

Analysis of the Efficacy and Safety of Different Endoscopic Surgery in Treatment of Upper Gastrointestinal Submucosal Tumors

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Abstract: To investigate the efficacy and safety of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) in treatment of upper gastrointestinal submucosal tumors (SMT), and the high risk factors of intraoperative perforation, 201 patients with upper gastrointestinal submucosal tumors treated in Department of Gastroenterology of the first Affiliated Hospital of Chongqing Medical University from June 2018 to June 2023 were selected and divided into EMR group and ESD group according to the mode of operation. The success rate, hospitalization cost, hospitalization time, postoperative fasting time, intraoperative and postoperative complications and postoperative follow-up were compared. According to the occurrence of intraoperative perforation, patients were divided into two groups: non-perforation group and non-perforation group. The clinical data of age, sex, smoking history, drinking history, diabetes, hypertension, tumor size, tumor location and origin were collected. Multivariate Logistic regression model was used to analyze the high risk factors of intraoperative perforation. There was no significant difference in complete resection rate, postoperative residual and recurrence rate, intraoperative bleeding rate and postoperative complication rate between EMR group and ESD group, but the fasting time and average hospital stay in ESD group were longer than those in EMR group, and the intraoperative perforation rate in EMR group was significantly lower than that in ESD group. The age in the perforation group was significantly older than that in non-perforation group, and the proportion of diabetes located in the fundus of the stomach, originating from the lamina propria and ESD treatment in the perforation group, was significantly higher than that in non-perforation group. The results of binary Logistic regression analysis showed that diabetes history, endoscopic treatment (ESD) and lesion origin (lamina propria) were independent risk factors for intraoperative perforation. Therefore, it is effective to treat SMT, EMR and ESD of upper digestive tract, but EMR has fewer complications, shorter hospitalization time and lower hospitalization cost than ESD. The history of diabetes, endoscopic treatment (ESD) and the origin of the lesion (lamina propria) are important factors affecting intraoperative perforation.

Keywords: SMT; EMR; ESD; perforation

1. Introduction

Upper gastrointestinal submucosal tumor (submucosal tumor, SMT) is a space-occupying lesion originating from tissues below the mucosal layer of human upper digestive tract (mucosal muscle layer, submucosa, proper muscle layer). Most of these lesions are lack of specific manifestations and are occasionally found in endoscopic physical examination, but with the progress of the disease and the increase of lesions, some lesions may lead to symptoms such as bleeding or obstruction^[1]. The pathological types of SMT are complex, mostly benign lesions, such as leiomyoma, stromal tumor, lipoma, ectopic pancreas, etc., but about 10-15% of the lesions may be malignant, so early diagnosis and timely treatment of SMT are of great significance^[2]. The latest consensus of experts in endoscopic diagnosis and treatment of digestive tract SMT in China^[3] suggests that patients with tumors suspected by preoperative examination or confirmed by pathology have malignant potential, or are suspected by preoperative examination or pathologically proved to be benign, but patients can not be followed up regularly or the tumor increases in a short time during the follow-up period and patients with strong desire for endoscopic treatment can be treated by endoscopy. At present, endoscopic mucosal resection (endoscopic mucosal resection, EMR) and endoscopic submucosal dissection (endoscopic submucosal dissection, ESD) are widely used in clinic, but there is no clear conclusion as to which method can

benefit patients more. The purpose of this study is to analyze the efficacy and safety of EMR and ESD in treatment of upper gastrointestinal SMT.

2. Objects and Methods

2.1 Objects

A total of 201 patients with upper digestive tract SMT treated in Department of Gastroenterology of the first Affiliated Hospital of Chongqing Medical University from June 2018 to June 2023 were divided into EMR group (n = 78) and ESD group (n = 123) according to different endoscopic resection methods, and were divided into non-perforation group (n = 141) and perforation group (n = 60) according to the occurrence of intraoperative perforation. Inclusion criteria are as follows: (1) SMT of upper digestive tract was diagnosed by endoscopic ultrasonography before operation, and the lesion grew into the lumen, single focus and no other site metastasis; (2) patients who took anticoagulants for a long time should stop taking anticoagulants for 7 days; (3) patients without other sites of malignant tumor; (4) patients who were voluntarily treated with EMR or ESD in our hospital signed informed consent form. Exclusion criteria are as follows: (1) patients with severe cardiac, pulmonary and brain dysfunction, who could not tolerate EBL, EMR or ESD or intravenous anesthesia; (2) patients with severe coagulation dysfunction; (3) submucosal tumors in other sites; (4) patients with incomplete clinical data.

This study has been approved by the Ethics Committee of the first affiliated Hospital of Chongqing Medical University (review batch number: K2024-063-01), and all patients have signed informed consent forms.

2.2 Methods

Before operation, blood routine, liver and kidney function, electrolyte, coagulation, pre-transfusion examination, electrocardiogram, chest X-ray and other examinations should be improved to make sure that there is no contraindication of endoscopic treatment. During operation, the left semi-recumbent position was taken and general intravenous anesthesia was used.

The EMR group was treated with EMR in the following procedures: (1) location around the lesion by electrocoagulation, (2) injection of normal saline along the marked point, (3) ligation of the focus with a trap, and (4) electrocoagulation to remove the focus.

ESD group was treated with ESD: (1) location around the lesion by electrocoagulation, (2) injection of methylene blue + epinephrine + glycerol-fructose mixture around the lesion to fully protrude the mucosa of the lesion, (3) incision of the mucosa around the lesion with Dual knife or IT knife, and (4) complete dissection of the focus with a special electric knife. Fasting for 1-3 days after operation, parenteral nutrition support, acid inhibition and stomach protection were given. At the same time, vital signs and complications such as fever, gastrointestinal bleeding, perforation and subcutaneous emphysema were observed, and corresponding measures were taken according to the situation.

2.3 Observation index

2.3.1 General clinical features

The clinical characteristics of the patients were age, sex, body mass index, personal history (smoking and drinking), past history (coronary heart disease, hypertension and diabetes), tumor size, tumor location, tumor origin and tumor surface mucosa.

2.3.2 Operation indicators

Operation indicators include: complete resection rate, postoperative focus residue and recurrence rate, intraoperative complications (bleeding, perforation), postoperative complications (bleeding, perforation, infection), postoperative fasting time, hospital stay, hospitalization expenses, postoperative follow-up and so on.

2.4 Statistical method

SPSS26.0 statistical software was used for statistical analysis. The continuous measurement data in

accordance with normal distribution were described by mean \pm standard deviation, the differences between groups were described by t-test, the data that did not accord with normal distribution were described by M (P25 ~ P75), the differences between groups were analyzed by nonparametric rank sum test, the counting data were expressed by cases and percentage (%), and the differences between groups were described by 2-test or Fisher exact probability method. The influencing factors of intraoperative perforation were analyzed by contingency table 2 test, and then multivariate Logistic regression analysis was used to analyze the influencing factors of intraoperative perforation.

3. Results

3.1 Comparison of general clinical features between EMR group and ESD group

The average age of EMR group was 54.55 ± 10.31 years, the range was 24.74 years old, the diameter of tumor was 0.92 ± 0.39 cm; ESD group, the age was 55.19 ± 11.88 years, the range was 24 ~ 91 years old, the diameter of tumor was 1.58 ± 0.97 cm. There was no significant difference in age, sex and tumor origin between the two groups (all $P > 0.05$), but there was significant difference in tumor size between the two groups ($P < 0.05$). See Table 1.

Table 1: Comparison of general clinical features between EMR group and ESD group

Project	EMR group (n=78)	ESD group(n=123)	z/ χ^2	P
Age	54(49,60)	54(48,64)	-0.090	0.929
Gender, male / female	29/49	52/71	0.515	0.473
Tumor origin level,n (%)			0.173	0.917
Muscularis mucosae	23(29.5%)	35(28.5%)		
Submucosa	11(14.1%)	20(16.3%)		
Lamina propria	44(56.4%)	68(55.3%)		
Tumor size,cm	0.86(0.66,1.00)	1.40(0.92,2.00)	-6.039	<0.001
Tumor size,n(%)			14.895	<0.001
<1cm	42(53.8%)	33(26.8%)		
≥ 1 cm	36(46.2%)	90(73.2%)		

3.2 Comparison of operative indexes between EMR group and ESD group

Compared with EMR group, ESD group had higher intraoperative perforation rate, longer postoperative fasting time and average hospitalization time, and higher hospitalization cost, but there was no significant difference in complete resection rate, intraoperative bleeding rate and postoperative complications (bleeding, perforation, infection) between the two groups. See Table 2.

Table 2: Comparison of operative indexes between EMR group and ESD group

Project	EMR group (n=78)	ESD group(n=123)	z/ χ^2	P
Complete resection,n(%)	78(100.0%)	120(97.6%)	0.629	0.428
Intraoperative complications,n(%)				
Perforation	15(19.2%)	45(36.6%)	6.865	0.009
bleeding	2(2.6%)	3(2.4%)	0.000	>0.999
Postoperative complications,n(%)			5.525	0.064
Perforation	0(0.0%)	2(1.6%)		
Bleeding	1(1.3%)	0(0.0%)		
Infection	2(2.6%)	11(8.9%)		
Postoperative fasting time, days	1.5(1,3)	2.0(1,3)	-2.960	0.003
Length of stay in hospital, days	6(5,7)	9(7,13)	-6.076	<0.001
Hospitalization expenses, yuan	9105.36(6691.31,12049.05)	20964.73(15382.76,27311.87)	-10.190	<0.001

3.3 Comparison of clinical data between perforation group and non-perforation group

The age in the perforation group was significantly older than that in the non-perforation group, and the proportion of diabetes, located in the fundus of the stomach, originating from the lamina propria and ESD treatment in the perforation group was significantly higher than that in the non-perforation group. There was no significant difference in other indexes between the two groups ($P > 0.05$). See Table 3. The results of binary Logistic regression analysis showed that diabetes history, endoscopic treatment (ESD) and lesion origin (lamina propria) were independent risk factors for intraoperative perforation. See Table 4.

Table 3: Univariate analysis of intraoperative perforation

Project	Perforation group (n = 60)	non-perforation group (n = 141)	z/ χ^2	P
Age,n(%)			5.205	0.023
<60 years old	34(56.7%)	103(73.0%)		
\geq 60 years old	26(43.3%)	38(27.0%)		
Sex,male/female	25/35	56/85	0.067	0.796
Smoking history,n(%)	12(20.0%)	32(22.7%)	0.179	0.672
drinking history,n(%)	12(20.0%)	21(14.9%)	0.800	0.371
Hypertension,n(%)	14(23.3%)	28(19.9%)	0.308	0.579
Diabetes,n(%)	13(21.7%)	7(5.0%)	13.104	<0.001
Coronary heart disease,n(%)	3(5.0%)	3(2.1%)	0.412	0.521
tumor site n(%)			6.040	0.014
non-gastric fundus	28(46.7%)	92(65.2%)		
gastric fundus	32(52.3%)	49(34.8%)		
Tumor size,n(%)			0.196	0.658
<1cm	21(35.0%)	54(38.3%)		
\geq 1cm	39(65.0%)	87(61.7%)		
Tumor origin layer,n(%)			12.884	<0.001
Non-lamina propria	15(25.0%)	74(52.5%)		
Lamina propria	45(75.0%)	67(47.5%)		
Surface mucosal conditio,n(%)			1.461	0.227
Smooth	59(98.3%)	131(92.9%)		
Hyperemia and erosion	1(1.7%)	10(7.1%)		
Endoscopic treatment,n(%)			6.865	0.009
EMR	15(25.0%)	63(44.7%)		
ESD	45(75.0%)	78(55.3%)		

Table 4: Multivariate binary Logistic regression analysis of intraoperative perforation

Influencing factors	B	SE	Wald	OR	95%CI	P
Age (\geq 60 years old)	0.497	0.364	1.861	1.644	0.805-3.357	0.173
Location of the tumor (fundus of stomach)	0.508	0.345	2.169	1.663	0.845-3.270	0.141
Layer of origin (lamina propria)	1.175	0.369	10.142	3.239	1.571-6.676	0.001
Endoscopic treatment (ESD)	0.990	0.375	6.980	2.692	1.291-5.612	0.008
Diabetes	1.496	0.545	7.534	4.466	1.534-13.002	0.006
Constant	-2.807	0.467	36.063	0.060		<0.001

4. Discussion

SMT in the upper digestive tract is a common gastrointestinal disease. Most endoscopic

examinations show that the incidence of SMT is not low. Some studies have found that SMT is found in 1 case out of every 300 endoscopic examinations^[4]. The histopathological types of upper digestive tract SMT are complex, including leiomyoma, stromal tumor, lipoma and ectopic pancreas, most of which are benign lesions, but about 15% of SMT may be malignant^[5]. The larger the lesion volume, the higher the degree of malignancy, the worse the prognosis. Therefore, the early diagnosis and timely treatment of SMT are of great significance. Surgical resection is a classic treatment for SMT of the upper digestive tract, but invasive surgery is often accompanied by many complications, such as postoperative bleeding, gastroesophageal reflux, late anastomotic stricture, etc, especially for tumors with small diameter, the surgical trauma is great, the normal structure of stomach is destroyed, and the quality of life is affected after operation^[6]. With the continuous development and maturity of endoscopic minimally invasive technology, endoscopic resection of SMT has gradually become a choice for more doctors and patients^[7-8]. At present, EMR and ESD are widely used in the treatment of upper digestive tract SMT. EMR separates the lesions of the mucosa and submucosa from the proper muscle layer by injecting drugs into the submucosa of the lesion, and then uses a trap or high-frequency electric knife to remove the focus. For EMR resection of SMT, a number of studies^[9-10] have confirmed that it is safe and effective in superficial SMT (originating from submucosa and muscularis mucosa), but the efficacy and safety of SMT, EMR in lamina propria are not sure. Endoscopic submucosal dissection (ESD) is developed on the basis of EMR. According to the size, location and depth of invasion of the lesion, this technique uses a special electric knife to gradually peel off the lesion under endoscope, and the peeling depth can reach the lamina propria. However, ESD surgery takes a long time and requires a high level of endoscopic surgery, which is always accompanied by high perforation and postoperative bleeding rate^[11-12].

The results of this study showed that compared with the EMR group, the postoperative fasting time and average hospitalization time of the SMT patients with different tumor size were longer and the hospitalization cost was higher in the ESD group. Analysis of the possible reasons: compared with EMR, ESD is easier to achieve complete resection of larger or deeper lesions, but it takes longer operation time and requires higher operation level and equipment of endoscopic surgeons, which leads to postoperative recovery, prolonged hospitalization time and increased hospitalization costs. However, there was no significant difference in complete resection rate, intraoperative bleeding rate and postoperative complications (bleeding, perforation, infection) between EMR group and ESD group. During the follow-up for 1 year, no residual or recurrent lesions were found in all patients who underwent endoscopic resection. Therefore, both SMT, EMR and ESD can be removed safely and effectively, but EMR has more benefits in reducing hospital stay, hospitalization cost and intraoperative perforation rate.

Intraoperative perforation is the main complication of endoscopic treatment. during the operation, a large amount of gas accumulates in the digestive tract, which can lead to perforation even if there are few lacerations in the muscular layer, thus increasing the risk of abdominal infection^[13]. In this study, the intraoperative perforation rate was high (23.3%). The possible reasons were analyzed: because most of the lesions were treated with ESD, the lesions located in the gastric fundus and originated from the lamina propria accounted for the majority, but the ESD itself was difficult to operate. when resecting the focus of the gastric fundus, because the tissue of the fundus of the stomach was weak, the focus was closely connected with the muscle layer, the operating space at the top of the small curve was small, and the visual field was limited, so it was difficult to remove the focus completely under endoscope. With the deepening of the infiltration level of the lesion, especially for the SMT of the lamina propria, the endoscopic operation becomes more difficult and the risk of perforation will be greatly increased^[14-15]. In this study, the age of the perforated group was significantly older than that of the non-perforated group, and the proportion of diabetes, originating from the lamina propria and ESD treatment in the perforated group was significantly higher than that in the non-perforated group, and the difference was statistically significant. It can be seen that age, diabetes, tumor location and origin, and endoscopic treatment may be associated with the occurrence of perforation. Further binary Logistic regression analysis of the above influencing factors showed that diabetes history, endoscopic treatment (ESD) and lesion origin (lamina propria) were independent risk factors for intraoperative perforation. Therefore, in order to reduce intraoperative perforation, the location and origin of the lesion should be identified by EUS and other examinations before operation. Patients with diabetes should be recommended regular hypoglycemic treatment before operation. At the same time, attention should be paid to the difficulty of ESD endoscopic operation, and the operation ability and proficiency of surgeons should be improved so as to reduce the occurrence of complications.

5. Conclusion

To sum up, both EMR and ESD are safe and effective in the treatment of upper gastrointestinal SMT, but the former has more advantages in shortening hospitalization time and reducing hospitalization costs, while ESD may be more suitable for large SMT that is difficult to be resected by EMR or originated from the lamina propria. For SMT patients with a history of diabetes, originating from the lamina propria, located in the fundus of the stomach and scheduled for ESD treatment, it is necessary to be highly vigilant about the occurrence of intraoperative perforation, comprehensive preoperative evaluation and individual accurate intraoperative treatment in order to reduce the occurrence of perforation. Nevertheless, there are still some limitations in this study. The study was conducted only in a single center with a relatively small sample size, and the control study required longer follow-up. Therefore, it is necessary to design prospective, multicenter, randomized controlled trials with large sample size to further study and formulate diagnostic and treatment criteria for patients with upper digestive tract SMT.

References

- [1] Liu Q, Ruan W, Liu Z, Li J, et al. Efficacy and Safety Analysis of Submucosal Tunnel Endoscopic Resection for Submucosal Masses in Esophageal Muscularis Propria[J]. *Comput Math Methods Med*, 2022, 2022:4457696.
- [2] Zhu Baojie, Chai Ningli, Liu Shengzhen, et al. Clinical study of super minimally invasive surgery under digestive endoscope in the treatment of superficial tumors of upper digestive tract with submucosal tumors [J]. *Chinese Journal of Digestive Endoscope*, 2023, 40 (8): 610-615.
- [3] Zhou Pinghong, Zhong Yunshi, Li Quanlin. Chinese expert consensus on endoscopic diagnosis and treatment of gastrointestinal submucosal tumors (2023 edition) [J]. *Chinese Journal of practical surgery*, 10-615.2023, 43(03):241-251.
- [4] Sharzehi K, Sethi A, Savides T. AGA clinical practice update on management of subepithelial lesions encountered during routine endoscopy: Expert review[J]. *Clin Gastroenterol Hepatol*, 2022, 20(11):2435-2443.
- [5] Sahakian AB, Aslanian HR. Endoscopic submucosal dissection for resection of submucosal tumors of the colon and rectum: Within reach, or the edge of tomorrow[J]? *Gastrointest Endosc*, 2018, 87(2):549-551.
- [6] Ebi M, Sakamoto K, Inoue S, et al. Esophageal leiomyosarcoma diagnosed by endoscopic ultrasound-guided fine-needle aspiration biopsy and cured with surgical resection[J]. *Internal Medicine*, 2019, 58(17):2479-2483.
- [7] Tan Y, Zhou B, Zhang S, et al. Submucosal tunneling endoscopic resection for gastric submucosal tumors: a comparison between cardia and non-cardia location[J]. *J Gastrointest Surg*, 2019, 23(11): 2129-2135.
- [8] Deprez PH, Moons LMG, O'Toole D, et al. Endoscopic management of subepithelial lesions including neuroendocrine neoplasms: European Society of Gastrointestinal Endoscopy (ESGE) Guideline[J]. *Endoscopy*, 2022, 54(4):412-429.
- [9] Zhu H, Shi D, Song H, et al. Snare-assisted endoscopic resection of gastric subepithelial tumors originating from the muscularis propria layer: a multicenter study[J]. *Surg Endosc*, 2020, 34(9): 3827-3832.
- [10] Geng Yanli. Efficacy of microscopic mucosal resection (EMR) in the treatment of flat gastrointestinal mucosal tumors [J]. *Contemporary medicine*, 2020, 26(35):128-129.
- [11] Tanaka S., Kashida H., Saito Y., et al. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection[J]. *Digestive Endoscopy*, 2020, 32(2):219-239.
- [12] Podboy A., Kolahi K. S., Friedland S., Louie C. Y. Endoscopic submucosal dissection is associated with less pathologic uncertainty than endoscopic mucosal resection in diagnosing and staging Barrett's-related neoplasia[J]. *Digestive Endoscopy*, 2020, 32(3):346-354.
- [13] Lin Xiaohua, Wan Xiuping, Liu Yuan, et al. Analysis of the efficacy and risk factors of postoperative complications of two endoscopic surgery methods in the treatment of submucosal tumors at the esophagogastric junction [J]. *Chinese Journal of Endoscope*, 2023, 29(8): 53-59.
- [14] Chai N, Zou J, Linghu E, et al. Autologous Skin-Grafting Surgery to Prevent Esophageal Stenosis After Complete Circular Endoscopic Submucosal Tunnel Dissection for Superficial Esophageal Neoplasms[J]. *The American Journal of Gastroenterology*, 2019, 114(5):822-825.
- [15] Ahmed Y, Othman M. EMR/ESD: Techniques, Complications, and Evidence[J]. *Curr Gastroenterol Rep*, 2020, 22(8):39-51.