Distal gastrectomy versus total gastrectomy for distal gastric cancer

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Abstract
Even though more than a century later, after the first case of gastrectomy has been successfully performed, the best surgical treatment for distal gastric cancer still remains controversial. Thus, the present study was designed to compare the survival impact of distal (DG) or total gastrectomy (TG) for distal gastric cancer. A total of 1262 distal gastric cancer patients were enrolled in current study including 1157 patients who underwent DG and 157 patients who underwent TG. The postoperative complications and 5-year overall survival were compared between the 2 groups. TG group presented a longer surgical time, a higher volume of intraoperative bleeding, and a larger number of excised lymph nodes (all \( P < 0.05 \)) compared with the DG group. The postoperative complications were comparable (all \( P > 0.05 \)). The 5-year overall survival rate of DG group was significantly higher than that of TG group (67.6% vs 44.3%, \( P < 0.001 \)). However, multivariate analysis showed that type of resection was not an independent prognostic factor for distal gastric cancer (\( P > 0.05 \)). The factor-stratified multivariate analysis showed that only in the subgroup of Tumor-node-metastasis staging system (TNM) stage III (\( P = 0.049 \)), TG was the independent prognostic factor for poor survival. In conclusion, DG was as feasible as TG; however, TG did not increase the survival rate. DG brought better long-term survival than TG in patients with TNM stage III tumor. We recommended that DG should be the optimal surgical procedure for distal gastric cancer under the premise of negative resection margin.

Abbreviations: CI = confidence interval, DG = distal gastrectomy, HR = hazard ratio, TG = total gastrectomy

Keywords: complication, distal gastrectomy, distal gastric cancer, prognosis, total gastrectomy

1. Introduction
Although a significantly decreasing incidence trend of gastric cancer has been observed worldwide, gastric cancer is still the second most common carcinoma in China.\(^1\) Surgical resection including proximal, distal (DG), or total gastrectomy (TG) with extended lymphadenectomy is the only curative treatment for gastric cancer by now. Even more than a hundred years later, since the first case of subtotal gastrectomy had been successfully performed in 1881 and 1897,\(^2,3\) respectively, the best surgical procedure for distal gastric cancer still remains controversial.

The type of resection for gastric cancer is assessed and determined by the tumor size and location as well as the distance of proximal resection edge.\(^4\) Complete resection with at least a 4 cm proximal margin length for gastric cancer is recommended by the 2016 edition of NCCN guidelines.\(^5\) However, McNeer et al\(^6\) proposed that TG should be performed even an R0 margin can be obtained by DG. There is no consensus on the selection of operations for distal gastric cancer under the premise of sufficient proximal margin length, since study based on a comparison of survival superiority between DG and TG was lacking. The preference of surgical resection for distal gastric cancer is much more dependent on surgeons’ experience and varies between different regions.\(^7–9\)

Therefore, the current study aimed to compare the survival impact between DG and TG for distal gastric cancer in order to achieve the optimal treatment strategy.

2. Patients and methods
From September 2008 to March 2015, a total of 1262 distal gastric cancer who received radical gastrectomy in Xijing Hospital, Fourth Military Medical University, were retrospectively enrolled in the present study. The inclusion criteria were listed as follows: (1) with a lower third gastric cancer; (2) without neoadjuvant chemotherapy; (3) without distal metastasis; (4) with radical gastrectomy; (5) with negative proximal margin; (6) with complete follow-up records. This study was approved by the Ethics Committee of Xijing Hospital, and written informed consent was obtained from all patients before surgery.

All of the patients received DG or TG according to the recommendation of Japanese Gastric Cancer Treatment guidelines.\(^10\) All the surgeries were performed by experienced surgeons in our center. The TNM stages were defined on the basis of 7th edition of AJCC cancer staging manual.\(^11\)
Clinicopathological data including age, gender, tumor size, histologic type, tumor depth, lymph node metastasis, and TNM stage were recorded and analyzed. The perioperative outcomes including surgical time, intraoperative bleeding, number of excised lymph nodes, pulmonary infection, wound dehiscence, wound infection, anastomotic leakage, chylous fistula, intraperitoneal hemorrhage, postoperative 30-day mortality, and hospital stay were also analyzed. Data were processed using SPSS 22.0 for Windows (SPSS Inc., Chicago, IL). Numerical variables were expressed as mean ± SD. Discrete variables were analyzed using the Chi-square test or Fisher's exact test. Risk factors for survival were identified by univariate analysis and Cox's proportional hazards regression model was employed for multivariate analysis. Overall survival was analyzed by the Kaplan-Meier method and differences between curves were compared using the log-rank test. P values were considered to be statistically significant at the 5% level.

3. Results

3.1. General features between DG and TG groups

The clinicopathological features were summarized in Table 1. There were 923 males and 339 females. The median age was 56 years (range 21–86 years). Among the enrolled patients, 1157 (91.7%) patients received DG and 105 (8.3%) patients received TG. The distribution of tumor size, histologic type, tumor depth, lymph node metastasis, and TNM stage were significantly different between the DG and TG groups (all P < 0.005).

### Table 1

| Characteristics                      | DG group (n = 1157) | TG group (n = 105) | P     |
|--------------------------------------|--------------------|-------------------|-------|
| Age                                  |                    |                   | 0.447 |
| ≤60                                  | 762 (65.9%)        | 73 (69.5%)        |       |
| >60                                  | 395 (34.1%)        | 32 (30.5%)        |       |
| Gender                               |                    |                   | 0.612 |
| Male                                 | 844 (72.9%)        | 79 (75.2%)        |       |
| Female                               | 313 (27.1%)        | 26 (24.8%)        |       |
| Tumor size                           |                    |                   | <0.001|
| ≤2 cm                                | 323 (27.9%)        | 14 (13.3%)        |       |
| 2.1-4 cm                             | 502 (43.4%)        | 36 (34.3%)        |       |
| ≥4.1 cm                              | 332 (28.7%)        | 55 (52.2%)        |       |
| Histologic type                      |                    |                   | 0.027 |
| Well                                 | 149 (12.9%)        | 4 (3.8%)          |       |
| Moderately                           | 276 (24.0%)        | 22 (21.0%)        |       |
| Poorly                               | 276 (24.0%)        | 22 (21.0%)        |       |
| Mucinous or signet ring cell         | 51 (4.4%)          | 6 (5.7%)          |       |
| Tumor depth                          |                    |                   | <0.001|
| T1                                   | 348 (30.1%)        | 18 (17.1%)        |       |
| T2                                   | 241 (20.8%)        | 9 (8.6%)          |       |
| T3                                   | 336 (29.0%)        | 26 (24.8%)        |       |
| T4                                   | 232 (20.1%)        | 52 (49.5%)        |       |
| Lymph node metastasis                |                    |                   | <0.001|
| N0                                   | 526 (45.5%)        | 26 (24.8%)        |       |
| N1                                   | 228 (19.7%)        | 13 (12.4%)        |       |
| N2                                   | 178 (15.4%)        | 18 (17.1%)        |       |
| N3                                   | 225 (19.4%)        | 48 (45.7%)        |       |
| TNM stage                            |                    |                   | <0.001|
| I                                    | 427 (36.9%)        | 19 (18.1%)        |       |
| II                                   | 345 (29.8%)        | 19 (18.1%)        |       |
| III                                  | 385 (33.3%)        | 67 (63.8%)        |       |

DG = distal gastrectomy, TG = total gastrectomy.

As showed in Table 2, the TG group presented a longer surgical time (224.65 min vs 199.09 min, P < 0.001), a higher volume of intraoperative bleeding (217.43 mL vs 185.22 mL, P = 0.014) and a larger number of excised lymph nodes (28.25 vs 23.66, P < 0.001) in comparison with the DG group. The postoperative complications including surgical time, intraoperative bleeding, number of excised lymph nodes, pulmonary infection, wound dehiscence, wound infection, anastomotic leakage, chylous fistula, intraperitoneal hemorrhage, postoperative 30-day mortality were comparable between the two groups (all P > 0.05). The postoperative hospital stay had no statistical difference either (median, 7 d vs 7 d, P = 0.257).

### Table 2

| Items                                | DG group (n = 1157) | TG group (n = 105) | P     |
|--------------------------------------|--------------------|-------------------|-------|
| Intraoperative outcomes, mean ± SD   |                    |                   |       |
| Surgical time, min                   | 199.09 ± 64.926    | 224.65 ± 74.66    | <0.001|
| Intraoperative bleeding, mL          | 185.22 ± 126.37    | 217.43 ± 147.41   | 0.014 |
| Number of excised lymph nodes        | 23.66 ± 9.77       | 28.25 ± 10.43     | <0.001|
| Perioperative complications, n, %    |                    |                   |       |
| Pulmonary infection                  | 27 (2.8%)          | 2 (2.3%)          | 1.00  |
| Wound dehiscence                     | 7 (0.7%)           | 0                 | 1.00  |
| Wound infection                      | 4 (0.4%)           | 0                 | 1.00  |
| Anastomotic leakage                  | 2 (0.2%)           | 0                 | 1.00  |
| Chylous fistula                      | 7 (0.6%)           | 0                 | 1.00  |
| Intraperitoneal hemorrhage           | 8 (0.8%)           | 1 (1.2%)          | 0.537 |
| Number of patients                   | 47 (4.1%)          | 3 (2.9%)          | 0.793 |
| Postoperative 30-day mortality, n, % | 2 (0.2%)           | 1 (1.2%)          | 0.224 |
| Postoperative hospital stay, median d| 7                  | 7                 | 0.257 |

DG = distal gastrectomy, TG = total gastrectomy.

3.2. Overall survival analysis

Survival was analyzed in 1262 distal gastric cancer patients with the range of follow-up from 0.17 to 76 months (mean, 29 months; median, 25.83 months). A 65.8% 5-year overall survival rate for the entire cohort was found in the current study. The 5-year overall survival rate of DG group was significantly higher than that of TG group (67.6% vs 44.3%, P < 0.001, Fig. 1). The presence of age, tumor size, histologic type, tumor depth, lymph
node metastasis, TNM stage, intraoperative bleeding, number of excised lymph nodes, and type of resection were associated with prognosis according to the univariate analysis (all P < 0.05, Table 3). However, multivariate analysis showed that type of resection was not an independent prognostic factor for distal gastric cancer (P > 0.05, Table 3).

3.3. Survival analysis according to subgroups

In order to further compare the survival of DG and TG groups, we analyzed the 5-year overall survival rates of patients according to the subgroups of all the clinicopathological factors listed in Table 1, using the Kaplan–Meier method (Table 4). The results showed that TG was associated with poor survival in subgroups of age (< 60, > 60), gender (male, female), tumor size (2.1–4 cm), histologic type (differentiated, undifferentiated), tumor depth (T4), lymph node metastasis (positive), and TNM stage (stage III) (all P < 0.05). The survival rates had no significant differences between the 2 groups in the rest of the subgroups (all P > 0.05).

We conducted univariate and multivariate analyses for each subgroup. In consistent with the Kaplan–Meier method, the same results were also found by univariate analysis (data not show). The multivariate analysis showed that only in the subgroup of TNM stage III, TG was the independent prognostic factor indicating poor survival (all P = 0.049, Table 5). The survival curves of the 2 subgroups were showed in Fig. 2.

4. Discussion

The current study focused on the survival impact of DG and TG for distal gastric cancer. We found that the 5-year overall survival rate after DG for distal gastric cancer patients was higher than that of TG, but the resection type was not an independent prognostic factor for the cohort. Only in TNM stage III, TG brought a worse prognosis for distal gastric cancer than DG according to multivariate analysis.

Although a variety of novel molecular targets have been found and the targeted therapies have shown encouraging results in gastric cancer patients,[12–16] curative resection is considered to be the ideal primary choice that not only brings favorable long-term survival but also causes a low morbidity rate.[17,18] However, consideration regarding the extent of surgical resection depends on multiple factors.[19,20] Till now, there was no consensus about the surgical procedure for distal gastric cancer. A previous extensive survey of 62 centers in Europe including 16,594 patients showed that 44% surgeons would chose TG for antrum tumor of stomach.[21] The national Cancer Data Base report of United States comprising 6400 patients showed that 44% surgeons would chose TG for antrum tumor of stomach. However, a previous randomized clinical trial demonstrated that the postoperative complications were comparable between DG.

### Table 3

| Characteristics          | β | Univariate analysis | P | β | Multivariate analysis | P |
|--------------------------|---|---------------------|---|---|-----------------------|---|
| Age                      | 0.012 | 1.012 (1.002–1.022) | 0.023 | 0.346 | 1.413 (1.102–1.811) | 0.006 |
| Gender                   | 0.030 | 1.030 (0.781–1.342) | 0.824 |
| Tumor size               | 0.865 | 2.375 (1.999–2.822) | <0.001 | 0.312 | 1.379 (1.127–1.687) | 0.002 |
| Histologic type          | 0.525 | 1.691 (1.429–2.001) | <0.001 | 0.001 | 2.022 (1.011–1.481) | 0.038 |
| Tumor depth              | 0.859 | 2.361 (2.070–2.692) | <0.001 |
| Lymph node metastasis    | 0.770 | 2.159 (1.942–2.401) | <0.001 |
| TNM stage                | 0.666 | 1.946 (1.769–2.141) | <0.001 | 0.530 | 1.699 (1.563–1.846) | <0.001 |
| Surgical time            | 0.000 | 1.000 (0.998–1.002) | 0.918 |
| Intraoperative bleeding  | 0.002 | 1.002 (1.001–1.002) | <0.001 | 0.001 | 1.001 (1.000–1.002) | 0.011 |
| No. of excised lymph nodes | 0.015 | 1.015 (1.004–1.026) | 0.008 |
| Type of resection        | -0.909 | 0.403 (0.289–0.562) | <0.001 |

CI = confidence interval, HR = hazard ratio.

### Table 4

| Factors                  | 5-year overall survival | χ² value | P |
|--------------------------|-------------------------|----------|---|
| Age                      |                         |          |   |
| <60                      | 69.9%                   | 39.6%    | 12.295 | <0.001 |
| >60                      | 65.1%                   | 36.0%    | 19.374 | <0.001 |
| Gender                   |                         |          |   |
| Male                     | 67.2%                   | 41.9%    | 23.737 | <0.001 |
| Female                   | 69.2%                   | 38.9%    | 4.908 | 0.027 |
| Tumor size               |                         |          |   |
| ≤2 cm                    | 87.3%                   | 90.0%    | 0.126 | 0.722 |
| 2.1–4 cm                 | 66.1%                   | 24.3%    | 14.279 | <0.001 |
| ≥4.1 cm                  | 50.1%                   | 47.8%    | 3.310 | 0.069 |
| Histologic type          |                         |          |   |
| Differentiated           | 78.0%                   | 51.7%    | 24.217 | <0.001 |
| Undifferentiated         | 61.4%                   | 40.2%    | 9.578 | 0.002 |
| Tumor depth              |                         |          |   |
| T1/2                     | 85.4%                   | 79.2%    | 0.978 | 0.323 |
| T3                       | 54.2%                   | 63.2%    | 0.012 | 0.914 |
| T4                       | 38.3%                   | 35.4%    | 5.015 | 0.025 |
| Lymph node metastasis    |                         |          |   |
| Negative                 | 83.4%                   | 90.5%    | 0.238 | 0.626 |
| Positive                 | 54.5%                   | 30.7%    | 17.328 | <0.001 |
| TNM stage                |                         |          |   |
| I                        | 91.6%                   | 100%     | 0.568 | 0.451 |
| II                       | 69.8%                   | 82.4%    | 0.065 | 0.799 |
| III                      | 35.7%                   | 16.4%    | 7.864 | 0.003 |

Differentiated = well or moderately differentiated degree.
Undifferentiated = poorly differentiated degree or mucinous or signet cell ring.
DG = distal gastrectomy, TG = total gastrectomy.
and TG.\textsuperscript{12,14} At the current time, the comparison of perioperative morbidity and mortality between the 2 groups were still under debate.\textsuperscript{13,23,24} In the present study, DG showed significant superiority to TG during the surgical procedure. The postoperative complications and hospital stay were comparable between the 2 groups. From the point of view of safety, DG instead of TG was feasible. Previous studies demonstrated that extended lymph node dissection had not shown any benefit for gastric cancer so far.\textsuperscript{17,27–29} In the current study, the number of excised lymph nodes was not an independent prognostic factor either.

Long-term survival is the most important criterion when choosing the extent of resection. A French prospective controlled study including 201 patients with gastric antrum cancer indicated that TG did not increase the survival rate compared with DG.\textsuperscript{30} In consistent with the conclusion above, another randomized clinical trial including 618 patients with tumor of the distal stomach from 28 institutions, demonstrated that there is no superiority in extending resection, which showed familiar 5-year survival rate between DG and TG groups.\textsuperscript{31} The similar results were also found in the other studies.\textsuperscript{32–34} In our study, DG brought a significantly better overall survival than TG for distal gastric cancer patients. But, the multivariate analysis showed that type of resection was not an independent prognostic factor for the entire cohort. The poor survival after TG may be due to the higher stage of tumor in the TG group.

Under this case, further clinicopathological factor-stratified survival analysis was necessary. Multivariate analysis indicated that TG was an independent risk factor for poor prognosis in subgroup of TNM stage III. Thus, patients with distal gastric cancer who received TG should be treated more carefully and followed up closely, when assessed as TNM stage III degree postoperatively by the pathologists. There are several limitations in our present study. First, it was a retrospective study of a single center’s experience. Multicenter studies are needed to verify the survival impact of these 2 types of gastrectomy. Second, the postoperative quality of life of patients who underwent either DG or TG was not analyzed. Third, the numbers of patients in the 2 groups were unbalanced.

5. Conclusions

Distal gastrectomy was as feasible as total gastrectomy for distal gastric cancer regarding the intraoperative procedure. Type of resection was not an independent prognostic factor for distal gastric cancer in the cohort. Distal gastrectomy was significantly superior to total gastrectomy in subgroup of TNM stage III. We recommended distal gastrectomy as the optimal surgical procedure for distal gastric cancer under the premise of negative resection margin.

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