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Original Article

Safety and efficacy of laparoscopy-assisted gastrectomy for advanced gastric cancer in the elderly

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Abstract: To evaluate safety and efficacy of laparoscopy-assisted radical gastrectomy (LARG) for advanced gastric cancer patients aged 70 years or older. Clinical data were retrospectively collected from patients with II_A-III_C gastric cancer who underwent LARG (n = 30) and open radical gastrectomy (ORG, n = 34) in Department of Gastrointestinal Surgery in the Ningbo First Hospital from January 2012 to December 2013. The mean operative time was longer in the LARG group than in the ORG group but there was no statistical difference between the two groups. The intraoperative blood loss (120 ± 52.7 ml vs 227.3 ± 146.9 ml), incidence of postoperative complication (23.0% vs 47%) were lower in the LARG group than those in the ORG group. In addition, the time to first flatus (2.9 ± 0.8 d vs 4.6 ± 1.2 d), time to first ambulation (1.2 ± 0.4 vs 4.1 ± 1.0 d), time of nasogastric intubation (2.5 ± 1.0 d vs 3.5 ± 1.4 d), and postoperative hospital stay (13.0 ± 4.2 d vs 16.9 ± 4.1 d) were significantly shorter in the LARG group than in the ORG group, respectively. No statistical difference in the number of harvested lymph nodes was noted between the two groups (30.2 ± 12.0 vs 28.1 ± 11.8, P > 0.05). LARG is safer, more effective and less invasive for the elderly patients with advanced gastric cancer.

Keywords: Laparoscopy-assisted gastrectomy, open gastrectomy, gastric cancer, clinical efficacy

Introduction

According to the "Statistical Communiqué of the People's Republic of China on the 2013 Social Service and Development" published by Ministry of Civil Affairs of China, 131.61 milllion people were aged 65 and over (9.7% of the total population) by the end of 2013 [1]. It is predicted that both the population and the proportion of elderly will continue to increase in China.

Gastric cancer is one of the most common malignant tumors worldwide, with a yearly incidence of about 900000. In China, more than 400000 cases of gastric cancer are diagnosed annually, of them, more than 90% are diagnosed at an advanced stage when they first present [2]. With the changing age distribution, the number of elderly patients with gastric cancer is increasing, especially in China. At present, radical D2 gastrectomy is the only effective treatment for gastric cancer with a potential to cure the disease [3]. Several previous studies have reported a high incidence of comorbid disease, postoperative complications, and mortality associated with elderly gastric cancer patients who have undergone open gastrectomy [4, 5]. Laparoscopy-assisted radical gastrectomy (LARG) has been reported as a less invasive surgical technique than open gastrectomy in terms of reduced postoperative morbidity, rapid return of gastrointestinal function, shortened hospital stay after operation, thus is a widely accepted treatment for gastric cancer nowadays [6-8]. On the other hand, disadvantages of LARG were also reported such as longer operation times and usually requiring a pneumoperitoneum, which can influence respiratory or cardiovascular function especially for those elderly patients who often have preoperative morbidities and reduced functional capacities [9, 10]. Therefore, the feasibility of LARG in elderly patients is still controversial. Some studies have suggested that LARG is an effective treatment for elderly patients with early gastric cancer [11, 12]. However, its suitability for the treatment of elderly patients with advanced gastric cancer has not previously been tested. The current study compared the surgical short-

term outcomes between LARG and open radical gastrectomy (ORG) cancer in elderly patients with advanced gastric cancer in our department.

Material and methods

Patient clinical data

A total of 103 patients aged ≥ 70 years with gastric cancer were treated with LARG or ORG in our Department from January 2012 to December 2013. Of those, 64 patients with II_A-III_C gastric cancer were enrolled in this study, of which 30 patients were underwent LARG, and 34 patients were underwent ORG. The other 43 patients with stage I or IV who had not been undergone radical gastrectomy with D2 lymph nodes dissection were excluded. The study including data collection and data analysis was approved by the Ethics Committee of Ningbo First Hospital, and all enrolled patients provided written informed consent. All the patients were confirmed pathologically as gastric adenocarcinoma at staging II_A-III_C based on the 2010 World Health Organization (WHO) classification [13]. Preoperative, intraoperative and postoperative parameters were compared between the LARG group and ORG group.

Preoperative evaluation of general condition

Chest X-rays, laboratory tests, electrocardiograms (ECG), echocardiography, computed tomography of the abdomen and respiratory function tests using spirometry were examined in all patients to assess preoperative cardiopulmonary function and other comorbidities. Patients were classified according to the American Society of Anesthesiologists (ASA) Classification of Physical Status guidelines so that patient comorbidity could be evaluated objectively.

Surgical procedures

LARG: Following general anesthesia, patients were placed in the supine position with their legs apart. LARG was performed under a pneumoperitoneum that was created by injection of carbon dioxide (CO_2) at 10-12 mmHg during surgery. However, an intraperitoneal pressure of 8-10 mmHg was sometimes selected if a lower cardiopulmonary reserve was expected. A total of five ports (each 5-12 mm) were inserted, and the operator was standing on the left side of the patient, while first assistant was standing on the right side, and the second assistant who was holding the laparoscope stood between the patient's legs. The procedure of LARG was conducted briefly as follows. After completion of the omentectomy, the roots of the right gastroepiploic vein and artery were isolated and sealed by harmonic scalpel with clips and lymph nodes (Group 6) were removed. Then, along the dissection of pancreatic capsule, the splenic artery, left gastric artery, left gastric vein and the common hepatic artery were exposed with the lymph nodes (Group 11p, 7, 8, 9) dissected; Along the gastroduodenal artery, the root of the right gastric artery and proper hepatic artery were exposed and the lymph nodes (Group 5, 12a) were dissected. Next, the lesser omentum was dissected from the lesser curvature, then left gastroepiploic artery and vein were dissedted after the isolation of splenic flexure with resection of the greater omentum from the greater curvature of the stomach (Group 1, 3, 4), thus the lymph node dissection was completed intracorporeally for radical distal gastrectomy. As to radical total gastrectomy, procedures were needed to further isolate the splenic flexure, and the short gastric vessels were resected at the origin. The splenic artery was isolated and the lymph nodes of Group 11 d and 10 were removed. After isolation of stomach from the gastric fundus and posterior stomach, 5 cm of the esophagus was exposed with the anterior and posterior vagal nerves resected, then the lymph nodes of Group 1 and 2 were dissected. Extrocorporeal reconstruction was performed using a 4-5 cm upper midline incision with Billroth-I or II for distal gastrectomy or Roux-en-Y reconstruction for total gastrectomy.

ORG: The operation was carried out under general anesthesia. Patients were placed in the supine position. An incision of 15-20 cm was made in the midline of the upper abdomen. The procedure of open radical gastrectomy was performed as described above.

Statistical analysis

Statistical analysis was performed using SPSS 18.0 (SPSS Inc., Chicago, IL, United States). All data are presented as mean ± SD, and were analyzed using Student's t test. Categorical data are presented as proportions, and were analyzed using the Chi square test or Fisher exact probability test. $P < 0.05$ was considered statistically significant.

Table 1. The characteristics of the included patients

	LARG (n = 30)	ORG (n = 34)	*P* value
Age (year)	74.4 ± 3.1	75.6 ± 3.0	*P = 0.132*
Gender (M/F)	25/5	22/12	*P = 0.092*
BMI (kg/m^2)	21.6 ± 2.7	21.6 ± 3.0	*P = 0.960*
Comorbidity			
Hypertension	15	16	*P = 0.814*
Diabetes mellitus	3	5	*P = 0.850*
COPD	6	6	*P = 0.810*
Heart disease	10	7	*P = 0.249*
ASA-PS			P = 0.995
1	1	1	
2	21	24	
3	8	9	
Tumor location			P = 0.313
Upper	3	6	
Middle	11	7	
Lower	16	21	
Type of operation			P = 0.146
Distal gastrectomy	14	22	
Total gastrectomy	16	12	
Intraoperative $PaCO_2$ (mmHg)	42.3 ± 5.7	38.1 ± 4.5	*P = 0.004*
Preoperative Hb (g/dl)	9.0 ± 2.4	8.7 ± 1.5	*P = 0.600*
Postoperative Hb (g/dl)	10.5 ± 2.3	10.1 ± 1.9	*P = 0.428*
Preoperative serum albumin (g/dl)	36.9 ± 4.3	35.5 ± 5.5	*P = 0.297*
Postoperative serum albumin (g/dl)	29.7 ± 3.6	29.3 ± 3.7	*P = 0.727*
Tumor size (cm)	4.1 ± 1.9	4.9 ± 2.6	*P = 0.153*
Tumor stage			P = 0.065
II_A-II_B	16	10	
III_A-III_B	5	14	
III_C	9	10	

Table 2. Comparison of surgical outcomes between LARG and ORG

Outcomes	LARG (n = 30)	ORG (n = 34)	*P* value
Operative time (min)	259.5 ± 53.76	236.09 ± 45.3	*P* = 0.068
Blood loss	120 ± 52.7	227.3 ± 146.9	*P < 0.01*
Number of retrieved lymph nodes	30.2 ± 12.0	28.1 ± 11.8	*P = 0.484*
Time to first flatus (d)	2.9 ± 0.8	4.6 ± 1.2	*P < 0.010*
Time of nasogastric intubation (d)	2.5 ± 1.0	3.5 ± 1.4	*P < 0.01*
Time to initiate oral intake (d)	4.5 ± 0.8	5.5 ± 1.0	*P < 0.01*
Time to ambulation (d)	1.2 ± 0.4	4.1 ± 1.0	*P < 0.01*
Hospital stay (d)	13.0 ± 4.2	16.9 ± 4.1	*P < 0.01*

Results

Patient characteristics

Patient demographics and clinical findings are listed in **Table 1**. Hypertension, chronic obstructive pulmonary disease (COPD), cardiovascular disease and diabetes mellitus were the most common comorbid diseases in both groups, but the distribution of comorbid diseases did not differ between the two groups. There were no significant differences with respect to other preoperative characteristics and postoperative pathologic features between the two groups.

Comparison of intraoperative characteristics and outcomes

LARG was successfully completed in the 30 patients without conversion to laparotomy. ORG was also successfully performed in 34 patients. Surgical indices are shown in **Table 2**. The mean operative time was a little longer in the LARG group than that in the ORG group (259.5.3 ± 53.76 min vs 236.09 ± 45.3 min, p > 0.05), but there was no significant difference between the two groups. There were no significant differences in the mean number of retrieved lymph nodes between the two groups (30.2 ± 12.0 vs 28.1 ± 11.8, p > 0.05). Whereas patients in the LARG group showed less intraoperative blood loss (120 ± 52.7 ml vs 227.3 ± 146.9 ml, p < 0.05), shorter time of nasogastric intubation (2.5 ± 1.0 d vs 3.5 ± 1.4 d), shorter time to first flatus (2.9 ± 0.8 d vs 4.6 ± 1.2 d), decreased time to first ambulation (1.2 ± 0.4 vs 4.1 ± 1.0 d), less

Table 3. Comparison of postoperative complications

Postoperative complications	LARG (n = 30)	ORG (n = 34)	*P* value
Overall, n (%)	7 (23)	16 (47)	*P = 0.048*
Anastomotic leakage (n)	0	1	*p = ?*
Pulmonary infection (n)	3	7	*p = ?*
Re-operation	0	0	*0*
Incision infection	1	0	*p = ?*
Urinary infection	1	2	*p = ?*
Heart failure	0	3	*p = ?*
Others	2	3	*p = ?*

time to initiate oral intake (4.5 ± 0.8 d vs 5.5 ± 1.0 d), and less postoperative hospital stay (13.0 ± 4.2 d vs 16.9 ± 4.1 d, p < 0.05). than those in the ORG group. The intraoperative arterial blood partial pressure of CO_2 ($PaCO_2$) was higher in the LARG group than that in the ORG group (42.3 ± 5.7 mmHg vs 38.1 ± 4.5 mmHg, P < 0.05).

Postoperative complications

Postoperative complications are listed in **Table 3**. The overall complication rate was significantly lower in the LARG group than that in the ORG group (23%, 7/30 vs 47%, 16/34, P < 0.05). The most frequent complications were respiratory or cardiovascular complications. One patient in the ORG group developed anastomotic leakage requiring image-guided drainage after esophagojejunostomy. No patient in the two groups needed a re-operation due to postoperative complication and no perioperative death occurred in either group.

Discussion

Since the first successful LARG by Kitano et al [14] for early gastric cancer in 1994, LARG has been widely accepted modality for early gastric cancer in Japan and Korea [15]. Whether LARG can be applied in the treatment of advanced gastic cancer is still controversial. Park et al [16] evaluated the long-term results of 239 patients who underwent LARG for the treatment of advanced gastric cancer and found that the major recurrence was distant metastasis whereas lymph node relapses were most frequent in para-aortic lymph node metastasis, thus believing that the dissection of lymph nodes around the stomach can be performed efficiently by LARG. Chen et al [17] made a systematic review and meta-analysis of laparoscopic and open gastrectomy for advanced gastric cancer, and alternative suggested that LARG is a safe technical alternative to ORG for advanced gastric cancer with a lower complication rate and enhanced postoperative recovery.

With the aging population, more elderly patients with advanced gastric cancer are being referred for radical gastric resection. Previous studies reported an adverse effect with high incidences of postoperative morbidity and mortality among elderly gastric cancer patients who undergone ORG [4, 5], therefore, the minimally invasive surgical procedure LARG which has many advantages such as less pain, less intraoperative bleeding, earlier bowel movements and postoperative recovery, is recommended for those older patients with a higher incidence of comorbid disease [18].

Although the World Health Organization defines elderly patients as those over 65 years of age, in the present study, elderly patients were defined as being 70 years old or older as other studies reported [19, 20]. Some studies reported that the incidence of postoperative complications after ORG in elderly patients was higher than that in younger patients due to preoperative comorbidities mainly including hypertension, COPD, cardiovascular disease and diabetes mellitus as revealed in present study [21, 22]. However, when taken the severity of postoperative complications into consideration, there was no statistical difference in the rates of postoperative complications between the elderly patients and young patients if the patients undergoing LARG [18]. Outcomes in the current study demonstrated that postoperative complication rate was quite lower in the LARG group than that in ORG group (23% vs 47%), and we consider that the decrease in postoperative morbidity particularly in respiratory complications is mainly attributed to the minimally invasive surgical procedure, because LARG is less painful, less intraoperative blood loss, earlier ambulation and shorter nasogastric intubation , all of which are crucial for better recovery for elderly patients.

It is also important to consider the potential negative effects of the pneumoperitoneum on cardiopulmonary reserve during LARG surgery particularly for elderly patients, which can

cause severe arrhthmia, decreased mean arterial blood pressure, and systemic vascular pressure. Normally, an intraperitoneal pressure of 10-12 mmHg was maintained during operation, but sometimes an intraperitoneal pressure of 8-10 mmHg was also selected for those limited cardiopulmonary reserve patients in order to reduce the pneumoperitoneum-related negative effects [23]. Operative time of LARG is another important factor concerning the negative effects of the pneumoperitoneum on patients' cardiopulmonary function [24]. However, as the technique improved and experience accumulated, the LARG operation time is similar to that of ORG [25]. In the present study, the operative time of LARG and ORG was 259.5.3 ± 53.76 min and 236.09 ± 45.3 min respectively, a little longer in the LARG group than that in the ORG group with no statistically significant difference between the two groups. Therefore, in our series, we did not experience any elderly patients who suffered from severe accidents related to the pneumoperitoneum during LARG although the intraoperative arterial blood partial pressure of CO_2 ($PaCO_2$) was higher in the LARG group than that in the ORG group.

The result that there were no significant differences in the mean number of retrieved lymph nodes between the two groups suggested that LARG can achieve the same D2 lymph node dissection effect as to that by ORG. Other early surgical outcomes demonstrated that LARG is a safe, effective, and minimally invasive approach for treatment of elderly patients with advanced gastric cancer.

There are some limitations associated with the present study. The long-term efficacy of LARG in elderly patients with advanced gastric cancer is needed to observe, and large-volume studies are also needed to further investigate.

In conclusion, with the advances in surgical technology, improved treatments for momorbid diseases, and appropriate prophylaxis of morbidity, the present study revealed satifactory short-term surgical outcomes after LARG compared to ORG in elderly patients with advanced gastric cancer. LARG should be considered as a treatment of choice in elderly patients with advanced gastric cancer.

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Disclosure of conflict of interest

None.

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