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Original Article

Clinical comparison of endoscopic mucosal resection and submucosal dissection on effectiveness and quality of life of patients with early-stage gastric cancer and precancerous lesions

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Abstract: Objective: To compare endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) on effectiveness and quality of life of patients with early gastric cancer and precancerous lesions. Methods: A total of 156 patients with early gastric cancer and precancerous lesions were selected and randomized into two groups, ESD group treated with ESD and EMR group treated with EMR. The treatment of the two groups was compared. Intraoperative conditions including blood loss, operation time, hospitalization time, and surgical resection, as well as perforation rate, six-month recurrence rate, Visual Analogue Scale (VAS) score, and Six-point Behavioral Scale (BRS-6) score of the two groups were compared. Meantime, quality of life of the patients in the two groups was evaluated and compared. Results: The total effective rate in ESD group was 94.87%, higher than that in EMR group (74.36%; P = 0.000). Compared with EMR group, the *en bloc* resection rate and curative resection rate of ESD group were significantly higher (both P = 0.000), the lesion excised diameter of ESD group was significantly smaller (P = 0.000), and the six-month recurrence rate of ESD group was significantly lower (χ^2 = 3.087; P = 0.024). After treatment, the score of quality of life of ESD group was significantly higher than that of EMR group (t = 16.670, P = 0.000); VAS score (t = 13.414, P = 0.000) and BRS-6 score (t = 9.433, P = 0.009) of ESD group were both significantly lower than those of EMR group. Conclusion: ESD surgery for patients with early gastric cancer and precancerous lesions can achieve relatively satisfactory effectiveness, improve quality of life of the patients, and effectively reduce the pain. It is therefore worthy of clinical promotion and application.

Keywords: ESD, EMR, gastric cancer, precancerous lesions, treatment effectiveness

Introduction

Gastric cancer is a clinically common malignant tumor of digestive system, and the fourth most common tumor in the world with relatively high incidence rate and poor effectiveness according to clinical statistics [1-3]. In the early time, a series of related surgical treatments were carried out for middle- and advanced-stage gastric cancer [4, 5]. With the continuous development of current digestive endoscopy technology, early diagnosis and treatment is often adopted for gastric cancer. Early-stage gastric cancer can be screened out through advanced diagnostic techniques. Cancerous cells of early-stage gastric cancer mostly infiltrate gastric submucosa and mucosa. Emaciation, vomiting, appetite hypofunction and gastric pain are the main clinical symptoms among the patients [6]. Previously, lymphadenectomy and surgical laparotomy are mostly adopted for early-stage gastric cancer with the lesions locating in mucosa and submucosa. With the continuous development of endoscopic diagnosis technology, ultrasonic endoscopy methods such as endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) are mostly used for early-stage cancer and precancerous lesions clinically. Such methods can remove the lesions at one time with smaller wound surface and fewer complications, and thus there has been increasing clinical application. Among them, EMR is characterized by low invasiveness and high safety as well as relatively low incidence of complications. Gastric perforation is a common complication in EMR as per clinical studies, with incidence rate of 0.06-5% only. However, low resection rate is the major defect

for EMR. Only 34% of total removal rate is obtained in treatment of early-stage rectal cancer using EMR, and the recurrence rate ranges from 10% to 23.5% due to residual lesions caused by piecemeal resection frequently adopted in EMR [7]. While the recurrence rate of rectal cancer after ESD is found to be only 0-9.1% on account of effective improvement on one-time resection rate using endoscopic submucosal dissection serving as a more advanced technology [8].

Endoscopic mucosal resection procedure has gained wider popularization and application in early-stage gastric cancer and precancerous lesions. However, no comprehensive and systematic clinically studies have been conducted on ESD and EMR for early-stage gastric cancer and precancerous lesions, with a lack of relevant clinical data of treatment effect. In order to better guide the treatment of early-stage gastric cancer and precancerous lesions, ESD and EMR were adopted in the patients with early-stage gastric cancer and precancerous lesions to compare the effectiveness as well as quality of life of the patients of the two methods.

Materials and methods

General clinical data

A total of 156 patients with early-stage gastric cancer and precancerous lesions in The People's Hospital of Danyang from January 2017 to November 2018 were recruited and randomly divided into two groups, ESD group and EMR group, with 78 cases in each group. In ESD group, 39 cases were male and 39 were female, with an average age of 60.3 years (SD = 7.9). In EMR group, 41 cases were male and 37 were female, with an average age of 59.9 years (SD = 6.2). There was no significant difference in general clinical data between the two groups, which was comparable (all $P>0.05$). The study was approved by the Medical Ethics Committee of The People's Hospital of Danyang, and informed consents were obtained from all the patients or their families.

Inclusive criteria were: patients who had not undergone decollement or dissection; patients who had differentiated intramucosal carcinoma; patients who had undifferentiated gastric intragastric carcinoma without ulceration, with lesion diameter of less than 2 cm; and patients who had differentiated superficial gastric submucosal carcinoma without ulceration, with lesion diameter of less than 3 cm. Exclusion criteria were: patients who had serious injuries to vital organs such as heart, liver and kidney; patients who had poor compliance; patients who had contraindications in general anesthesia or endoscopic operation; patients who had received radiotherapy and chemotherapy before; and patients who had extragastric metastasis.

Methods

Patients in EMR group were treated by endoscopic mucosal resection. The lesions of a patient were observed under endoscope after successful general anesthesia. Depressed lesions were suctioned into a cap under negative pressure attraction through the tip of the endoscope (Olympus Medical Systems, Tokyo, Japan). Once retracted completely into the cap, the lesions were captured by snare with mucosal resection. The eminence lesions were captured by snare (Olympus, Tokyo, Japan), followed by mucosal resection. If basal mucosa was involved as a lesion, the resection border around the lesion was marked at 2-3 mm away from the margin of the basal mucosa, followed by injection of 10 mL of epinephrine (0.1 mg/mL; Hangzhou Minsheng Pharmaceutical Group Co., Ltd., China) at the lesion. After injection, the elevated and pale lesion was observed and captured by electrocautery snare with mucosal resection [9].

ESD group adopted endoscopic submucosal dissection. After general anesthesia, the lesions of a patient were observed and marked using soft coagulation current at 5 mm away from the margin of the lesions with a distance of about 2 mm between marks, followed by injection of physiological saline solution with epinephrine at each mark. Then a KD-610 IT-knife (Olympus, Tokyo, Japan) was used to cut open the lesion to submucosa and dissect the submucosal layer beneath the lesion. Minor oozing from small blood vessels was treated using Dual knife (Olympus, Tokyo, Japan), and more significant bleeding or bleeding from large blood vessel rupture was stopped using electrocoagulation, and blood vessels were exposed by electrothermal bipolar coagulation after complete dissection [10].

Table 1. Comparison of general clinical data of the patients of the two groups

	EMR group (n = 78)	ESD group (n = 78)	P
Age (year)	59.9±6.2	60.3±7.9	0.725
Sex (male/female)	41/37	39/39	1.000
Operation time (min)	65.67±7.09	62.99±6.54	0.054
Lesion diameter (cm)	1.56±0.12	1.54±0.11	0.280
BMI (kg/m^2)	21.32±2.11	21.09±2.09	0.065
Lesion site (n)			
Sinuses ventriculi	34	37	1.000
Fundus gastricus/pars cardiaca	20	20	1.000
Corpus gastricum	14	14	1.000
Gastric angulus	10	7	1.000
Pathological type (n)			
Low-grade intraepithelial neoplasia	19	20	1.000
High-grade intraepithelial neoplasia	39	36	1.000
Early-stage gastric cancer	20	22	1.000

Note: EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection; BMI: body mass index.

Outcome measures

The clinical treatment effect was divided into three levels according to resection degree of lesions, with complete resection being markedly effective, massive resection being effective, and non-resection being ineffective. The total effective rate = (markedly effective cases + effective cases)/total cases × 100%. The amount of intraoperative blood loss, operation time and the postoperative hospitalization time were recorded. Postoperative treatment conditions including the *en bloc* excision (complete and *en bloc* resection, instead of multiple excision or incomplete excision of lesion mucosa) and curative resection no lesion tissue exposure at specimen margin, no vascular infiltration, and depth of infiltration (could not exceed 500 μm beneath mucosal muscle), and the lesion excised diameters in patients were recorded. Presence or absence of the gastric perforation occurred after operation was observed. All patients were followed up for six months, and their recurrence condition was recorded for estimating six-month recurrence rate. The condition that neoplastic lesion grew from the original scar of EMR or ESD, or lesion within 1-2 mm close to the original scar of ESD or EMR with surrounding mucosa bunched up was considered as recurrence.

Quality of Life Questionnaire Core 30 (QLQ-C30) scale is a cancer patient-oriented scoring scale, with a total of 30 items, 7 points in each item; the higher the score, the higher the quality of life, and the better the patient's condition [11]. The pain degree was assessed using Visual Analogue Scale (VAS), and the pain degree of the patient was expressed by a 0-to-10 scale with 11 rating options, wherein 0 represented painless and 10 represented severe pain, and the lower the score, the lower the pain degree [12]. Six-point Behavioral Scale (BRS-6) was also used to assess the pain degree containing six grades, grade 1 with no pain (score: 0), grade 2 with mild pain that could be ignored (score: 1), grade 3 with mild pain that could not be ignored (score: 2), grade 4 with moderate pain (score: 3), grade 5 with severe pain (score: 4), and grade 6 with extreme severe pain (score: 5) [13].

Statistical analysis

All the data obtained in this study were analyzed using the SPSS software version 19.0. The measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± sd), on which intra-group comparison was performed by *t*-test. The enumeration data was expressed as cases/percentage (n/%), on which intra-group comparison was carried out by chi-square test. *P* values of <0.05 were considered statistically significant.

Results

General clinical data

There were no significant differences in age, sex, operation time, lesion diameter, body mass index (BMI), lesion location, and pathological type between the two groups, which were comparable (all P>0.05). See **Table 1**.

Treatment effect

In EMR group, there were 30 cases being markedly effective and 28 cases being effective, with a total effective rate of 74.36%. While in ESD group, there were 59 cases being mark-

Table 2. Comparison of treatment effect of the patients of the two Groups

	Markedly effective (n)	Effective (n)	Ineffective (n)	Total effective rate (n/%)
EMR (n = 78)	30	28	20	58 (74.36)
ESD (n = 78)	59	15	4	74 (94.87)
χ^2		0.000		12.606
P				

Note: EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection.

Table 3. Comparison between the two groups in intraoperative conditions and hospitalization time

	Intraoperative amount of blood loss (mL)	Operation time (min)	Postoperative hospitliztion time (d)
EMR (n = 78)	134.67±11.77	91.67±8.97	8.31±0.97
ESD (n = 78)	138.67±14.09	92.09±9.43	8.51±1.09
t	1.924	0.287	1.205
P	0.056	0.775	0.230

Note: EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection.

Table 4. Comparison of surgical resection between two groups

	En bloc resection (n/%)	Curative resection (n/%)	Lesion excised diameter (mm)
EMR group (n = 78)	55 (70.51)	35 (44.87)	29.67±3.09
ESD group (n = 78)	74 (94.87)	60 (76.92)	15.98±1.98
t/χ^2	24.157	16.825	13.690
P	0.000	0.000	0.000

Note: EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection.

Table 5. Comparison between two groups in perforation and six-month recurrence rate (n, %)

	Perforation	Six-month recurrence
EMR group	14 (17.95%)	22 (28.20%)
ESD group	15 (19.23%)	13 (16.67%)
χ^2	0.042	3.087
P	0.837	0.024

Note: EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection.

edly effective and 15 cases being effective, with a total effective rate of 94.87%. The total effective rate in ESD group was significantly higher than that in EMR group (χ^2 = 12.606, P = 0.000). See **Table 2**.

Intraoperative conditions and hospitalization time

There were no significant differences between EMR group and ESD group in the amount of intraoperative blood loss, operation time and postoperative hospitalization time (P = 0.056, P = 0.775, P = 0.230). See **Table 3**.

Surgical resection of two groups

There were 55 cases of resection and 35 cases of curative resection in EMR group. While in ESD group, there were 74 cases of *en bloc* resection and 60 cases of curative resection presented. The lesion excised diameters in EMR group and ESD group were 29.67±3.09 mm and 15.98±1.98 mm, respectively. The *en bloc* resection rate and curative resection rate in ESD group were significantly higher than those in EMR group (both P = 0.000), and the lesion excised diameter in ESD group was significantly smaller than that in EMR group (P = 0.000). See **Table 4**.

Perforation rate and six-month recurrence rate

The perforation rates of ESD group and EMR group were 19.23% and 17.95%, respectively, with no significant difference (χ^2 = 0.042, P = 0.837). The six-month recurrence rates of ESD group and EMR group were 16.67% and 28.20%, respectively. The six-month recurrence rate of ESD group was significantly lower than that of EMR group (χ^2 = 3.087, P = 0.024). See **Table 5**.

Comparison of postoperative quality of life scores between two groups

After treatment, the quality of life scores of ESD group and EMR group were 59.18±8.41 and 42.51±6.63, respectively. The score of ESD

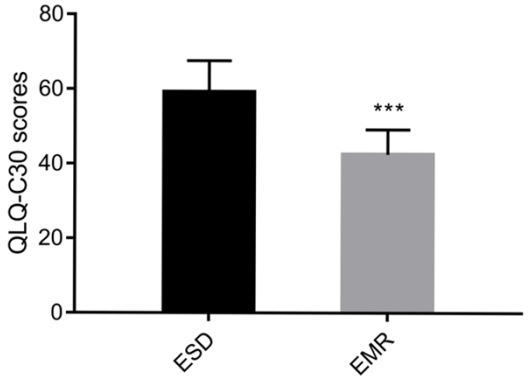

Figure 1. Comparison of postoperative QLQ-C30 scores between two groups. Compared with ESD group, ***P = 0.000. EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection; QLQ-C30: Quality of Life Questionnaire Core 30.

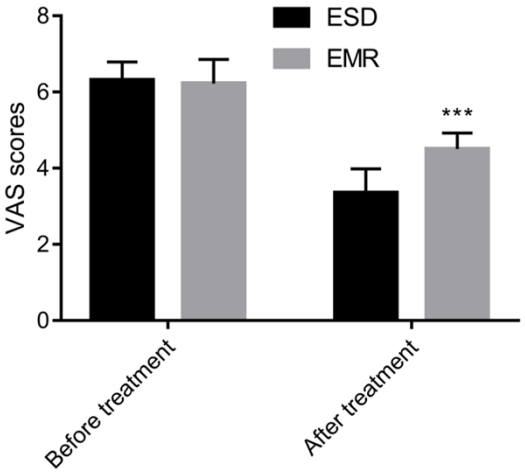

Figure 2. Comparison of VAS scores between the two groups before and after treatment. Compared with ESD group, ***P = 0.000. EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection; VAS: Visual Analogue Scale.

group was significantly higher than that of EMR group (t = 16.670, P = 0.000). See **Figure 1**.

Comparison of VAS scores between two groups before and after treatment

The VAS scores of ESD group and EMR group before treatment were 6.31±0.48 and 6.23±0.63, respectively, while the scores of ESD group and EMR group after treatment were 3.35±0.64 and (4.50±0.42), respectively. After treatment, the VAS scores of ESD group were significantly lower than those of EMR group (t = 13.414, P = 0.000). See **Figure 2**.

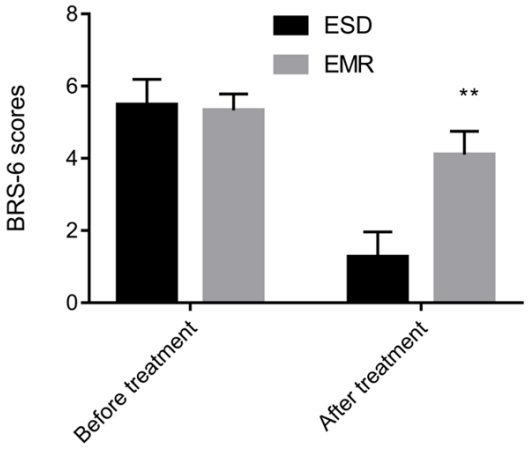

Figure 3. Comparison of BRS-6 scores between two groups before and after treatment. Compared with ESD group, **P = 0.009. EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection; BRS-6 score: the 6-point behavioral rating scale.

Comparison of BRS-6 scores between two groups before and after treatment

The BRS-6 scores of ESD group and EMR group before treatment were 5.54±0.32 and 5.23±0.54, respectively. After treatment, the scores of EMR group and ESD group were 3.98±0.41 and 1.23±0.11, respectively. The BRS-6 scores of the patients in both groups were decreased, and the BRS-6 scores of ESD group were significantly lower than those of EMR group (t = 9.43, P = 0.009). See **Figure 3**.

Discussion

Gastric cancer has been referred as one of the malignant tumors that seriously threaten human life and health due to its high incidence rate. Gastric cancer ranks fourth in the number of newly diagnosed cases in cancer field worldwide every year. In China, the detection rate of gastric cancer through gastroscopy is as high as 3.13% due to unobvious clinical symptoms of gastric cancer in the early stage with most cases having atypical symptoms and rapid progression [14]. Most cases of gastric cancer in patients are in the middle and advanced stage when receiving confirmed diagnosis. Previously, surgery is the top choice usually adopted for middle and advanced gastric cancer. However, the treatment effect is unsatisfactory due to dilatoriness at the best treatment time. Clinical statistics show that gastric cancer, as one of the common malignant tumors of digestive

tract, ranks second in mortality among cancers [14]. However, surgical resection brings great damage to the patients with dramatic reduction in the quality of life, presenting only 25% of five-year survival rate after conventional surgical resection [15, 16].

With the continuous improvement of endoscopic diagnosis technology, the endoscopic results are usually used as the diagnostic basis for gastrointestinal tumors. The clear image presented by endoscopy is greatly helpful for preliminary diagnosis on the mucosa, blood vessels and pathological tissues, thus improving the detection rate of pathological parts. In previous studies, endoscopic ultrasonography was compared with CT in diagnosis for gastrointestinal tumors, with a diagnostic rate of 64.4%, which shows superiority to CT presenting a diagnostic rate of 58.4% [17, 18]. At present, minimally invasive endoscopic techniques, EMR and ESD, are used as the main treatment methods for early cancers and precancerous lesions of digestive tract. Such endoscopic techniques have obvious curative effect and less trauma, which provides reliable data for clinical research in this field. While EMR increases the possibility of recurrence due to the difficulty in resecting the lesion tissue *en bloc* in clinic, as well as the difficulty in resecting submucosal lesions. ESD can peel off the lesion tissue at one time, which makes up for the deficiency of EMR to a certain extent. In patients with colorectal cancer, the *en bloc* resection rate of ESD is 94.87%, which is significantly higher than that of EMR presenting 70.51% [19]. ESD can completely preserve pathological tissues, and can peel off the lesions for pathological diagnosis to evaluate the effect of *en bloc* resection; however, this method is relatively strict in technical operation, and as well has difficulty in a surgery [20]. This study showed that the total effective rate of EMR group was 74.36%, which was significantly higher than that of ESD group (94.87%), indicating that the treatment effect of ESD was better than that of EMR group. In clinical ESD surgery, gastrointestinal lesions and normal submucosa of patients were gradually peeled off by high-frequency electrotome to improve the purpose of *en bloc* resection of the lesions. This surgery, compared with EMR, can provide clear field of lesion tissues under endoscope, which can improve the *en bloc* resection rate of the lesion tissues. In this study, the *en bloc* resection rate and curative resection rate of ESD group were significantly higher than those of EMR group, and the lesion excised diameter of ESD group was significantly smaller than that of EMR group. This may be related to differences in operational approach between the two methods. Lesions are suctioned into the transparent cap by negative pressure in EMR surgery. If the lesion is irregular, there could be residual lesions existing after surgery, even with the help of high-frequency electrotome for lesion resection, resulting in a low rate of one-time resection. While ESD can better control the scope and shape of the lesions, and can completely excise mucosal lesion tissues *en bloc* along the outer margin of the lesions [21]. This study found that the six-month recurrence rate of ESD group was significantly lower than that of EMR group. Presumably, ESD surgery using endoscopic submucosal dissection causes less trauma to the patients, and accurately location of the lesions on the submucosal level under endoscope brings clear *en bloc* dissection, which largely reduces the probability of lesion residual, thus effectively reducing the possibility of recurrence. Quality of life has been taken as an important indicator for evaluating the therapeutic effect of malignant tumors. Clinically, it is believed that the quality of life of patients with malignant tumors can better reflect the treatment effect and health status of the patients. Therefore, quality of life score has been taken as an important evaluation factor for clinical treatment effect of malignant tumors in clinical trials. QLQ-C30 is a quality of life survey questionnaire most commonly used in cancer patients, which includes physical function, emotional function, social function and role-playing function, etc. Additionally, physiological symptoms of the patients such as nausea, vomiting, pain, constipation, and diarrhea are evaluated. The scale is widely applied in quality of life evaluation of patients with malignant tumors including gastric cancer. Patients with early-stage gastric cancer and precancerous lesions are mostly characterized by stomachache, vomiting, nausea, loss of appetite, and decrease in quality of life. In this study, the quality of life score of ESD group was significantly higher than that of EMR group, and the VAS score and BRS-6 score of ESD after treatment were significantly lower than those of EMR group, indicating that ESD can reduce the

pain of the patients to a certain extent as well as improve their quality of life. Consistent to these findings, Zhu found that the hospitalization cost and time in the group treated with ESD were significantly less than those in the group treated with radical surgery for patients with early-stage gastric cancer, and the quality of life scores evaluated by QLQ-C30 scale in the ESD group were significantly higher than those in the radical surgery group [22].

The main shortcoming of this study is that the follow-up period was only half a year. In the future research, follow-up period should be extended to track the post-operative recurrence of the patients. In addition, sample size should be expanded as well to improve the accuracy of results of the following research.

In summary, ESD surgery for patients with early gastric cancer and precancerous lesions can achieve relatively satisfactory effectiveness, improve quality of life of the patients, and effectively reduce the pain, which provides scientific basis for clinical treatment of early-stage gastric cancer and precancerous lesions, and is worthy of clinical promotion and application.

Disclosure of conflict of interest

None.

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