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单切口腹腔镜在结直肠手术中的应用效果及对炎症因子与应激反应的影响*

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摘要 目的:探讨单切口腹腔镜在结直肠手术中的应用效果及对炎症因子与应激反应的影响。方法:选择2018年1月至2019年10月我院接诊的98例结直肠癌患者,通过随机数表法分为2组,每组49例。观察组使用单切口腹腔镜结直肠癌根治术,对照组使用传统腹腔镜结直肠癌根治术,常规5孔操作法。比较两组围术期相关情况、手术前后血清炎症因子水平的变化、手术后应激反应及并发症的发生情况。结果:两组淋巴结清扫个数、中转开腹例数、术后排气时间比较差异均无统计学意义($P>0.05$),观察组手术时间明显长于对照组,脐切口长度、住院时间、术中出血量均显著短于或低于对照组;两组术后1 d、3 d、5 d时高敏C反应蛋白(hs-CRP)、肿瘤坏死因子-α(TNF-α)、白细胞介素-6(IL-6)、去甲肾上腺素(NE)、肾上腺素(E)、皮质醇(Cor)水平均明显高于术前($P<0.05$);且观察组术后1d、3d、5d时hs-CRP、TNF-α、IL-6、NE、E、Cor较对照组显著降低($P<0.05$);两组吻合口瘘、吻合口狭窄、吻合口出血、小肠穿孔、肠梗阻、感染的总发生率比较差异无统计学意义($P>0.05$)。结论:和传统5孔操作法相比,单切口腹腔镜结直肠癌根治术治疗结直肠癌患者的手术时间更长,但术后炎症因子表达更低,应激反应更小,有利于患者术后恢复。

关键词:结直肠癌;腹腔镜结直肠癌根治术;单切口;炎症因子;应激反应

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Efficacy of Single Incision Laparoscopy in the Treatment of Colorectal Surgery and Its Influence on Inflammatory Factors and Stress Response*

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ABSTRACT Objective: To study the efficacy of single incision laparoscopy in the treatment of colorectal surgery and its influence on the inflammatory factors and stress response. Methods: 98 patients of colorectal cancer who were treated from January 2018 to October 2019 in our hospital were selected, and divided into the observation group and the control group according to the random number table, with 49 cases in each group. The observation group was given single incision laparoscopic colorectal cancer radical operation, the control group was treated by traditional laparoscopic colorectal cancer radical operation, conventional 5-hole operation. The perioperative condition, changes of serum inflammatory factors levels before and after operation, stress response after operation and the occurrence of complications were compared between the two groups. Results: There was all no significant difference in the number of lymphadenectomy, conversion to laparotomy and postoperative exhaust time between the two groups ($P>0.05$); the operation time of observation group was significantly longer than that of the control group, the length of umbilical incision, length of stay and intraoperative hemorrhage were shorter or lower than those of the control group; the high sensitive C-reactive protein (hs CRP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), norepinephrine (NE), epinephrine (E) and cortisol (Cor) in the two groups on postoperative 1st, 3rd and 5th day were significantly higher than those before operation ($P<0.05$); and the levels of hs-CRP, TNF-α, IL-6, NE, E and cor on postoperative 1st, 3rd and 5th day in the observation group were significantly decreased compared with the control group ($P<0.05$); there was no significant difference in the total incidence of anastomotic leakage, anastomotic stenosis, anastomotic bleeding, intestinal perforation, intestinal obstruction and infection between the two groups ($P>0.05$). Conclusion: Compared with the traditional 5-hole operation, the single incision laparoscopic radical surgery has longer operation time for colorectal cancer patients, which can relieve inflammatory responses and stress response and is beneficial to the recovery of patients.

Key words: Colorectal cancer; Laparoscopic radical resection of colorectal cancer; Single incision; Inflammatory factors; Stress response

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前言

结直肠癌是临床上常见的消化道恶性肿瘤，包含结肠癌、直肠癌。随着近年来人们生活水平的提高、饮食结构的变化，结直肠癌发病率呈逐年增长的趋势[1,2]。结直肠癌患者早期通常无症状或者症状不明显，随着病情发展，可出现大便习惯改变、便血、腹痛、腹部包块、肠梗阻等症状，多数需接受手术切除治疗[3,4]。微创外科技术目前已在临床上取得较大进展，尤其以腹腔镜技术作为代表，已成为结直肠癌患者的首选治疗方案。和传统的开腹手术相比，腹腔镜结直肠癌根治术具有创伤小、恢复快、安全性高等优点，且疗效和开腹手术相似[5,6]。

单切口腹腔镜手术是在传统腹腔镜手术基础上进一步发展而成的一种新的手术方式，主要特点是可减少腹腔镜端口，避免静脉留置针相关并发症发生率风险等，但该术式在临床上应用时间较短，其是否可以获得和传统多孔腹腔镜手术相同的疗效，是否可以减少对患者的伤害等方面仍不完全段[7,8]。因此，本研究旨在探讨单切口腹腔镜在结直肠手术中的应用效果，以及其对炎症因子与应激反应的影响，现报道如下。

1 资料与方法

1.1 一般资料

选择 2018 年 1 月至 2019 年 10 月我院接诊的 98 例结直肠癌患者纳入研究。纳入标准[9]：①通过实验室检查、直肠镜检查、病理检查等，确诊为结直肠癌；②具有腹腔镜手术适应症，全身状况良好，无远处转移，肿瘤直径≤ 5 cm；③美国麻醉医师协会分级(ASA)I~II 级；④签署研究知情同意书。排除标准[10]：①腹腔镜内严重粘连，对手术过程有影响；②急性肠梗阻或肠穿孔；③合并躯体重大疾病，包括心、脑、肺等，或合并其余恶性肿瘤；④有腹部手术史；⑤术前血常规异常，凝血功能障碍；⑥精神障碍。通过随机数表法分为 2 组，每组 49 例，观察组和对照组一般资料见表 1，差异无统计学意义($P>0.05$)。

表 1 两组一般资料的比较[$\bar{x}\pm s$，n(%)]

Table 1 Comparison of the general information between two groups[$\bar{x}\pm s$, n(%)]

Item		A group(n=49)	B group(n=49)
Gender	Male	29(59.18)	31(63.27)
	Female	20(40.82)	18(36.73)
Age(years)		61.89± 7.50	62.04± 7.21
BMI(kg/m^2)		23.11± 2.69	23.05± 2.81
ASA	I	24(48.98)	26(53.06)
	II	25(51.02)	23(46.94)
Tumor diameter(cm)		3.95± 0.40	3.88± 0.49
Dukes staging	A	11(22.45)	10(20.41)
	B	28(57.14)	26(53.06)
	C	10(20.41)	13(26.53)

1.2 治疗方法

观察组使用单切口腹腔镜结直肠癌根治术，于脐孔左侧开小切口，长度 1 cm，建立 CO_2 人工气腹，压力维持于 13 mmHg，并经切口将 10 mm Trocar 置入，在腹腔镜下全麻对腹腔进行探查，确认腹腔无粘连、转移，并评估肿瘤位置大小等后，相应延长切口至 2 cm，仅切开皮肤和皮下筋膜，将腹直肌前鞘保留，于原 Trocar 上方分别将 5 mm 和 12 mm 的 Trocar 置入，三枚 Trocar 排列方式呈倒三角。对照组使用传统腹腔镜结直肠癌根治术，常规 5 孔操作法，于脐上或脐孔做观察孔，将右髂前上棘内侧偏下穿刺孔作为手术操作孔，将左右脐旁腹直肌外缘、左髂前上棘内侧偏下的部位各作一穿刺孔作为辅助操作孔。两组手术过程均根据肿瘤治疗原则，保证手术切除范围，根据手术部位选择 Miles 术、Dixon 术、直肠前切术等[11]，遵循无瘤操作。

1.3 观察指标

1.3.1 围术期情况　包括手术时间、术中出血量、脐切口长度、淋巴结清扫个数、中转开腹、术后排气时间和住院时间。

1.3.2 炎症因子　收集术前、术后 1 d、3 d、5 d，收集两组患者静脉血 8 mL，使用 3500 r/min 的转速，离心 10 min，收集上层血清液储存于冷冻箱中备检，检测指标包括高敏 C 反应蛋白(hs-CRP)、肿瘤坏死因子 -α(TNF-α)、白细胞介素 -6(IL-6)，试剂盒使用美国 R&D 公司生产的酶联免疫吸附法(ELISA)试剂盒检测；

1.3.3 应激反应　留取上述血清液样本 4 mL，检测指标包括去甲肾上腺素(NE)、肾上腺素(E)、皮质醇(Cor)，所使用的 ELISA 试剂盒由上海研谨生物科技有限公司提供；

1.3.4 术后并发症

1.4 统计学分析

以 spss18.0 软件进行统计学分析，计量资料用($\bar{x}\pm s$)表示，组间比较采用 t 检验，计数资料组间比较采用 x^2 检验，以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组围术期相关情况的比较

两组淋巴结清扫个数、中转开腹例数、术后排气时间比较

差异无统计学意义($P>0.05$)，观察组手术时间长于对照组，脐切口长度、住院时间短于对照组，术中出血量少于对照组($P<0.05$)，见表 2。

表 2 两组围术期相关情况的比较[$\bar{x}\pm s$，n(%)]

Table 2 Comparison of the perioperative related information between two groups[$\bar{x}\pm s$, n(%)]

Groups	Operation time (min)	Intraoperative hemorrhage(mL)	Length of umbilical incision(cm)	Lymphadenecto-my(pcs)	Conversion to laparotomy[n(%)]	Postoperative exhaust time(h)	Length of stay(d)
Observation group(n=49)	158.56± 31.04*	101.74± 10.91*	3.26± 0.54*	12.43± 2.17	1(2.04)	32.28± 2.62*	7.04± 1.53*
Control group (n=49)	141.84± 33.61	116.82± 12.05	5.75± 0.47	12.27± 2.40	2(4.08)	32.67± 2.29	7.98± 1.20

Vs the control group, *$P<0.05$.

2.2 两组手术前后血清炎症因子水平的比较

两组术后 1 d、3 d、5 d 时血清 hs-CRP、TNF-α、IL-6 均明显高于术前($P<0.05$)，且观察组术后 1 d、3 d、5 d 时血清 hs-CRP、TNF-α、IL-6 水平明显低于对照组($P<0.05$)，见表 3。

表 3 两组手术前后炎症因子比较($\bar{x}\pm s$)

Table 3 Comparison of the inflammatory factors between two group before and after operation($\bar{x}\pm s$)

Groups		hs-CRP(mg/L)	TNF-α(pg/mL)	IL-6(pg/mL)
Observation group(n=49)	Preoperation	7.94± 1.50	22.74± 3.61	8.45± 1.29
	1 d postoperation	54.84± 4.48*#	44.10± 3.85*#	31.81± 2.85*#
	3 d postoperation	40.01± 3.51*#	37.19± 2.94*#	22.03± 2.19*#
	5 d postoperation	21.27± 2.65*#	30.08± 3.21*#	14.63± 2.40*#
Control group(n=49)	Preoperation	7.85± 1.77	22.62± 3.85	8.39± 1.46
	1 d postoperation	76.96± 6.91*	56.84± 4.20*	44.03± 3.18*
	3 d postoperation	52.18± 4.94*	49.03± 3.28*	38.12± 2.45*
	5 d postoperation	39.36± 3.74*	41.22± 3.84*	21.07± 2.06*

Note: Compared with preoperation, *$P<0.05$; Compared with the control group, #$P<0.05$.

3 讨论

结直肠癌是临床上常见的恶性肿瘤，2016 年的一项研究中显示每年有 15.9 万人死于结直肠癌，位于中国恶性肿瘤的发病率、死亡率第 5 位，而每年新发的结直肠癌患者约 33.1 万，位于第 4 位，经济发展、生活水平的提高、膳食结构的转变是导致结直肠癌发病、死亡的重要因素[12,13]。目前，结直肠癌的治疗仍以手术为主，也是治愈该病的唯一手段，传统的开腹手术是腹腔镜手术广泛应用之前最常用的方案，可有效切除肿瘤并完成淋巴结清扫[14,15]。但也有出血量多、创伤大、感染率高、术后肠道功能恢复慢等缺点。自 1991 年 Jacobs 等提出腹腔镜辅助治疗结肠切除术后，该方式也逐渐在结直肠癌患者中得到普及，并成为现今治疗该病的经典术式[16]。随着近年来微创技术的不断完善，其手术方式、操作技术已相对完善[17,18]。但临床实践中，有报道显示传统的腹腔镜手术为多孔操作，腹壁会留下 4~5 个 0.5~2.0 mm 的小切口，在一定程度上会影响术后恢复[19,20]。

单切口腹腔镜手术是由多孔腹腔镜手术演变而来的一种术式，在 2008 年 Bucher 等[21]首次成功应用于 1 例良性结肠疾病患者。此外，单切口腹腔镜手术并发症发生率、开腹中转率以及淋巴结清扫数量和传统腹腔镜手术相似[22]。Sangster W 等[23]通过对比 308 例单切口腹腔镜手术、318 例传统腹腔镜手术患者，发现两组手术时间、住院时间、术后 60d 再入院率均相似。但单切口腹腔镜手术在我国的开展时间较短，其疗效和安全性仍处于探讨阶段。

本研究通过研究围术期相关指标，发现单切口腹腔镜手术和传统腹腔镜手术的治疗效果相似，也可实现直肠系膜的完整切除和环周切缘阴性。Borowski DW 等[24]报道也得出了相似结论。但本研究显示使用单切口腹腔镜手术的患者手术时间更长，脐切口长度、住院时间更短，且术中出血量更少。在手术时间方面，由于单切口腹腔镜手术在我国的应用情况不如国外普及，尚处于探索和发展初期，且手术过程中容易出现视觉限制，即便是具有丰富经验的腹腔镜外科医师在最初开展单切口腹腔镜手术时也会觉得较为困难，因此延长了手术时间。Daher R 等[25]通过对术者加强学习曲线经验累积后发现单切口腹腔镜手术的手术时间有逐渐缩短的趋势。此外，由于单切口腹腔镜手术切口较小，术中出血量减少，术后恢复时间缩短。

腹腔镜手术属于一种有创性手术，术中必定会对患者机体产生影响，主要表现为大量炎症细胞生成、应激反应加强等，其反应程度和机体损伤程度密切相关[26,27]。hs-CRP 是反映机体炎症状态的重要指标，在遭受到组织损伤后数小时就可出现升高，并在 48 h 内达到高峰，随着机体损伤的缓解，其表达可逐步降低[28]。TNF-α 作为一种单核细胞因子，具有触发、启动局部

炎症反应的作用，被认为是机体最强的内源性炎症指标。IL-6则是急性期损伤的早期反应物质，属一类促炎因子，其升高程度和炎症反应呈正相关。而NE、E、Cor则是机体在应激反应下所释放的具有代表性的应激因子，在手术等刺激下，其表达可在短时间内出现升高，和机体应激反应程度密切相关。本研究中，使用单切口腹腔镜手术的患者术后1 d、3 d、5 d时hs-CRP、TNF-α、IL-6、NE、E、Cor水平比传统腹腔镜手术的患者更低，提示和传统5孔操作法相比，使用单切口腹腔手术可减少多切口对组织的损伤，避免术后炎症因子、应激指标的剧烈升高。

目前，单切口腹腔镜结直肠癌根治术在临床上并未得到广泛应用，主要是由于手术对人体工学的要求高、手术时间长、成本高等。本研究证实单切口腹腔镜手术应用于结直肠癌患者是一种安全性有效的方式，通过总结经验，我们认为在手术过程中应注意以下几点，①主刀医生手术所操作的手和扶镜的手需保持距离，例如适当倾斜手术台或使用细长的器械，避免操作距离过近出现镜头起雾等现象，影响手术效果；②充分游离结肠，便于经脐切口拉入体外；③对于低位直肠病变的患者，单切口条件下较为狭窄，对于骨盆内的直肠病灶远端的切除上难度较大，可选择病灶近端切断，再把下段直肠由肛门翻转拉出体外；④加强医师对该术式的学习曲线，缩短手术时间；⑤不宜选择过于肥胖的患者，避免出现术中操作困难中转开腹手术，严格把握手术适应症。但本研究也存在部分不足，例如未持续患者短期和长期的生存率等，且样本量过少，此后仍需进一步深入研究来验证本结论。

综上所述，和传统5孔操作法相比，单切口腹腔镜结直肠癌根治术治疗结直肠癌患者的手术时间更长，但术后炎症因子表达更低，应激反应更小，有利于患者术后恢复。

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