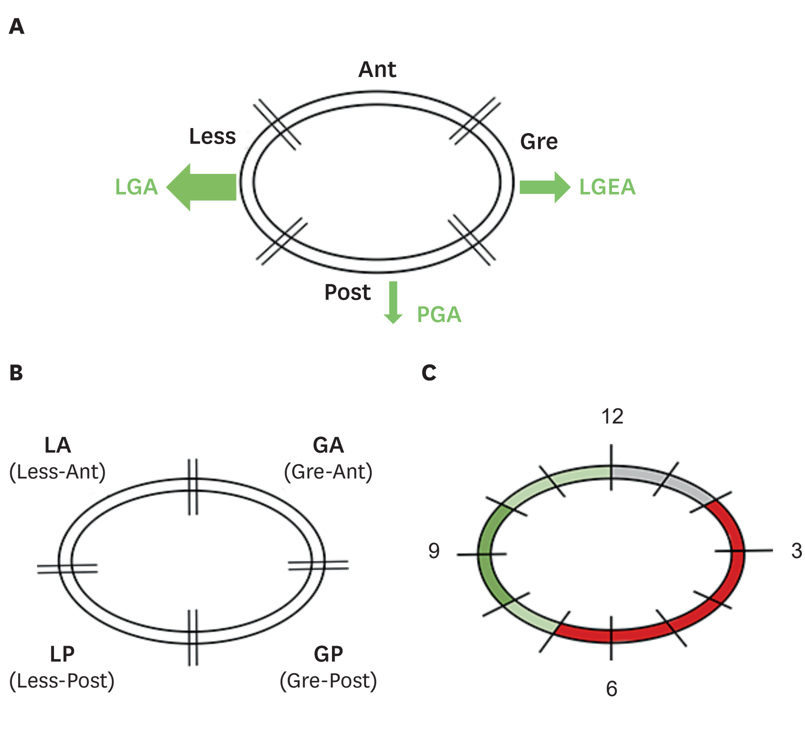

Fig. 3. Current circumferential classification of the stomach according to the Japanese Classification of Gastric Carcinoma [14]. Green arrows show the lymphatic flows, and the width of the arrows represents the amount of lymphatic flow. (A) Proposal of a new quadrant circumferential classification. The borders are the midlines of the anterior and posterior walls and lesser and greater curvatures. (B) A clock-like classification. The colors indicate possible application of LGA-BD. Green denotes better indication; light green denotes potential indication; red denotes contraindication; gray indicates unknown. (C) Algorithm for the possible application of local resection + LGA-BD (gray, broken line). The current standard algorithm is indicated by a solid blue line.
Ant = anterior wall; Gre = greater curvature; Post = posterior wall; Less = tumor located in lesser curvature; LGA = left gastric artery; LGEA = left gastroepiploic artery; PGA = posterior gastric artery; ESD = endoscopic submucosal dissection; LGA-BD = LGA basin dissection; <4 cm = tumor smaller than 4 cm; Frozen Bx = intraoperative frozen section biopsy; pN0 = pathologically negative lymph node metastasis; R0 = no residual tumor.

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indications for endoscopic treatment were established using this method [28]. Therefore, this study is significant in u-EGC patients to prevent unnecessary radical gastrectomy. In the future, a prospective feasibility study will be conducted to evaluate the efficacy of LR + LGA-BD.

In conclusion, u-EGC, which has a low risk of LN metastasis but is ineligible for endoscopic resection, may achieve complete cancer removal through LR with prophylactic LGA-BD without SN navigation. The indications for LGA-BD are as follows: 1) u-EGC (upper-third, pT1a or pT1b), 2) tumor located in the lesser curvature, and 3) relatively smaller tumor (<40 mm as the cut-off) (**Fig. 3D**). This procedure has less risk of post-gastrectomy dysfunction compared with radical gastrectomy, such as TG or PG; therefore, it is a better treatment option if oncological safety is confirmed.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Pathological risk factors for lymph node metastases

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Supplementary Table 2

Correlation between lymph node metastasis in the left gastric artery and other lymphatic basins

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Supplementary Fig. 1

Study flow diagram showing the patients in experimental dataset and case sorting in the external validation dataset.

Click here to view

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