

doi: 10.13241/j.cnki.pmb.2022.11.031

内镜黏膜下剥离术与腹腔镜手术治疗直径 ≤ 5 cm 胃间质瘤的疗效比较 及对术后应激反应和胃肠激素的影响*

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摘要 目的:对比内镜黏膜下剥离术(ESD)与腹腔镜手术(LAP)治疗直径 ≤ 5 cm 胃间质瘤(GIST)的疗效及对术后应激反应和胃肠激素的影响。**方法:**回顾性分析 2015 年 1 月至 2018 年 3 月期间临汾市人民医院收治的 170 例直径 ≤ 5 cm GIST 患者的临床资料。本研究按照手术方式的不同,将行 LAP 的患者 83 例纳入 A 组,将行 ESD 的患者 87 例纳入 B 组。对比两组疗效、围术期指标、术后应激反应和胃肠激素水平、并发症发生率。**结果:**与 A 组相比,B 组住院总费用、术中出血量更少,术后首次进食流质时间、术后住院时间、术后排气时间、手术时间更短($P<0.05$)。两组肿瘤完整切除率对比未见明显差异($P>0.05$)。两组术后 3 d 血清肾上腺素(E)、去甲肾上腺素(NE)水平均升高,但 B 组低于 A 组($P<0.05$)。两组术后 3 d 血清胃泌素(GAS)、胃动素(MTL)水平均下降,但 B 组高于 A 组($P<0.05$)。两组并发症发生率对比,组间无统计学差异($P>0.05$)。**结论:**ESD、LAP 治疗直径 ≤ 5 cm GIST,疗效相当,其中 ESD 相对而言手术创伤更小、术后恢复更快,可能与减轻应激反应及减轻对胃肠激素的影响有关。

关键词:内镜黏膜下剥离术;腹腔镜手术;胃间质瘤;疗效;应激反应;胃肠激素

中图分类号:R656.61 **文献标识码:**A **文章编号:**1673-6273(2022)11-2157-04

Comparison the Efficacy of Endoscopic Submucosal Dissection and Laparoscopic Surgery in the Treatment of Gastric Stromal Tumors with Diameter ≤ 5 cm and its Effects on Postoperative Stress Response and Gastrointestinal Hormones*

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ABSTRACT Objective: To compare the efficacy of endoscopic submucosal dissection (ESD) and laparoscopic surgery (LAP) in the treatment of gastric stromal tumors (GIST) with diameter ≤ 5 cm and the effects on postoperative stress response and gastrointestinal hormones. **Methods:** The clinical data of 170 patients with GIST with diameter ≤ 5 cm who were treated in Linfen People's Hospital from January 2015 to March 2018 were analyzed retrospectively. According to different surgical methods, 83 patients undergoing LAP were included in group A, and 87 patients undergoing ESD were included in group B. The efficacy, perioperative indexes, postoperative stress response, gastrointestinal hormones levels and the incidence rate of complications were compared between the two groups. **Results:** Compared with group A, group B had less total hospitalization cost, less intraoperative bleeding, shorter first postoperative fluid intake time, postoperative hospitalization time, postoperative exhaust time and operation time($P<0.05$). There was no significant difference in the complete tumor resection rate between the two groups ($P>0.05$). The levels of serum epinephrine (E) and norepinephrine (NE) at 3d after operation in two groups increased, but group B was lower than group A ($P<0.05$). The levels of serum gastrin (GAS) and motilin (MTL) at 3 d after operation in two groups decreased, but group B was higher than group A ($P<0.05$). There was no significant difference in the incidence rate of complications between the two groups ($P>0.05$). **Conclusion:** ESD and LAP are equally effective in treating GIST with diameter ≤ 5 cm. ESD has relatively less surgical trauma and faster postoperative recovery, which may be related to reducing stress response and reducing the impact on gastrointestinal hormones.

* 基金项目:山西省教育厅高校科技创新计划项目(2020L0224);国家自然科学基金项目(82170658)

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(收稿日期:2022-01-07 接受日期:2022-01-28)

Key words: Endoscopic submucosal dissection; Laparoscopic surgery; Gastric stromal tumor; Efficacy; Stress response; Gastrointestinal hormones

Chinese Library Classification(CLC): R656.61 **Document code:** A

Article ID: 1673-6273(2022)11-2157-04

前言

胃间质瘤(GIST)是来源于胃肠间叶组织的一种肿瘤,由于GIST存在非定向分化和潜在恶性生物学行为,故应及时给予手术治疗^[1,2]。内镜黏膜下剥离术(ESD)^[3]、腹腔镜手术(LAP)^[4]均是治疗直径 ≤ 5 cm GIST的常用微创手术,其可行性和安全性均已得到广泛报道。但两种手术方式都有其局限性,其中LAP在气腹建立后胃前壁的视野相对较好,但如果是位于胃后壁的肿瘤则相对视野不佳,一定程度上受限于肿瘤部位^[5]。而ESD虽然可弥补上述缺陷,但也存在内镜下手术是否能最大化切除瘤体的争议^[6]。因此,本研究通过对比ESD、LAP治疗直径 ≤ 5 cm GIST患者的疗效及对术后应激反应和胃肠激素的影响,以期为此类患者临床术式选择提供一定依据。

1 资料与方法

1.1 一般资料

回顾性分析2015年1月至2018年3月期间临汾市人民医院收治的170例直径 ≤ 5 cm GIST患者的临床资料。纳入标准:(1)GIST的发病部位在胃部;(2)行腹部电子计算机断层扫描(CT)或磁共振成像(MRI)检查显示无淋巴结转移、无周围器官转移;(3)TNM分期I~II期,术前完善超声、胃镜检查,患者肿瘤直径 ≤ 5 cm;(4)临床资料完整者。排除标准:(1)其他系统严重疾病或其他恶性肿瘤共存的患者;(2)常规内镜、手术治疗禁忌证者;(3)中途转为开腹手术者。本研究按照手术方式的不同,将行LAP的患者83例纳为A组,将行ESD的患者87例纳为B组。其中A组男45例,女38例,年龄32~69岁,平均 (49.72 ± 5.41) 岁;TNM分期:I期38例;II期45例;肿瘤部位:胃底部38例,胃体部29例,胃窦部11例,贲门部5例;肿瘤直径2~5 cm,平均 (3.29 ± 0.57) cm。B组男49例,女38例,年龄30~70岁,平均 (49.16 ± 4.68) 岁;TNM分期:I期35例;II期52例;肿瘤部位:胃底部37例,胃体部28例,胃窦部13例,贲门部9例;肿瘤直径2~5 cm,平均 (3.34 ± 0.66) cm。两组患者一般资料对比,差异无统计学意义($P>0.05$)。

1.2 方法

术前准备:两组患者均完善血型、血尿粪常规、血凝、生化、心电图、肿瘤标志物、胸片、肺功能检查等。胃镜及上腹部CT评估患者病变大小、病变深度,确定肿瘤位置。向家属交代手术的相关风险,告知手术的具体过程,家属均签署手术同意书。A组:行LAP,全身麻醉,取脐上部位作一切口,置入10 mm Trocar。建立气腹,使用超声刀游离组织,根据肿瘤位置作以下处理:肿瘤位于胃底时,先切断胃脾韧带、肝十二指肠韧带和胃结肠韧带,翻转后行胃楔形切除术;肿瘤位于胃后壁处时,切断胃结肠韧带及胃脾韧带,随后行手术切除;肿瘤位于胃后壁小弯侧时,需先切断肝胃韧带,向后、向下翻转后行手术切除;肿瘤位于胃窦前壁和胃体时,直接手术切除;肿瘤位于近胃前壁小弯侧时,

切断肝胃韧带后行切除术。B组:行ESD,术前肌注注射用丁溴东莨菪碱(成都天台山制药有限公司,国药准字H20080375,规格:20 mg)20 mg抑制胃蠕动,口服二甲基硅油(四川麦克福瑞制药有限公司,国药准字H51021603,规格:25 mg)祛除胃内泡沫以建立清晰的手术视野。采用Daul刀在隆起边缘进行电凝标记,于标记点外侧多点黏膜下注射。使用Daul刀沿病灶边缘切开黏膜下层,暴露瘤体,对肿瘤进行完整剥离,剥离过程中创面出血时采用热活检钳止血、切开刀前端电凝或者肾上腺素盐水冲洗。术后创面穿孔处采用钛夹或荷包缝合。术后处理:两组患者术后均禁食2~3 d,常规胃肠减压,同时给予常规补液营养支持,纠正电解质紊乱,2~3 d后根据情况给予半流质或流质饮食。

1.3 观察指标

(1)观察两组患者的肿瘤完整切除率及围术期指标(包括术后首次进食流质时间、术后排气时间、手术时间、住院总费用、术后住院时间、术中出血量)。(2)术前、术后3 d取患者静脉血5 mL,经离心处理(离心半径9 cm,速率3600 r/min,时长12 min),取上清液保存待检测。采用放射免疫法检测血清胃肠激素水平:胃泌素(GAS)、胃动素(MTL),检测试剂盒购自天津阿斯尔生物科技有限公司。采用酶联免疫吸附法检测血清肾上腺素(E)、去甲肾上腺素(NE)水平,检测试剂盒购自无锡云萃生物科技有限公司。(3)对比两组患者并发症(感染、继发性出血、穿孔)发生情况。

1.4 统计学方法

研究数据采用SPSS23.0软件进行统计分析。并发症发生率、性别比例、肿瘤部位等计数资料以例数或率表示,组间比较采用 χ^2 检验。经检验正态分布的E、NE、肿瘤直径等计量资料以 $(\bar{x} \pm s)$ 表示,组间、组内比较采用成组t检验或配对t检验。检验标准设为 $\alpha=0.05$ 。

2 结果

2.1 两组疗效及围术期指标对比

与A组相比,B组住院总费用、术中出血量更少,术后首次进食流质时间、术后住院时间、术后排气时间、手术时间更短($P<0.05$)。两组肿瘤完整切除率对比未见明显差异($P>0.05$)。如表1所示。

2.2 两组应激反应指标变化

两组患者术前血清E、NE水平组间对比无统计学差异($P>0.05$)。两组术后3 d血清E、NE水平均升高,但B组低于A组($P<0.05$),见表2。

2.3 两组胃肠激素水平变化

两组患者术前血清MTL、GAS水平组间对比无统计学差异($P>0.05$)。两组术后3 d血清MTL、GAS水平均下降,但B组高于A组($P<0.05$),见表3。

2.4 两组并发症发生率对比

两组并发症发生率对比,组间无统计学差异($P>0.05$),见

表 4。其中继发性出血的患者出血较多者及时进行了内镜下干预。针对穿孔者及时进行了修补治疗。预或外科手术。针对感染者给予了合适的抗生素行抗感染治

表 1 两组疗效及围术期指标对比($\bar{x} \pm s$)Table 1 Comparison of efficacy and perioperative indexes between the two groups($\bar{x} \pm s$)

Groups	Operation time (min)	Postoperative exhaust time (min)	Postoperative hospitalization time(d)	Total hospitalization cost(yuan)	Intraoperative bleeding(mL)	First postoperative fluid intake time (d)	Complete tumor resection rate (%)
Group A(n=83)	84.29± 5.75	2.23± 0.52	7.53± 0.76	33611.19± 183.22	47.19± 3.35	3.78± 0.31	72(86.75)
Group B(n=87)	73.73± 5.82	1.64± 0.38	6.28± 0.61	25384.71± 165.15	18.23± 2.24	2.54± 0.37	74(85.06)
t/ χ^2	11.863	8.474	11.853	39.764	66.539	23.628	0.100
P	0.000	0.000	0.000	0.000	0.000	0.000	0.752

表 2 两组应激反应指标变化($\bar{x} \pm s$, ng/mL)Table 2 Changes of stress response indexes in the two groups($\bar{x} \pm s$, ng/mL)

Groups	E		NE	
	Preoperative	3 d after operation	Preoperative	3 d after operation
Group A(n=83)	54.15± 7.09	107.69± 6.92*	48.91± 7.24	106.38± 6.91*
Group B(n=87)	54.28± 6.73	86.38± 7.65*	49.67± 8.37	87.37± 6.74*
t	-0.123	19.018	-0.632	18.157
P	0.903	0.000	0.528	0.000

Note: * compared with preoperative, the difference was statistically significant.

表 3 两组胃肠激素水平变化($\bar{x} \pm s$, pg/mL)Table 3 Changes of gastrointestinal hormone levels in the two groups($\bar{x} \pm s$, pg/mL)

Groups	MTL		GAS	
	Preoperative	3 d after operation	Preoperative	3 d after operation
Group A(n=83)	139.43± 11.52	75.72± 11.19*	328.65± 16.32	205.75± 28.46*
Group B(n=87)	138.48± 8.45	92.76± 10.82*	329.61± 25.47	268.06± 31.29*
t	0.615	-9.958	-0.921	-13.563
P	0.539	0.000	0.771	0.000

Note: * compared with preoperative, the difference was statistically significant.

表 4 两组并发症发生率对比 [例(%)]

Table 4 Comparison of incidence rate of complications between the two groups [(%)]

Groups	Secondary hemorrhage	Infect	Perforation	Total incidence rate
Group A(n=83)	2(2.41)	1(1.20)	1(1.20)	4(4.82)
Group B(n=87)	6(6.90)	0(0.00)	3(3.45)	9(10.34)
χ^2				1.836
P				0.715

3 讨论

随着我国医疗卫生事业的发展以及健康体检的普及,越来越多的小间质瘤(直径 ≤ 5 cm)患者在健康体检中被检出^[7,8]。GIST 均有潜在恶变倾向,因 GIST 疾病的发展具有不可预测性,患者在保守治疗过程中压力较大,故而多数倾向于接受手

术切除治疗^[9]。手术治疗的关键之处在于完全切除病灶,且尽可能保留胃功能^[10]。临床上对于直径 >5 cm 患者,多推荐采用开腹手术切除;而对于直径 ≤ 5 cm 的 GIST 患者,多建议微创手术治疗,如 LAP 等^[11,12]。现有的临床操作表明^[13],LAP 也存在一定的弊端,如针对较小内生型 GIST,腹腔镜存在定位困难的缺陷;而针对较大的肿瘤时需要扩大切口取出瘤体,增加术中损

伤。近年来,有研究表明^[14],ESD 应用于 GIST 具有一定的疗效。内镜直视下可清楚观察病灶大小、质地与边界,而且无需腹部钻孔,快速切除病灶^[15]。以往学者们认为 GIST 多起源于固有肌层,其生长方式多样,与周围组织紧密连接,镜下难以彻底分离,完整切除瘤体存在一定的困难,且术后并发症发生率较高,故而一直未能将 ESD 定为瘤体直径稍大的 GIST 患者的首选治疗方案^[16-18]。近来随着内镜下治疗技术的不断进步,使得其在直径 ≤ 5 cm GIST 应用的优先级提高。

本次研究结果显示,两组肿瘤完整切除率对比未见明显差异,提示两种术式疗效相当。但与 A 组相比,B 组住院总费用、术中出血量更少,术后首次进食流质时间、术后住院时间、术后排气时间、手术时间更短。这说明,ESD 具有术中创伤小、术后恢复快、且手术花费少,经济性高等诸多优势。主要是因为与 LAP 相比,ESD 拥有可以快速发现病灶、可处理腹腔镜下难处理的贲门部病灶、直观了解肿瘤的大小、质地和边界等优点,从而改善围术期指标^[19-21]。GIST 作为一项重大的负性生活事件,术前即可对患者造成一定程度的应激反应,加上 LAP、ESD 手术过程中气腹建立、麻醉刺激、手术牵拉刺激等多方面刺激,机体产生应激反应,而强烈的应激反应会影响机体其他组织的正常运行^[22-24]。本次研究发现,两组术后 3 d 血清 E、NE 水平均升高,但 B 组低于 A 组,说明 ESD 可有效减轻直径 ≤ 5 cm GIST 患者的术后应激反应。考虑可能与 ESD 精准定位病灶,彻底切除病灶,减少对腹腔脏器的干预,最大限度地维持正常组织生理结构功能有关^[25-27]。胃肠激素是一组多肽类神经-体液物质,GAS 能促进胃底舒张、胃窦收缩^[28],MTL 则可启动消化间期内移动性运动复合波^[29]。两者作为客观生化指标,可有效反应人体胃肠功能恢复情况。相关报道指出^[30],腹部手术因对胃肠道牵拉、手术创伤等,均会损伤胃肠功能,导致血清 MTL、GAS 含量明显降低。本研究中,ESD 手术可更有效地减轻对胃肠激素的影响,可能与 ESD 可精准定位病灶,减轻对周围脏器的继发性损伤有关。这也可能是患者住院时间、术后进食时间明显短于 LAP 的主要原因。本次研究中,两组并发症发生率对比,组间无统计学差异,但值得注意的是,本研究显示 ESD 术后发生率较高的并发症为穿孔和继发性出血,ESD 切除过程中须小心、轻柔,术中无需盲目追求剥离速度,尽量减少穿孔的发生;同时 ESD 切除过程中应在黏膜下注射足够厚的水垫,充分暴露黏膜下层,以避免触碰肿瘤导致手术性种植转移;此外,手术过程中可采用多种内镜止血方案进行止血,最大程度的降低继发性出血发生率。如何更好地减少 ESD 术后并发症发生率,也将是未来的研究方向之一。

综上所述,ESD、LAP 治疗直径 ≤ 5 cm GIST,疗效较好,其中 ESD 相对而言手术创伤更小、术后恢复更快,可能与减轻应激反应及减轻对胃肠激素的影响有关。本研究局限性在于未设置术后随访,有关 ESD 治疗直径 ≤ 5 cm GIST 的预后和安全性有待进一步的研究。

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