

Distal gastrectomy versus total gastrectomy for distal gastric cancer

Zhen Liu, MM, Fan Feng, MD, Man Guo, B.Med, Shushang Liu, MM, Gaozan Zheng, MM, Guanghui Xu, MM, Xiao Lian, MS.tat, Daiming Fan, PhD, Hongwei Zhang, PhD*

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 and total gastrectomy had been successfully performed in 1881 and 1897,^[2,3] respectively, the best surgical procedure for distal gastric cancer still remains controversial.

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Division of Digestive Surgery, Xijing Hospital of Digestive Diseases, The Fourth Military Medical University, Xi'an, Shaanxi Province, China.

* Correspondence: Hongwei Zhang and Fan Feng, Division of Digestive Surgery, Xijing Hospital of Digestive Diseases, The Fourth Military Medical University, Xi'an, Shaanxi Province, China (e-mails: zhanghwfmmu@126.com [HZ]; surgeonfengfan@163.com [FF]).

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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 \pm 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
Clinicopathological features of distal gastric cancer patients between DG and TG group.

Characteristics	DG group (n=1157)	TG group (n=105)	<i>P</i>
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
≤ 2cm	323 (27.9%)	14 (13.3%)	
2.1–4 cm	502 (43.4%)	36 (34.3%)	
≥ 4.1 cm	332 (28.7%)	55 (52.4%)	
Histologic type			0.027
Well	149 (12.9%)	4 (3.8%)	
Moderately	276 (24.0%)	22 (21.0%)	
Poorly	676 (58.7%)	73 (69.5%)	
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.

Table 2

Perioperative outcomes of distal gastric cancer patients between DG and TG groups.

Items	DG group (n=1157)	TG group (n=105)	<i>P</i>
Intraoperative outcomes, mean \pm SD			
Surgical time, min	199.09 \pm 64.926	224.65 \pm 74.66	<0.001
Intraoperative bleeding, mL	185.22 \pm 126.37	217.43 \pm 147.41	0.014
Number of excised lymph nodes	23.66 \pm 9.77	28.25 \pm 10.43	<0.001
Postoperative complications, n, %			
Pulmonary infection	27 (2.8%)	2 (2.3%)	1.000
Wound dehiscence	7 (0.7%)	0	1.000
Wound infection	4 (0.4%)	0	1.000
Anastomotic leakage	2 (0.2%)	0	1.000
Chylous fistula	7 (0.6%)	0	1.000
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.

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 2 groups (all $P > 0.05$). The postoperative hospital stay had no statistical difference either (median, 7 d vs 7 d, $P = 0.257$).

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

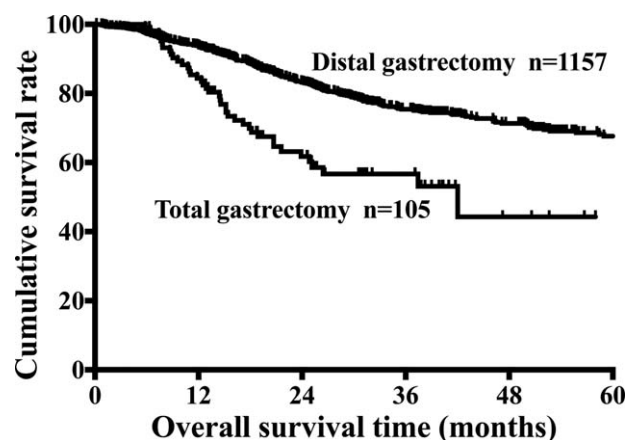


Figure 1. Comparison of 5-year survival rates of distal gastric cancer patients between DG and TG groups. DG = distal gastrectomy, TG = total gastrectomy.

Table 3**Univariate and multivariate analyses of prognostic factors for patients with distal gastric cancer.**

Characteristics	Univariate analysis			Multivariate analysis		
	β	HR (95% CI)	P	β	HR (95% CI)	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	0.321	1.379 (1.127–1.687)	0.002
Histologic type	0.525	1.691 (1.429–2.001)	<0.001	0.202	1.224 (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.

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 ($\leq 60, > 60$), 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.

Table 4**Kaplan–Meier survival analysis of patients' clinicopathological factors.**

Factors	5-year overall survival		χ^2 value	P
	DG group	TG group		
Age				
≤ 60	69.0%	39.6%	13.295	<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%	14.270	<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%	87.2%	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%	95.0%	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.

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 approximately 12.3% distal gastric cancer patients received TG.^[9] In our cohort, only 8.3% patients received TG which was obviously lower than the proportion reported previously.

Actually, TG could cause several complications such as weight loss, diarrhea, anorexia, and metabolic changes.^[22] Meanwhile, there is also some superiority of TG compared with DG; for instance, avoiding tumor local recurrence and reducing the occurrence risk of remnant gastric cancer.^[23] However, a previous randomized clinical trial demonstrated that the postoperative complications were comparable between DG

Table 5**Univariate and multivariate analyses of prognostic factors for patients with stage III distal gastric cancer.**

Characteristics	Univariate analysis			Multivariate analysis		
	β	HR (95% CI)	P	β	HR (95% CI)	P
Age	0.383	1.467 (1.095–1.965)	0.010	0.393	1.481 (1.101–1.993)	0.009
Gender	-0.057	0.945 (0.695–1.284)	0.717			
Tumor size	0.328	1.388 (1.090–1.768)	0.008			
Histologic type	0.347	1.414 (1.093–1.829)	0.008	0.275	1.316 (1.013–1.710)	0.040
Tumor depth	0.300	1.350 (1.077–1.691)	0.009	0.441	1.554 (1.227–1.967)	<0.001
Lymph node metastasis	0.472	1.603 (1.268–2.026)	<0.001	0.592	1.808 (1.418–2.306)	<0.001
Surgical time	0.001	1.001 (0.999–1.004)	0.223			
Intraoperative bleeding	0.001	1.001 (1.000–1.002)	0.033			
No. of excised lymph nodes	-0.003	0.997 (0.982–1.012)	0.706			
Type of resection	-0.542	0.582 (0.407–0.831)	0.003	-0.367	0.693 (0.481–0.999)	0.049

CI=confidence interval, HR=hazard ratio.

and TG.^[24] At the current time, the comparison of perioperative morbidity and mortality between the 2 groups were still under debate.^[22,25,26] 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.^[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 criteria 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.^[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.^[31] The similar results were also found in the other studies.^[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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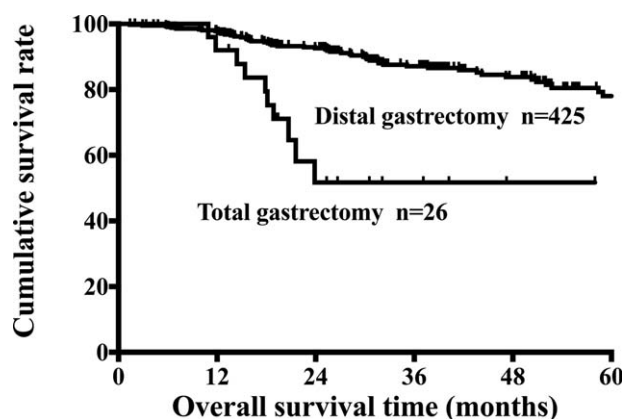


Figure 2. Survival curves of patients with TNM stage III distal gastric cancer between DG and TG groups. DG = distal gastrectomy, TG = total gastrectomy, TNM = tumor-node-metastasis staging system.

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