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Long-term outcomes of laparoscopy-assisted distal gastrectomy versus open distal gastrectomy for gastric cancer: a 10-year single-institution experience

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Abstract

Background Laparoscopy-assisted distal gastrectomy (LADG) for gastric cancer has been widely applied; however, its oncologic efficacy has yet been well established. The study aimed to compare the long-term oncologic outcomes of LADG versus open distal gastrectomy (ODG) on gastric cancer.

Methods The clinicopathologic data of gastric cancer patients who underwent distal gastrectomy with curative intent from October 2004 through September 2014 were included and analyzed in a retrospective cohort. The last follow-up was September 2016.

Results 769 eligible patients (LADG 414 vs. ODG 355) were included in the study. No significant difference was observed between the groups in 5-year DFS (LADG 61.2% vs. ODG 59.1%; $p=0.384$) and OS rates (LADG 65.8% vs. ODG 66.3%; $p=0.750$). During surgery, though LADG group had longer operating time, the blood loss was less than ODG group. LADG group had faster postoperative recovery course including shorter time to oral intake, ambulation, and discharge time. Postoperative complication rate within 30 days showed no significant difference between the groups (LADG 15.7% vs. ODG 13.0%; $p=0.281$). Age over 65 years old, blood loss > 200 ml, postoperative complication, and advanced T and N stage were identified as independent risk factors for DFS and OS.

Conclusions LADG could yield similar oncologic outcomes compared with ODG in treating distal gastric cancer. However, the findings need to be further confirmed through ongoing prospective randomized controlled trials.

Keywords Gastric cancer · Laparoscopy · Gastrectomy · Oncologic outcome · Long term

Gastric cancer, as the world's third leading cause for cancer-related deaths, brought more than 300,000 deaths in China annually [1, 2]. Even with the rapid development of multiple treatment modalities [3–5], for localized resectable distal gastric cancer, radical distal gastrectomy with sufficient lymphadenectomy still remains the primary treatment.

Laparoscopy-assisted distal gastrectomy (LADG), as a minimally invasive alternative to traditional open distal gastrectomy (ODG), has been applied worldwide in recent years. Reports concerning the safety, feasibility, and oncologic outcomes for LADG have shown that it could yield comparable efficacy with ODG, especially in treatment of early gastric cancer [6, 7]. For locally advanced distal gastric cancer, multicenter prospective trials comparing the oncologic outcomes for LADG with ODG, including CLASS-01 (China), KLASS-02 (Korea), and JLSSG 0901 (Japan) trials are still ongoing. To mention that, the interim report of CLASS-01 has already demonstrated the safety and feasibility of LADG, the long-term oncologic results are still awaited [8]. Before publication of the final results of these randomized controlled trials (RCTs), the efficacy of LADG for distal gastric cancer was primarily supported by retrospective studies [9–11]. However, the evidence level of these

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studies was limited, mainly due to the retrospective design and lack of advanced-stage diseases.

As one of the leading laparoscopic gastrointestinal surgical centers in China, Nanfang Hospital started the first case of laparoscopic distal gastrectomy for distal gastric cancer in 2004. Accordingly, a prospective collected gastric cancer database including clinicopathologic, surgical, and follow-up information was established and adopted as the official database for Chinese Laparoscopic Gastrointestinal Surgery Study (CLASS) group [12]. Through our 10 years' experience (2004–2014) of performing LADG for distal gastric cancer, we aimed to investigate the long-term oncologic outcomes of LADG with ODG for distal gastric cancer and to further identify the potential risk factors for survival through the study.

Materials and methods

Patient

Between October 2004 and September 2014, 1427 gastric cancer patients who received gastrectomy in our center were identified from the above-mentioned database [12]. Among them, 422 patients who underwent total gastrectomy, 118 who underwent proximal gastrectomy, and one patient who underwent segmental resection were not included in the study. One hundred and seventeen patients with stage IV disease were also excluded. Finally, 769 eligible patients underwent distal gastrectomy (LADG: 414 vs. ODG: 355) with curative intent were subsequently analyzed (Fig. 1).

The study complied with the principles set forth in the Declaration of Helsinki. The data collection protocol was approved by the Ethics Committee of Nanfang Hospital, Southern Medical University. For all patients, full explanations of the advantages, disadvantages, risks, along with possible outcomes and expenses were provided before operations to all the patients. Surgical procedures were determined based on the patients' own choices. Written informed consent was obtained from all the patients in the study.

Surgical indications and procedures

Preoperative diagnosis was performed by endoscopic biopsy and histological examination. Clinical stage was confirmed by endoscopic ultrasound, enhanced abdominal computed tomography, and positron emission computed tomography if necessary. The 7th edition of AJCC Cancer Staging was applied to determine the stages of the disease [13].

Surgery was attempted for tumors staged T1−4, with lymph nodes involvement limited to the perigastric tier, and without distant metastasis according to preoperative assessment. After the learning curve of laparoscopic distal gastrectomy with D2 lymphadenectomy was overcome, the indication of LADG was identical with ODG [14]. Open and laparoscopic distal gastrectomies were following the identical oncologic treatment principles. All the surgeries (both open and laparoscopic distal gastrectomies) were performed by the same group of surgeons in our institution. During surgery, D1 or D1+ lymphadenectomy was conducted for early gastric cancer, D2 lymphadenectomy was conducted for advanced gastric cancer. The principles for gastrectomy, lymphadenectomy, and extent of omentectomy were

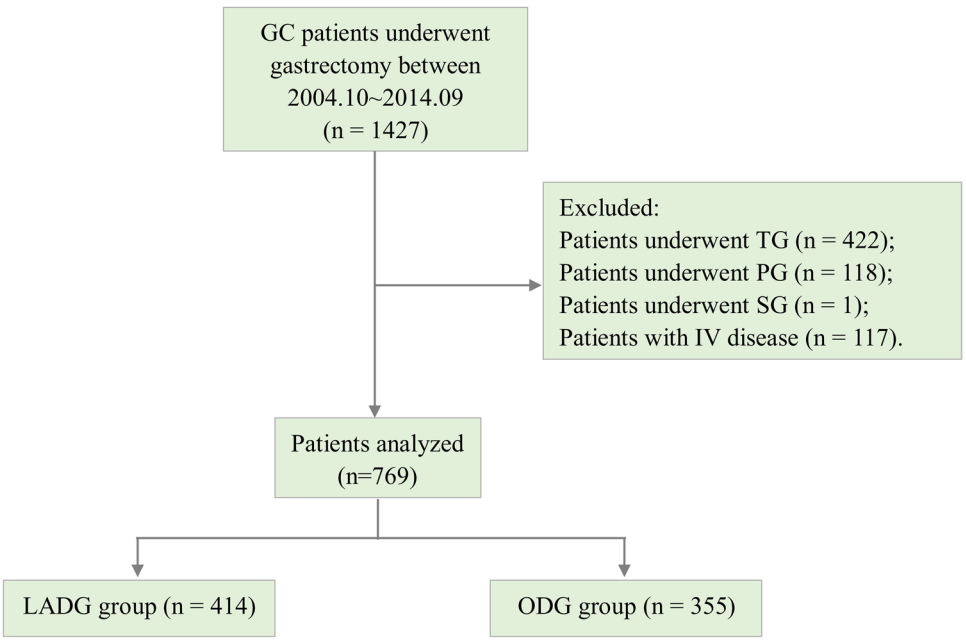

Fig. 1 Flow chart showing study cohort. *GC* gastric cancer, *TG* total gastrectomy, *PG* proximal gastrectomy, *SG* segmental gastrectomy, *LADG* laparoscopy-assisted distal gastrectomy, *ODG* open distal gastrectomy

determined according to the gastric cancer treatment guidelines in Japan [15, 16]. The procedure of LADG has been described previously [17]. Reconstruction was performed according to the surgeon's preference and experience, either Billroth-I gastroduodenostomy, Billroth-II gastrojejunostomy, or Roux-en-Y gastrojejunostomy was adopted during surgery.

Adjuvant chemotherapy and follow-up

The indication for adjuvant chemotherapy was strictly evaluated based on the tumor's pathologic results and patients' decision. Despite the changes in first-line chemotherapy regimens for gastric cancer during the past decade, 5-FU-based regimens including XELOX, FOLFOX, and mFOLFOX were applied in T3–4 or any N+ patients. The adjuvant treatment period was 6 months.

All patients were followed up until death or last follow-up in September 2016. The follow-up scheme was 3-month interval during the first 2 years after surgery, and 6-month in the next 3 years, and annually afterward.

Statistical analysis

Data are presented as mean ± standard deviation for continuous variable (for those with non-normal distribution, median and range are shown) and as number (%) for categorical variables. The Student's t test and Mann–Whitney U test were used to compare continuous variables, and the χ^2 test and Fisher's exact test were used to compare categorical variables, as appropriate. Survival probability was estimated with the Kaplan–Meier method and compared by log-rank test. Risk factors for survival were evaluated by uni- and multivariate analyses using Cox regression models. Variables with statistical significance ($p < 0.05$) in univariate analysis as well as the critical factor in present analysis, surgical procedure (i.e., LADG or ODG) were entered into the multivariable model and were analyzed by using an "Enter" method. $p < 0.05$ (two-tailed) was considered statistically significant. The statistical software SPSS version 17.0 for Windows (SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses.

Results

Clinicopathologic characteristics

The clinical and pathologic characteristics of patients are shown in Table 1. There were 276 men in the LADG group and 229 men in the ODG group ($p = 0.529$). Mean age in the LADG and ODG groups was 56 and 54 years ($p = 0.061$), with a mean body mass index of 21.88 and 21.68 kg/m^2 ($p = 0.328$). Mean tumor size was 3.27 cm in LADG group and 3.45 cm in ODG group ($p = 0.108$), respectively, with a median of one metastatic lymph node in both two groups ($p = 0.884$). There were no significant differences between LADG and ODG groups in terms of previous abdominal surgery, comorbidity, or tumor location. The number of patients in each disease stage was as follows (LADG vs. ODG): stage I, 132 (31.9%) versus 93 (26.2%); stage II, 101 (24.4%) versus 100 (28.2%); stage III, 181 (43.7%) versus 162 (45.6%). TNM stage between LADG and ODG groups did not differ significantly ($p = 0.191$).

Surgical characteristic, postoperative recovery courses, and complications

The surgical and postoperative outcomes are presented in Table 2. The median operating time of LADG group was longer than ODG group (202 vs. 170 min; $p < 0.001$). However, the median estimated blood loss in LADG group was less than ODG group (100 vs. 200 ml; $p < 0.001$). Also, less patients needing blood transfusion during operation was observed in LADG group, compared with ODG group (3.1 vs. 9.0%; $p < 0.001$). There was no significant difference between the two groups in terms of length of proximal resection margin. No positive resection margin was observed in all patients. Two groups showed different distributions in reconstruction ($p < 0.001$), with more Billroth-I observed in LADG group (66.4%) and more Billroth-II in ODG group (60.8%). Lymphadenectomy and the number of lymph nodes retrieved were similar between the groups. Among patients in LADG group, 13 (3.1%) experienced conversion to open surgery due to bulky tumor (eight patients), technical difficulties (two patients), severe adhesion (one patient), uncontrolled bleeding (one patient), and intolerance to pneumoperitoneum (one patient). In term of recovery course, time to first flatus, first liquid intake, first soft diet and ambulation, and postoperative hospital stay were significantly shorter in LADG group than ODG group (all $p < 0.001$).

Postoperative morbidity and mortality are listed in Table 3. A total of 81 postoperative complications occurred in 65 (15.7%) patients in LADG group and 56 complications in 46 (13.0%) patients in ODG group. There was no significant difference in total number of patients occurring complications between the groups ($p = 0.281$). Among all the complications (anastomotic leakage, wound problem, intraabdominal bleeding, intraabdominal abscess, ileus, intraabdominal lymphorrhagia, gastroparesis, pancreatic fistula, cholecystitis, pulmonary, cardio-cerebrovascular and renal complication, and others), no significant difference was observed between the groups. According to the Clavien–Dindo classification of surgical complications [18], the severity of complications was similar between the two

Table 1 Clinicopathologic characteristics

	LADG ($n=414$) *N* (%) or mean (SD)	ODG ($n=355$) *N* (%) or mean (SD)	*p*
Age (years)	56.03 (12.74)	54.37 (11.44)	0.061
Gender (men)	276 (66.7)	229 (64.5)	0.529
Body mass index (kg/m^2)	21.88 (2.94)	21.68 (2.47)	0.328
Previous abdominal surgery	43 (10.4)	28 (7.9)	0.233
Comorbidity			0.583
0	286 (69.1)	257 (72.4)	
1	96 (23.2)	75 (21.1)	
≥2	32 (7.7)	23 (6.5)	
Tumor location			0.876
Middle third	59 (14.3)	52 (14.6)	
Lower third	355 (85.7)	303 (85.4)	
Tumor size (cm)	3.27 (1.45)	3.45 (1.57)	0.108
No. of metastatic LNs[a]	1.00 (0–47)	1.00 (0–65)	0.884
Received chemotherapy	238 (57.5)	209 (58.9)	0.698
Clinical T stage			0.002
T1	88 (21.3)	45 (12.7)	
T2 ~ T4	326 (78.7)	310 (87.3)	
Clinical N stage			0.093
N0	192 (46.4)	166 (46.8)	
N1	61 (14.7)	46 (13.0)	
N2	71 (17.1)	74 (20.8)	
N3	35 (8.5)	40 (11.3)	
Nx	55 (13.3)	29 (8.2)	
Pathological T stage			0.006
T1	117 (28.3)	70 (19.7)	
T2 ~ T4	297 (71.7)	285 (80.3)	
Pathologic N stage			0.046
N0	196 (47.3)	172 (48.5)	
N1	75 (18.1)	44 (12.4)	
N2	65 (15.7)	77 (21.7)	
N3	78 (18.8)	62 (17.5)	
TNM stage			0.191
I	132 (31.9)	93 (26.2)	
II	101 (24.4)	100 (28.2)	
III	181 (43.7)	162 (45.6)	
Chronological distribution			< 0.001
2004–2010	133 (32.1)	272 (76.6)	
2011–2014	281 (67.9)	83 (23.4)	

LADG laparoscopy-assisted distal gastrectomy, *ODG* open distal gastrectomy, *SD* standard deviation

[a]Data are presented as median (range)

groups ($p=0.950$). One patient in ODG group died due to severe pancreatitis.

Long-term oncologic outcomes

The patients were followed up for a median of 45 months (range 1–146 months). The 5-year DFS rate was 61.2% (95% confidence interval [CI] 55.2−67.1%) in LADG group and 59.1% (95% CI 53.6−64.6%) in ODG group, with no significant difference between the groups (hazard ratio [HR] 1.11; 95% CI 0.88–1.41; $p=0.384$) (Fig. 2A). Both LADG and ODG groups yielded a similar 5-year OS rate [65.8% (95% CI 59.9−71.7%) vs. 66.3% (95% CI 61.0−71.6%); HR 1.04, (95% CI 0.81−1.35); $p=0.750$] (Fig. 2B). When stratified by tumor stage, patients yielded similar 5-year DFS and OS rates between the two groups in each stage (Fig. 2C, D).

Table 2 Surgical outcomes and postoperative recovery course

	LADG ($n=414$) *N* (%) or mean (SD)	ODG ($n=355$) *N* (%) or mean (SD)	*p*
Operating time (min)[a]	202 (120–560)	170 (102–400)	< 0.001
Estimated blood loss (ml)[a]	100 (10–800)	200 (15-1500)	< 0.001
Intraoperative blood transfusion	13 (3.1)	32 (9.0)	< 0.001
Proximal resection margin (mm)	43.05 (21.77)	44.37 (16.41)	0.349
Positive resection margin	0 (0.0)	0 (0.0)	1.000
Reconstruction			< 0.001
Billroth-I	275 (66.4)	130 (36.6)	
Billroth-II	115 (27.8)	216 (60.8)	
Roux-en-Y	24 (5.8)	9 (2.5)	
Lymphadenectomy			0.072
D0	14 (3.4)	8 (2.3)	
D1	58 (14.0)	41 (11.5)	
D1+	51 (12.3)	27 (7.6)	
D2	285 (68.8)	276 (77.7)	
D2+	6 (1.4)	3 (0.8)	
No. of retrieved LNs[a]	27 (2-128)	33 (2-145)	0.722
Conversion	13 (3.1)	–	
Bulky tumor	8 (61.5)	–	
Technical difficulties	2 (15.4)	–	
Severe adhesion	1 (7.7)	–	
Uncontrolled bleeding	1 (7.7)	–	
Intolerance to pneumoperitoneum	1 (7.7)	–	
Time to ambulation (day)	2.54 (1.51)	4.06 (2.23)	< 0.001
Time to first flatus (day)	3.46 (1.56)	5.08 (1.92)	< 0.001
Time to first liquid intake (day)	4.17 (1.76)	5.64 (2.34)	< 0.001
Time to first soft diet (day)	5.26 (2.82)	7.56 (3.33)	< 0.001
Postoperative hospital stay (day)	9.31 (4.21)	13.86 (16.97)	< 0.001

LADG laparoscopy-assisted distal gastrectomy, *ODG* open distal gastrectomy, *SD* standard deviation, *LNs* lymph nodes, *D1* No. 1, 3, 4sb, 4 days, 5, 6, 7, *D0* lymphadenectomy less than D1, *D1+* D1 plus No. 8a, 9, *D2* D1 plus No. 8a, 9, 11p, 12a, *D2+* D2 plus one or more of No. 12 b/p, 14, and 16

[a]Data are presented as median (range)

Risk factors for survival

Uni- and multivariate analyses of risk factors for survival are presented in Table 4. Univariate analyses revealed that age over 65 years, bearing more than one comorbidity, tumor located at the lower third, tumor size > 4.0 cm, estimated blood loss over 200 ml, intraoperative blood transfusion, postoperative complication, and advanced tumor T and N stage were risk factors for either DFS or OS. Furthermore, multivariate analyses indicated that age over 65 years, estimated blood loss > 200 ml, postoperative complication, and advanced tumor T and N stage were independent risk factors for DFS and OS. Notably, LADG was not identified as a risk factor for both OS and DFS, compared with ODG.

Discussion

Since its introduction for early gastric cancer by Kitano et al. [19], LADG has gradually gained popularity in the management of distal gastric cancer in East Asia [20–22]. After the first report of LADG for distal gastric cancer in China in 2000 [23], our center also started LADG for early distal gastric cancer in 2004. From 2004 to 2014, with the accumulation of laparoscopic surgical experience and improvement in surgical techniques, the indications of LADG have gradually been extended from early-staged disease to resectable locally advanced diseases. To date, some of the prospective results about LADG for early gastric cancer including short- and long-term outcomes have demonstrated its comparable efficacy with ODG [6, 7, 24]; however, RCTs relating LADG

Table 3 Postoperative morbidity and mortality

	LADG ($n=414$) *N* (%)	ODG ($n=355$) *N* (%)	*p*
Postoperative complication	65 (15.7)	46 (13.0)	0.281
Anastomotic leakage	1 (0.2)	3 (0.8)	0.340
Wound problem	10 (2.4)	7 (2.0)	0.677
Intraabdominal bleeding	5 (1.2)	3 (0.8)	0.732
Intraabdominal abscess	9 (2.2)	3 (0.8)	0.138
Ileus	11 (2.7)	8 (2.3)	0.719
Intraabdominal lymphorrhagia	9 (2.2)	3 (0.8)	0.138
Gastroparesis	2 (0.5)	5 (1.4)	0.258
Pancreatic fistula	1 (0.2)	0 (0.0)	1.000
Cholecystitis	1 (0.2)	0 (0.0)	1.000
Pulmonary complication	22 (5.3)	17 (4.8)	0.741
Cardio-cerebrovascular complication	3 (0.7)	1 (0.3)	0.628
Renal complication	2 (0.5)	4 (1.1)	0.423
Others	5 (1.2)	2 (0.6)	0.461
Mortality	0 (0.0)	1 (0.2)	1.000
Clavien–Dindo classification			0.950
I	9 (13.8)	7 (14.9)	
II	44 (67.7)	30 (63.8)	
IIIa	3 (4.6)	3 (6.4)	
IIIb	6 (9.2)	4 (8.5)	
IVa	3 (4.6)	2 (4.3)	
V	0 (0.0)	1 (2.1)	

LADG laparoscopy-assisted distal gastrectomy, *ODG* open distal gastrectomy

versus ODG for advanced gastric cancer are still lacking, especially from the long-term aspects [25]. There were also a few retrospective reports on the laparoscopic distal gastrectomy with lymphadenectomy in treating gastric cancer, and these reports came to similar conclusion of our study [26, 27]. Since the final results of the large-scale RCTs comparing LADG and ODG for locally advanced gastric cancer are still being awaited, herein, we retrospectively analyzed our center's 10-year data of LADG for gastric cancer with emphasis on the long-term oncologic outcomes.

In this study, there were no significant differences in 5-year DFS and OS between LADG and ODG groups. While stratified by stages, the survival rates for stage I, II, and III were also similar between the groups, which might help support that LADG could yield comparable oncologic outcomes with ODG for distal gastric cancer. Since different from other studies, in our analyzed cohorts, the majority of patients were with advanced-staged diseases, it is inappropriate to directly compare our 5-year survival rates with others'. For example, the 5-year OS in our study was 65.8% in LADG group; however, in a Japanese study, where more clinical stage I patients (243 out of 278) were included, the 5-year OS was 85.6% [28]. However, when analyzing by stages, our survival data of stage I, II, and III diseases in LADG and ODG were similar with other reports [7, 9, 10, 29].

In our study, we found that postoperative complication and advanced tumor T and N stage were independent risk factors for both DFS and OS, which have also been demonstrated in other studies [30–32]. Also, age over 65 years was identified as risk factor for survival in our study, which was similar with results from two recent Korean studies [33, 34]. By explanation, a poorer prognosis in elderly patients might be partly attributed to the weaker host-defense mechanisms [35, 36]. In addition, we found that intraoperative blood loss over 200 ml was also a risk factor for survival. In Mizuno et al.'s [37] and Ishino et al.'s [38] studies, they found that excessive intraoperative blood loss was associated with poorer prognosis. Although the mechanisms of negative effect of excessive blood loss on long-term outcomes are not fully understood, but evidence showed that excessive blood loss may, by itself, impair immunity against cancer cells and nutritional status via loss of plasma constituents [39], which might be associated with poor survival. Notably in our study, the surgical procedure of LADG versus ODG was not a risk factor for DFS or OS, which might indicate that LADG was an oncologically efficient treatment alternative to ODG in distal gastric cancer.

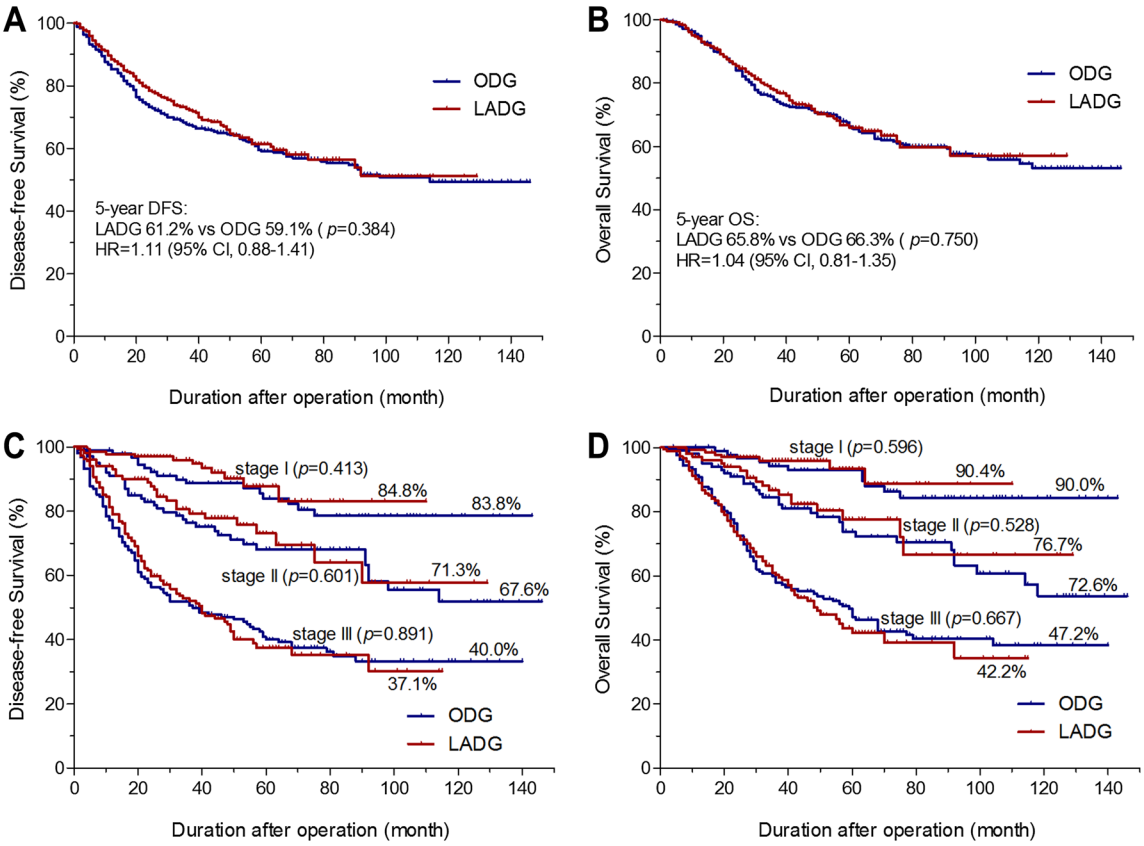

Fig. 2 Comparison of cumulative survival rates for LADG and ODG groups in terms of **A** 5-year disease-free survival, **B** 5-year overall survival, and **C** 5-year disease-free survival according to tumor stages and **D** 5-year overall survival according to tumor stages

Regarding postoperative complication, a total rate of postoperative complication after LADG reported by other authors range between 11.0 and 19.9% [6, 8, 22, 34, 40]. In our study, the postoperative complication rate was 15.7% in LADG group and 13.0% in ODG group. Complication rate and severity were both similar between the groups, hence, LADG could be equally safe and feasible with ODG. In our cohort, no matter in LADG group or ODG group, the most common complication was pulmonary infection after surgery. This phenomenon was identical with CLASS-01's interim report [8]. The reason might be that after upper abdominal surgeries, reduced diaphragmatic activity and microatelectasis would cause decreased pulmonary function, which eventually resulted in pulmonary infection [41, 42].

For surgical findings and recovery course, our study demonstrated similar minimally invasive benefits including less blood loss, shorter times of recovery (ambulation, first flatus, oral intake, and hospital stay) as with other studies [8, 20, 24, 43, 44]. For reconstruction after gastrectomy, in LADG group, Billroth-I reconstruction was preferred by surgeons while more Billroth-II reconstruction was adopted by open surgeons. This was mainly due to the different distributions of T stage tumors between the groups. Usually, in our center, Billroth-I reconstruction was preferred in T1 stage tumors before 2012 as long as sufficient resection margin could be ascertained. However, since 2012, after observation of three cases of recurrent tumor at the anastomosis after Billroth-I reconstruction, the difficulty of performing second surgery reminded us of modifying our reconstruction preference after distal gastrectomy. Ever since then, Billroth-II or Roux-en-Y reconstruction was adopted in either LADG of ODG.

Our results have several limitations. First, its retrospective design has the weakness of being observational or non-experimental in nature. Second, the imbalance of T and N stage between the groups might influence the long-term outcomes though the TNM stage distribution was similar. Third, during a decade's period, the changes of treatment concepts, surgical preferences might also create bias in the analyses. Despite these limitations, our study evaluating our 10 years' experience of LADG in views of long-term oncologic outcomes, would represent the development of Chinese laparoscopic gastric cancer surgery during the past decade, since our center is one of the first centers in China to perform LADG for distal gastric cancer. In conclusion, the findings of this study might suggest comparable safety and oncologic efficacy of LADG in treating distal gastrectomy

Table 4 Univariate and multivariate Cox regression analyses of risk factors for survival

Factor	Disease-free survival				Overall survival			
	Univariate		Multivariate		Univariate		Multivariate	
	HR[a] (95% CI)	*p*	HR[a] (95% CI)	*p*	HR[a] (95% CI)	*p*	HR[a] (95% CI)	*p*
Procedure (LADG vs. ODG)	1.11 (0.88, 1.41)	0.386	0.96 (0.75, 1.23)	0.747	1.04 (0.81, 1.35)	0.751	1.01 (0.77, 1.32)	0.974
Age (> 65 vs. ≤ 65 years)	1.71 (1.31, 2.22)	< 0.001	1.64 (1.24, 2.16)	0.001	1.93 (1.46, 2.55)	< 0.001	1.86 (1.38, 2.49)	< 0.001
Gender	1.03 (0.80, 1.31)	0.834			0.98 (0.75, 1.27)	0.866		
BMI (> 30.0 vs. ≤ 30.0 kg/m^2)	0.88 (0.65, 1.56)	0.365			0.91 (0.68, 1.34)	0.553		
Previous abdominal surgery	1.00 (0.66, 1.50)	0.985			0.92 (0.57, 1.47)	0.719		
Comorbidity (> 1 vs. ≤ 1)	1.88 (1.30, 2.73)	0.001	1.36 (0.92, 2.00)	0.124	1.84 (1.23, 2.77)	0.003	1.21 (0.80, 1.85)	0.371
Tumor location (lower vs. middle)	1.78 (1.21, 2.61)	0.003	1.38 (0.92, 2.05)	0.119	1.93 (1.25, 2.96)	0.003	1.51 (0.96, 2.37)	0.073
Tumor size (> 4.0 vs. ≤ 4.0 cm)	1.80 (1.41, 2.30)	< 0.001	1.06 (0.82, 1.38)	0.666	1.82 (1.40, 2.36)	< 0.001	1.03 (0.78, 1.37)	0.832
Operating time (> 240 vs. ≤ 240 min)	1.10 (0.78, 1.54)	0.581			1.05 (0.72, 1.53)	0.814		
Estimated blood loss (> 200 vs. ≤ 200 ml)	1.44 (1.05, 1.96)	0.022	1.47 (1.06, 2.03)	0.021	1.43 (1.03, 1.98)	0.032	1.45 (1.03, 2.05)	0.032
Intraoperative blood transfusion	1.59 (1.05, 2.40)	0.027	0.89 (0.57, 1.37)	0.589	1.63 (1.05, 2.52)	0.030	0.96 (0.60, 1.53)	0.867
Conversion	1.43 (0.87, 4.43)	0.483			1.53 (0.79, 4.91)	0.581		
Postoperative complication	1.57 (1.16, 2.13)	0.004	1.39 (1.02, 1.91)	0.040	1.93 (1.40, 2.65)	< 0.001	1.75 (1.26, 2.42)	0.001
Pathologic T stage		< 0.001		< 0.001		< 0.001		< 0.001
T2 versus T1	1.59 (0.91, 2.80)	0.105	1.17 (0.65, 2.09)	0.599	2.16 (1.14, 4.08)	0.018	1.60 (0.83, 3.09)	0.161
T3 versus T1	3.92 (2.08, 7.39)	< 0.001	2.56 (1.33, 4.93)	0.005	5.01 (2.41, 10.43)	< 0.001	3.18 (1.49, 6.77)	0.003
T4 versus T1	4.19 (2.81, 6.25)	< 0.001	2.32 (1.51, 3.59)	< 0.001	5.23 (3.23, 8.48)	< 0.001	2.89 (1.73, 4.85)	< 0.001
Pathologic N stage		< 0.001		< 0.001		< 0.001		< 0.001
N1 versus N0	1.98 (1.36, 2.90)	< 0.001	1.73 (1.16, 2.57)	0.007	2.03 (1.34, 3.08)	0.001	1.78 (1.15, 2.74)	0.010
N2 versus N0	3.06 (2.22, 4.22)	< 0.001	2.17 (1.54, 3.06)	< 0.001	3.11 (2.19, 4.43)	< 0.001	2.13 (1.46, 3.09)	< 0.001
N3 versus N0	5.32 (3.90, 7.24)	< 0.001	3.73 (2.64, 5.25)	< 0.001	5.56 (3.96, 7.80)	< 0.001	3.86 (2.65, 5.61)	< 0.001

LADG laparoscopy-assisted distal gastrectomy, *ODG* open distal gastrectomy, *BMI* body mass index, *HR* hazard ratio, *CI* confidence interval

[a]HR was calculated from Cox regression model

in experienced centers. However, the long-term multicenter prospective randomized controlled trials would still be awaited.

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Compliance with ethical standards

Disclosures Drs. Hao Wang, Tingyu Mou, Hao Chen, Yanfeng Hu, Tian Lin, Tuanjie Li, Jiang Yu, Hao Liu, and Guoxin Li have no conflicts of interest or financial ties to disclose.

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