JBUON 2019; 24(6): 2509-2516
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
Email: editorial_office@jbuon.com

ORIGINAL ARTICLE

A comparative study on endoscopic submucosal dissection and laparoscopy-assisted radical gastrectomy in the treatment of early gastric carcinoma

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Summary

Purpose: *To compare the clinical efficacy and safety of endoscopic submucosal dissection (ESD) and laparoscopy-assisted radical gastrectomy (LARG) in the treatment of early gastric carcinoma (EGC) with different risks of lymph node metastasis.*

Methods: *The clinical data of 194 EGC patients who underwent ESD (ESD group, n=58) or LARG (LARG group, n=136) in our hospital from January 2014 to January 2016 were collected. The baseline data, pathological features of tumor, perioperative indexes and long- and short-term complications were compared between the two groups, the overall survival (OS) rate of patients was recorded through follow-up, and the tumor-free survival (TFS) rate was compared after ESD and LARG for EGC with different risks of lymph node metastasis.*

Results: *The general clinical features were comparable between the two groups of patients, and there was no perioperative death. The pathological features of the tumor had no statistically significant differences between the two groups (p>0.05). The operation time in ESD group (73.57±21.30 min) was significantly shorter than that in LARG group (159.22±39.40 min) (p<0.001), and the time of first ambulation after operation in ESD group (1.6±0.8 d) was also overtly shorter than that in LARG group (3.5±1.7 d) (p<0.001). Postoperatively, no drainage tube was placed in the ESD group, while it was placed for 5.7±2.4 days on average in the LARG group. The time of first flatus after operation, time of first liquid diet after operation, and total hospitalization time in the ESD group were significantly compared with the LARG group (p<0.001). The incidence rate of short-term complications after surgery was 10.3% and 7.4% in the two groups, (p=0.570), while long-term complications were 17.6% (9/51) and 20.9% (24/115) in the two groups (p=0.631). The in situ tumor recurrence by the end of follow-up was 3.92% (2/51) and 0.87% (1/115) in the two groups, while the ectopic recurrence rate was 5.89% (3/51) and 0.87% (1/115) (p=0.173, p=0.087). OS survival was 96.1% (49/51) and 97.4% (112/115) in the two groups (p=0.751). The postoperative TFS of EGC patients with a low risk of lymph node metastasis was 93.8% (30/32) and 98.6% (70/71) in the two groups, again without significant difference (p=0.197). The postoperative TFS of EGC patients with a high risk of lymph node metastasis was 84.2% (16/19) and 97.7% (43/44) in the two groups, with statistically significant difference (log-rank, p=0.034).*

Conclusions: *ESD is characterized by small trauma, rapid postoperative recovery, postoperative recurrence and survival comparable to those after surgical operation and high safety for EGC with a low risk of lymph node metastasis. LARG can reduce the postoperative recurrence rate of EGC in patients with high risk of lymph node metastasis.*

Key words: *endoscopic submucosal dissection, laparoscopy-assisted radical gastrectomy, early gastric carcinoma, efficacy*

Introduction

In early gastric carcinoma (EGC), the carcinoma tissues are confined to the mucosa or submucosa, regardless of the presence or absence of lymph node metastasis. The detection rate of EGC

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Received: 18/04/2019; Accepted: 22/05/2019

has increased year by year with the continuous development of endoscopy and the gradual improvement of people's health consciousness [1-3]. It has increased from 18% to 70% in the past 3 decades in Japan, and also significantly improved in China, accounting for 10-15% of gastric carcinoma [4]. The traditional treatment means for EGC is the radical surgical resection, and the postoperative 5-year survival rate can reach more than 90.0% [3], while the survival rate of EGC without lymph node metastasis can be as high as 94.2% [5]. In 1994, the laparoscopy-assisted distal gastrectomy (LADG) was performed for the first time and reconstructed the digestive tract using the Billroth I anastomosis, and then the safety and feasibility of LADG were gradually verified, so laparoscopic surgery has been applied more and more widely in the treatment of EGC [6,7]. In 2014, laparoscopy-assisted radical gastrectomy (LARG) was listed as a conventional operation method for stage I gastric carcinoma in the fourth edition of the Gastric Cancer Treatment Guideline. Endoscopic submucosal dissection (ESD), an emerging endoscopic treatment technique, enables the local resection of lesions through the endoscope, which is characterized by small trauma, quick recovery, low cost and few complications, and can retain the normal anatomical structure and physiological function of the diseased organs, so that the patients have a high quality of life after operation [8,9]. ESD has gradually become a preferred treatment method for EGC patients with a low risk of lymph node metastasis [10].

In the present study, the clinical data of 194 patients undergoing LARG or ESD in the General Surgery Department of our hospital from January 2014 to January 2016 were retrospectively analyzed, and the clinical efficacy and safety of the two operation methods were compared.

Methods

General data

The clinical data of 194 EGC patients undergoing ESD (ESD group, n=58) or LARG (LARG group, n=136) from January 2014 to January 2016 were retrospectively analyzed, and it was pathologically confirmed that the tumor infiltration was confined to the mucosa or submucosa, regardless of the presence or absence of lymph node metastasis.

Inclusion criteria: 1) patients diagnosed with early primary gastric carcinoma (depth of tumor infiltration: pTis, pT1a and pT1b, with or without lymph node metastasis) according to postoperative pathological findings; and 2) patients conforming to the absolute or relative indications for endoscopy of EGC (Japanese Gastric Cancer Treatment Guidelines 2010 [11]).

Exclusion criteria: 1) patients with a history of malignant tumors or complicated with malignant tumors in other systems found before operation; 2) patients who received definitive treatment, such as radiotherapy, chemotherapy or immunotherapy; 3) patients with severe hepatic or renal insufficiency, or underlying diseases such as circulatory system or blood system diseases, failing to tolerate the operation; or 4) patients with contraindications for laparoscopic surgery. The general clinical data had no statistically significant differences between the two groups, such as age, gender, history of chronic gastric disease, family history of gastric carcinoma and complications, and they were comparable (Table 1). All patients enrolled adhered to the Declaration of Helsinki, and they were informed of the study and signed the informed consent. The two kinds of operations were performed by surgeons in the same medical group. This study was approved by the ethics committee of Xiang-

Table 1. Baseline demographic and clinical characteristics of the studied patients

Parameters	*ESD group*	*LARG group*	*p value*
	n=58	*n=136*	
	n (%)	*n (%)*	
Age, years, mean±SD	58.84±10.71	56.93±9.45	0.217
Gender			0.519
Male	34 (58.6)	87 (64.0)	
Female	24 (41.4)	49 (36.0)	
Chronic gastric disease	43 (74.1)	109 (80.1)	0.349
Family history of gastric cancer	9 (15.5)	18 (13.2)	0.657
Systemic disease	17 (29.3)	36 (26.5)	0.726
Hypertension	7 (12.1)	17 (12.5)	
Diabetes mellitus	5 (8.6)	9 (6.6)	
Coronary heart disease	4 (6.9)	7 (5.1)	
Chronic bronchitis	1 (1.7)	2 (1.5)	
Asthma	0 (0)	1 (0.7)	

ESD: endoscopic submucosal dissection, LARG: laparoscopic assisted radical gastrectomy

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Operation methods

ESD: The single-pore endoscope (GIF-Q260J, Olympus) was used, and the operation process was as follows: The transparent cap (D-201-11804, Olympus) was mounted on the head of the endoscope. An annular marker was made at least 5 mm along the edge of the lesion using the Dual knife (KD-650L, Olympus), from which methylene blue (0.04 mg/mL) + adrenaline hydrochloride (0.002 mg/mL) + 500 mL of normal saline were submucosally injected using needle (25G, Boston) to fully separate the mucosa and submucosa from the inherent muscular layer. Then, an annular incision was made at least 5 mm along the edge of the marker using the Dual knife (KD-650L, Olympus) and peeled along the submucosa under the endoscope. The visible vessels on the wound were treated with the hot biopsy forceps (FD-410LR, Olympus). Finally, the specimens were spread and fixed using pins and foam plates, immersed in 10% formaldehyde and sliced into thin sections in parallel with the edge of lesion at an interval of 2 mm.

LARG: According to the site and size of tumor, distal subtotal gastrectomy, proximal subtotal gastrectomy or total gastrectomy were performed. The range of lymph node dissection was based on the tumor size, depth of infiltration, pathological type and presence or absence of suspicious enlargement of lymph nodes. D2 lymph node dissection is often adopted in our hospital. In distal subtotal gastrectomy, the 1st, 3rd, 4th, 5th, 6th, 7th, 8th, 11p, 12a and 13th groups of lymph nodes were dissected. In proximal subtotal gastrectomy, the 1st, 2nd, 3rd, 4th, 5th, 6th, 7th, 8th, 9th, 10th, 11th, 12th, 13th, 14th, 19th and 20th [12] groups of lymph nodes were dissected. The digestive tract was reconstructed using the Billroth I anastomosis, Billroth II anastomosis and Roux-en-Y gastrojejunostomy in distal gastrectomy, using the esophagus-gastric remnant anastomosis in proximal gastrectomy, and using esophagus-jejunum anastomosis or Roux-en-Y esophagus-jejunum anastomosis in total gastrectomy.

Pathological evaluation

The resected specimens were fixed, sliced, examined by professional pathologists using standardized scheme, and evaluated according to the related provisions of the Japanese Gastric Cancer Association [13], including the circumferential margin and basal margin of lesion, histological type, grade of differentiation, depth of infiltration of cancer cells, and whether the vascular tumor, vascular invasion and nerve invasion were involved. Complete resection: The whole lesion is resected without invasion of cancer cells at the horizontal and basilar parts. Incomplete resection: The lesion is resected piecemeal or there is invasion of cancer cells at the horizontal and basilar parts. Curative resection: The lesion is resected completely, and tumor diameter is ≤2 cm. Differentiated carcinoma: The cancer cells infiltrate to the lamina propria or the mucosal muscle layer, and both horizontal and vertical margins are negative, without vascular tumor.

Observation indexes

Indexes of short-term efficacy: The operation time, time of first ambulation after operation, time of first flatus after operation, time of first liquid diet after operation and hospitalization time after operation in both groups were recorded. After first flatus and withdrawal of gastric tube, the patients began to have a little water first, and then liquid diet, semifluid diet and digestible solid diet. When the patients had a diet normally and defecated normally, and the blood indexes were all normal, they could be discharged from hospital. First ambulation after operation refers to walking for at least 5 m under help or independently.

Indexes of long-term efficacy: The *in situ* recurrence rate of tumor, ectopic tumor recurrence rate, incidence of long-term complications and survival after operation were compared between the two groups. *In situ* recurrence of tumor: New lesions are found within 12 months after endoscopic treatment, namely the secondary lesions that had existed but missed when endoscopic treatment is performed and been found within 12 months after operation. Ectopic recurrence of tumor: New lesions are found beyond 12 months after treatment, and most lesions are near the primary lesion, with the same histopathological type. EGC with a low risk of lymph node metastasis: Tumor diameter ≤2 cm, the infiltration is confined to the mucosal layer, and it is differentiated carcinoma. EGC with a high risk of lymph node metastasis: Tumor diameter >2 cm, the infiltration reaches submucosa, and it is poorly differentiated adenocarcinoma or signet-ring cell carcinoma.

The patients were followed up for the first time at 3 months after ESD to confirm the surgical wound healing. Then, they were examined by endoscope and abdominal CT examination once every 6 months to determine whether there was lymph node metastasis or recurrence in any form. Within 2 years after LARG, the patients were examined by endoscope and abdominal CT examination once every 6 months, or once every other year within 2-5 years after operation. All of the patients were followed up until January 2019.

Statistics

SPSS 22.0 software (IBM, Armonk, NY, USA) was used for statistical analyses. The measurement data were expressed as mean±standard deviation (x±s), and t-test was performed for the comparison between two groups. The enumeration data were expressed as percents, and x^2 test was performed for the comparison between two groups. Kaplan-Meier curves were plotted for survival analysis, and log-rank test was used for comparisons. $P<0.05$ suggested that the difference was statistically significant.

Results

Comparisons of tumor's pathological features

In ESD and LARG group, the tumor was mainly located at the 1/3 of the lower stomach [39 cases (67.2%) *vs.* 95 cases (69.9%), p=0.275]. The endoscopic

classification was mainly type II (flat type) [52 cases (89.7%) *vs.* 106 cases (78.0%), p=0.096]. Moderate and poor differentiation dominated in the histological type [moderate differentiation: 27 cases (46.6%) *vs.* 61 cases (44.9%); poor differentiation: 24 cases (41.4%) *vs.* 50 cases (36.8%), p=0.539]. In the two groups, the mean tumor diameter was 2.36±1.31 cm and 2.54±1.59 cm (p=0.193), and the tumor infiltration was mainly confined to the mucosa [39 cases (67.2%) *vs.* 98 cases (72.1%), p=0.500]. There were 3 cases (5.2%) and 9 cases (6.6%) of vascular invasion in the two groups (p=0.702), and stage I tumor dominated [56 cases (96.6%) *vs.* 132 cases (97.1%), p=0.852]. Moreover, both complete resection rate and curative resection rate in LARG group were significantly higher than those in ESD group (p=0.007, p<0.001) (Table 2).

Comparisons of perioperative indexes

The operation time in ESD group (73.57±21.30 min) was significantly shorter than that in LARG group (159.22±39.40 min) (p<0.001), and the time of first ambulation after operation in ESD group (1.6±0.8 d) was also significantly shorter than that in LARG group (3.5±1.7 days) (p<0.001). After operation, no drainage tube was placed in ESD group, while it was placed for 5.7±2.4 days on average in LARG group (90.4%; 123/136). The time of first flatus after operation, time of first liquid diet after operation and total hospitalization time in ESD group were significantly shorter than those in LARG group (p<0.05). The incidence rate of short-term complications after operation was 10.3% and 7.4% in the two groups, showing no statistically significant difference (p=0.570) (Table 3).

Comparisons of long-term efficacy indexes

Fifty one and 115 patients in both groups completed the follow-up, and were followed-up for 43.6±8.1 months and 45.2±9.7 months on average, respectively. The incidence rate of long-term complications was 17.6% (9/51) and 20.9% (24/115) in the two groups, showing no statistically significant difference (p=0.631). In the two groups, there was 1 case and 4 cases of emaciation, 0 case and 2 cases of diarrhea, 2 cases and 4 cases of upper abdominal

Table 2. Comparison of tumor pathological characteristics of the studied patients

Parameters	*ESD group*	*LARG group*	*p value*
	n=58 *n (%)*	*n=136* *n (%)*	
Tumor location			0.275
Upper 1/3 stomach	4 (6.9)	17 (12.5)	
Middle 1/3 stomach	15 (25.9)	24 (17.6)	
Lower 1/3 stomach	39 (67.2)	95 (69.9)	
Tumor diameter (cm), mean±SD	2.36±1.31	2.54±1.59	0.193
Endoscopic classification			0.096
I	5 (8.6)	17 (12.5)	
II	52 (89.7)	106 (78.0)	
III	1 (1.7)	13 (9.5)	
Differentiation grade			0.539
High	7 (12.1)	25 (18.4)	
Moderate	27 (46.6)	61 (44.9)	
Low	24 (41.4)	50 (36.8)	
Invasive depth			0.500
Mucous layer	39 (67.2)	98 (72.1)	
Submucous layer	19 (32.8)	38 (27.9)	
Vascular invasion	3 (5.2)	9 (6.6)	0.702
Pathological stage			0.852
I	56 (96.6)	132 (97.1)	
II	2 (3.4)	4 (2.9)	
Complete resection rate	94.8% (55/58)	100%	0.007
Curative resection rate	63.8% (37/58)	100%	0.001

ESD: endoscopic submucosal dissection, LARG: laparoscopic assisted radical gastrectomy

Table 3. Comparison of perioperative parameters of patients in the two groups

Parameters	*ESD group*	*LAR group*	*p value*
	n=58 *n (%)*	*n=136* *n (%)*	
Operation time (min)*	73.57±21.30	159.22±39.40	0.001
First time out of bed (day)*	1.6±0.8	3.5±1.7	0.001
First flatus time (day)*	2.4±3.1	3.9±2.8	0.001
Postoperative catheter drainage time (day)*	0	5.7±2.4	0.001
First fluid intake time (day)*	3.6±1.6	5.4±2.3	0.001
In-hospital stay (day)*	9.7±4.1	11.3±5.3	0.042
Short-term complications§	6 (10.3)	10 (7.4)	0.570
Incision infection	0 (0)	1 (0.7)	
Hemorrhage	3 (5.2)	1 (0.7)	
Perforation	2 (3.4)	0 (0)	
Anastomotic fistula	0 (0)	2 (1.5)	
Adhesive intestinal obstruction	0 (0)	4 (2.9)	
Blood transfusion	1 (1.7)	2 (0.7)	

ESD: endoscopic submucosal dissection, LARG: laparoscopic assisted radical gastrectomy, *mean±SD, §n (%)

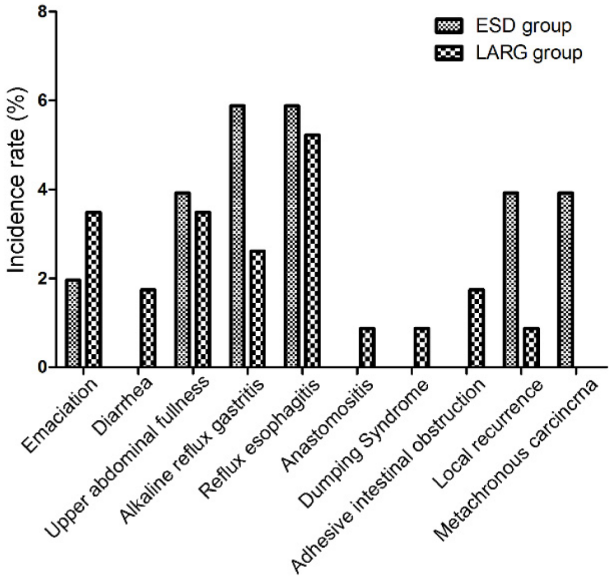

Figure 1. The incidence rate of long-term complications of patients in ESD group and LARG group. The overall incidence rate of long-term complications were 17.6% and 20.9% in ESD group and LARG group, respectively. The difference between incidence rate of the two groups had no statistical significance (p=0.631).

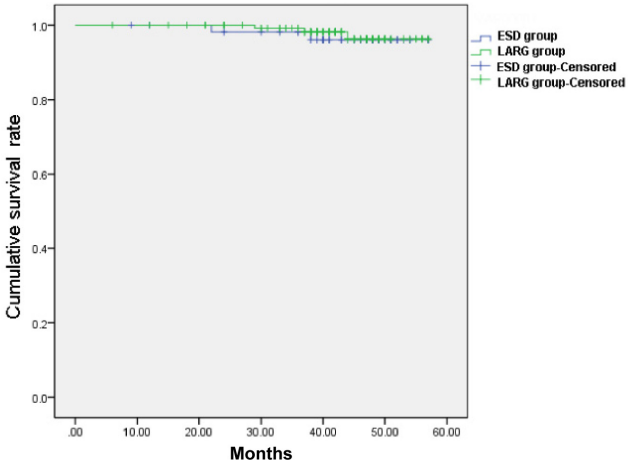

Figure 2. Kaplan-Meier survival curves of patients in ESD group and LARG group. The overall survival rate of patients in ESD group had no significantly difference compared with that of LARG group (p=0.751).

fullness, 3 cases of alkaline reflux gastritis, 3 cases and 6 cases of reflux esophagitis, 0 case and 1 case of anastomositis, 0 case and 1 case of dumping syndrome, and 0 case and 2 cases of adhesive intestinal obstruction. The *in situ* tumor recurrence rate was 3.92% (2/51) and 0.87% (1/115) in the two groups, while the ectopic recurrence rate was 5.89% (3/51) and 0.87% (1/115), displaying no statistically significant differences (p=0.173, p=0.087) (Figure 1).

Survival

By the end of follow-up, 2 patients had died in ESD group (1 death from cerebral hemorrhage at 22 months, and 1 death from hepatic metastasis at 39 months), and 3 patients had died in LARG group (1 death from myocardial infarction at 29 months, 1 death from cerebral infarction at 37 months, and 1 death from tumor recurrence at 44 months). The OS rate was 96.1% (49/51) and 97.4% (112/115) in the two groups, showing no statistically significant difference (p=0.751). The postoperative TFS rate of EGC patients with low risk of lymph node metastasis was 93.8% (30/32) and 98.6% (70/71) in the two groups, again without statistically significant

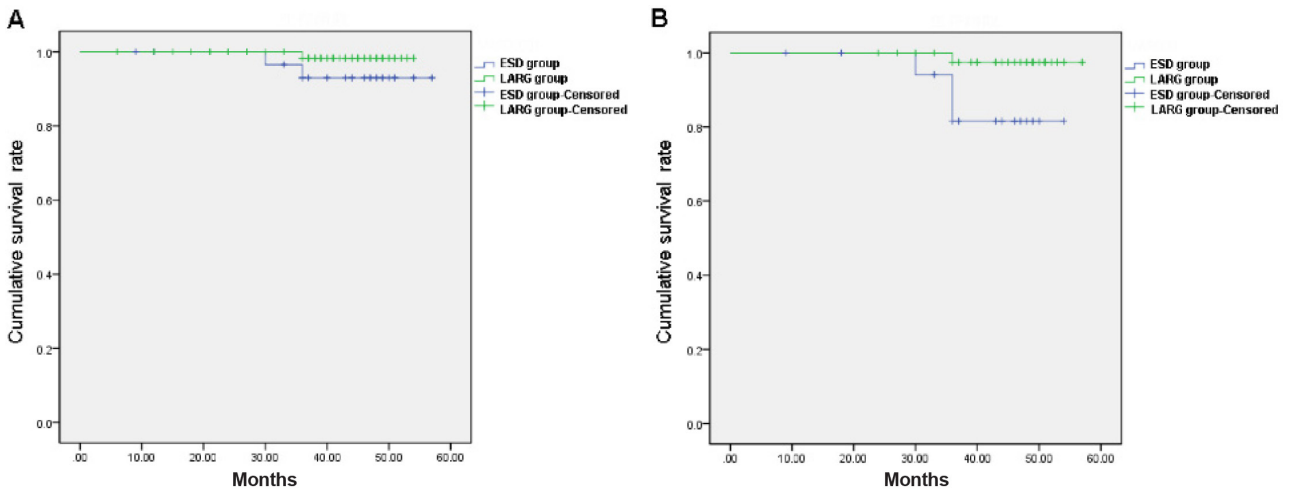

Figure 3. Kaplan-Meier survival curves of patients in ESD group and LARG group. **(A):** For early gastric cancer with low lymph node metastasis risk, the tumor-free survival rate of patients in ESD group had no significantly difference compared with that of LARG group (p=0.197). **(B):** For early gastric cancer with high risk of lymph node metastasis, the tumor-free survival rate of patients in ESD group was significantly lower compared with that of LARG group (p=0.034).

difference (p=0.197). Besides, the postoperative TFS of EGC patients with high risk of lymph node metastasis was 84.2% (16/19) and 97.7% (43/44) in the two groups, and the difference was statistically significant test (log-rank p=0.034). The Kaplan-Meier survival curves are shown in Figures 2 and 3.

Discussion

With the continuous improvement of imaging techniques, the diagnostic rate of EGC is constantly increasing, accounting for 10-15% of gastric carcinoma in China. The prognosis of EGC is significantly superior to that of advanced gastric carcinoma, and the postoperative 5-year OS is as high as 90%. Therefore, the treatment of EGC needs to not only guarantee the long-term survival but also retain the physiological function of the gastrointestinal tract as far as possible based on the radical operation, so as to improve the quality of life of patients after operation [14]. Currently, the operation methods of EGC include endoscopic treatment and surgical treatment. Compared with LARG, ESD can retain the complete gastrointestinal functions and has few postoperative complications, but lymph node dissection cannot be performed in ESD due to risk of postoperative ectopic recurrence. Moreover, its therapeutic indications remain controversial in China, and there are few comparative studies on both methods [15].

In the present study, ESD had a short operation time, small trauma, shortened time of ambulation and rapid recovery of gastrointestinal function, consistent with literature reports [16,17]. Before ESD, however, the size of lesion, depth of infiltration and lymph node metastasis need to be accurately evaluated, and the indications should be determined, so auxiliary examinations such as narrow band imaging, magnifying endoscopy, ultrasonic endoscopy and CT should be performed before operation, trying to effectively reduce ESD beyond the scope of indications. It was found that the complete resection and curative resection rate in ESD group were lower than those in LARG group. According to foreign studies, the complete resection and curative resection rate of ESD were 84-94.7% and 75.0-95%, respectively [18,19]. In this study, ESD group had a complete resection rate of 94.8% and a curative resection rate of 63.8%, significantly lower than the LARG group. The possible reason is that the number of ESD cases enrolled was smaller, leading to data deviation from previous reports. Besides, the incidence of complications after ESD was 1.3-25.3% in a study [20]. In this study, there were 3 cases of postoperative hemorrhage and 2 cases of perforation (8.6%) in ESD group. The hemostasis was successful in bleeding patients, without operation performed in other departments. The perforation patients were strictly fasted before ESD, the perforation was small and the resulting signs of peritonitis were mild, conforming to the indications for conservative treatment, so the intraoperative clamping using metal clips, postoperative fasting, gastrointestinal decompression, acid suppression, anti-inflammation and fluid infusion were performed, after which they were cured and discharged. Also, short-term complications occurred in 10 cases (7.4%) in LARG group, lower than that in a previous report (24.5-32.5%) [16]. The possible reason is that with the constant development and maturity of laparoscopic operation techniques in recent years, the operation time and resulting

trauma are obviously reduced, thereby lowering the incidence rate of complications. In this study, the incidence rate of long-term complications had no statistically significant difference between the two groups, and the safety of the two kinds of operations was somewhat similar.

The postoperative recurrence and survival time are important indexes for evaluating the efficacy of an operation. In this study, it was found that the OS was 96.1% (49/51) and 97.4% (112/115) in the two groups, and the difference was not statistically significant (p=0.751). After the effects of confounding factors were excluded, the recurrence rate of patients with different risks of lymph node metastasis was further analyzed. The results showed that the postoperative TFS of EGC patients with a low risk of lymph node metastasis had no statistically significant difference (p=0.197), but the postoperative TFS rate of EGC patients with a high risk of lymph node metastasis had a statistically significant difference between the two groups (p=0.034), significantly higher in LARG group than that in ESD group, indicating that LARG can significantly reduce the postoperative tumor recurrence in EGC with high risk of lymph node metastasis.

There are some limitations in the present study. First, this was a single-center retrospective study, there was a lack of randomized controlled trials, and the number of cases enrolled was small, especially in the ESD group. Second, no questionnaire survey and comparative analysis were conducted on the quality of life of patients during follow-up. Therefore, the conclusions made in this study remain to be further confirmed by multicenter large-sample prospective randomized studies in the future.

Conclusions

ESD is characterized by small trauma, rapid postoperative recovery, postoperative recurrence and survival comparable to those after surgical operation and high safety for EGC with a low risk of lymph node metastasis. LARG can reduce the postoperative recurrence rate of EGC with a high risk of lymph node metastasis.

Conflict of interests

The authors declare no conflict of interests.

References

1. Ajani JA, Bentrem DJ, Besh S et al. Gastric cancer, version 2.2013: featured updates to the NCCN Guidelines. J Natl Compr Canc Netw 2013;11:531-46.
2. Zygogianni A, Fotineas A, Platoni K et al. A five split-field three dimensional conformal technique versus an anterior-posterior on in postoperative radiotherapy for gastric carcinoma: a multicenter comparative study using quality of life measurements as well as clinical and dosimetric parameters. JBUON 2018;23:1020-8.
3. Gong Y, Wang B, Wang H. A propensity score-matching analysis comparing oncological outcomes of laparoscopic and open gastrectomy in patients with gastric carcinoma. JBUON 2017;22:134-40.
4. Watanabe M, Ito H, Hosono S et al. Declining trends in prevalence of Helicobacter pylori infection by birth-year in a Japanese population. Cancer Sci 2015;106:1738-43.
5. Ueda Y, Shiroshita H, Etoh T, Inomata M, Shiraishi N. Laparoscopic proximal gastrectomy for early gastric cancer. Surg Today 2017;47:538-47.
6. Liu J, Yang K, Chen XZ et al. Quality of life following laparoscopic-assisted distal gastrectomy for gastric cancer. Hepatogastroenterology 2012;59:2207-12.
7. Misawa K, Fujiwara M, Ando M et al. Long-term quality of life after laparoscopic distal gastrectomy for early gastric cancer: results of a prospective multi-institutional comparative trial. Gastric Cancer 2015;18:417-25.
8. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003;58:S3-S43.
9. Oka S, Tanaka S, Kaneko I et al. Advantage of endoscopic submucosal dissection compared with EMR for early gastric cancer. Gastrointest Endosc 2006;64:877-83.
10. Ono H, Yao K, Fujishiro M et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. Dig Endosc 2016;28:3-15.
11. Japanese gastric cancer treatment guidelines 2010 (version 3). Gastric Cancer 2011;14:113-23.
12. An JY, Heo GU, Cheong JH, Hyung WJ, Choi SH, Noh SH. Assessment of open versus laparoscopy-assisted gastrectomy in lymph node-positive early gastric cancer: a retrospective cohort analysis. J Surg Oncol 2010;102:77-81.
13. Japanese GCA. Japanese Classification of Gastric Carcinoma (2nd English Edition). Gastric Cancer 1998;1:10-24.
14. Takeuchi H, Goto O, Yahagi N, Kitagawa Y. Function-preserving gastrectomy based on the sentinel node concept in early gastric cancer. Gastric Cancer 2017;20:53-9.
15. Oda I, Suzuki H, Yoshinaga S. Endoscopic Submucosal Dissection for Early Gastric Cancer: Getting It Right! Adv Exp Med Biol 2016;908:317-30.

16. Chiu PW, Teoh AY, To KF et al. Endoscopic submucosal dissection (ESD) compared with gastrectomy for treatment of early gastric neoplasia: a retrospective cohort study. Surg Endosc 2012;26:3584-91.
17. Libanio D, Braga V, Ferraz S et al. Prospective comparative study of endoscopic submucosal dissection and gastrectomy for early neoplastic lesions including patients' perspectives. Endoscopy 2019;51:30-9.
18. Kim MY, Cho JH, Cho JY. Ever-changing endoscopic treatment for early gastric cancer: yesterday-today-tomorrow. World J Gastroenterol 2014;20:13273-83.
19. Uedo N, Takeuchi Y, Ishihara R. Endoscopic management of early gastric cancer: endoscopic mucosal resection or endoscopic submucosal dissection: data from a Japanese high-volume center and literature review. Ann Gastroenterol 2012;25:281-90.
20. Oda I, Suzuki H, Nonaka S, Yoshinaga S. Complications of gastric endoscopic submucosal dissection. Dig Endosc 2013;25 (Suppl 1):71-8.