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Original Article

The short-term effect of endoscopic submucosal dissection on gastric stromal tumors and its effect on immune function

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Abstract: Objective: To investigate the short-term effect of endoscopic submucosal dissection (ESD) on gastric stromal tumors (GST) and its effect on immune function. Methods: A retrospective study was conducted on 120 patients with GST. The patients were divided into an observation group (n=60) and a control group (n=60) according to the treatment method each received. The patients in the control group were treated by laparotomy, and the patients in the observation group were treated by ESD. Clinically relevant indicators, such as the immune function, the gastrointestinal hormones, the quality of life, and the postoperative complications, were compared between the two groups. The complete tumor resection rates and the postoperative recurrence rates of the two groups were calculated. Results: Compared with the control group, the observation group had less surgical blood loss, shorter operation times, shorter postoperative first anal exhaust times, and shorter hospital stays (all P<0.001). After the operations, the CD4+ level and the CD4+/CD8+ ratio and the serum gastrin, and motilin levels in the two groups were lower, but the CD8+ levels were higher than they were before the operation, and the level of each indicator in the observation group was better than it was in the control group (all P<0.001). After the operations, the concise quality of life scale scores of the two groups were higher compared with before the operations (P<0.001), but there was no significant difference between the two groups after the operations (P>0.05). There was no significant difference in the incidence of postoperative complications between the two groups (P>0.05). Compared with the control group, the observation group had a higher complete tumor resection rate and a lower postoperative recurrence rate (both P<0.05). Conclusion: The application of ESD in the treatment of GST is helpful in the recovery of gastrointestinal function and in the improvement of immune function. Moreover, the tumor resection is thorough, and the postoperative recurrence rate is low.

Keywords: Endoscopic submucosal dissection, gastric stromal tumor, immune function, quality of life, short-term effect

Introduction

Clinically, gastrointestinal stromal tumors are a high-incidence tumor that can occur both as a benign or malignant tumor. According to clinical statistics, the incidence of this disease is increasing worldwide, and there is a higher incidence in men than in women [1]. Meanwhile, gastrointestinal stromal tumors can exist in any part of the body, among which gastric stromal tumors (GSTs) account for the highest proportion, up to 60% [2, 3]. At present, surgery is the main method used to treat GST clinically. Traditional laparotomy can completely remove the focus and its adjacent focus, especially for smaller tumors that are not easy to operate on under an endoscope. However, laparotomy also has the disadvantages of large postoperative wounds and a significant stress response in patients. At the same time, laparotomy can easily induce a variety of complications, and some patients are unsatisfied with the treatment results [4]. At present, the evolving, minimally invasive technology has attracted more and more attention from clinicians, because it provides a new method of surgical treatment for

patients with GST, among which endoscopic submucosal dissection (ESD) is more widely used in clinical practice. ESD is highly practical, effective, and safe in the treatment of GST [5, 6]. However, there are a few clinical reports on the effects of ESD on immune function, gastrointestinal hormones, and the quality of life in GST patients. Thus, this study aimed to investigate the therapeutic effect of ESD on GST patients and its effects on the immune function and on gastrointestinal hormones.

Materials and methods

General information

A retrospective study was conducted on 120 patients with GST who were admitted to Jilin Province People's Hospital from May 2017 to July 2019 and who met the diagnosis and treatment criteria. The patients were divided into the observation group (n=60) and the control group (n=60) according to the treatment method each received. This study was approved by the Ethics Committee of Jilin Province People's Hospital, and all the enrolled patients or their families signed the informed consent.

Inclusion criteria: (1) Patients who met the *Consensus of Chinese experts in the diagnosis and treatment of gastrointestinal stromal tumor (2011 edition)* criteria and whose GST was confirmed by a pathological biopsy [7]; (2) Patients with complete clinical data; (3) Patients with tumor diameters less than 40 mm; (4) Patients without cognitive impairment; (5) Patients whose tumors originated from the muscularis propria with clear tumor boundaries and a uniform texture; (6) Patients without an abnormal coagulation function.

Exclusion criteria: (1) Patients who didn't follow the doctors' advice and who didn't cooperate with the doctors during the treatment; (2) Patients under 20 years old or over 75 years old; (3) Patients with heart and lung function intolerance; (4) Patients suffering from other malignant tumors; (5) Patients with immune system disorders; (6) Patients with other severe, chronic underlying diseases.

Methods

The patients in control group received conventional laparotomies [8]. An incision of about 10 cm was made in the middle of the patient's upper abdomen, and the location and scope of the focus were determined after entering the abdomen layer by layer, and the tumor was removed through a wedge resection of the stomach. The patients in observation group received ESD [9]. Preoperative preparation: the patients consumed no solids and liquids before the operation, and they were anesthetized using an intravenous injection of propofol (Xi'an Libang Pharmaceutical Co., Ltd., China) to induce anesthesia, followed by endotracheal intubation. Intraoperative operation: electrocoagulation markers were performed at a distance of 5 mm from the focus, and 0.9% NaCl solution (Shandong Qidu Pharmaceutical Co., Ltd., China), adrenaline, and indigo carmine mixture (Chengdu Lianhe Chemical Pharmaceutical Co., Ltd., China) were injected into the submucosa at the same time. The mucosal layer of the patient was cut along the previous mark points, and the submucosa was stripped to fully expose the focus. For a few residual lesion tissues, electrocoagulation and electroresection were performed with a snare to achieve the goal of complete resection. The tissues removed during the operations were fixed on a formaldehyde solution plate and promptly sent for the pathological examination. After the operation, the patients were asked to take a supine position. Gastrointestinal decompression was performed, the patients were not permitted to consume solids or liquids for one to two days, the vital signs were closely monitored, and the following measures were taken: acid suppression and anti-inflammatories were administered, their water and electrolyte balances were maintained, and nutritional support was provided. The patients in both groups were followed up for 6 months.

Outcome measures and clinical efficacy evaluation

(1) The clinical indicators of the two groups were compared. (2) 5 mL of fasting venous blood was collected from the patients of both groups before and on the third day after the operations respectively, and the supernatant was taken after the centrifugation, and it was stored at -20°C to be tested later. Cell immune function: the CD4+ and CD8+ levels were determined using a Beckman flow cytometer (Beckman Coulter Co., Ltd., USA), and the CD4+/CD8+ ratio was calculated. Gastrointestinal hormones: the serum gastrin (GAS) and motilin (MTL) levels were determined using an automatic biochemical analyzer (Beckman Coulter

Table 1. Comparison of the clinical data (n, $\bar{x}$ ± sd)

Group	Observation group (n=60)	Control group (n=60)	t/χ^2	P
Gender (n)			0.034	0.854
Male/female	24/36	25/35		
Age (year)	53.4±3.5	53.5±3.4	0.159	0.874
BMI (kg/m^2)	22.18±2.14	22.19±2.13	0.026	0.980
Tumor location (n)			0.308	0.857
Cardia	4	3		
Fundus of the stomach	44	43		
Gastric body	12	14		
NIH classification (n)			0.804	0.669
Very low risk	48	46		
Low risk	9	12		
Middle risk	2	1		
High risk	1	1		

Note: BMI: body mass index.

Co., Ltd., USA). (3) The concise quality of life scale (SF-36) was used to evaluate the patients' quality of life in the two groups before and at 6 months after their operations [10]. The scale has a total of 36 items and 8 dimensions. Through linear transformation, the total score of the 8 dimensions can be standardized within a range of 0-100, and the score is proportional to the quality of life. (4) The incidence of postoperative complications and recurrence at three months after the operations were analyzed in the two groups, and the complete tumor resection rates by CT examination at 72 h of both groups were calculated.

Statistical analysis

SPSS 20.0 software was used for the statistical analysis of the experimental data. The measurement data conforming to a normal distribution were expressed as the mean ± standard deviation ($\bar{x}$ ± sd), and the enumeration data were expressed as case number/percentage (n/%). Paired t tests were used for the comparisons before and after the operations within the same group, and independent sample t tests were used for the comparison between two groups. There was a significant difference at P<0.05.

Results

Comparison of the clinical data

The statistical analysis found no significant differences between the two groups in terms of gender, age, body mass index, tumor location, or NIH classification (P>0.05). See **Table 1**.

Comparison of the clinical indicators

Compared with the control group, the observation group had less surgical blood loss, shorter operation times, shorter postoperative first anal exhaust times, and shorter hospital stays (all P<0.001). See **Table 2**.

Comparison of the immune function before and after operation

Before the operations, there was no significant difference in the immune function levels in the two groups (all P>0.05). After the operations, the CD4+ level and the CD4+/CD8+ ratios in both groups were significantly lower than they were before the operations (all P<0.001), but the levels in the observation group were significantly higher than the levels in the control group (all P<0.001), and after the operations, the CD8+ levels in both groups were significantly higher than they were before the operations (P<0.001), but observation group was significantly lower than control group (P<0.001). See **Table 3**.

Comparison of the gastrointestinal hormones before and after the operations

Before the operations, there was no significant difference in the gastrointestinal hormone levels in the two groups (all P>0.05). After the operations, the GAS and MTL levels in both groups were significantly lower than they were before the operations (both P<0.001). Compared with the control group, the level of each indicator in the observation group was higher (all P<0.001). See **Table 4**.

Comparison of the quality of life before and after the operations

Compared with before the operations, the SF-36 scores were higher in the two groups after the operations (P<0.001). However, there was no significant difference in the SF-36

Table 2. Comparison of the clinical indicators ($\bar{x}$ ± sd)

Group	Surgical blood loss (mL)	Operation time (min)	Postoperative first anal exhaust time (d)	Hospital stay (d)
Observation group (n=60)	50.33±8.68	99.55±15.37	2.91±0.50	9.91±1.21
Control group (n=60)	106.71±22.67	120.05±14.41	3.70±0.60	12.70±1.82
t	17.990	7.537	7.835	9.888
P	<0.001	<0.001	<0.001	<0.001

Table 3. Comparison of the immune function before and after the operations ($\bar{x}$ ± sd)

Group	CD4+ (%)		CD8+ (%)		CD4+/CD8+	
	Before the operations	After the operations	Before the operations	After the operations	Before the operations	After the operations
Observation group (n=60)	41.75±4.47	33.09±3.68	24.21±2.55	30.02±2.77	1.72±0.18	1.10±0.11
Control group (n=60)	41.80±4.39	28.45±3.54	24.23±2.60	34.17±2.79	1.73±0.20	0.83±0.13
t	0.062	7.039	0.043	8.176	0.288	12.281
P	0.951	<0.001	0.966	<0.001	0.774	<0.001
t and P within the observation group	t=11.586; P=0.000		t=11.953; P=0.000		t=22.766; P=0.000	
t and P within the control group	t=18.337; P=0.000		t=20.189; P=0.000		t=29.226; P=0.000	

Table 4. Comparison of the gastrointestinal hormones before and after operations (pg/mL, $\bar{x}$ ± sd)

Group	GAS		MTL	
	Before the operations	After the operations	Before the operations	After the operations
Observation group (n=60)	320.29±24.26	251.11±30.24	152.48±21.75	91.03±12.32
Control group (n=60)	321.02±23.27	223.79±26.30	152.47±21.68	79.41±10.59
t	0.168	5.280	0.003	5.540
P	0.867	<0.001	0.998	<0.001
t and P within observation group	t=13.822; P=0.000		t=19.042; P=0.000	
t and P within control group	t=21.447; P=0.000		t=23.455; P=0.000	

Note: GAS: gastrin; MTL: motilin.

scores between the two groups before and after the operations (P>0.05). See **Table 5** and **Figure 1**.

Comparison of the postoperative complications

There was no significant difference in the incidences of postoperative complications between the two groups (P>0.05). See **Table 6**.

Comparison of the complete tumor resection rate and the postoperative recurrence rate

Compared with the control group, the observation group had a higher complete tumor resection rate and a lower postoperative recurrence rate (P<0.05). See **Table 7**.

Discussion

Gastric stromal tumors (GST) usually originate from the muscularis propria of the body, are a kind of tumor with potentially malignant lesions. According to clinical statistics, the incidence of malignant lesions in GST is about 3.6% [11]. At present, the clinically recommended method for the treatment of non-metastatic GST is surgery, and traditional laparotomy is applicable to any tumor in principle. However, the long incision, the heavy bleeding, and the relatively high-risk of laparotomy make its application in clinical practice subject to certain limitations. At present, with the rapid development of endoscopic technology and the rare occurrence of lymph node metastasis in GST, lymph node dissection is not required during the operation. Therefore, endoscopic local resection can be performed only when the negative resection edge and the tumor body are not ruptured. The safety, effectiveness, and economy of ESD in the treatment of GST have also been confirmed [12, 13]. For GSTs ≤5 cm, ESD can effectively avoid wound healing problems in laparotomy and has a good prognosis [14]. The principle of

Table 5. Comparison of the quality of life before and after the operations (score, $\bar{x} \pm sd$)

Group	SF-36 score	
	Before operation	After operation
Observation group (n=60)	77.98±8.33	87.04±10.64
Control group (n=60)	77.04±8.37	86.98±10.76
t	0.617	0.031
P	0.537	0.976
t and P within the observation group	t=5.193; P=0.000	
t and P within the control group	t=5.648; P=0.000	

Note: SF-36: concise quality of life scale.

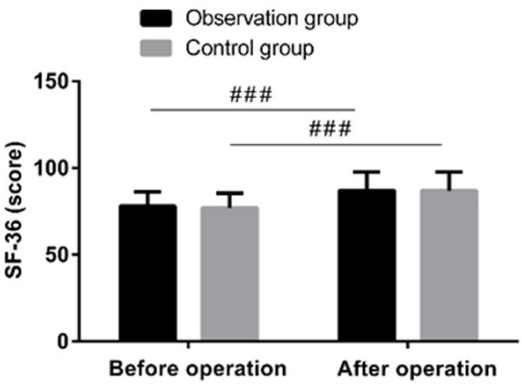

Figure 1. Comparison of the quality of life before and after the operations. Compared with the same group before the operations, ###P<0.001. SF-36: concise quality of life scale.

ESD for the treatment of GSTs in the clinic is: (1) the diameter of the tumor is relatively small; (2) the boundary of the tumor is clear and the capsule is complete; (3) there is no metastasis or infiltration of the focus [15].

ESD can quickly detect the focus enabling surgeons to perform a rapid dissection to remove tumors, with less damage to the body and no recurrence after a 1-year follow-up [16]. In this study, different treatment methods were applied to the enrolled patients, and the results showed that compared with the control group, observation group had less surgical blood loss, shorter operation times, shorter postoperative first anal exhaust times, and shorter hospital stays. This indicates that ESD will not cause significant damage to the body, for it can be administered through the lacunar channel of the body without involving the surrounding tissues, thus enabling the surgeon to accurately complete the intraoperative operation. However, any operation is a stress operation, and it will induce different degrees of stress response in the body. This kind of operation is manifested as the body's self-protection, but the overreaction can still cause immune suppression and affect the postoperative efficacy and recovery effect [17]. The cellular immune function of the body is usually expressed by the proportion of T-lymphocytes, in which the changes in the levels of the CD4+ and CD8+ T-lymphocytes can directly reflect the cellular immune state of the body, and a decrease in the ratio of the two indicates that the cellular immune function of the body is inhibited [18]. The results of this study showed that, after the operations, both CD4+ level and CD4+/CD8+ ratio in the observation group were higher than those in the control group, but the CD8+ level was lower than it was in the control group. This shows that, compared with the traditional laparotomy, ESD will not cause deeper damage or destruction to the body's immune system, which is helpful for the postoperative recovery of patients. It may be that under the direct vision of an endoscope, ESD can accurately achieve the localization and resection of the focus, minimize the influence of the operation on the viscera, and inhibit further stress response, so that the immune function can be effectively restored. The gastrointestinal function will be damaged to different degrees when the surgeon performs operations such as gastrointestinal tract pulling, cutting and squeezing. MTL and GAS are sensitive biochemical indicators for the evaluation of gastrointestinal function, among which GAS is beneficial to the relaxation of the gastric fundus and the contraction of the gastric antrum, and thus significant for the improvement of esophageal sphincter pressure [19]. The results of this study showed that after the operations, the GAS and MTL levels in the two groups were lower than they were before the operation, but the level of each indicator in the observation group was better than it was in the control group. Meanwhile, after the operations, the SF-36 scores in the two groups were significantly improved compared with the scores

Table 6. Comparison of the postoperative complications (n (%))

Group	Perforation (n)	Infection of incisional wound (n)	Postoperative bleeding (n)	Others (n)	Total incidence (n (%))
Observation group (n=60)	3	1	2	2	8 (13.33)
Control group (n=60)	0	5	4	4	13 (21.67)
χ^2	-	-	-	-	1.443
P	-	-	-	-	0.230

Table 7. Comparison of the complete tumor resection rate and the postoperative recurrence rate (n, %)

Group	Complete tumor resection rate	Postoperative recurrence rate
Observation group (n=60)	58 (96.67)	4 (6.67)
Control group (n=60)	51 (85.00)	13 (21.67)
χ^2	4.904	5.551
P	0.027	0.018

before the operations. The results show that the implementation of ESD is of great significance to the recovery of gastrointestinal function and to the improvement of the quality of life after an operation. It is speculated that endoscopic detection can effectively avoid the interference of various factors on GST, and can directly obtain the location, size, and echo characteristics of the tumor, so as to accurately operate and avoid any damage to the gastrointestinal function [20]. Hemorrhage, perforation and infection are common postoperative complications of ESD [21]. The results of this study showed that there was no significant difference in the incidence of postoperative complications between the two groups, but compared with the control group, the observation group had a higher complete tumor resection rate and a lower postoperative recurrence rate. This suggests that ESD can directly carry out tumor dissection through the basal layer of the gastrointestinal mucosa of the body, and the intraoperative resection of the lesion tissues occurring in the submucosa can be performed using an electric coil, which maximally improves the integrity of tumor resection.

However, the cohort in this study was small, and the exact effect of ESD on gastrointestinal function has not been studied in depth, so it still needs to be studied with a larger cohort and in a multi-center setting in the future.

In summary, for patients with GST, the application of ESD is conducive to the improvement of gastrointestinal function, and it plays an important role in the recovery of immune function.

Disclosure of conflict of interest

None.

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