Is proximal gastrectomy indicated for locally advanced cancer in the upper third of the stomach?

Abstract

Aim: To treat upper third gastric cancer, proximal gastrectomy (PG), a function-preserving procedure, is recommended for early lesions when at least half the distal stomach can be preserved, while total gastrectomy (TG) is standard for locally advanced lesions. Oncological feasibility, when applying PG for such lesions, remains unknown.

Methods: We reviewed patients undergoing TG for clinical (c) T2–T4 upper third gastric cancer between 2006 and 2015. Preoperative tumor locations were further classified into the cardia, fornix, and gastric body based on endoscopic findings. The metastatic rate and therapeutic value index for lymph node (LN) dissection were determined, and characteristics of patients with distal LN (No. 4d, 5, and 6) metastasis (DLNM) were reviewed. In addition, patients with pathological tumor invasion to the middle third (M) region were investigated.

Results: We studied 167 patients. There were 8 (4.8%) with DLNM and 41 (24.6%) with pathological tumor invasion to the M region. As to regional stations, therapeutic indices for LN dissection at stations No. 4d, 5, 6, and 12a were zero or extremely low. No DLNM was detected in cT2 lesions or cT3/T4 lesions located within the cardia and/or the fornix. In addition, none of the lesions located within the cardia and/or the fornix by preoperative endoscopy extended to the M region in the pathological specimen.

Conclusions: For upper third gastric cancer, PG without No. 12a dissection might be acceptable for cT2–T4 lesions located within the cardia and/or the fornix when considering the risk of DLNM and cancer-positivity in the distal stump.

Keywords
distal margin, locally advanced gastric cancer, lymph node metastasis, proximal gastrectomy, therapeutic index, upper third gastric cancer
1 | INTRODUCTION

Worldwide, gastric cancer is among the most life-threatening malignant neoplasms.1,2 The incidence of gastric cancer in the upper third of the stomach has recently been rising in both Western and Asian countries.3–5 As a therapeutic strategy for upper third gastric cancer indicated for surgical treatment, proximal gastrectomy (PG), a function-preserving procedure, is advocated for lesions diagnosed at an early stage when more than half of the distal stomach can be preserved.6 In contrast, total gastrectomy (TG) is now the standard procedure for locally advanced lesions in the upper third of the stomach.6

Comparing TG and PG for early gastric cancer, PG is considered to be more advantageous in mitigating body weight loss, maintaining nutritional status, and not causing deterioration of quality of life postoperatively.7,9 Therefore, provided that oncological safety is assured, PG may also be the preferred surgical treatment for locally advanced gastric cancer in the upper third region. As to esophageogastric junctional (EGJ) cancer, PG can be selected even for an advanced tumor if the primary lesion is less than 4 cm in size, based on the oncological safety of lymph node (LN) metastasis, as stated in the Japanese gastric cancer treatment guidelines.6

However, there are oncological concerns when applying PG for advanced upper third gastric malignancies other than EGJ tumors. That is, an optimal extent of LN dissection in performing PG for advanced cancer has not yet been established, with only a few reports focusing on this issue.10,11 nor has the relationship between actual locations of primary lesions and LN metastasis been investigated in sufficient detail. Moreover, it is essential to ensure an adequate distal tumor margin and sufficient volume of the remnant stomach after gastric dissection.

Here we evaluated pathological metastasis involving the aforementioned regional LNs and the distal tumor margin in patients undergoing TG for clinically advanced gastric cancer in the upper third of the stomach. The present results are anticipated to contribute to determining the criteria for applying PG to advanced lesions.

2 | METHODS

2.1 | Patients

From January 2006 to December 2015, patients who underwent TG for cT2–4 gastric cancer, preoperatively diagnosed as being located within the upper third region of the stomach without or with esophageal invasion, at the Department of Gastroenterological Surgery, Cancer Institute Hospital, Tokyo, Japan, were registered in this study. Although D2 LN dissection was usually performed during TG for advanced lesions, a few patients underwent TG with D1/D1+LN dissection at the discretion of the main surgeon, based on patient background factors such as age, performance status, comorbidities, and so on. The exclusion criteria were as follows: (a) EGJ cancer with its center located within 2 cm of the EGJ, as defined by the Japanese gastric cancer treatment guidelines,12 (b) macroscopic type 4 (diffuse infiltrative) lesion, (c) remnant gastric cancer, (d) simultaneous multiple gastric cancers, (e) the presence of other primary malignant disease, (f) history of preoperative chemotherapy, and (g) R1/R2 resection. This study was approved by the Institutional Review Board of the Cancer Institute Hospital (No. 2017-1187).

2.2 | Assessment of clinical staging

For clinical T factor diagnosis, findings obtained by endoscopy and the features noted on computed tomography (CT) by an experienced radiologist were reviewed, and the depth of tumor invasion of the wall was finally determined at the gastric cancer team conference including surgeons, endoscopists, and chemotherapists. Regional LNs with a long-axis diameter of 10 mm or more on CT were diagnosed as metastatic nodes and their station numbers were also examined. Clinical stages were determined according to the 14th edition of the Japanese Classification of Gastric Carcinoma.13

2.3 | Pathological metastasis and therapeutic value index for LNs at each station

As to the regional LNs to be dissected, the rate of LN metastasis and the therapeutic value index for dissection of LNs at each station were examined, including LNs not defined as meeting the extent of lymphadenectomy in PG for early cancer. The rate of metastasis was calculated by dividing the number of patients with metastasis at the nodal station by the number of patients in whom that station was retrieved. Moreover, the therapeutic values of each dissected LN were determined using the therapeutic value index proposed by Sasako et al.14 This index was obtained by multiplying the rate of nodal metastasis by the 5-y overall survival (OS) for each nodal station. The 5-y OS in patients with LN metastasis was calculated for each station, irrespective of nodal metastasis at other stations. In addition, clinical details of patients with distal LN metastasis (DLNM), that is, metastasis to LNs at stations No. 4d, 5, and/or 6, which could not be removed during PG, were investigated.

2.4 | Evaluation of tumor location based on preoperative endoscopy and pathological specimen

We assessed tumor location preoperatively based on the endoscopic findings. In particular, the locations of the distal tumor border were further divided into three regions, ie, the cardia, the fornix, and the gastric body (Figure 1). The location of the cardia was defined as being within 2 cm of the EGJ in the stomach. Representative endoscopic photographs of tumors included in this study are presented in Figure 2. In addition, tumor locations were also determined postoperatively using the pathological specimen, and divided into the upper third or middle third (M) regions of the stomach.
### 3 | STATISTICAL ANALYSIS

The patient background characteristics, surgical details, and pathological findings were collected from our database and information contained in electronic medical records. The relationships between clinical characteristics and pathological findings, including LN metastasis and tumor location, were investigated. All continuous variables are expressed as median values. Statistical analyses were conducted using the Mann–Whitney U-test and the chi-squared test. A $P$-value less than .05 was considered to indicate a statistically significant difference. All statistical analyses were performed with JMP Pro 13 (SAS Institute Japan, Japan) for windows.

### 4 | RESULTS

#### 4.1 | Clinicopathological characteristics

Patient clinical characteristics are shown in Table 1. In total, 167 patients were included in this study. As to the location of the distal tumor border according to preoperative endoscopy, 12 patients (7.2%) had lesions limited to the cardia or the fornix. Although 23
patients (13.8%) were clinically diagnosed as having LN metastasis, none of them had swollen LNs at stations No. 4d, 5, and/or 6. As to pathological findings (Table 2), there were 8 patients (4.8%) with DLNM, and 41 (24.6%) showing tumor invasion to the M region in the pathological specimen.

4.2 | Rate of LN metastasis and therapeutic value index of LN dissection

Table 3 shows the LN metastasis rate, 5- y OS, and the therapeutic value index for dissection of each LN station. In patients with cT2 lesions, the metastatic rate and the therapeutic index of LN were both zero at stations No. 4d, 5, and 6. On the other hand, the LN metastasis rate was zero only at station No. 6 of the three stations examined patients with cT3/T4 tumors. Among the regional stations examined, however, the therapeutic indices of LN dissection at stations No. 4d and 5 were extremely low, at 1.0 and 1.4, respectively. The therapeutic index for dissection of LNs at station No. 12a was also zero in all patients.

### Table 1 Characteristics of the patients

|                          | All (n = 167) |
|--------------------------|--------------|
| Sex, n (%)               |              |
| Male                     | 116 (69.5)   |
| Female                   | 51 (30.5)    |
| Age, years [IQR]         | 67 [59-73]   |
| Tumor location, n (%)    |              |
| U                        | 151 (90.4)   |
| UE                       | 16 (9.6)     |
| Location of distal tumor border by endoscopy, n (%) | |
| Cardia or fornix         | 12 (7.2)     |
| Gastric body             | 155 (92.8)   |
| Tumor circumference, n (%) |           |
| Less                     | 46 (27.5)    |
| Gre                      | 22 (13.2)    |
| Ant                      | 24 (14.4)    |
| Post                     | 71 (42.5)    |
| Circ                     | 4 (2.4)      |
| Preoperative tumor size, mm [IQR] | 40 [30-55] |
| Clinical T factor, n (%) |              |
| T2                       | 65 (38.9)    |
| T3                       | 41 (24.6)    |
| T4                       | 61 (36.5)    |
| Clinical N factor, n (%) |              |
| N0                       | 144 (86.2)   |
| N+                       | 23 (13.8)    |
| Region of clinical lymph node metastasis |              |
| Left area of cardia (No. 2) | 1 (4.2)     |
| Lesser curvature (No. 1 and 3) | 21 (87.5)   |
| Supra-pancreas (No. 7, 8a, 9 and 11p) | 2 (8.3)     |
| Splenic hilum (No. 10)   | 0 (0)        |
| Distal area (No. 4d, 5 and 6) | 0 (0)      |
| Surgical approach, n (%) |              |
| Open                     | 163 (97.6)   |
| Laparoscopic             | 4 (2.4)      |
| Type of lymph node dissection, n (%) |     |
| D2 or more               | 156 (93.4)   |
| D1 or D1+                | 11 (6.6)     |

Abbreviation: IQR, interquartile range.

### Table 2 Pathological findings

|                          | All (n = 167) |
|--------------------------|--------------|
| Pathological tumor size, mm [IQR] | 50 [38-75] |
| Histology, n (%)         |              |
| Differentiated           | 72 (43.1)    |
| Undifferentiated         | 92 (55.1)    |
| Others                   | 3 (1.8)      |
| Pathological T factor, n (%) |          |
| T1                       | 16 (9.6)     |
| T2                       | 29 (17.4)    |
| T3                       | 55 (32.9)    |
| T4                       | 67 (40.1)    |
| Pathological N factor, n (%) |           |
| N0                       | 78 (46.7)    |
| N1                       | 34 (20.4)    |
| N2                       | 26 (15.6)    |
| N3                       | 29 (17.4)    |
| Pathological stage, n (%) |            |
| I                        | 39 (23.4)    |
| II                       | 63 (37.7)    |
| III                      | 61 (36.5)    |
| IV                       | 4 (2.4)      |
| DLNM, n (%)              |              |
| Yes                      | 8 (4.8)      |
| No                       | 159 (95.2)   |
| Pathological tumor invasion to the M region, n (%) | |
| Yes                      | 41 (24.6)    |
| No                       | 126 (75.4)   |

Abbreviations: DLNM, distal lymph node (stations No. 4d, 5, and 6) metastasis; IQR, interquartile range; M region, middle third of the stomach.
**4.3 | Patients with DLNM**

Table 4 shows the clinicopathological and demographic characteristics of eight patients with DLNM. All primary lesions extended to the gastric body, and all had a depth of cT3 or cT4. All but one of the seven patients were diagnosed at far advanced stages of disease, pStage III or IV, with extensive LN metastasis.

**5 | DISCUSSION**

We evaluated the pathological status of regional LNs, the therapeutic index for each nodal station, and the pathological tumor location in patients undergoing TG for cT2–4 upper third gastric cancer, to...
explore the possibility of applying PG for these lesions. The following findings were obtained in the present study. Among the regional LNs examined, the therapeutic indices for dissection of LNs at stations No. 4, 5, 6, and 12a were zero or extremely low. Moreover, no DLNM was detected in cT2 lesions or cT3/T4 lesions located within the cardia/fornix. In addition, the lesions located within the cardia/fornix by preoperative endoscopy did not extend to the M region in the pathological specimen. Therefore, PG without No. 12a dissection might be indicated for lesions within the cardia/fornix, considering the oncological aspects of DLNM and the risk of cancer-positivity in the distal margin.

Several studies have focused on the frequency of DLNM in locally advanced cancers in the upper third of the stomach, and all obtained similar results.10,11,14 In particular, Yura et al suggested that the frequency of DLNM in pT2/T3 lesions in the upper region was extremely low, and that no therapeutic effect was obtained by dissecting these LNs.11 However, patients were not studied according to clinical T factors, but instead only according to pathological T factors in all of the previous investigations. Given that surgical treatment is determined based on the preoperative diagnosis including the clinical T factor and that clinicopathological discrepancies among T categories are possible, the results obtained from the present study, which included taking clinical T factors into account, appear to be reliable.

Moreover, tumor locations were further divided into three regions based on preoperative endoscopic findings, revealing that DLNM is unlikely to develop in locally advanced lesions, even with serosal invasion, when they are located above the gastric body. Although greater tumor diameter is considered to carry a risk of deeper wall invasion,15-17 PG might be acceptable for such lesions because a sufficient distal margin can be maintained. In addition, given that all patients with DLNM were pathologically diagnosed as having far advanced disease stages, ie, pStage IIIC or IV, except in one case, surgical treatment alone would not have achieved satisfactory long-term survival. Thus, patients with DLNM require perioperative multidisciplinary treatments.

As specified in the current guidelines,6 lymph node dissection with D1 or D1 plus can be applied in PG for early lesions, while the optimal extent of lymphadenectomy in PG for advanced stage cancer remains unknown. Although LNs at the distal stations cannot be removed because blood flow to the remnant stomach must be preserved, it is possible to dissect LNs at stations No. 10, 11d, and 12a, which are not included among the LNs defined as being suitable for PG with D1 or D1 plus. Based on several reports indicating that No. 12a LN dissection has no therapeutic effect, which is consistent with the results of the present study,10,11,14 it may be reasonable to omit lymphadenectomy of station No. 12a when performing PG for advanced lesions. On the other hand, the frequency of No. 10 LN metastasis in proximal advanced gastric cancer is not low, reportedly being 10.7%-16.5%,18-20 which is similar to the result obtained in this study. Splenectomy for No. 10 LN dissection should be determined according to the results of a randomized controlled trial.21

Insufficient volume of the remnant stomach after PG is reportedly associated with deterioration of postoperative quality of life and skeletal muscle loss.22,23 In practice, the aim is generally to preserve more than 2/3 of the preoperative gastric volume in performing PG for early lesions.7,24 Even when applying PG to advanced tumors, it is apparently essential that at least half of the distal stomach, as recommended in the guidelines, be preserved.6 Large tumors and pathologically advanced T stage are reportedly risk factors for

### Table 4: Characteristics of patients with DLNM

| No. | Gender | Age, years | Distal border of tumor | Clinical macroscopic type | Preoperative tumor size, mm | cT factor | Histology | pT factor | pN factor | pStage |
|-----|--------|------------|------------------------|--------------------------|-----------------------------|-----------|-----------|-----------|-----------|--------|
| 1   | Female | 67         | Gastric body           | Type 3                   | 100                         | cT4a      | Undiff.   | pT4a      | pN3b      | IIIC   |
| 2   | Female | 61         | Gastric body           | Type 3                   | 55                          | cT3       | Undiff.   | pT4a      | pN3a      | IVA    |
| 3   | Male   | 71         | Gastric body           | Type 3                   | 60                          | cT4a      | Undiff.   | pT4a      | pN3b      | IIIC   |
| 4   | Male   | 79         | Gastric body           | Type 3                   | 60                          | cT4b      | Undiff.   | pT4b      | pN3b      | IVA    |
| 5   | Male   | 59         | Gastric body           | Type 3                   | 40                          | cT3       | Diff.     | pT4a      | pN3a      | IIIC   |
| 6   | Male   | 81         | Gastric body           | Type 3                   | 60                          | cT4a      | Diff.     | pT4a      | pN3a      | IIIC   |
| 7   | Male   | 73         | Gastric body           | Type 1                   | 35                          | cT3       | Diff.     | pT1b      | pN1       | IB     |
| 8   | Female | 48         | Gastric body           | Type 3                   | 50                          | cT4a      | Undiff.   | pT4a      | pN3a      | IIIC   |

Abbreviations: DLNM, distal lymph node (stations No. 4d, 5, and 6) metastasis; Undiff., undifferentiated type.
a positive resection margin in gastric cancer surgery, similar to the characteristics of patients with pathological tumor invasion to the M region in this study.25-27 However, this study suggested that more than half of the stomach might be preserved even with locally advanced gastric cancer, provided that the lesion is located within the cardia and/or the fornix.

This study has several limitations. First, this was a retrospective study with a small sample size conducted at a single institution. Moreover, we were not able to perform a multivariate analysis because there were too few patients with DLNM in this cohort. The most recent cases could not be included in the present study due to this being a 5-y survival analysis. Second, the

| TABLE 5 Comparison between patients with and without pathological tumor invasion to the M region |
|-----------------------------------|-----------------------------------------------|----------------|
|                                  | No pathological invasion to M region (n = 126) | Pathological invasion to M region (n = 41) | P value |
| Sex, n (%)                        |                                           |                                           |         |
| Male                              | 93 (73.8)                                  | 23 (56.1)                                  | .032    |
| Female                            | 33 (26.2)                                  | 18 (43.9)                                  |         |
| Age, years [IQR]                  | 67 [60-73]                                 | 63 [54-75]                                 | .142    |
| Tumor location, n (%)             |                                           |                                           |         |
| U                                 | 116 (92.1)                                 | 35 (85.4)                                  | .205    |
| UE                                | 10 (7.9)                                   | 6 (14.6)                                   |         |
| Location of distal tumor border by endoscopy, n (%) | | |
| Cardia or fornix                  | 12 (9.5)                                   | 0 (0)                                      | .040    |
| Gastric body                      | 114 (90.5)                                 | 41 (100)                                   |         |
| Clinical macroscopic type, n (%)  |                                           |                                           |         |
| 0                                 | 25 (19.8)                                  | 10 (24.4)                                  | .444    |
| 1                                 | 13 (10.3)                                  | 1 (2.4)                                    |         |
| 2                                 | 29 (23.0)                                  | 10 (24.4)                                  |         |
| 3                                 | 56 (44.4)                                  | 20 (48.8)                                  |         |
| 5                                 | 3 (2.4)                                    | 0 (0)                                      |         |
| Preoperative tumor size, mm [IQR] | 40 [30-50]                                 | 50 [40-60]                                 | <.001   |
| Clinical T factor, n (%)          |                                           |                                           |         |
| T2                                | 56 (44.4)                                  | 9 (22.0)                                   | <.001   |
| T3                                | 34 (27.0)                                  | 7 (17.1)                                   |         |
| T4                                | 26 (28.6)                                  | 25 (61.0)                                  |         |
| Histology, n (%)                  |                                           |                                           | .605    |
| Differentiated                    | 57 (45.2)                                  | 15 (36.6)                                  |         |
| Undifferentiated                  | 67 (53.2)                                  | 25 (61.0)                                  |         |
| Others                            | 2 (1.6)                                    | 1 (2.4)                                    |         |
| Pathological tumor size, mm [IQR] | 48 [35-62]                                 | 80 [52-95]                                 | <.001   |
| Pathological T factor, n (%)      |                                           |                                           | .030    |
| T1                                | 15 (11.9)                                  | 1 (2.4)                                    |         |
| T2                                | 24 (19.1)                                  | 5 (12.2)                                   |         |
| T3                                | 44 (34.9)                                  | 11 (26.8)                                  |         |
| T4                                | 43 (34.1)                                  | 24 (58.5)                                  |         |
| Pathological stage, n (%)         |                                           |                                           | .124    |
| I                                 | 34 (27.0)                                  | 5 (12.2)                                   |         |
| II                                | 48 (38.1)                                  | 15 (36.6)                                  |         |
| III                               | 42 (33.3)                                  | 19 (46.3)                                  |         |
| IV                                | 2 (1.6)                                    | 2 (4.9)                                    |         |

Abbreviations: IQR, interquartile range; M region, middle third of the stomach.
therapeutic effect of dissecting LNs at station No. 11d remains unclear due to the insufficient number of cases. In addition, whether dissection of No. 3b LNs has any clinical benefit could not be evaluated because not all of the No. 3 LNs were recorded separately, ie, as No. 3a or 3b LNs, in our database. This is because the nodes at station No. 3 were divided into 3a and 3b LNs according to the revision of the 14th edition of the Japanese Classification of Gastric Carcinoma in 2010.13 When performing PG for locally advanced lesions, complete dissection of LNs at station No. 3 including the nodes at station No. 3b might be essential, along with not leaving a significant volume of the remnant stomach due to the necessity of securing an appropriate margin. The optimal extent of LN dissection at station No. 3 is a topic for future study. Third, functions of the remnant stomach such as peristalsis and retention after PG for locally advanced cancer were not evaluated. A multicenter study with a large sample size is required to clarify these issues and overcome the limitations of this study.

In conclusion, for locally advanced gastric cancer in the upper third of the stomach, PG without No. 12a dissection might be acceptable for lesions located within the cardia and/or the fornix, given that neither DLNM nor a distal cancer-positive margin was detected in these cases.

DISCLOSURE
The protocol for this research project was approved by the Institutional Review Board of the Cancer Institute Hospital and conforms to the provisions of the Declaration of Helsinki. Approval No. 2017-1187. Informed consent was obtained from all of the subjects. Conflict of Interest: The authors have no conflicts of interest regarding this article to declare.

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REFERENCES
1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359–86.
2. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65(2):87–108.
3. Wu H, Rusiecki JA, Zhu K, Potter J, Devesa SS. Stomach carcinoma in 2010. Cancer Epidemiol Biomarkers Prev. 2010;19(5):1251–60.
4. Wu H, Rusiecki JA, Zhu K, Potter J, Devesa SS. Stomach carcinoma in 2010. Cancer Epidemiol Biomarkers Prev. 2010;19(5):1251–60.
5. Deans C, Yeo MSW, Soe MY, Shabbir A, Ti TK, So JBY. Cancer of the upper third of the stomach. Ann Surg Oncol. 2017;24(6):1635–42.
6. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer. 2021;24:1–21.
7. Hayami M, Hiki N, Nunobe S, Mine S, Ohashi M, Kumagai K, et al. Clinical outcomes and evaluation of laparoscopic proximal gastrectomy with double-flap technique for early gastric cancer in the upper third of the stomach. Ann Surg Oncol. 2017;24(6):1635–42.
8. Tanioka T, Waratchanont R, Fukuyo R, Saito T, Umebayashi Y, Kanemoto E, et al. Surgical and nutritional outcomes of laparoscopic proximal gastrectomy versus total gastrectomy: a meta-analysis. Surg Endosc. 2020;34(3):1061–9. https://doi.org/10.1007/s00464-019-07352-2
9. Takiguchi N, Takahashi M, Ikeda M, Inagawa S, Ueda S, Nobuoka T, et al. Long-term quality-of-life comparison of total gastrectomy and proximal gastrectomy by postgastrectomy syndrome assessment scale (PGSAS-45): a nationwide multi-institutional study. Gastric Cancer. 2015;18(2):407–16.
10. Haruta S, Shinozuka H, Hosogi H, Ohkura YU, Kobayashi N, Mizuno A, et al. Proximal gastrectomy with exclusion of no. 3b lesser curvature lymph node dissection could be indicated for patients with advanced upper-third gastric cancer. Gastric Cancer. 2017;20(3):528–35.
11. Ueda M, Yoshikawa T, Otsuki S, Yamagata Y, Morita S, Katai H, et al. Oncological safety of proximal gastrectomy for T2/T3 proximal gastric cancer. Gastric Cancer. 2019;22(5):1029–35.
12. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer. 2017;20(1):1–19.
13. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer. 2011;14(2):101–12.
14. Sasaki 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.
15. Wang X, Wang F, Pan J, Yu GZ, Chen Y, Wang JH. Tumor size: a non-negligible independent prognostic factor for gastric cancer. J Surg Oncol. 2008;97(3):236–40.
16. Wang HM, Huang CM, Zheng CH, Li P, Xie J-W, Wang J-B, et al. Tumor size as a prognostic factor in patients with advanced gastric cancer in the lower third of the stomach. World J Gastroenterol. 2012;18(38):5470–5.
17. Guo P, Li Y, Zhu Z, Sun Z, Chong LU, Wang Z, et al. Prognostic value of tumor size in gastric cancer: an analysis of 2,379 patients. Tumour Biol. 2013;34(2):1027–35.
18. Shin SH, Jung H, Choi SH, An JY, Choi MG, Noh JH, et al. Clinical significance of splenic hilar lymph node metastasis in proximal gastric cancer. Ann Surg Oncol. 2009;16(5):1304–9.
19. Sasada S, Ninomiya M, Nishizaki M, Harano M, Ojima Y, Matsukawa H, et al. Frequency of lymph node metastasis to the splenic hilus and effect of splenectomy in proximal gastric cancer. Anticancer Res. 2009;29(8):3347–51.
20. Kosuga T, Ichikawa D, Okamoto K, Komatsu S, Shiozaki A, Fujiwara H, et al. Survival benefits from splenic hilar lymph node dissection by splenectomy in gastric cancer patients: relative comparison of the benefits in subgroups of patients. Gastric Cancer. 2011;14(2):172–7.
21. 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.
22. Shin SH, Jung H, Choi SH, An JY, Choi MG, Noh JH, et al. Clinical significance of splenic hilar lymph node metastasis in proximal gastric cancer. Ann Surg Oncol. 2009;16(5):1304–9.
23. Sasada S, Ninomiya M, Nishizaki M, Harano M, Ojima Y, Matsukawa H, et al. Frequency of lymph node metastasis to the splenic hilus and effect of splenectomy in proximal gastric cancer. Anticancer Res. 2009;29(8):3347–51.
24. Kosuga T, Ichikawa D, Okamoto K, Komatsu S, Shiozaki A, Fujiwara H, et al. Survival benefits from splenic hilar lymph node dissection by splenectomy in gastric cancer patients: relative comparison of the benefits in subgroups of patients. Gastric Cancer. 2011;14(2):172–7.
25. 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.
24. Hosoda K, Washio M, Mieno H, Moriya H, Ema A, Ushiku H, et al. Comparison of double-flap and OrVil techniques of laparoscopy-assisted proximal gastrectomy in preventing gastroesophageal reflux: a retrospective cohort study. Langenbecks Arch Surg. 2019;404(1):81–91.

25. Lee JH, Ahn SH, Park DJ, Kim HH, Lee HJ, Yang HK. Clinical impact of tumor infiltration at the transected surgical margin during gastric cancer surgery. J Surg Oncol. 2012;106(6):772–6.

26. Bissolati M, Desio M, Rosa F, Rausel S, Marrelli D, Baiocchi GL, et al. Risk factor analysis for involvement of resection margins in gastric and esophagogastric junction cancer: an Italian multicenter study. Gastric Cancer. 2017;20(1):70–82.

27. Kumazu Y, Hayashi T, Yoshikawa T, Yamada T, Hara K, Shimoda Y, et al. Risk factors analysis and stratification for microscopically positive resection margin in gastric cancer patients. BMC Surg. 2020;20(1):95.

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