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Original Article

Perioperative clinicopathological outcomes of laparoscopic and open total gastrectomy for gastric cancer of cardia and fundus: results from a retrospective study

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Abstract: We analyzed perioperative clinicopathological outcomes of total gastrectomy by laparoscopic and open approach for patients with gastric cancer of cardia and fundus in order to provide reference for the improvement of surgical treatment. From January 1, 2014, to December 31, 2016, in the Department of General Surgery, Beijing Shijitan Hospital, Capital Medical University, clinical and pathological data of 33 cases of patients with gastric cancer of cardia and fundus that underwent laparoscopic total gastrectomy and 29 cases of patients with gastric cancer of cardia and fundus that underwent open total gastrectomy were collected and compared. Last follow up was completed on June 30, 2017, 6 months after the last patient completed total gastrectomy. Estimated blood loss in operations was significantly less in the laparoscopic group than in open group (P<0.001). Operation time was significantly shorter in laparoscopic group than in open group (P<0.001). Length of incision was significantly shorter in laparoscopic group than in open group (P<0.001). Time passed until the first flatus was shorter after laparoscopic surgery than after open surgery (P<0.001). The life ability score at discharge was higher in the laparoscopic group than in open group (P<0.001). Time of postoperative hospitalization was shorter in laparoscopic group than in open group (P<0.001). The distance between tumor edge and proximal margin was longer in laparoscopic group than in open group (P = 0.047). Patients whose KPS Score at 2 and 4 weeks after operation were less than 70 points, and had to delay adjuvant chemotherapy, were less in the laparoscopic group than in open group (P = 0.029 and P = 0.044). No recurrence, metastasis, or death was reported in either group. Compared with open approach, laparoscopic total gastrectomy for gastric cancer of cardia and fundus had less intraoperative bleeding, shorter operation time, shorter incision, shorter postoperative hospitalization, quicker recovery of postoperative intestinal function and life ability, and longer distance between the tumor edge and proximal margin. Laparoscopic total gastrectomy could get better short-term outcomes than open total gastrectomy for patients with gastric cancer of cardia and fundus.

Keywords: Perioperative, clinicopathological, laparoscopic, open, gastrectomy, gastric cancer, cardia and fundus

Introduction

Gastric cancer is the fourth most common cancer and third leading cause of cancer-related deaths in the world. There were an estimated 951,600 new cases and 723,100 deaths in 2012 [1]. About 35 percent of the world's stomach cancer cases occur in China, seriously endangering the health of citizens. In recent years, incidence of gastric cancer in developed countries and big cities in China has been decreasing yearly but it is still flat or growing in vast rural areas and there has been no decrease in gastric cancer of cardia and fundus all over the world. Treatment of gastric cancer is relatively mature, some patients can survive long-term after tumor surgical removal. Data shows that lymph node metastases above and under the pylorus were 25% and 20%, respectively, in patients with gastric cancer of cardia and fundus. If total gastrectomy is not done, it is difficult to achieve the radical excision goal. Five-year survival rate was 83% after total gastrectomy and only 16% after proximal gastric resection in patients with gastric cancer of cardia and fundus. Mortality of anastomotic

Table 1. Baseline characteristics

Items	Laparoscopic group (n = 33)	Open Group (n = 29)	*P* value
Age (yrs)	60.8 ± 13.2	63.6 ± 11.0	0.372
Gander (n)			
Male	23	19	0.725
Female	10	10	
BMI (kg/M^2)	23.8 ± 3.01	23.7 ± 2.54	0.982
Diabetes Mellitus (n)	5	5	0.823
Life ability score on admission (points)	97.9 ± 5.45	93.4 ± 12.0	0.060

BMI = Body Mass Index.

Table 2. Operation related data

Items	Laparoscopic group (n = 33)	Open Group (n = 29)	*P* value
Operation time (min)	230 ± 58.0	290 ± 126	<0.001
EBL (ml)	244 ± 263	285 ± 223	<0.001
Length of incision (cm)	10.3 ± 4.71	18.3 ± 7.20	<0.001
Time to pass first flatus (days)	5.22 ± 3.56	6.40 ± 3.44	<0.001
Life ability score at discharge (points)	90.0 ± 11.5	86.3 ± 16.1	<0.001
Postoperative hospitalization (days)	16.7 ± 7.89	20.1 ± 14.8	<0.001
Postoperative bleeding (n)	2	4	0.304
Intestinal obstruction (n)	3	2	0.752
Anastomotic fistula (n)	1	1	0.926

EBL = Estimated Blood Loss.

fistula after proximal gastrectomy is higher and refractory reflux esophagitis after surgery influences postoperative quality of life. Therefore, total gastrectomy is the best surgical approach for gastric cancer of cardia and fundus. Since laparoscopic gastrectomy was first reported in 1994 for treatment of early stage gastric adenocarcinoma [2], this technique has been rapidly adopted within East Asia. Although laparoscopic surgery produces less trauma and a quicker recovery in comparison to open surgery [3], there have been few reports whether laparoscopic total gastrectomy for gastric cancer of cardia and fundus can achieve the same effect as open total gastrectomy. Thus, in this study, perioperative clinicopathological outcomes of laparoscopic and open total gastrectomy for patients with gastric cancer of cardia and fundus were compared and analyzed.

Material and methods

General information

This study was reviewed and approved by the Ethics Committee of Beijing Shijitan Hospital, Capital Medical University, and all patients provided written informed consent. From January 1, 2014, to December 31, 2016, in the Department of General Surgery, Beijing Shijitan Hospital, Capital Medical University, clinical and pathological data of 33 cases of patients with gastric cancer of cardia and fundus that underwent laparoscopic total gastrectomy and 29 cases of patients with gastric cancer of cardia and fundus that underwent open total gastrectomy were collected and compared. Last follow up was completed on June 30, 2017, 6 months after the last patient completed total gastrectomy. Baseline characteristics of patients in the two groups such as age, gender, body mass index, diabetes mellitus, and life ability score on admission were compared and analyzed (**Table 1**). Operation related data of patients in the two groups such as operation time, estimated blood loss, length of incision, time to pass first flatus, life ability score at discharge, postoperative hospitalization, postoperative bleeding, intestinal obstruction, and anastomotic fistula were compared and analyzed (**Table 2**). Pathological characteristics of specimens from patients in the two groups such as tumor differentiation, pTNM stage, distance between tumor edge and distal margin, distance between tumor edge and proximal margin, size of the tumor, harvested lymph nodes, and number of positive lymph nodes was compared and analyzed (**Table 3**). KPS scores of patients in the two groups were compared and analyzed 2 weeks after operation, 4 weeks after operation, and 6 weeks after operation (**Table 4**).

All patients with gastric cancer of cardia and fundus that were clinically diagnosed as cT1-4aN0-3M0 lesions based on abdominal enhanced CT, abdominal enhanced MRI, and endoscopic ultrasonography, were eligible for inclusion into our study. Exclusion criteria

Table 3. Pathological characteristics of specimens

Items	Laparoscopic group (n = 33)	Open Group (n = 29)	*P* value
Tumor differentiation (n)			
Well or moderately differentiated	10	8	0.814
Poorly differentiated/Signet-ring	23	21	
pTNM stage (n)			
Stage I	3	4	0.164
Stage II	14	12	
Stage III	16	13	
The distance between the tumor edge and the distal margin (cm)	10.3 ± 2.34	10.4 ± 1.98	0.779
The distance between the tumor edge and the proximal margin (cm)	2.52 ± 1.19	2.09 ± 1.10	0.047
Size of the tumors (cm)	4.77 ± 1.89	4.99 ± 1.72	0.319
Harvested lymph nodes (n)	29.5 ± 9.71	28.4 ± 12.7	0.441
The number of positive lymph nodes (n)	5.71 ± 10.2	7.07 ± 6.97	0.218

Table 4. KPS score after operation for adjuvant chemotherapy

Items	Laparoscopic group (n = 33)	Open Group (n= 29)	*P* value
2 weeks after operation			
≥70	30	20	0.029
<70	3	9	
4 weeks after operation			
≥70	32	23	0.044
<70	1	6	
6 weeks after operation			
≥70	33	28	0.282
<70	0	1	

KPS = Karnofsky Performance Status.

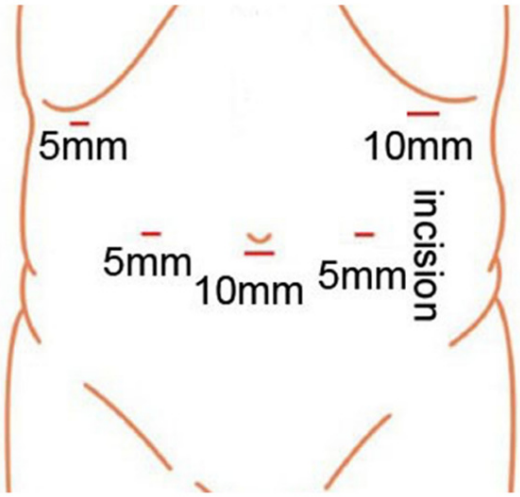

Figure 1. The five locations of trocars and incision for removing the specimen in laparoscopic total gastrectomy.

included gastric cancer of parts other than cardia and fundus, gastric tumors of other pathologic types except adenocarcinoma, recurrent gastric cancer, a synchronous distant metastasis, invasion of adjacent tissues and organs, another malignancy, severe cardiac or pulmonary disease, and pregnancy.

Operation procedures

Surgery was performed by two surgeons from Beijing Shijitan Hospitals with full experience performing laparoscopic and open total gastrectomy. All patients underwent total gastrectomy under general anesthesia. The extent of resection was identical for the laparoscopic and open method.

Laparoscopic approach: Typically, one periumbilical trocar (10 mm) was inserted and four additional trocars were introduced under laparoscopic guidance (**Figure 1**). With a pneumoperitoneum of 12 to 14 mmHg, the left lobe of the liver was retracted. The greater omentum was divided with ultrasonic shears at the midportion of the transverse colon 4 to 5 cm away from the gastroepiploic arcades toward the lower pole of the spleen. Roots of the left gastroepiploic vessels were then exposed and divided with clips. Several short gastric vessels were dissected with ultrasonic shear, and the greater curvature side was completely mobilized from the splenic hilum and left side of the diaphragm. The right gastroepiploic vein and

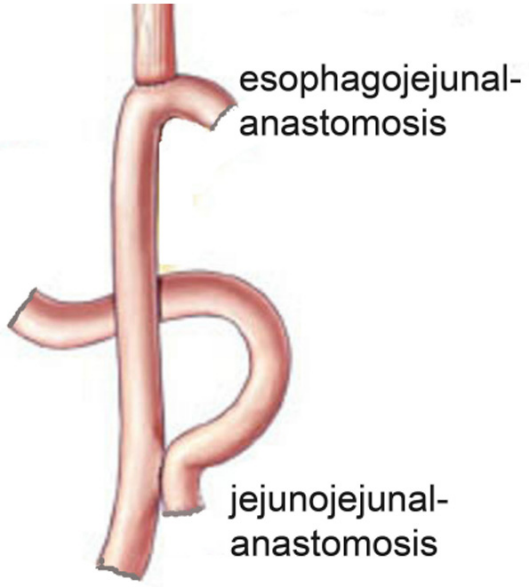

Figure 2. The two intracorporeal anastomosises completed by OrVil™ system in laparoscopic total gastrectomy.

artery were divided individually at their roots with clips and clearing of the pancreatic head area was done. The right gastric artery was then exposed and divided at its origin with clips after dissection of the anterior portion of the hepatoduodenal ligament. The duodenum was transected at 2 cm distal from the pylorus with an endoscopic linear stapler. Lymph node-bearing soft tissues along the common hepatic artery, proximal splenic artery, and celiac axis were dissected. The root of the left gastric artery was exposed and divided with double clips. Meticulous dissection was continued along the splenic vessels to clear the No. 11 lymph node. No. 10 lymph node dissection was also performed. Perigastric lymph nodes were dissected along the lesser curvature up to the esophagogastric junction with division of both vagus nerves. The abdominal esophagus was then freely mobilized after dissection of No.1 and 2 lymph nodes. Once the stomach was completely mobilized and after an adequate proximal resection margin was guaranteed, endoscopic linear stapling devices were introduced and the stomach was transected. The 10 mm trocar site at the left upper quadrant was extended to about 10 cm in length and through it the stomach was pulled out. An OrVil™ tube was then transorally introduced into the esophagus by the anesthesiologist. OrVil™ was introduced through the patient mouth with a rubbery gastric tube, at first. As the operator identified the OrVil™ tube reaching the esophageal stump, a small hole was made on the esophageal stump. The tube was then extracted through the hole until the anvil reached the esophageal stump. Then, the tube was disconnected from the anvil by cutting the connecting thread and removed from the abdominal cavity. Jejunum was brought through the anterocolic route after dividing the jejunum 30 cm from the ligament of Treitz, then the shaft of the circular stapler was introduced into the jejunum through the incision and anastomosed to the esophageal stump in an end-to-side manner. The entry site of the jejunal stump was closed using an endoscopic linear stapler. Side-to-side jejunojejunal anastomosis was performed using an endoscopic circular stapler (**Figure 2**), the length between the esophagojejunostomy and jejunojejunal anastomosis was approximately 40 cm [4]. Reinforcement sutures were made, including the double stapling point.

Open approach: A 20 cm upper midline laparotomy was made and the stomach was then pulled out through the wound. Esophageal transection was performed using linear stapling devices and the anvil of a circular stapler was inserted into the esophageal stump through the abdominal cavity, directly. The remaining steps were identical to the laparoscopic approach.

Follow up methods

Patients were followed up at two-week intervals, postoperatively, for the first 6 months. In postoperative follow up, KPS scores were recorded every two weeks after surgery, CEA test and chest radiography every 3 months, and abdominal enhanced CT at 6 months. Last follow up was completed on June 30, 2017, 6 months after the last patient completed total gastrectomy. No patients were lost to follow up or found with recurrence, metastasis, or death.

Statistical methods

All major clinicopathological parameters were subjected to statistical analysis. Measurement data were compared with t-test. Count data were compared with χ^2 test and confounding factors were analyzed using multiple linear

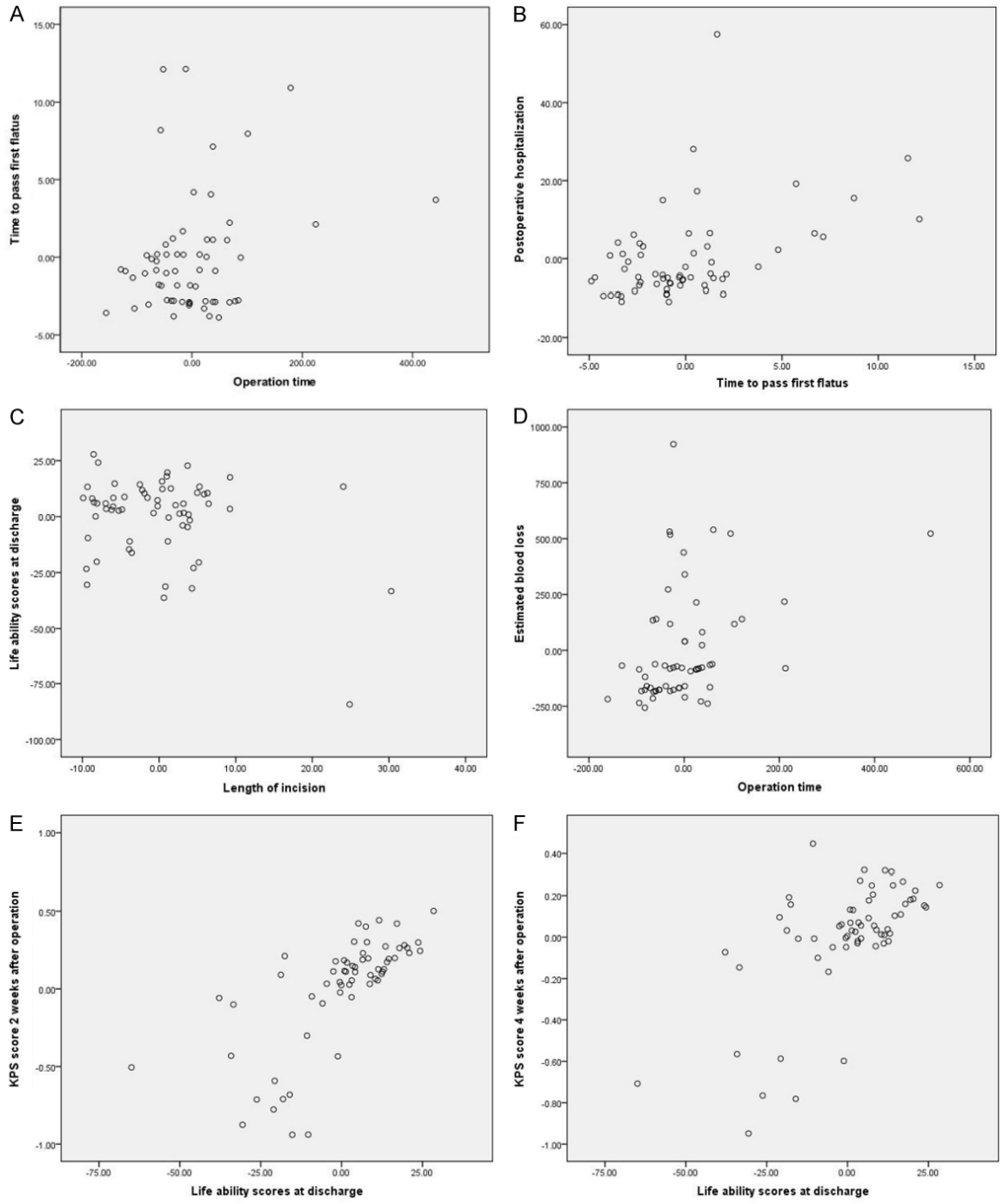

Figure 3. Operation time is the confounding factor of time to pass first flatus (the correlation coefficient = 0.285, *P* = 0.045), shown in the scatter diagram (A). Time to pass first flatus is the confounding factor of postoperative hospitalization (the correlation coefficient = 0.473, *P<0.001*) shown in the scatter diagram (B). Length of incision is the confounding factor of life ability scores at discharge (the correlation coefficient = 0.305, P = 0.016) shown in the scatter diagram (C). Operation time is the confounding factor of estimated blood loss (the correlation coefficient = 0.382, *P* = 0.003) shown in the scatter plot (D). The life ability score at discharge was positively correlated with KPS score 2 weeks after operation (the correlation coefficient = 0.718, *P<0.001*) and KPS score 4 weeks after operation (the correlation coefficient = 0.646, *P<0.001*), shown in the scatter plot (E) and (F).

regression. Differences were considered statistically significant if P<0.05. All statistical analyses were performed using SPSS 17.0 (SPSS, Inc., Chicago, IL, USA) software.

Results

Age, gender, body mass index, diabetes mellitus, and life ability score on admission were similar between the two groups (**Table 1**). Estimated blood loss during operation was significantly less in the laparoscopic group than in open group (**Table 2**). Operation time was significantly shorter in the laparoscopic group than in open group (**Table 2**). Length of incision was significantly shorter in the laparoscopic group than in open group (**Table 2**). The time passed until first flatus was shorter after laparoscopic surgery than after open surgery (**Table 2**). Life ability score at discharge was higher in laparoscopic group than in open group (**Table 2**). Time of postoperative hospitalization was shorter in laparoscopic group than in open group (**Table 2**). Postoperative complication rates of intestinal obstruction, postoperative bleeding, and anastomotic fistula were similar between the two groups (**Table 2**). The distance between tumor edge and proximal margin was longer in laparoscopic group than in open group (**Table 3**). Tumor differentiation, pTNM stage, distance between the tumor edge and distal margin, and size of tumors were similar between the two groups (**Table 3**). Harvested lymph nodes and number of positive lymph nodes were also similar between the two groups (**Table 3**). Patients with KPS Scores less than 70 points 2 and 4 weeks after operation, having to delay adjuvant chemotherapy, were fewer in the laparoscopic group than in open group (**Table 4**).

The above outcomes were identified by regression to adjust potential confounding factors (**Figure 3**). When postoperative exhaust time was listed as a dependent variable, it was concluded that operation time was the confounding factor (correlation coefficient = 0.285, P = 0.045), shown in scatter diagram A. When postoperative hospitalization was listed as a dependent variable, it was concluded that postoperative exhaust time was the confounding factor (correlation coefficient = 0.473, P<0.001), shown in scatter diagram B. When life ability scores at discharge were listed as dependent variable, it was concluded that incision length was the confounding factor (correlation coefficient = 0.305, P = 0.016), shown in scatter diagram C. When estimated blood loss was listed as dependent variable, it was concluded that operation time was the confounding factor (correlation coefficient = 0.382, P = 0.003), shown in scatter plot D. Length of the incision was determined by the surgical method. Distance between the tumor edge and proximal margin was not related to length of the incision (correlation coefficient = -0.157, P = 0.236) and operation time (correlation coefficient = -0.039, P = 0.769, but only related to surgical method (P = 0.047). Life ability score at discharge was positively correlated with KPS score 2 weeks after operation (the correlation coefficient = 0.718, P<0.001) and KPS score 4 weeks after operation (the correlation coefficient = 0.646, P<0.001), as shown in scatter plots E and F.

Discussion

Gastric cancer is one of the most common malignancies worldwide and surgical treatment remains the only curative management option [5, 6]. Recently, laparoscopic surgery for gastric cancer has become an alternative treatment option. As the popularity of laparoscopic surgery has grown, it has been associated with rapid recovery and reduced complications. In this study, compared with the open approach, laparoscopic total gastrectomy for gastric cancer of cardia and fundus had less intraoperative bleeding, shorter operation time, shorter incision, shorter postoperative hospitalization, quicker recovery of postoperative intestinal function and life ability, and longer distance between tumor edge and the proximal margin. The above outcomes show the technical advantages of laparoscopic approach over open approach. As a result of patients not leaving the hospital until incision stitching was removed and half liquid diet was restored, together with the fact that several patients got intestinal obstruction, postoperatively, and stayed in the hospital for a long time, the mean length of hospital stay of both groups was long (16.7 ± 7.89 days and 20.1± 14.8 days).

The cardia lies between the end of the esophagus and the body of the stomach. It is a small macroscopically indistinct zone that lies immediately distal to the gastroesophageal junction. Gastric cancer of cardia and fundus is associated with more advanced staging and less favorable clinicopathological features compared with gastric cancer of other parts [7]. Gastric cancer of cardia and fundus is generally

small and can be removed through a small incision during laparoscopic surgery. In particular, laparoscopic surgery vision has an advantage over open surgery in the dissociation of the lower esophageal segment. In this study, ratios of well or moderately differentiated adenocarcinoma to poorly differentiated adenocarcinoma or signet-ring cell cancer in the two group were 10/23 and 8/21, having no significant difference ($P = 0.814$), but both associated with less favorable pathological features in high proportion (**Table 3**). Ratios of stage I to stage II and stage III in the two group was 3/30 and 4/25, with no significant differences between the two group ($P = 0.164$), but both were associated with more advanced staging in high proportion (**Table 3**).

Total number of harvested lymph nodes was an independent prognostic factor for patients with gastric cancer [8]. Multivariate analysis revealed that T factor, N factor, and severe complications were independent factors for survival [9]. In this study, harvested lymph nodes of the laparoscopic group and open group were 29.5 ± 9.71 and 28.4 ± 12.7 ($P = 0.441$), having no significant differences. Number of positive lymph nodes of the two groups were 5.71 ± 10.2 and 7.07 ± 6.97 ($P = 0.218$), with no significant differences. The above outcomes indicate that laparoscopic total gastrectomy can reach a similar oncological operative effect as the open approach.

Daily life ability score includes the following items: eating, bathing, grooming, dressing, control of bowel movement, control of urine, going to the toilet, moving desk and chair, walking on the ground, up and down the stairs. A perfect score is 100 points. In our study, daily life ability scores on admission had no significant differences between the two groups (97.9 ± 5.45 and 93.4 ± 12.0, $P = 0.060$) but laparoscopic group got a higher score at discharge, compared to open group (90.0 ± 11.5 and 86.3 ± 16.1, $P<0.001$). Adjuvant chemotherapy performed at an earlier time could benefit patients after total gastrectomy. Early chemotherapy after surgery may, therefore, prevent tumor growth [10]. Thus, adjuvant chemotherapy should be performed as early as possible. Patients with KPS scores less than 70 points were not suitable for adjuvant chemotherapy. Patients with laparoscopic total gastrectomy recovered more quickly after surgery than those with open approach and patients with KPS scores of more than 70 points 2 and 4 weeks after operation in laparoscopic group were more than those in open group, accordingly (**Table 4**). Laparoscopic total gastrectomy of gastric cancer of cardia and fundus is beneficial in allowing patients to receive adjuvant chemotherapy earlier, thus, achieving a better therapeutic effect.

Orvil™ stapling device, which is inserted into the esophagus through the mouth, is convenient and feasible [11]. Intracorporeal esophagojejunostomy after laparoscopic total gastrectomy is technically difficult as it is performed in a narrow field in the abdomen. Placement of the anvil of a circular stapling device into the esophagus and connecting the instrument to the anvil are extremely difficult steps of this surgery. Placing the hammer head anvil through the mouth to make the esophagus jejunum anastomosis would greatly simplify the operation. OrVil™ is safe and reliable for digestive tract reconstruction, providing an ideal solution. The slanting design of the anvil head can help it to pass through the mouth and esophageal stenosis and the anvil head will automatically go back to its normal position when the stapling device is connected to the anvil head. Orvil™ device design is very unique. It makes a difficult and complicated operation easier.

Postoperative venous analgesic pumps were used in the two groups conventionally, therefore, additional analgesic drugs were not used. In this study, number of post-operative pain medication was not counted.

Laparoscopic total gastrectomy has just recently been carried out in our hospital, therefore, there was no data of 3-year or 5-year OS (overall survival rate) and DFS (disease-free survival rate) for large samples. There have been some reports of no statistical difference in long-term OS and DFS between laparoscopic total gastrectomy and open total gastrectomy from other national centers and centers abroad [12]. Evaluation of long-term OS and DFS of patients after laparoscopic total gastrectomy with gastric cancer of cardia and fundus will be the next step of future studies.

Conclusion

Laparoscopic total gastrectomy could improve short-term outcomes more than the open ap-

proach for patients with gastric cancer of cardia and fundus. Laparoscopic approach can get a similar oncological effect as open approach in cases of lymph nodes harvesting. The laparoscopic approach is beneficial in allowing patients to receive adjuvant chemotherapy at an earlier stage, thus, achieving a better comprehensive therapeutic effect.

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Disclosure of conflict of interest

None.

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