Optimal extent of lymph node dissection for remnant advanced gastric carcinoma after distal gastrectomy: a retrospective analysis of more than 3000 patients from the nationwide registry of the Japanese Gastric Cancer Association

Hitoshi Katai¹ · Takashi Ishikawa² · Kohei Akazawa² · Takeo Fukagawa³ · Yoh Isobe⁴ · Isao Miyashiro⁵ · Ichiro Oda⁶ · Shunichi Tsujitani⁷ · Hiroyuki Ono⁸ · Satoshi Tanabe⁹ · Souya Nunobe¹⁰ · Satoshi Suzuki¹¹ · Yoshihiro Kakeji¹¹ · the Registration Committee of the Japanese Gastric Cancer Association

Received: 28 February 2020 / Accepted: 3 May 2020 / Published online: 17 May 2020
© The International Gastric Cancer Association and The Japanese Gastric Cancer Association 2020

Abstract

Background No guidelines are available for defining the extent of lymph node (LN) dissection in patients with remnant gastric carcinoma (RGC). Hence, this retrospective study aimed to determine the optimal extent of LN dissection in patients with RGC.

Methods We retrospectively evaluated the therapeutic outcomes of node dissection for RGC from a nationwide registry. When the metastatic rate or 5-year survival rate exceeded 10%, dissection was recommended. We calculated the dissection index by multiplying the incidence of metastasis at that nodal station by the 5-year survival rate of patients with metastasis at the station. A dissection index of > 1.0 was considered significant.

Results We included 1133 patients with RGC (T2–T4 tumor) who had undergone distal gastrectomy as the primary surgery for the evaluation of the survival benefit of nodal dissection. Any regional node station was considered significant. When the primary surgery was for malignant disease, the index was high for Nos. 3 (10.2), 7 (9.5), 1 (7.1), and 9 (8.0) nodes. For nodes at the splenic hilum, the index value was 4.4, which was higher than that for the perigastric nodes (Nos. 4sa and 4sb). The index for No. 10 nodes was the highest (10.5) when tumors involved a greater curvature.

Conclusions The therapeutic strategy for RGC remains the same, regardless of the histology of the primary disease during the initial surgery. Total gastrectomy and dissection of the perigastric LNs (Nos. 1–4), suprapancreatic LNs (Nos. 7–9 and 11), and LNs at the splenic hilum (No. 10) are justified.

Keywords Upper GI · Remnant gastric carcinoma · Lymph node dissection

✉ Hitoshi Katai
hkatai@ncc.go.jp

¹ Department of Gastric Surgery, National Cancer Center Hospital, 5-1-1 Tsukiji, chuo-ku, Tokyo 104-0045, Japan

² Department of Medical Informatics, Niigata University Medical and Dental Hospital, Niigata, Japan

³ Department of Surgery, Teikyo University School of Medicine, Tokyo, Japan

⁴ Department of Surgery, National Hospital Organization Tokyo Medical Center, Tokyo, Japan

⁵ Cancer Control Center, Osaka International Cancer Institute, Osaka, Japan

⁶ Endoscopy Division, National Cancer Center Hospital, Tokyo, Japan

⁷ Department of Gastroenterological Surgery, Tottori University, Tottori, Japan

⁸ Endoscopy Division, Shizuoka Cancer Center, Shizuoka, Japan

⁹ Department of Advanced Medicine Research and Development Center for New Medical Frontiers, Kitasato University School of Medicine, Kanagawa, Japan

¹⁰ Department of Gastroenterological Surgery, Cancer Institute Ariake Hospital, Tokyo, Japan

¹¹ Division of Gastrointestinal Surgery, Department of Surgery, Kobe University Graduate School of Medicine, Kobe, Japan

Introduction

The beneficial effect of systematic lymph node (LN) dissection for primary gastric carcinoma is well documented and acknowledged. On the basis of retrospective historical data of the involved nodes in patients with gastric carcinoma, the Japanese gastric cancer treatment guidelines define the optimal extent of lymphadenectomy for this cancer [1]. Meanwhile, the optimal extent of LN dissection for remnant gastric carcinoma (RGC) cases remains undefined, not only in the aforementioned guidelines but also in any international guidelines for gastric cancer treatment.

The lymphatic flow in RGC cases may be altered by the LN dissection, vascular dissection, and anastomosis type at the initial surgery of a primary tumor, as well as by the development of adhesions after the initial surgery.

The proportion of remnant gastric carcinoma was 2.4% of entire gastric carcinoma [2]. Defining the optimal extent of node dissection in RGC cases is difficult, mainly because of the relative rarity of this disease. Only small sample sizes have been analyzed. Even though the number of patients is particularly small, with the guidelines, surgeons can make a positive decision on extent of surgery. For patients, the guidelines is an important decision factor in promoting their treatment while communication with the attending surgeon. Since lymph node dissection is a pillar of gastric cancer treatment, there is a clinical question in the Japanese gastric cancer treatment guidelines; what is the optimal extent of lymph node dissection? The guidelines recommend that non-dissected gastric lymph nodes be dissected during the first surgery [3]. However, the significance of dissection of jejunal LN and splenic LN is uncertain. The Japanese Gastric Cancer Association Guideline Committee requested that an optimal dissection range be determined.

Therefore, we present the results of a large-scale study conducted using data from a nationwide registry.

Patients and methods

Hospitals affiliated to the Japanese Gastric Cancer Association (JGCA) voluntarily downloaded and fulfilled the requirements for the database requested by the JGCA and the sent data of patients 5 years after they had undergone resection. We had retrospectively collected data on 54 items, including the surgical procedures performed, pathological diagnosis, and prognosis, pertaining to patients with RGC who had been treated surgically between 2002 and 2008. The JGCA Registration Committee reviewed and analyzed the accumulated patient data according to

previously reported methods [2]. Furthermore, the items were defined and documented according to the JGCA Japanese Classification of Gastric Carcinoma [4].

RGC encompasses all carcinomas arising in the remnant stomach following gastrectomy, irrespective of the histology (benign or malignant), risk of recurrence, extent of resection, or method of reconstruction following the resection of the primary lesion [4].

Using the Kaplan–Meier method, we calculated the 5-year overall survival rates (5YOSs) for various subsets of prognostic factors. Deaths from the primary disease and from any cause observed during the 5-year postoperative period were counted as events in the survival analysis. This nationwide registration program was approved by the ethics committee of the JGCA. Every hospital discloses information to the patients about the nationwide registry of the JGCA. Patients were excluded in this analysis only when they specifically indicated that they were unwilling to participate.

Handling of the resected specimen and giving the station numbers to the lymph nodes are carried out according to Japanese classification of gastric carcinoma [4].

For each patient, surgeon assessed gastric LN specimens immediately after the resection, separating the perigastric tissue into LN stations and identifying and harvesting. The left gastric artery was not transected at that root for the benign group and occasionally for the malignant group. Under these circumstances we can recognize No. 7 LN during operation. Lymph nodes of stations No. 8, No. 9, and No. 11p were usually removed and identified separately during operation. This assessment was followed by evaluation by a pathologist.

To evaluate the therapeutic value of LN dissection at any nodal station, we determined the frequency of metastasis at that nodal station and calculated the cumulative 5YOS of patients with metastasis at that nodal station, irrespective of the presence/absence of metastasis at other nodal stations. We calculated the frequency of LN metastasis, with the number of dissected cases as the denominator and the number of positive cases of LN metastasis as the numerator. An index of the benefit gained by the dissection of each station was calculated by multiplying the frequency of metastasis at the LN station and the 5-year survival rate of patients with metastasis at that station.

Dissection was recommended when the metastatic rate or 5-year survival rate exceeded 10%. We also regarded the value of dissection as significant for indices exceeding 1.0. This cutoff value exceeds the minimum value of the index in the regional nodes (Japanese Classification of Gastric Carcinoma, 13th Edition) of the primary advanced gastric cancer [5, 6].

Results

Characteristics of the patients

This study enrolled 3405 patients with RGC from 234 institutions in Japan. Of these patients, 3205 had undergone gastric resection, obtaining a resection rate of 94.1% (3205/3405). Of the total number of participating patients, 31 did not have adenocarcinoma. After exclusion of these aforementioned patients, the data of the 3174 remaining patients who had undergone gastric resection were included in the analysis (Table 1).

The overall median time interval between the initial surgery and the second surgery for RGC was 16 (range 0–63) years; it was 7 (range 0–52) years in patients with malignant primary disease, and 36 (range 0.3–63) years in those with benign primary disease.

When the follow-up period was < 1825 days, the patients were regarded as “lost to follow-up.” Of the 3174 patients, 432 were lost to follow-up, yielding a follow-up rate of 86.4%. The 25th, 50th, and 75th percentile follow-up periods in the lost-to-follow-up patients were 212, 729, and 1296 days after the operation, respectively.

The patient demographics are summarized in Table 1. The median patient age was 71 years, the proportion of patients who were > 80 years old was 11.9%, and the male-to-female ratio was 5.2:1.

Regarding the histology of the primary disease, 37.6% of the cases were benign (Benign group), whereas 58.0% of the cases were malignant (Malignant group).

Table 1 also summarizes the surgical procedures adopted for the initial surgery. Distal gastrectomy was performed in 88.0% of patients, indicating the predominantly performed procedure. Meanwhile, pylorus-preserving gastrectomy, proximal gastrectomy, and local resection were performed in 2.4%, 4.8%, and 3.8% of cases, respectively.

Moreover, Billroth I reconstruction (BI) was the predominant type of reconstruction performed after primary gastrectomy, accounting for 50.2% of patients, followed by Billroth II reconstruction (BII) (35.4%) and then Roux-en-Y reconstruction (RY) (2.8%).

The most frequent macroscopic tumor type was type 0 (45.8%), followed by types 3 (16.9%), 2 (16.4%), and 1 (8.9%). The ratio of the differentiated type to the undifferentiated type of cancer was 1.2:1. Early gastric cancer (T1) was confirmed pathologically in 41.2% of the patients. Additionally, the ratio of mucosa to submucosa was 0.96:1.

Adjacent organ involvement was observed in 10.4%. The pancreatic tail (35.0%), liver (27.2%), and transverse colon (19.0%) were the most frequently involved.

In the 2793 patients who had undergone distal gastrectomy as the primary surgery, 37.4% of them experienced invasion of the anastomosis.

Of the total subject population, 28.9% had nodal involvement, and 13.0% had metastasis beyond pN2 (Anatomical Classification of the JGCA, 13th Edition). Peritoneal washing cytology was performed in 47.7% of all the patients, and 3.6% of them acquired a positive cytology rate. In addition, synchronous liver metastases and peritoneal seeding were found in 1.9% and 4.7%, respectively.

The surgical procedures adopted for the RGC are also summarized. Total gastrectomy was performed in 92.0% of the patients, indicating the predominantly performed type of gastrectomy, followed by subtotal gastrectomy (7.8%) and pancreatoduodenectomy (0.3%).

The spleen (17.7%), pancreatic tail and spleen (4.4%), transverse colon (3.6%), and liver (2.7%) were frequently resected.

R0 resection was performed in 85.4% of the patients, whereas R1 or R2 resection was performed in 13.1%.

Survival in patients after distal gastrectomy (Fig. 1)

Distal gastrectomy was performed in 2793 patients. We excluded patients who had not undergone reconstruction by the BI, BII, or RY procedure after primary gastrectomy, who underwent second surgery other than total gastrectomy, and who had missing values. Conversely, we included the data of the 2081 remaining patients who had undergone R0 total gastrectomy. Finally, we included 1133 T2–T4 patients who had undergone total gastrectomy with reconstruction by the BI, BII, or RY procedure after primary gastrectomy.

Splenectomy was performed in 553 (48.8%) of 1133 overall cases.

Moreover, we conducted the analysis separately according to the primary disease type (benign or malignant) for which the initial surgery was performed.

Survival in patients with pT2–T4 tumors (Tables 2 and 3)

The frequencies of LNs remaining at Nos. 1 and 3 stations were 43.8% and 24.3%, respectively, which were high even after the initial gastrectomy for malignant disease.

The frequency of involvement of Nos. 1, 2, 3, 4sa, and 4sb LNs was high, regardless of the reconstruction method employed after the primary gastrectomy in both the Malignant and Benign groups. The 5YOS by involvement at each nodal station was 15.9%–35.3% overall, and these LNs were recommended for dissection.

With regard to the suprapancreatic LNs (Nos. 7, 8, 9, and 11p LNs), at least 13% of the patients had remaining LNs at

Table 1 Patient characteristics
(3174 resected cases)

Category	Number of patients	%
Age (years), Median		
≤ 39	15	0.5
40–59	462	14.6
60–79	2319	73.1
≥ 80	378	11.9
Missing value	0	0
Gender		
Male	2659	83.8
Female	515	16.2
Missing value	0	0
Histology of the primary disease (resected cases)		
Benign	1194	37.6
Malignant	1841	58.0
Missing value	138	4.3
Procedures of primary surgery (resected cases)		
Distal gastrectomy	2793	88.0
Pylorus-preserving gastrectomy	76	2.4
Proximal gastrectomy	152	4.8
Local resection	120	3.8
Missing value	33	1.0
Reconstruction after primary surgery (resected cases)		
Billroth I	1594	50.2
Billroth II	1124	35.4
Roux-en-Y	88	2.8
Gastro-gastrostomy	111	3.5
Jejunal interposition	71	2.2
Esophagogastrostomy	87	2.7
Missing value	99	3.1
Tumor location		
U	1779	56.0
M	1105	34.8
L	237	7.5
Esophageal invasion	12	0.4
Duodenal invasion	5	0.5
Jejunal invasion	16	0.5
Entire remnant stomach	12	0.4
Missing value	8	0.3
Macroscopic type (JGCA)		
Type 0	1455	45.8
Type 1	283	8.9
Type 2	519	16.4
Type 3	536	16.9
Type 4	230	7.2
Type 5	149	4.7
Missing value	2	0.1
Histologic type		
Differentiated type	1729	54.5
Undifferentiated type	1423	44.8
Other types	22	0.7
Missing value	0	0
pT		

Table 1 (continued)

Category	Number of patients	%
M	642	20.2
SM	668	21.0
MP	425	13.4
SS	591	18.6
SE	503	15.8
SI	331	10.4
Missing value	14	0.4
Adjacent organ involvement (331 SI disease cases)		
Pancreas	116	35.0
Liver	90	27.2
Transverse colon	63	19.0
Diaphragm	18	5.4
Transverse mesocolon	13	3.9
Spleen	9	2.7
Small intestine	9	2.7
Abdominal wall	4	1.2
Gallbladder	2	0.6
Others	6	1.8
Missing value	1	0.3
Invasion of the anastomosis (2793 distal gastrectomy cases)		
Negative	1596	57.1
Positive	1045	37.4
Missing value	152	5.4
pN (JGCA 13th)		
0	2149	67.7
1	494	15.6
2	313	9.9
3	99	3.1
Missing value	119	3.7
pN (JGCA 14th)		
0	2137	67.3
1	453	14.3
2	281	8.9
3a	132	4.2
3b	50	1.6
Missing value	121	3.8
Cytology (resected cases)		
0	1398	44.0
1	115	3.6
X	1661	52.3
Hepatic metastasis		
0	3080	97.0
1	61	1.9
Missing value	33	1.0
Peritoneal metastasis		
0	2982	94.0
1	149	4.7
Missing value	43	1.4
M		
0	3043	95.9
1	97	3.1

Table 1 (continued)

Category	Number of patients	%
Missing value	34	1.1
Operative procedure		
Total gastrectomy	2919	92.0
Subtotal gastrectomy	246	7.8
Pancreatoduodenectomy	9	0.3
Missing value	0	0
Combined resection		
Spleen	561	17.7
Pancreas, spleen	139	4.4
Transverse colon	113	3.6
Liver	86	2.7
Small intestine	78	2.5
Thoracic esophagus	29	0.9
Diaphragm	11	0.3
Others	352	11.1
Not done	1795	56.6
Missing value	10	0.3
Residual tumor		
R0	2711	85.4
R1	175	5.5
R2	241	7.6
Missing value	47	1.5

these stations, which were dissected even after gastrectomy for malignant disease.

The frequency of metastatic LNs at this station was also high overall, regardless of the reconstruction method employed after the primary gastrectomy.

The 5YOS by involvement at each nodal station was within the range of 10.2–40.3% overall, and dissection was recommended for these LNs.

Metastasis of LNs at the splenic hilum was observed in 14.1% of cases overall in the Malignant group. The 5YOS in patients with involvement of this group of LNs was 30.9%, thereby recommended for dissection. The frequency of No. 10 metastasis was 19.2% in patients from the benign group. In total, 24.7% of the patients with metastasis survived > 5 years.

The proportion of patients with metastasis in No. 10 LNs invading the greater curvature was 31.5%, which was higher than that in patients with tumors not invading the greater curvature (11.7%) (Table 4). The 5YOS of patients with metastasis at this node station was 20.0% in those with tumors involving the greater curvature and 32.9% in those with tumors not involving the greater curvature. No significant difference was observed.

The frequency of involvement of the jejunal LNs was high in patients who had undergone BII/RV in both the Malignant and Benign groups (21.9% and 38.6%, respectively). The 5YOS in patients with involvement at this nodal station was

50.0% and 44.0%, respectively, and resection was recommended for this LN.

Index of the estimated benefit of LN dissection for pT2–T4 tumors (Table 5)

The LN metastasis trend and the 5-year survival rates were similar between patients who had undergone BI and BII/RV, in both the Malignant and Benign groups. We calculated the index of the estimated benefit from LN dissection for each LN station, with the analysis combined for patients who had undergone BI and BII/RV reconstruction methods. This index was calculated by multiplying the frequency of metastasis at the relevant LN station by the 5-year survival rate of the patients with metastasis at that station. The index was only calculated for those LN stations that required dissection in > 10% of cases.

In the Malignant group, the index was high for Nos. 3 (10.2), 7 (9.5), 1 (7.1), and 9 (8.0) LNs. The index value for the LNs at the splenic hilum was 4.4, which was higher than that for Nos. 4sa and 4sb LNs (perigastric LNs).

The index for No. 10 LNs was the highest (10.5) when tumors involved the greater curvature.

Comparison of the indices between the Malignant and Benign groups revealed that the indices for all stations were higher in the Malignant group, except for Nos. 3, 4sa, 4sb, 10 (non-G), 11d, and J stations.

Fig. 1 Flow diagram of patients in this study

Discussion

The median time interval between the initial surgery and second surgery for RGC was 7 years in the Malignant group and 16 years in the Benign group [7]. Hence, the median interval was shorter in the Malignant group than that in the Benign group, consistent with a previous report [7, 8].

The proportion of patients with malignant disease was higher than that of patients with benign disease at the time of the initial surgery, inconsistent with a previous large-scale retrospective study [7]. Considering that H2-blockers became available for use in clinical practice from the late 1980s to the early 1990s, the number of gastric surgeries for benign disease has decreased remarkably since 1990 in Japan.

In the Malignant group, Nos. 1 and 3 LNs would be expected to have been dissected during the initial distal gastrectomy; however, the frequencies of the remaining LNs at these stations were higher than we expected.

If the initial surgery for malignant disease involved a complete dissection on the lesser curvature side (Nos. 1, 3, and 7), even RGCs located on the lesser curvature could be

associated with LN metastases on the greater curvature side (Nos. 4sb, 4sa, and 10) because of the altered lymphatic flow [9, 10]. However, in this study, the proportion of metastatic LNs between the Malignant and Benign groups had no difference, conforming to a systematic review by the task force of the JGCA [8]. Therefore, no answers to this clinical question could be obtained from this study, considering that the proportion of the remaining LNs in the lesser curvature area remained high even after the initial surgery for malignant disease.

The type of reconstruction (BI vs. BII/RY) and nature of the primary disease (malignant/benign) during the initial surgery did not affect the incidence of LN metastasis associated with RGC, consistent with the findings of a previous study [7].

All the lymph nodes showed in Table 5 satisfied the following condition: metastatic rate or 5-year survival rate exceeded 10%. Dissection was recommended for these nodes.

Involvement of LNs in the jejunal mesentery is peculiar to RGC developing after BII/RY. In this study, among patients with T2–T4 disease, 21.9% in the Malignant

Table 2 pT2–T4 Malignant

	Billroth I			Billroth II, Roux-en-Y			Overall		
	No. of patients undergoing dissection	No. of patients with positive nodes	5YSR of node-positive patients (%)	No. of patients undergoing dissection	No. of patients with positive nodes	5YSR of node-positive patients (%)	No. of patients undergoing dissection	No. of patients with positive nodes	5YSR of node-positive patients (%)
1	181 (43.7%)	53 (29.3%)	27.3	66 (44.0%)	12 (18.2%)	27.3	247 (43.8%)	65 (26.3%)	27.1
2	250 (60.4%)	63 (25.2%)	23.1	81 (54.0%)	19 (23.5%)	15.8	331 (58.7%)	82 (24.8%)	21.1
3	89 (21.5%)	32 (36.0%)	23.7	48 (32.0%)	12 (25.0%)	58.2	137 (24.3%)	44 (32.1%)	31.8
4	28 (6.8%)	7 (25.0%)	50.0	14 (9.3%)	1 (7.1%)	100	42 (7.4%)	8 (19.0%)	57.1
4sa	179 (43.2%)	24 (13.4%)	24.6	69 (46.0%)	10 (14.5%)	37.5	248 (44.0%)	34 (13.7%)	27.7
4sb	101 (24.4%)	10 (9.9%)	30.0	38 (25.3%)	4 (10.5%)	37.5	139 (24.6%)	14 (10.1%)	33.3
5	4 (1.0%)	1 (25.0%)	100	4 (2.7%)	1 (25.0%)	100	8 (1.4%)	2 (25.0%)	100
6	10 (2.4%)	2 (20.0%)	100	6 (4.0%)	1 (16.7%)	0	16 (2.8%)	3 (18.8%)	66.7
7	51 (12.3%)	15 (29.4%)	34.3	30 (20.0%)	4 (13.3%)	66.7	81 (14.4%)	19 (23.5%)	40.3
8	63 (12.3%)	17 (27.0%)	27.5	20 (13.3%)	2 (10.0%)	0	83 (14.7%)	19 (22.9%)	24.6
9	59 (14.3%)	16 (27.0%)	31.3	16 (10.7%)	2 (12.5%)	50.0	75 (13.3%)	18 (24.0%)	33.3
10	115 (27.8%)	15 (13.0%)	41.7	55 (36.7%)	9 (16.4%)	0	170 (30.1%)	24 (14.1%)	30.9
11	31 (7.5%)	4 (12.9%)	25.0	13 (8.7%)	4 (30.8%)	Not reached	44 (7.8%)	8 (18.2%)	16.7
11p	78 (18.8%)	21 (26.9%)	6.9	29 (19.3%)	9 (31.0%)	33.3	107 (19.0%)	30 (28.0%)	16.2
11d	63 (15.2%)	12 (19.0%)	8.3	31 (20.7%)	3 (9.7%)	33.3	94 (16.7%)	15 (16.0%)	13.3
12	35 (8.5%)	4 (11.4%)	25.0	6 (4.0%)	0		41 (7.3%)	4 (9.8%)	25.0
13	15 (3.6%)	4 (26.7%)	25.0	1 (0.7%)	1 (100%)	100	16 (2.8%)	5 (31.3%)	40.0
14	10 (2.4%)	4 (40.0%)	0	2 (1.3%)	1 (50.0%)	0	12 (2.1%)	5 (41.7%)	0
15	6 (1.4%)	2 (33.3%)	0	2 (1.3%)	0		8 (1.4%)	2 (25.0%)	50.0
16	19 (4.6%)	9 (47.4%)	27.8	9 (6.0%)	3 (33.3%)	50.0	28 (5.0%)	12 (42.9%)	32.7
J	5 (1.2%)	2 (40.0%)	0	32 (21.3%)	7 (21.9%)	50.0	37 (6.6%)	9 (24.3%)	38.1
17	1 (0.2%)	1 (100%)	0	0	0		1 (0.2%)	1 (100%)	0
18	0	0		0	0		0	0	
19	12 (2.9%)	2 (16.7%)	50.0	1 (0.7%)	0		13 (2.3%)	2 (15.4%)	50.0
20	11 (2.7%)	1 (9.1%)	100	5 (3.3%)	0		16 (2.8%)	1 (6.3%)	100
110	10 (2.4%)	2 (20.0%)	50.0	0	0		10 (1.8%)	2 (20.0%)	50.0
111	3 (0.7%)	3 (100%)	0	0	0		3 (0.5%)	3 (100%)	0
112	3 (0.7%)	0		0	0		3 (0.5%)	0	

N=564 (Billroth I, 414; Billroth II or Roux-en-Y, 150)

group and 38.6% in the Benign group had jejunal node metastasis. The reported incidence ranges from 0 to 20.8% [8, 10, 11].

Optimal management of metastasis in the LNs at the splenic hilum in RGC cases is an important issue under the condition wherein the effectiveness of prophylactic splenectomy for advanced gastric cancer involving the upper third of the stomach not invading the greater curvature has not been proven by clinical trials and guidelines do not recommend splenectomy [12]. LN metastasis at the splenic hilum has a relatively high incidence in patients with RGC [9–11]. Preceding LN dissection for malignant disease possibly increases the lymphatic flow from the remnant stomach to these LNs. Conversely, the incidence of metastasis associated with RGC after initial gastrectomy for benign disease

without dissection may be the same as that for PGC, given that the lymphatic flow after the initial surgery did not alter.

According to the index for primary gastric cancer, a clear pattern can be seen: the indices decreased as the lymph node tier increased [11]. Although the indices in Table 5 are less likely to show any pattern, the indices exceeded 1.0 in all lymph node stations except for No.9 in the Benign group. The index for the remaining suprapancreatic LNs was high and the index for jejunal LN was also high, regardless of the nature of the disease during the initial surgery.

The proportion of LN metastasis in No. 10 LNs in T2–T4 RGC was 14.1% and 19.2% in the Malignant and Benign groups, respectively. Thus, the proportion of patients with metastasis at this LN station between the Malignant and Benign groups had no difference. When we compared the

Table 3 pT2–T4 Benign

	Billroth I			Billroth II, Roux-en-Y			Overall		
	No. of patients undergoing dissection	No. of patients with positive nodes	5YSR of node-positive patients (%)	No. of patients undergoing dissection	No. of patients with positive nodes	5YSR of node-positive patients (%)	No. of patients undergoing dissection	No. of patients with positive nodes	5YSR of node-positive patients (%)
1	138 (82.1%)	39 (28.3%)	25.9	300 (74.8%)	48 (16.0%)	27.6	438 (77.0%)	87 (19.9%)	26.9
2	102 (60.7%)	20 (19.6%)	18.7	217 (54.1%)	17 (7.8%)	12.5	319 (56.1%)	37 (11.6%)	15.9
3	129 (76.8%)	45 (34.9%)	38.3	298 (74.3%)	80 (26.8%)	33.5	427 (75.0%)	125 (29.3%)	35.3
4	25 (14.9%)	7 (28.0%)	42.9	52 (13.0%)	10 (19.2%)	46.7	77 (13.5%)	17 (22.1%)	44.8
4sa	73 (43.5%)	13 (17.8%)	22.8	174 (43.4%)	26 (14.9%)	29.2	247 (43.4)	39 (15.8%)	27.8
4sb	69 (41.1%)	17 (24.6%)	29.9	161 (40.1%)	37 (23.0%)	30.0	230 (40.4%)	54 (23.5%)	29.7
5	6 (3.6%)	3 (50.0%)	66.7	6 (1.5%)	2 (33.3%)	Not reached	12 (2.1%)	5 (41.7%)	75.0
6	16 (9.5%)	3 (18.8%)	Not reached	2 (0.5%)	1 (50.0%)	0	18 (3.2%)	4 (22.2%)	66.7
7	106 (63.1%)	14 (13.2%)	34.8	254 (63.3%)	27 (10.6%)	30.3	360 (63.3%)	41 (11.4%)	31.9
8	83 (49.4%)	12 (14.5%)	27.3	177 (44.1%)	10 (5.6%)	0	260 (45.7%)	22 (8.5%)	14.3
9	41 (24.4%)	4 (9.8%)	0	114 (28.4%)	5 (4.4%)	20.0	155 (27.2%)	9 (5.8%)	12.7
10	60 (35.7%)	10 (16.7%)	13.3	133 (33.2%)	27 (20.3%)	28.1	193 (33.9%)	37 (19.2%)	24.7
11	25 (14.9%)	4 (16.0%)	25.0	54 (13.5%)	10 (18.5%)	0	79 (13.9%)	14 (17.7%)	7.7
11p	50 (29.8%)	5 (10.0%)	40.0	118 (29.4%)	14 (11.9%)	21.4	168 (29.5%)	19 (11.3%)	26.3
11d	39 (23.2%)	7 (17.9%)	26.7	80 (20.0%)	9 (11.3%)	42.9	119 (20.9%)	16 (13.4%)	37.3
12	25 (14.9%)	3 (12.0%)	0	28 (7.0%)	1 (3.6%)	0	53 (9.3%)	4 (7.5%)	0
13	3 (1.8%)	1 (33.3%)	0	7 (1.7%)	1 (14.3%)	100	10 (1.8%)	2 (20.0%)	50.0
14	6 (3.6%)	0		16 (4.0%)	3 (18.8%)	66.7	22 (3.9%)	3 (13.6%)	66.7
15	2 (1.2%)	0		1 (0.2%)	0		3 (0.5%)	0	
16	12 (7.1%)	5 (41.7%)	0	9 (2.2%)	1 (11.1%)	100	21 (3.7%)	6 (28.6%)	22.2
J	6 (3.6%)	1 (16.7%)	100	114 (28.4%)	44 (38.6%)	44.0	120 (21.1%)	45 (37.5%)	45.3
17	0	0		3 (0.7%)	1 (33.3%)	0	3 (0.5%)	1 (33.3%)	0
18	0	0		2 (0.5%)	0		2 (0.4%)	0	
19	1 (0.6%)	1 (100%)	0	3 (0.7%)	0		4 (0.7%)	1 (25.0%)	0
20	3 (1.8%)	1 (33.3%)	0	7 (1.7%)	3 (42.9%)	0	10 (1.8%)	4 (40.0%)	0
110	5 (3.0%)	2 (40.0%)	0	2 (0.5%)	0		7 (1.2%)	2 (28.6%)	0
111	1 (0.5%)	0		0	0		1 (0.2%)	0	
112	1 (0.6%)	1 (100%)	0	0	0		1 (0.2%)	1 (100%)	0

N=569 (Billroth I, 168; Billroth II or Roux-en-Y, 401)

Table 4 Proportion of cases with metastasis in the No. 10 lymph nodes and 5-year survival rate by tumor location

pT2–T4	Benign			Malignant			Overall		
	No. of patients undergoing dissection	Proportion of No. 10 positive patients	5YSR of node-positive patients (%)	No. of patients undergoing dissection	Proportion of No. 10 positive patients	5YSR of node-positive patients (%)	No. of patients undergoing dissection	Proportion of No. 10 positive patients	5YSR of node-positive patients (%)
Involving the greater curvature	47/157 (29.9%)	14/47 (29.8%)	7.7	38/102 (37.3%)	14/38 (36.8%)	28.6	92/284 (32.4%)	29/92 (31.5%)	20.0
Not involving the greater curvature	149/478 (31.2%)	23/149 (15.4%)	36.0	137/486 (28.2%)	10/137 (7.3%)	32.0	298/1006 (29.6%)	35/298 (11.7%)	32.9

Table 5 Index of the estimated benefit from lymph node dissection (pT2–T4)

	Malignant					Benign				
	Proportion of patients with positive node (%)	95% CI	5YSR of node-positive patient (%)	95% CI	Index	Proportion of patients with positive node (%)	95% CI	5YSR of node-positive patients (%)	95% CI	Index
1	26.3	20.8–31.8	27.1	15.9–38.3	7.1	19.9	16.1–23.6	26.9	16.9–36.9	5.3
2	24.8	20.1–29.5	21.1	11.9–30.3	5.2	11.6	8.1–15.1	15.9	3.2–28.6	1.8
3	32.1	24.3–40.0	31.8	16.9–46.7	10.2	29.3	25.0–33.6	35.3	26.5–44.1	10.3
4 ^a	13.7	9.4–18.0	27.7	10.6–44.8	3.8	15.8	11.3–20.3	27.8	12.5–43.1	4.4
4 ^b	10.1	5.0–15.2	33.3	7.6–59.0	3.4	23.5	18.0–29.0	29.7	16.6–42.8	7.0
7	23.5	14.2–32.7	40.3	16.2–64.4	9.5	11.4	8.1–14.7	31.9	16.8–47.0	3.6
8	22.9	13.9–31.9	24.6	4.6–44.6	5.6	8.5	5.1–11.8	14.3	N/A	1.2
9	24.0	14.2–33.8	33.3	11.5–55.1	8.0	5.8	2.1–9.5	12.7	N/A	0.7
10(all)	14.1	8.8–19.4	30.9	10.5–51.3	4.4	19.2	13.7–24.7	24.7	9.8–39.6	4.7
10 (G ^a)	36.8	21.3–52.3	28.6	2.3–54.9	10.5	31.1	17.4–44.8	7.7	N/A	2.4
10(NG ^b)	7.6	3.1–12.1	32.0	N/A	2.4	15.5	9.6–21.4	36.0	14.8–57.2	5.6
11 ^p	28.0	19.4–36.7	16.2	1.9–30.5	4.5	11.3	6.4–16.2	26.3	6.5–46.1	3.0
11 ^d	16.0	8.5–23.4	13.3	N/A	2.1	13.4	7.4–19.5	37.3	8.5–66.1	5.0
J ^c	21.9	7.4–36.4	50.0	10.0–90.0	10.9	38.6	29.6–47.6	44.0	28.7–59.3	17.0

N/A: 95% confidence interval cannot be calculated due to small sample size

^a involving the Greater curvature^b not involving the greater curvature^c Analyzed for Billroth II and Roux-en-Y only

proportion of cases with metastasis at No. 10 LN station by the tumor location, the incidence was approximately three times higher for tumors involving the greater curvature than for those not involving the greater curvature overall.

The index for No. 10 LNs was high in the case of tumors invading the greater curvature. However, even in cases where the tumor did not invade the greater curvature, the index exceeded 1.0 and was similar to that for Nos. 4sa, 4sb, and 11d LNs.

The JCOG conducted a multi-institutional randomized controlled trial (JCOG0110) [12]. Proximal gastric adenocarcinoma of T2-4/N0-2/M0 not invading the greater curvature was eligible. Of 254 patients in the splenectomy group, 6 patients (2.4%) had histological metastasis in No. 10 nodes and all of them developed recurrence and died; the index was calculated as 0. No.10 lymph nodes in Table 5 showed also satisfied the following condition; metastatic rate or 5-year survival rate exceeded 10% regardless of the tumor location.

These findings, taking into consideration the previous reports [9, 10, 13], have led to the recommendation of thorough dissection of No. 10 LN, contrary to the case of primary gastric cancer involving the upper third of the stomach not invading the greater curvature.

However, this study has a limitation in terms of the calculation of the precise incidence of metastasis in the LN stations. In remnant stomach cases, LNs in some LN station had been already dissected during the previous gastrectomy, and during the second surgery, those LNs no longer existed. Therefore, the number of retrieved nodes in some LN station was frequently zero even after the dissection during the second surgery. When no LNs were retrieved, it was difficult to determine whether there were actually no LNs at the time of the operation, or the surgeon might have missed removing the nodes.

In conclusion, the therapeutic strategy for advanced RGC does not differ by the disease type (malignant or benign) for which the first surgery was performed. Total gastrectomy and dissection of the perigastric LNs (Nos. 1–4), suprapancreatic LNs (Nos. 7–9 and 11), and LNs at the splenic hilum (No. 10) are recommended for advanced-stage tumors. Considering that the efficacy of spleen-preserving dissection of LNs at the splenic hilum remains unconfirmed, splenectomy is also necessary. Furthermore, jejunal LNs should be dissected after BII/RV reconstruction.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

Compliance with ethical standards

Conflict of interest We certify that we have no conflicts of interests to declare.

Human and animal rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and in compliance with the Helsinki Declaration of 1964 and later versions. Every hospital discloses information to the patients about the nationwide registry of the JGCA. Participating patients were excluded only when they specified that they were unwilling to participate.

References

1. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer*. 2017;20(1):1–19.
2. Katai H, Ishikawa T, Akazawa K, Isobe Y, Miyashiro I, Oda I, et al. Five-year survival analysis of surgically resected gastric cancer cases in Japan: a retrospective analysis of more than 100,000 patients from the nationwide registry of the Japanese Gastric Cancer Association (2001–2007). *Gastric Cancer*. 2018;21(1):144–54.
3. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edn). *Gastric Cancer*; 2018. (Epub ahead of print)
4. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer*. 2011;14(2):101–12.
5. Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma: 2nd English Edition. *Gastric Cancer*. 1998;1(1):10–24.
6. Sasako M, McCulloch P, Kinoshita T, Maruyama K. New method to evaluate the therapeutic value of lymph node dissection for gastric cancer. *Br J Surg*. 1995;82(3):346–51.
7. Tanigawa N, Nomura E, Lee SW, Kaminishi M, Sugiyama M, Aikou T, et al. Current state of gastric stump carcinoma in Japan: based on the results of a nationwide survey. *World J Surg*. 2010;34(7):1540–7.
8. Shimada H, Fukagawa T, Haga Y, Oba K. Does remnant gastric cancer really differ from primary gastric cancer? A systematic review of the literature by the Task Force of Japanese Gastric Cancer Association. *Gastric Cancer*. 2016;19(2):339–49.
9. Ohashi M, Morita S, Fukagawa T, Kushima R, Katai H. Surgical treatment of non-early gastric remnant carcinoma developing after distal gastrectomy for gastric cancer. *J Surg Oncol*. 2015;111(2):208–12.
10. Honda S, Bando E, Makuuchi R, Tokunaga M, Tanizawa Y, Kawamura T, et al. Effects of initial disease status on lymph flow following gastrectomy in cases of carcinoma in the remnant stomach. *Gastric Cancer*. 2017;20(3):457–64.
11. Sasako M, Maruyama K, Kinoshita T, Okabayashi K. Surgical treatment of carcinoma of the gastric stump. *Br J Surg*. 1991;78(7):822–4.
12. Sano T, Sasako M, Mizusawa J, Yamamoto S, Katai H, Yoshikawa T, et al. Randomized controlled trial to evaluate splenectomy in total gastrectomy for proximal gastric carcinoma. *Ann Surg*. 2017;265(2):277–83.
13. Sugita H, Oda E, Hirota M, Ishikawa S, Tomiyasu S, Tanaka H, et al. Significance of lymphadenectomy with splenectomy in radical surgery for advanced (pT3/pT4) remnant gastric cancer. *Surgery*. 2016;159(4):1082–9.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.