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· 临床研究 ·

腹腔镜胃间质瘤切除的可行性与安全性的肿瘤位置匹配对照研究

王进, 贾宗良, 樊林, 王海江, 敬亚恒, 车向明

(西安交通大学第一附属医院 普通外科, 陕西 西安 710061)

摘要

目的: 评估腹腔镜手术切除胃间质瘤的可行性及安全性。

方法: 收集2010年1月—2016年1月期间行胃间质瘤手术切除并符合研究条件的患者资料, 将行腹腔镜手术与行开腹手术肿瘤位置相同的患者作1:1匹配, 最终腹腔镜组与开腹组各纳入36例, 比较两组患者的相关临床指标。

结果: 两组患者基本资料具有可比性。肿瘤位于近贲门处各5例, 胃体小弯侧各12例, 胃体(或胃底)各13例, 近幽门处各6例。腹腔镜组与开腹组切除方式(楔形切除: 26例 vs. 23例; 胃部分切除: 8例 vs. 10例)无明显差异($P>0.05$)。与开腹组比较, 腹腔镜平均手术时间、术中出血量减少(114 min vs. 140 min; 90 mL vs. 138 mL); 平均肛门排气时间、经口进流食时间、术后住院天数均减少(2.6 d vs. 3.1 d; 4.1 d vs. 5.3 d; 6.0 d vs. 8.3 d); 围手术期总并发症发生率降低(0.0% vs. 16.7%), 差异均有统计学意义(均 $P<0.05$)。两组术后病理指标、复发率、总生存率、无病生存率差异均无统计学意义(均 $P>0.05$)。

结论: 对于原发性胃间质瘤, 腹腔镜手术安全有效, 且在肿瘤位置相同的条件下, 比开腹手术创伤小、并发症少、患者恢复快。

关键词

胃肿瘤; 胃肠道间质肿瘤; 腹腔镜
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Feasibility and safety of laparoscopic resection for gastric stromal tumor: a tumor location matched case-control study

WANG Jin, JIA Zongliang, FAN Lin, WANG Haijiang, JING Yaheng, CHE Xiangming

(Department of General Surgery, the First Affiliated Hospital, Medical School of Xi'an Jiaotong University, Xi'an 710061, China)

Abstract

Objective: To evaluate the feasibility and safety of laparoscopic resection for gastric stromal tumors.

Methods: The data of patients who underwent surgical resection for gastric stromal tumors and met the study requirements from January 2010 to January 2016 were collected. Patients undergoing laparoscopic and open surgery were matched in a 1:1 ratio according to the tumor location, with 36 cases each in laparoscopic group and open surgery group finally enrolled. The main clinical variables between the two groups of patients were compared.

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作者简介: 王进, 西安交通大学第一附属医院硕士研究生, 主要从事胃肠道肿瘤的基础与临床方面的研究。

通信作者: 车向明, Email: chexiang@mail.xjtu.edu.cn

Results: The general data of the two groups of patients were comparable. The tumor in 5 cases was located near the cardia of the stomach, in 12 cases located at the lesser curvature of the stomach and in 13 cases located in the body or fundus of the stomach. The type of gastric resection performed in the laparoscopic and open surgery group (gastric wedge resection: 26 cases vs. 23 cases; gastric partial resection: 8 cases vs. 10 cases) had no statistical difference ($P < 0.05$). In laparoscopic group compared with open surgery group, the average operative time and intraoperative blood loss were reduced (114 min vs. 140 min; 90 mL vs. 138 mL), the average time to flatus and oral liquid food intake as well as length of postoperative hospital stay were shortened (2.6 d vs. 3.1 d; 4.1 d vs. 5.3 d; 6.0 d vs. 8.3 d), and incidence of overall perioperative complications was decreased (0.0% vs. 16.7%), and all differences had statistical significance (all $P < 0.05$). There was no statistical difference in postoperative pathological variables, recurrence rate, and overall survival and disease free survival rate between the two groups (all $P > 0.05$).

Conclusion: For primary gastric stromal tumor, laparoscopic surgery is safe and feasible, and compared with open surgery, it has the advantages of less trauma, few complications and quicker recovery of the patients under the condition of same tumor location.

Key words Stomach Neoplasms; Gastrointestinal Stromal Tumors; Laparoscopes

CLC number: R735.2

胃间质瘤是常见的胃肠道间叶组织肿瘤，来源于卡哈尔细胞（Cajal cell），绝大多数间质瘤特异性表达CD117与DOG1^[1-2]。具有潜在恶性，恶性程度与肿瘤直径、核分裂象密切相关^[3]。整个胃肠道都可发生间质瘤，其中胃间质瘤约占70%^[4]。目前，对于原发性胃间质瘤，手术切除仍是唯一可能治愈的治疗方式^[5]。手术切除应做到完整切除肿瘤，避免肿瘤破裂，显微镜下阴性切缘^[6]。鉴于胃间质瘤极少通过淋巴系统扩散转移，因此手术通常不需要行淋巴清扫^[7]。目前，腹腔镜技术已广泛应用于各专业的手术治疗^[8-11]。腹腔镜具有显著地微创优势。众多研究^[12-15]已经证实对于直径不大于5 cm的胃间质瘤，腹腔镜手术切除是技术上可行且肿瘤学安全的。最近有报道^[16-18]腹腔镜手术切除同样适用于肿瘤直径>5 cm的胃间质瘤，其围手术期临床效果同样具有显著优势，在远期生存率与复发率方面则无明显差异。然而，肿瘤大小并不是唯一左右手术方式的因素，肿瘤位置是另一个非人为因素而影响手术方式的因素，因此，本研究将肿瘤位置匹配后，评估腹腔镜手术切除胃间质瘤的可行性及安全性。

1 资料与方法

1.1 基本资料

2010年1月—2016年1月期间在我科行胃间质

瘤手术切除的患者共105例。排除术前接受伊马替尼治疗及既往上腹部手术史的患者7例，最终98例患者纳入本研究。其中，腹腔镜手术36例（腹腔镜组），开腹手术共69例（开腹组）。按照肿瘤位置，从开腹组中选取与腹腔镜组肿瘤位置相同的患者作为数量1:1的对照组，两组各有36例。术后经病理结果免疫组化证实为胃间质瘤。按照肿瘤的位置分为4部分：(1) 近贲门；(2) 小弯侧；(3) 大弯侧；(4) 近幽门处。手术切除部分根据肿瘤的位置及有无临近脏器侵犯不同可分为：胃楔形部分切除，胃部分（次全胃）切除，全胃切除，以及联合脏器切除。根据肿瘤位置和大小决定手术具体方式：(1) 胃楔形部分切除术，适用于肿瘤较小的胃间质瘤，至少距肿瘤切缘1~2 cm，必要时术中送病理确定切缘阴性；(2) 胃部分（次全胃）切除术，适用于肿瘤位于贲门、幽门周围以及胃窦部较大的间质瘤，采用胃部分（次全胃）切除术；(3) 全胃切除，适用于肿瘤直径较大，位于胃小弯侧；(4) 联合脏器切除，适用于侵犯附近脏器的胃间质瘤患者。

1.2 随访具体方法

通过定期门诊复查及电话随访出院患者。对于极低及低危险度的患者每半年复查1次腹部CT或者上消化道超声内镜，持续2年，如果未见复发或者转移，以后每年复查1次腹部CT或者上消化道超声内镜。中度及高度危险度等级与口服伊马替尼

的患者每半年复查1次腹部CT/PET-CT或者上消化道超声内镜。

1.3 统计学处理

通过查阅电子病历系统,收集患者的临床数据以及随访信息。分类变量的数据比较采用Pearson χ^2 或者Fisher精确检验。连续变量比较采用t检验。以 $P<0.05$ 作为具有统计学差异的标准。数据分析应用数据分析软件IBM SPSS 19.0。

2 结果

2.1 两组患者基本资料与肿瘤部位

两组患者基本资料差异均无统计学意义(均 $P>0.05$),具有可比性(表1)。按肿瘤位置1:1匹配,两组患者肿瘤位于近贲门处各5例,胃体小弯侧各12例,胃体(或胃底)各13例,近幽门处各6例。

表1 两组患者基本资料比较 [$n=36, n(\%)$]

Table 1 Comparison of the general data between the two groups of patients [$n=36, n(\%)$]

资料	腹腔镜组	开腹组	P
性别			
男	17 (47.2)	19 (52.8)	0.64
女	19 (52.8)	17 (47.2)	
年龄(岁)	63.0 \pm 9.4	61.0 \pm 9.3	0.27
BMI (kg/m ²)	23.4 \pm 3.5	23.8 \pm 3.7	0.71
ASA 分级			
1	21 (58.3)	16 (44.4)	
2	13 (36.1)	15 (41.7)	0.35
3	2 (5.6)	5 (13.9)	
临床症状			
上腹不适	14 (38.9)	13 (36.1)	
呕血/黑便	17 (47.2)	20 (55.6)	0.81
腹部包块	1 (2.8)	1 (2.8)	
体检发现	4 (11.1)	2 (5.6)	

2.2 两组患者手术相关指标

两组楔形切除分别26与23例,胃部分切除(近端胃切除与远端胃切除总和)8与10例,每组均有1例患者因肿瘤体积较大(腹腔镜组8.5 cm,开腹组10 cm),行全胃切除术,两组各有1例患者行联合脏器切除。在切除部位方面,两组差异无统计学意义($P=0.85$)。腹腔镜平均手术时间比开腹组少26 min,差异具有统计学意义($P=0.012$)。术中出血量腹腔镜组明显少于开腹

组($P=0.008$)(表2)。

表2 两组患者手术相关数据比较 [$n=36, n(\%)$]

Table 2 Comparison of the relevant surgical variables between the two groups of patients [$n=36, n(\%)$]

变量	腹腔镜组	开腹组	P
切除部位			
楔形切除	26 (72.2)	23 (63.9)	
胃部分切除	8 (22.2)	10 (27.8)	0.85
全胃切除	1 (2.8)	1 (2.8)	
联合脏器切除	1 (2.8)	2 (2.6)	
手术时间(min)	114 \pm 42	140 \pm 44	0.012
术中出血量(mL)	90 \pm 50	138 \pm 85	0.008

2.3 两组患者术后病理指标

开腹组患者肿瘤平均直径大于开腹组(5.1 cm vs. 4.6 cm)($P=0.35$);两组核分裂指数无统计学差异($P=0.47$);根据Fletcher危险度分级($P=0.11$)、组织学类型($P=0.91$)两组无统计学差异;绝大多数肿瘤表达CD117、DOG1,未见两者均未表达者,两组在分子表达上亦无统计学差异(均 $P>0.05$)(表3)。

表3 两组患者术后病理比较 [$n=36, n(\%)$]

Table 3 Comparison of the postoperative pathological variables between the two groups of patients [$n=36, n(\%)$]

变量	腹腔镜组	开腹组	P
肿瘤大小(cm)	4.6 \pm 1.8	5.1 \pm 3.0	0.35
核分裂指数			
≤ 5	30 (83.3)	28 (77.8)	
6~10	4 (11.1)	3 (8.3)	0.47
>10	2 (5.6)	5 (13.9)	
Fletcher 危险度分级			
极低危	5 (13.9)	2 (5.6)	
低位	18 (50.0)	15 (41.7)	0.11
中危	12 (33.3)	12 (33.3)	
高危	1 (2.8)	7 (19.4)	
组织学类型			
上皮细胞	23 (63.9)	22 (61.1)	
梭形细胞	10 (27.8)	10 (27.8)	0.91
混合细胞	3 (8.3)	4 (11.1)	
DOG1			
(+)	33 (91.7)	34 (94.4)	
(-)	3 (8.3)	2 (5.6)	1.00
CD117			
(+)	35 (97.2)	33 (91.7)	
(-)	1 (2.8)	3 (8.3)	0.61

2.4 两组患者术后恢复与随访情况

术后胃肠道功能恢复,腹腔镜组优于

开腹组；腹腔镜组术后未出现并发症，开腹组术后出现吻合口瘘 1 例，上呼吸道感染 2 例，伤口感染 1 例，相关指标比较有统计学差异 ($P < 0.05$) (表 4)。两组分别有 11 例与 15 位患者术后口服伊马替尼。腹腔镜组 1 例复查发现肝脏转移。开腹组有 1 位出现胃间质瘤复发，1 例患者出现肝脏转移。

所有患者平均随访周期为 30 (6~72) 个月。总生存率 (OS) 腹腔镜组为 94.4%，开腹组为 94.4%，差异无统计学意义 ($P = 0.679$) (图 1A)；无病生存率 (DFS) 腹腔镜组为 97.2%，开腹组为 97.2%，差异无统计学意义 ($P = 0.499$) (图 1B)。

表 4 两组患者术后恢复指标及随访情况比较 [$n = 36, n (\%)$]

Table 4 Comparison of the postoperative recovery variables and follow-up data between the two groups of patients [$n = 36, n (\%)$]

变量	腹腔镜组	开腹组	P
肛门排气时间(d)	2.6 ± 0.8	3.1 ± 0.6	0.008
进流质时间(d)	4.1 ± 1.0	5.3 ± 1.0	<0.001
术后住院时间(d)	6.0 ± 3.1	8.3 ± 2.3	0.001
围手术期并发症			
无	36 (100.0)	30 (83.3)	0.03
有	0 (0.0)	6 (16.7)	
具体并发症			
吻合口瘘	0 (0.0)	1 (2.8)	0.81
上呼吸道感染	0 (0.0)	2 (5.6)	0.47
伤口感染	0 (0.0)	3 (8.3)	0.24
口服伊马替尼			
有	11 (30.6)	15 (41.7)	0.33
无	25 (69.4)	21 (58.3)	
肿瘤复发			
有	1 (2.8)	2 (5.6)	1.0
无	35 (97.2)	34 (94.4)	

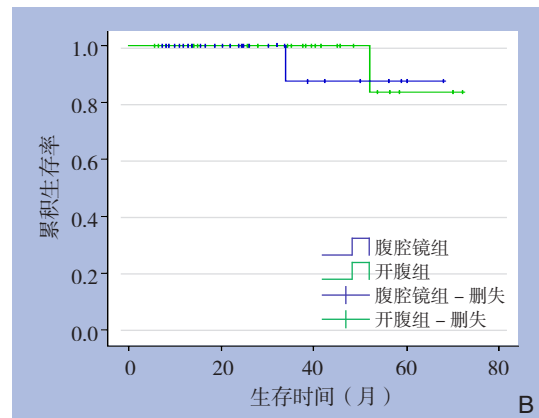
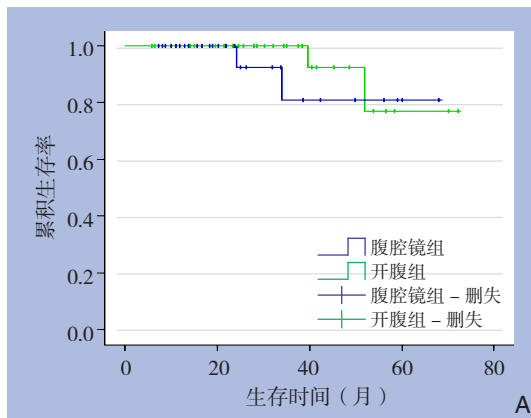


图 1 两组患者术后生存情况比较 A: OS 曲线; B: DFS 曲线

Figure 1 Comparison of postoperative survival between the two groups of patients A: OS curves; B: DFS curves

3 讨论

胃间质瘤是消化道最常见的源于间叶组织的肿瘤，其生物学行为具有潜在恶性^[19]，对于原发性肿瘤手术切除仍是目前治疗的金标准^[20]。手术应保证肿瘤完整切除，对于不能完整切除的局部复发或临近器官转移的患者应首先接受靶向药物治疗^[21]。腹腔镜技术对患者创伤小，患者术后康复快，已经逐渐应用于腹腔各类手术^[22-24]，自 1992 年 Lukaszczuk 等^[25]首次应用腹腔镜行胃间质瘤切除术，腹腔镜胃间质瘤手术越来越多的应用于临床实践中，而之前的许多禁忌证也被打破，

2010 版 NCCN 胃间质瘤指南已不再将肿瘤直径作为腹腔镜限制条件^[7]。由于肿瘤破裂会造成腹腔内播散种植，因此在腹腔镜操作过程中务必遵守无瘤操作原则加以细致轻柔实施，但是绝不能拒绝中转开腹。

众多比较腹腔镜与开腹手术切除胃间质瘤的研究并未将肿瘤位置匹配，这使得研究结果存在偏倚。本研究按肿瘤位置，1:1 匹配腹腔镜组与开腹组病例，两组基本资料具有可比性。两组患者的手术均由经验丰富的医生完成，遵循无瘤原则，其中腹腔镜手术标本装入标本袋从原有 Trocar 或者从稍扩大的 Trocar 切口取出，所有患者术后病

理证实切缘阴性。本研究纳入的病例中,大多数肿瘤位于胃底或胃体(50/72),高危度分级比例较少,占11.1%(8/72),这与吕柯等^[26]报道一致。腹腔镜组与开腹组各有36例两组楔形切除分别26/23例,胃部分切除(近端胃切除与远端胃切除总和)8/10例,腹腔镜平均手术时间比开腹组少26 min(114 min vs. 140 min, $P=0.012$),术中出血量少(93 mL vs. 138 mL, $P=0.008$)两者差异均具有统计学意义。在术后胃肠道功能恢复方面腹腔镜组具有显著优势,肛门首次排气时间腹腔镜组比开腹组平均早0.5 d(2.6 d vs. 3.1 d, $P=0.008$),腹腔镜组平均进流食时间比开腹组早1.2 d(4.1 d vs. 5.3 d, $P<0.001$),腹腔镜组术后住院天数比开腹组平均少2.3 d(6.0 d vs. 8.3 d, $P=0.001$),这些结果趋势与众多近期已发表研究一致^[12-13, 17, 27-30]。腹腔镜组围手术期并发症少于开腹组。两组OS无显著性差异($P=0.679$),DFS亦无显著性差异($P=0.499$)。腹腔镜与开腹组OS相同为94.4%,DFS 97.2%。因此,腹腔镜手术与开腹手术长期预后结果相似。De Vogelaere等^[13]纳入53例的回顾性研究发现,行腹腔镜手术的患者长期总生存率优于开腹组,这可能与其随访时间较长有关(最长达15年)。笔者也将继续随访,观察两组更长期的预后情况。

通过以上研究总结发现,对于原发性胃间质瘤,肿瘤位置分布相同的条件下,由技术熟练经验丰富的医师实施手术,腹腔镜手术患者与开腹手术患者相比围手术期胃肠道功能恢复快,并发症少,患者术后住院时间短。长期随访肿瘤复发率与生存率两组无明显差异。腹腔镜手术是安全有效可行的胃间质瘤切除方式。这些发现仍需要大规模的前瞻性具有长期随访的随机对照研究来证实。

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