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Retrospective Study

Efficacy and safety of endoscopic submucosal dissection for early gastric cancer and precancerous lesions in elderly patients

Wen-Si Xu, Hui-Yu Zhang, Shuang Jin, Qi Zhang, Hong-Dan Liu, Ming-Tao Wang, Bo Zhang

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With advancements in the development of endoscopic technologies, the endoscopic submucosal dissection (ESD) has been one of the gold-standard therapies for early gastric cancer.

AIM

To investigate the efficacy and safety ESD in the treatment of early gastric cancer and precancerous lesions in the elderly patients.

METHODS

Seventy-eight elderly patients with early gastric cancer and precancerous lesions admitted to the Third Affiliated Hospital of Qiqihar Medical University were selected and classified into two groups according to the different surgical therapies they received between January 2021 and June 2022. Among them, 39 patients treated with ESD were included in an experimental group, and 39 patients treated with endoscopic mucosal resection (EMR) were included in a control group. We compared the basic intraoperative conditions, postoperative short-term recovery, long-term recovery effects and functional status of gastric mucosa between the two groups; the basic intraoperative conditions included lesion resection, intraoperative bleeding and operation time; the postoperative short-term recovery assessment indexes were length of hospital stay and incidence of surgical complications; and the long-term recovery assessment indexes were the recurrence rate at 1 year postoperatively and the survival situation at 1 year and 3 years postoperatively; and we compared the preoperative and pre-discharge serum pepsinogen I (PG I) and PG II levels and PG I/PG II ratio in the two groups before surgery and discharge.

RESULTS

The curative resection rate and the rate of *en bloc* resection were higher in the

experimental group than in the control group. The intraoperative bleeding volume was higher in the experimental group than in the control group. The operation time was longer in the experimental group than that in the control group, and the rate for base residual focus was lower in the experimental group than that of the control group, and the differences were all statistically significant (all $P < 0.05$). The length of hospital stay was longer in the experimental group than in the control group, and the incidence of surgical complications, 1-year postoperative recurrence rate and 3-year postoperative survival rate were lower in the experimental group than in the control group, and the differences were statistically significant (all $P < 0.05$). However, the difference in the 1-year postoperative survival rate was not statistically significant between the two groups ($P > 0.05$). Before discharge, PG I and PG I/PG II ratio were elevated in both groups compared with the preoperative period, and the above indexes were higher in the experimental group than those in the control group, and the differences were statistically significant (both $P < 0.05$). Moreover, before discharge, PG II level was lower in both groups compared with the preoperative period, and the level was lower in the experimental group than in the control group, and the differences were all statistically significant (all $P < 0.05$).

CONCLUSION

Compared with EMR, ESD surgery is more thorough. It reduces the rate of base residual focus, recurrence rate, surgical complications, and promotes the recovery of gastric cells and glandular function. It is safe and suitable for clinical application.

Key Words: Endoscopic submucosal dissection; Endoscopic mucosal resection; Early gastric cancer; Serum pepsinogen; Elderly

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Core Tip: Endoscopic submucosal dissection is one of the most commonly used minimally invasive therapies for early gastric cancer and precancerous lesions. The present study compared the primary intraoperative conditions, postoperative short- and long-term recovery and functional status of gastric mucosa between elderly patients undergoing endoscopic submucosal dissection vs those undergoing endoscopic mucosal resection to evaluate the efficacy and safety of these two operations.

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INTRODUCTION

Early gastric cancer mainly refers to the condition that cancer tissues occurred in the submucosa or mucosa[1]. With the progress in the therapy instruments and technological advancement in endoscopic examination[2-4], endoscopic submucosal dissection (ESD) has become one of the main therapies for early gastric cancer, and is widely used in clinical practice achieving inspiring comparable efficacy with radical resection. ESD, which originated in Japan, is characterized by a high rate of *en bloc* resection and low recurrence rate. Several studies[5-7] showed the long- and short-term outcomes of patients eligible for ESD are comparable with those undergoing gastric resection. Moreover, ESD is associated with less complications, shorter hospital stays and better quality of life. In the clinical practice, identifying risk factors for cancer recurrence and then developing corresponding therapeutic strategies is essential for the intervention in elderly patients with early gastric cancer and precancerous lesions. The present study discussed the efficacy and safety of ESD in the elderly population.

MATERIALS AND METHODS

Participants

Seventy-eight elderly patients with early gastric cancer and precancerous lesions treated at The Third Affiliated Hospital of Qiqihar Medical University were selected and classified into two groups based on the different surgical therapies they received between January 2021 and June 2022. Among them, 39 patients who underwent ESD were included in an experimental group and 39 patients who underwent endoscopic mucosal resection (EMR) were included in a control group. The present study was approved by the Hospital Ethics Committees. Eligible patients were patients aged 65 or older with early gastric cancer and precancerous lesions confirmed by histological biopsy and indications for ESD and EMR based on Japanese Gastric Cancer Treatment Guidelines 2010[8]. All patients were informed about the research and signed the

consent form. Patients younger than 65 years old with intrinsic muscle layer invasive gastric cancer, acute exacerbation, coagulopathy or major organ dysfunction were excluded from the study. Patients in the experimental group were aged 66 years to 81 years, 23 were male, 16 were female, and body mass index (BMI) was 19 kg/m² to 27 kg/m² (23.58 ± 9.31). Gastric lesions were located in the gastric antrum in 22 patients, gastric body in 11 patients, and gastric cardia and fundus in 6 patients. Pathological diagnostic results showed that 5 patients had intramucosal carcinoma, 20 patients had high-grade intraepithelial neoplasia, and 14 patients had low-grade intraepithelial neoplasia. The mean lesion diameter was 1.2 cm to 4.2 cm (1.46 ± 0.36) and the mean tumor area was 1.0 cm² to 7.6 cm² (6.59 ± 1.72). Patients in the control group were aged 65 years to 81 years (74.54 ± 12.43), 22 were male, 17 were female, and the BMI was 20 kg/m² to 26 kg/m² (24.12 ± 8.69). Gastric lesions were located in the gastric antrum in 21 patients, gastric body in 12 patients, and gastric cardia and fundus in 6 patients. Pathological diagnostic results showed that 6 patients had intramucosal carcinoma, 18 patients had high-grade intraepithelial neoplasia and 15 patients had low-grade intraepithelial neoplasia. The mean lesion diameter was 1.0 cm to 3.8 cm (1.57 ± 0.61) and the mean tumor area was 1.1 cm² to 7.5 cm² (7.14 ± 1.69). There was no significant difference in the general information between the two groups ($P > 0.05$).

Therapies

Patients in the experimental group underwent ESD. First, the superficial lesions were stained with 0.4% Indigo Rouge after general anesthesia to help identify the circumferential range. Second, resection area was identified through argon electrocoagulation marking at 0.5 cm surrounding the lesion with a 0.2 cm margin between markers[9]. Third, mixed solutions which mainly composed of adrenaline, glycerol, glucose and normal saline were multi-point injected outside electrocoagulation marking points to lift the lesion. Fourth, a Hook knife was used to cut through the lesions to the submucosal fibers around the outside of the electrocoagulation marking points and mixed solutions were injected into the submucosa so that the lesions could be completely resected. Electrocautery was used in case bleeding points formed. A negative pressure suction device was used to create clear vision. During the operation, the hemostatic agent sucralfate gel was sprayed on the wound surface if necessary. The removed tissues were sent to the Department of Pathology for detailed examination. The patients received symptomatic treatment after the procedure. The type of anesthesia and electrocoagulation marking applied in the control group was comparable to those of the experimental group. Small lesions were removed by ligation-assisted (banding). EMR techniques and cap-assisted endoscopic resection was applied for the bigger lesions. To be specific, a transparent cap was attached to the distal end of the endoscope and in the meantime a high-frequency snare was inserted into the cap. Then, a negative pressure suction device was used to suck the lesional mucosa to the cap. When the lesional mucosa is fully retracted through the transparent cap, the band-ligation device was tightened up to remove the lesion. The way for lesion management is comparable to that of the experimental group.

Outcome measures

Basic information during the operation, and short- and long-term recovery and the function of gastric mucosa after the operation were compared between the two groups[10-13]. First, intraoperative basic information included lesion resection, intraoperative bleeding and the operation time. Lesion resection had two measures of *en bloc* resection and curative resection. The former was performed to remove the lesion as a whole and the latter was performed to prevent lymphatic metastasis. Second, postoperative short-term recovery involved length of hospital stay and incidence of surgical complications which included fever, bleeding, perforation, *etc.* Overall incidence of postoperative complications was the composite of these complications. Third, the assessment of long-term recovery refers to 1-year recurrence rate and 1- and 3-year survival rate. Fourth, the level of serum pepsinogen (PG) I and PG II and PG I/II ratio were compared between the two groups before the operation and discharge, respectively.

Statistical analysis

SPSS statistics 22.0 was used to process the data. Measurement data was presented as mean ± SD and *t* test was used when comparing the differences between the two groups. Count data was presented as *n* (%) and Pearson's χ^2 test was used when comparing the differences between the two groups. A $P < 0.05$ represented that there was a significant difference.

RESULTS

General intraoperative information

Both *en bloc* resection rate and curative resection rate were higher in the experimental group than in the control group. Moreover, the intraoperative blood loss was greater in the experimental group than in the control group. However, rate of residual tumors at the base of the primary tumors was lower in the experimental group than in the control group (all $P < 0.05$, Table 1).

Postoperative recovery

Length of hospital stay was longer in the experimental group than in the control group. However, the incidence of surgical complications and postoperative recurrence rates at 1 year and 3 years were lower in the experimental group than in the control group (all $P < 0.05$, Table 2 and Table 3). There was no significant difference in the 1-year survival rate between the two groups ($P > 0.05$).

Table 1 Comparison of general intraoperative information between the two groups

Group	n	En bloc resection	Curative resection	Rate of residual tumors at the base of the primary tumors	Intraoperative blood loss in mL	Operation time in min
Experimental group	39	38 (97.44)	29 (74.36)	1 (2.56)	102.21 ± 9.31	85.32 ± 8.93
Control group	39	28 (71.79)	20 (51.28)	11 (28.21)	76.53 ± 7.83	68.22 ± 7.34
χ^2/t value		12.733	10.721	17.412	6.426	5.315
P value		0.001	0.001	0.001	0.001	0.001

Data are n (%).

Table 2 Comparison of postoperative recovery between the two groups

Group	n	Length of hospital stay in d	1-yr recurrence rate	1-yr survival rate	3-yr survival rate
Experimental group	39	13.41 ± 3.25	0 (0.00)	37 (94.87)	29 (74.36)
Control group	39	10.38 ± 2.84	5 (12.82)	33 (84.62)	25 (64.10)
χ^2/t value		6.359	7.534	7.683	6.706
P value		0.001	0.001	0.001	0.001

Data are n (%).

Table 3 Comparison of surgical complications between the two groups

Group	n	Fever	Intraoperative perforation	Postoperative bleeding	Overall incidence of surgical complications
Experimental group	39	11 (28.21)	1 (2.56)	2 (5.13)	14 (35.90)
Control group	39	10 (25.64)	0 (0.00)	8 (20.51)	18 (46.15)
χ^2 value		0.834	0.000	8.476	6.580
P value		0.361	1.000	0.001	0.001

Data are n (%).

Changes in the function of gastric mucosa

No significant difference was observed in PG I, PG II and PG I/II between the two groups before the operation ($P > 0.05$). However, PG I and PG I/II increased in both groups before the discharge compared with those before the operation and these levels were higher in the experimental group than in the control group (all $P < 0.05$, Table 4). On the contrary, PG II decreased in both groups before the discharge compared with those before the operation and it was lower in the experimental group than in the control group (all $P < 0.05$, Table 4).

DISCUSSION

The case fatality rate of advanced gastric cancer accounted for 13.6% of cancer fatality rates in China. After standardized treatment, 5-year survival rate for patients with early-stage gastric cancer was over 90%. The earliest diagnosis and precision therapy thus are crucial to improving the survival rate and should be highlighted. ESD is low cost and minimally invasive, and patients undergoing ESD generally have a better quality of life after surgery. The efficacy of ESD for distal early-stage gastric cancer and precancerous lesions is comparable with that for proximal ones in the elderly. However, the risk of postoperative fever is higher for ESD in patients with distal gastric cancer and precancerous lesions than in patients with proximal ones, and the surgery may cause greater trauma in the former. This may be attributed to biological characteristics and structural features related to the location of the lesions[14,15]. ESD allows endoscopists to achieve *en bloc* resection of flat lesions larger than 2 cm including early-stage gastric cancer. The ESD procedure requires greater endoscopic management skills compared with EMR. The incidence of surgical complications in ESD procedures is relatively high. Factors influencing ESD operational challenges include location and size of lesions, presence of ulcer and scar as well as intraoperative bleeding. Intraoperative hemorrhage may lead to extended operation time and perforation

Table 4 Comparison of changes in the function of gastric mucosa between the two groups

Group	n	PG I		PG II		PG I/II	
		Before the operation	Before the discharge	Before the operation	Before the discharge	Before the operation	Before the discharge
Experimental group	39	65.31 ± 12.32	95.36 ± 19.26 ^a	23.28 ± 2.51	14.20 ± 2.35 ^a	2.72 ± 0.31	5.97 ± 1.52
Control group	39	66.38 ± 12.48	75.42 ± 13.48 ^a	24.03 ± 3.04	18.05 ± 1.03 ^a	2.71 ± 0.29	4.76 ± 1.21
t value		0.359	153.313	0.728	6.706	0.000	12.832
P value		0.501	0.001	0.342	0.001	1.000	0.001

^aP < 0.05 vs those before the operation.

PG: Pepsinogen.

due to the blurry visual field it caused[16]. Postoperative bleeding should be prevented to better assess the risk in the surgery. Endoscopic ultrasound can be used to evaluate the depth of invasion in early gastric cancer before ESD surgery. In addition, patient's medication status, *e.g.*, whether antiplatelets are used, coagulation monitoring, and platelet tests can help evaluate the risk for bleeding[17]. In general, studies have shown the advantages of ESD over EMR in the aspect of *en bloc* resection rate, complete resection rate and local recurrence rate.

The present study showed that the curative resection rate, *en bloc* resection rate, 1- and 3-year survival rate were higher in patients undergoing ESD than in those undergoing EMR, although ESD was associated with greater intraoperative hemorrhages and longer length of hospital stays. The relatively long duration of operation and length of hospital stay and greater intraoperative hemorrhage may attribute to surgical difficulty, wide resection range, *etc* in elderly patients with early gastric cancer and precancerous lesions. PG is a pepsin precursor, and its level can indicate the function of gastric mucosa. PG I, PG II and PG I/PG II ratio can be used to evaluate the number of gastric parietal cells, the function of gastric mucosa and the degree of gastric mucosal atrophy[18,19]. The results manifested that ESD can protect the function of the gastric mucosa by conserving most parts of the mucosa of the stomach.

CONCLUSION

Above all, ESD can improve treatment efficacy and reduce postoperative complications in elderly patients with early gastric cancer and precancerous lesions. It can be widely used in clinical practice.

ARTICLE HIGHLIGHTS

Research background

Endoscopic submucosal dissection (ESD) can realize curative *en bloc* resection of gastrointestinal superficial lesions as well as organ preservation in spite of some surgical risks such as perforation, intraoperative bleeding and prolonged operative duration.

Research motivation

Age is an important risk factor for the development of gastric cancer and meanwhile it influences the treatment options for gastric cancer, especially for the older patients who are more vulnerable to laparotomy.

Research objectives

This study aimed to investigate the efficacy and safety of ESD for the treatment of elderly patients with early gastric cancer and precancerous lesions.

Research methods

Surgical indexes, postoperative complications, recovery and prognosis were compared between patients with early gastric cancer and precancerous lesions undergoing ESD with those undergoing endoscopic mucosal resection (EMR).

Research results

ESD shows greater benefits in the aspects of the primary intraoperative conditions, postoperative short- and long-term recovery and functional status of gastric mucosa over EMR.

Research conclusions

ESD is a more effective option than EMR in the treatment of early gastric cancer and precancerous lesions in the elderly.

Research perspectives

Curative criteria after ESD for early gastric carcinoma should be considered in further studies to maximize the benefits of ESD for the recipients and provide evidence for the subsequent follow-up and treatment decision-making.

FOOTNOTES

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