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内镜黏膜下剥离术和挖除术治疗上消化道肿瘤的疗效及安全性分析*

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摘要 目的:分析内镜黏膜下剥离术(ESD)和黏膜下挖除术(ESE)治疗上消化道肿瘤的疗效及安全性。方法:回顾性分析 2017 年 1 月至 2019 年 4 月我院消化内科接受 ESD 或 ESE 治疗的 68 例上消化道肿瘤住院患者的临床资料,收集患者基础疾病、手术时间、病变部位大小、整块切除率、并发症等资料,同时采用 Logistic 回归分析对术中穿孔进行危险因素分析。结果:64 例患者完整切除瘤体(94.12%),肿瘤平均直径(16.98 ± 8.29)mm。食管病灶病理类型以高级别上皮内瘤变为主,有 15 例(22.06%);胃部病灶分布以胃体、胃底和胃窦居多,分别有 18 例(26.47%)、16 例(23.53%)和 12 例(17.65%),病理类型以间质瘤最多,占 36.76%;11 例患者发生并发症(16.18%),4 例患者出现术后出血(5.88%),经过内镜下止血后好转,8 例患者术中穿孔(11.76%),均行内镜下尼龙绳联合钛夹行荷包缝合,其中 1 例患者术中穿孔合并术后迟发性出血;病灶最大直径(≥ 25 mm, $P=0.036$)和病灶部位(胃底, $P=0.015$)是导致 ESD 或 ESE 术中穿孔的独立危险因素。结论:ESD 和 ESE 治疗上消化道肿瘤安全有效,但需注意病灶大小和胃底病变,因其是导致术中穿孔的独立危险因素。

关键词: 内镜黏膜下剥离术;内镜黏膜下挖除术;上消化道肿瘤;危险因素

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Efficacy and Safety of Upper Gastrointestinal Tumor Treated by Endoscopic Submucosal Dissection and Endoscopic Submucosal Excavation*

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ABSTRACT Objective: To analyze the efficacy and safety of upper gastrointestinal tumor treated by endoscopic submucosal dissection (ESD) and endoscopic submucosal excavation (ESE). **Methods:** Clinical data of 68 hospitalized patients with upper gastrointestinal tumor who underwent ESD or ESE in our hospital from January 2017 to April 2019 were collected, such as basic diseases, the size, operation time, complete resection rate and complication. According to the Logistic regression equation analysis, the risk factors for the complications of perforation were analyzed. **Results:** The tumors of 64 cases (94.12%) of patients were en-bloc resected, and the average tumor size was (16.98 ± 8.29 mm). Pathological results showed that high grade intraepithelial neoplasia was the most, 15 cases (22.06%) in the lesion of esophagus. The top three were gastric body, gastric fundus and gastric antrum in gastric lesions, there were 18 cases (26.47%), 16 cases (23.53%) and 12 cases (17.65%), respectively. Pathological results showed that stromal tumor was the most (36.76%). Complications occurred in 11 cases (16.18%), included 4 cases (5.88%) of delayed bleeding (all of them were treated successfully by endoscopic hemostasis therapy), and 8 patients (11.76%) with perforation (all of them were successfully treated by coagulation hemostasis and hemoclip), including 1 patient with perforation and delayed bleeding. Lesion diameter (≥ 25 mm, $P=0.036$) and lesion locating at the gastric fundus ($P=0.015$) were the independent risk factors for perforation in ESD or ESE. **Conclusion:** ESD and ESE are safe and effective technique for upper gastrointestinal tumor. However, lesion diameter and lesion locating at the gastric fundus should be paid attention as they are the risk factors for perforation.

Key words: Endoscopic submucosal dissection; Endoscopic submucosal excavation; Upper gastrointestinal tumor; Risk factors

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前言

上消化道肿瘤是一种常见的消化系统肿瘤,通常发生于患者的食管和胃部^[1],临床上最常见的是胃肠道间质瘤和食管平滑肌瘤,虽然食管平滑肌瘤属于良性肿瘤,但是随着肿瘤的增

大,会对临近脏器产生压迫而导致一系列临床症状^[2],严重威胁患者的生命健康。因此及早发现并切除对患者远期预后有着重要的意义。既往对于消化道肿瘤常采用外科手术治疗,但是术后并发症较多、住院时间长,导致患者恢复较慢。随着内镜技术的迅速发展,内镜黏膜下剥离术(ESD)和内镜黏膜下挖除术

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(ESE) 已广泛用于治疗消化道肿瘤性病变。我院作为基层医院,ESD 和 ESE 技术起步较晚,从 2016 年正式实施。本研究回顾性分析 2017 年 1 月至 2019 年 4 月我院消化内科接受 ESD 或 ESE 治疗的上消化道肿瘤住院患者临床特点,并对术中穿孔进行危险因素分析,旨在为基层医院行 ESD 或 ESE 安全性提供参考。

1 资料与方法

1.1 病例资料

2017 年 1 月至 2019 年 4 月阜阳市人民医院消化内科共收治 68 例诊断为上消化道肿瘤并行 ESD 或 ESE 术的住院患者。收集患者的基本情况如性别、年龄;基础疾病如高血压病、2-型糖尿病、脑梗死等;手术情况如手术时间、病灶部位、病灶大小等;并发症如穿孔、出血等;病理类型等。

1.2 纳入与排除标准

本研究纳入人数需同时满足以下条件:(1)内镜检查(超声胃镜和 CT)发现上消化道病变且经术后病理确诊为上消化道肿瘤;(2)接受 ESD 或 ESE 术治疗;(3)患者及家属签署知情同意书;(4)术前排除转移性肿瘤。排除标准:(1)病理资料不全者;(2)麻醉风险评分为高危者;(3)非 ESD 或 ESE 术治疗者;(4)术前已有消化道出血、穿孔者;(5)术后病理示息肉者;(6)存在内镜检查的禁忌症如不能停用华法林等抗凝药物。

1.3 ESD 手术操作流程

(1)标记病灶:通过内镜视野确定肿物的位置,用电凝法标记病灶;(2)黏膜下注射:在病灶周围多点注射美蓝、靛胭脂、生理盐水、甘油果糖、玻璃酸钠(少数使用);(3)黏膜切开:使用 Dual 刀切开病灶周围黏膜;(4)黏膜剥离:使用 Dual 刀、IT 刀对病灶从黏膜下层反复剥离,根据手术实际情况使用套圈器辅助取出病灶,对于术中出血使用止血钳止血,对于术中有穿孔者,可使用尼龙绳联合钛夹行荷包缝合创面。(5)将切除标本送病理学检查。

1.4 ESE 手术操作流程

采用 ESD 术将病灶周围黏膜预切开,从瘤体基底部将黏膜下层与部分固有基层剥离后,整块切除,根据手术实际情况,对创面进行处理。

1.5 ESD 和 ESE 并发症判定标准

ESD 和 ESD 治疗主要的并发症有出血和穿孔^[3,4]。其中出血分为术中出血和术后迟发性出血。由于本回顾性分析发现术中出血均通过内镜下止血后,再未发现活动性出血,因此出血并发症只统计术后迟发性出血。术后迟发性出血[5-8]是指出血时间在术后 48h 以上,并满足以下条件中的两个:(1)症状有呕血、黑便等;(2)血红蛋白较术前下降 20 g/L;(3)胃镜检查提示出血;(4)术后血压下降超过 20 mmHg 或心率增加超过 20 次/min。穿孔定义为术中内镜直视下发现穿孔,术后 CT 检查提示穿孔。

1.6 统计学方法

采用 SPSS 20.0 软件对数据进行统计学分析,计量资料采用 $\bar{x} \pm SD$ (标准差)表示,计数资料使用 χ^2 或 Fisher 精确检验。对于差异有统计学意义的单因素,采用 Logistic 回归分析进行多因素分析, $P < 0.05$ 表示有统计学差异。

2 结果

2.1 基本资料

共收集 68 例患者其中男性 31 例,女性 37 例;年龄 34~81 岁,平均年龄(60.09 $\pm$ 12.97)岁;肿瘤直径 3~40 mm,平均直径(16.98 $\pm$ 8.29) mm;手术平均时间(104.69 $\pm$ 53.50)min。

2.2 病变部位及病理分类

食管病变中以食管中段(距中切牙 23~32cm)最多,有 12 例患者(17.65%),病理类型主要以高级别上皮内瘤变为主,有 15 例(22.06%)。胃部病灶分布以胃窦、胃体、胃底居多,分别有 12 例(17.65%)、18 例(26.47%)和 16 例(23.53%),病理类型以间质瘤最多,25 例(36.76%)。行 ESD 术 48 例,ESE 术 20 例,其中食管黏膜下肿瘤均行 ESD 术。具体病变部位及病理分类和 ESD/ESE 两组患者资料见表 1。

表 1 68 例患者的一般资料

Table 1 General information of the 68 patients

Information	Case(%)	ESD group (n=48)	ESE group (n=20)
Sex			
Man	31(45.59)	21	10
Woman	37(54.41)	27	10
Lesion site Esophagus	17(25.00)	17	0
Upper esophageal (from central incisor 16~23 cm)	2(2.94)	2	0
Middle esophageal (from central incisor 23~32 cm)	12(17.65)	12	0
Middle and inferior esophageal (from central incisor 27~37cm)	1(1.47)	1	0
Inferior esophageal (from central incisor 32~40 cm)	2(2.94)	2	0
Stomach	51(75.00)	31	20
Gastric antrum	12(17.65)	9	3
Gastric body	18(26.47)	11	7
Gastric fundus	16(23.53)	8	8

Pathological type	Cardia	4(5.88)	3	1
	Gastric angle	1(1.47)	0	1
	Esophagus	17(25.00)	17	0
	High grade intraepithelial neoplasia	15(22.06)	15	0
	Esophagus leiomyoma	2(2.94)	2	0
	Stomach	51(75.00)	31	20
	Stromal tumor	25(36.76)	13	12
	Leiomyoma	5(7.35)	1	4
	Ectopic pancreas	7(10.29)	5	2
	High grade intraepithelial neoplasia	4(5.88)	4	0
	Spindle cell tumor	4(5.88)	4	0
	Neuroendocrine tumor	2(2.94)	1	1
	Adenoma	2(2.94)	1	1
	High differentiated adenocarcinoma	1(1.47)	1	0
	Lipoma	1(1.47)	1	0

2.3 手术结果及并发症

64 例 (94.12%) 患者完整切除瘤体,4 例不完全切除病例中,1 例患者瘤体较大,选择择期再行内镜下剥离术;2 例患者因病灶边界不清楚,考虑肿瘤较大,转入普外科行外科治疗,普外科行胃窦部肿块切除术发现肿瘤 4×4 cm,腔内生长的胃窦腺瘤;1 例患者因术中注射美蓝、靛胭脂、生理盐水后抬起不明显,予以 DUAL 刀和 IT 刀周边切开困难,出血量大,进一步剥离困难,转入普外科行外科治疗。

术后有 33 例患者表现出不同程度的上腹部隐痛,其中 29 例患者症状较轻,经过对症治疗后好转,4 例患者出现术后出血(5.88%),表现为黑便、呕血,经过内镜下止血后好转。8 例术中穿孔(11.76%),均行内镜下尼龙绳联合钛夹行荷包缝合,其中 1 例患者术中穿孔合并术后迟发性出血。68 例患者术中和术后发生并发症共 11 例(16.18%),ESD 组和 ESE 组在术后出血和术中穿孔差异上无统计学意义(P 均 >0.05),见表 2。

表 2 ESD 和 ESE 并发症
Table 2 Complications of ESD and ESE

Complications	Case(%)	ESD group(n=48)	ESE group(n=20)	χ^2	P
Bleeding	4(5.88)	4	0	0.585	0.444
Perforation	8(11.76)	4	4	0.898	0.343
Complications	11(16.18)	8	3	0.029	0.864

2.4 术中穿孔危险因素分析

对术中穿孔进行危险因素分析,将 68 例患者分为穿孔组和未穿孔组,从表 3 可知,穿孔组和未穿孔组在病灶最大直径(≥ 25 mm, $P=0.042$)、病灶部位($P=0.028$)、病理类型($P=0.013$)和浸润深度(固有肌层, $P=0.020$)上对比差异有统计学意义。分析发现胃底部位发病和病理类型为间质瘤的穿孔发生率明显

高于其他亚组,将病灶最大直径(≥ 25 mm)、病灶部位(胃底)、病理类型(间质瘤)和浸润深度(固有肌层)4 种危险因素带入 Logistic 回归方程进行多因素分析,结果显示,病灶最大直径(≥ 25 mm, $P=0.036$)和病灶部位(胃底, $P=0.015$)是导致 ESD 或 ESE 手术术中穿孔的独立危险因素,见表 4 所示。

表 3 穿孔的单因素分析
Table 3 Univariate analysis of perforation

Risk factors	Case	Perforation group (n=8)	Non- perforation group(n=60)	χ^2	P
Sex				0.012	0.912
	Man	31	3		
	Woman	37	5		
Age				1.712	0.191
	≥ 65	32	6		
	<65	36	2		

Lesion diameter					4.131	0.042
	≥ 25 mm	18	5	13		
	<25 mm	50	3	47		
Lesion site					10.399	0.028
	Esophagus	17	0	17		
	Gastric antrum	12	1	11		
	Gastric body	18	1	15		
	Gastric fundus	16	6	10		
	Cardia	4	0	4		
	Gastric angle	1	0	1		
Pathological type					7.980	0.013
Esophagus						
	Esophageal tumor	17	0	17		
Stomach						
	Stromal tumor	26	7	19		
	Other tumors	25	1	24		
Invasion depth					5.395	0.020
	Muscularis propria	16	5	11		
	Other propria	52	3	49		
Surgery					0.898	0.343
	ESD	48	4	44		
	ESE	20	4	16		
Tumor shape					0.002	0.962
	Round	64	7	57		
	Irregular	4	1	3		
Ulcer surface					0.118	0.381
	Yes	10	2	8		
	NO	58	6	52		
Basic disease					0.152	1.000
Diabetes						
	Yes	6	1	5		
	NO	62	7	55		
Cerebral infarction					1.154	0.283
	Yes	12	3	9		
	NO	56	5	51		
Coronary heart disease					2.481	0.115
	Yes	15	4	11		
	NO	53	4	49		
Heart failure					0.353	1.000
	Yes	5	1	4		
	NO	63	7	56		
Hypertension					0.001	0.977
	Yes	10	2	8		
	NO	58	8	50		

3 讨论

ESD 和 ESE 是在内镜黏膜切除术(EMR)的基础上发展而来的。与 EMR 相比,ESD 和 ESE 主要优势体现在可以一次性

表 4 穿孔的多因素 Logistic 分析

Table 4 Multivariate Logistic regression analysis of risk factors for perforation

Risk factors	B	S.E.	f	P	95%CI
Lesion diameter (≥ 25 mm)	2.330	1.109	1	0.036	1.170~90.294
Lesion site (Gastric fundus)	3.028	1.241	1	0.015	1.814~235.038
Pathological type (Stromal tumor)	0.742	1.411	1	0.599	0.132~33.367
Invasion depth (Muscularis propria)	2.159	1.213	1	0.075	0.803~93.368

完整切除直径 >20 mm 病灶,能够取得完整的病理组织,并解决了术后复发的问題。如修辉等^[9]报道了 ESD 与 EMR 在治疗早期食管癌及癌前病变的有效性和安全性 Meta 分析,结果显示 ESD 在整块切除率、完全性切除率和局部复发率上明显优于 EMR,建议在内镜治疗该类疾病首选 ESD。ESD 和 ESE 不但能很好的治疗消化道黏膜上皮病变,而且对消化道黏膜下病变也有着良好的表现,尤其是生长在黏膜肌层和下层的消化道肿瘤,或者固有肌层肿瘤^[10]。因此,本文回顾性分析了 ESD 和 ESE 治疗上消化道肿瘤的疗效和安全性。

本研究 ESD 和 ESE 整体切除率为 94.12%,与其他报道相一致^[16]。ESD 和 ESE 主要的并发症有出血和穿孔,不同文献报道的发生率不同,如 ESD 在治疗胃黏膜病变中急性出血的发生率为 2.9%~22.2%^[11-17],ESD 治疗消化道黏膜下肿瘤的穿孔发生率为 13%~42.3%,ESE 则为 0%~20.0%^[18-21],而本研究发生率 11.76%,虽然在报道范围内,但是发生率较出血高。为了探讨术中穿孔发生率高的原因,对术中穿孔进行单因素和多因素分析。本研究未发现食管行 ESD、ESE 术发生穿孔,术中穿孔均集中在胃部 ESD 和 ESE 术中。不同文献报道胃 ESD/ESE 术中穿孔的危险因素不同:Toyokawa 等^[22]对 1123 例行 ESD 术的早期胃肿瘤患者进行穿孔危险因素分析,结果发现位于胃上部肿瘤是导致穿孔的独立危险因素。张周娟等^[23]对 60 例 ESD 治疗胃肠道间质瘤术中穿孔危险因素分析得出穿孔与肿瘤大小、位置和浸润深度有密切关系。Zhang 等^[18]分析了 212 例行 ESE 治疗的胃上皮固有肌层肿瘤患者术中穿孔的影响因素,发现肿瘤位于胃底和胃体术中穿孔率明显高于胃窦($P=0.036$),术后病理胃肠道间质瘤的穿孔率明显高于平滑肌瘤($P=0.01$)。其它危险因素如病灶位于胃上部肿瘤、大面积黏膜下浸润、伴有溃疡瘢痕、手术时间长等相继被报道^[24-28]。而本研究多因素 Logistic 回归方程分析,得出病灶最大直径(≥ 25 mm, $P=0.036$)和病灶部位(胃底, $P=0.015$)是术中穿孔的独立危险因素,与文献报道的有所不同,可能与纳入人群特点、疾病、例数不同有关。本研究发现病灶直径 ≥ 25 mm 者穿孔率越高,与赖则宾等^[29]报道的病变直径在 18~28 mm 以及 >28 mm 者发生穿孔的风险明显高于直径 ≤ 18 mm($P=0.001$)相一致。病灶位于胃底的穿孔率明显高于胃部其他部位,可能原因为胃底薄弱,病灶与肌层组织连接紧密,小弯顶部操作空间小,视野受限,内镜下完整切除病灶难度较大,易发生穿孔^[23,30]。

综上所述,ESD 和 ESE 在治疗上消化道肿瘤安全有效,穿孔和出血是 ESD 和 ESE 主要并发症,对于病灶直径 ≥ 25 mm 或病灶部位位于胃底的患者,需要术前综合评估,术中个体化精准治疗,以减少穿孔的发生。

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