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直肠癌根治术治疗直肠癌的疗效及对 b FGF、MTL 及 GDF-15 的影响 *

马 聪 王 琦 赵 泓 周先锋 王建春

（安徽理工大学第一附属医院 普外三科 安徽 淮南 232007）

摘要 目的：探讨直肠癌根治术治疗直肠癌的疗效及对重组人碱性成纤维细胞生长因子（b FGF）、胃动素（MTL）及生长分化因子-15（GDF-15）的影响。**方法**：选择 2016 年 01 月 -2019 年 12 月在我院接受治疗的 104 例直肠癌患者，采用抽签法分为观察组（n=54）和对照组（n=50）。对照组给予传统开腹直肠癌根治术治疗，观察组给予腹腔镜直肠癌根治术治疗。比较手术情况、血清 b FGF、MTL、GDF-15、C 反应蛋白（CRP）、超氧化物歧化酶（SOD）、丙二醛（MDA）、血管活性肠肽、胃泌素变化情况及并发症发生情况。**结果**：观察组手术时间显著高于对照组，术中出血量、住院时间、术后排气时间及切口长度均显著低于对照组，差异显著（$P<0.05$）；治疗前，两组血清 b FGF、MTL 及 GDF-15 水平无明显差异；治疗后，两组血清 b FGF、MTL 及 GDF-15 水平均显著降低，且观察组上述指标均低于对照组（$P<0.05$）；治疗前，两组应激反应水平无明显差异；治疗后，两组血清 CRP、MDA 水平均显著升高，且观察组上述指标均低于对照组，两组 SOD 均显著下降，观察组高于对照组（$P<0.05$）；治疗前，两组胃肠激素水平无明显差异；治疗后，两组血管活性肠肽均显著升高，且观察组低于对照组，胃泌素水平均显著降低，且观察组均高于对照组（$P<0.05$）；两组并发症总发生率为 5.56%、26.00%，差异具有统计学意义（$P<0.05$）。**结论**：在直肠癌患者中应用腹腔镜直肠癌根治术效果显著，可有效改善患者血清 b FGF、MTL 及 GDF-15，且并发症较少。

关键词：直肠癌根治术；直肠癌；碱性成纤维细胞生长因子；胃动素；生长分化因子 -15

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Curative Efficacy of Radical Surgery for Rectal Cancerin Treatment of Colorectalcancer and Its Effectson b FGF, MTL and GDF-15*

MA Cong, WANG Qi, ZHAO Feng, ZHOU Xian-feng, WANG Jian-chun

(Department of general surgery, the First Affiliated Hospital of Anhui University of science and technology, Huainan, Anhui, 232007, China)

ABSTRACT Objective: To studyCurative efficacy of Radical surgery for rectal cancerin treatment of Colorectalcancerand its effectson Basic fibroblast growth factor (BFGF), motilin (MTL) and growth differentiation factor-15 (gdf-15). **Methods:** 104 patients with rectal cancer who were treated in our hospital from January 2016 to December 2019 were selected and divided into observation group (n=54) and control group (n=50) by drawing lots. The control group was treated with traditional open radical resection of rectal cancer, and the observation group was treated with laparoscopic radical resection of rectal cancer. The operation, serum b FGF, MTL, gdf-15, c-reactive protein (CRP), superoxide dismutase (SOD), malondialdehyde (MDA), vasoactive intestinal peptide, gastrin and complications were compared. **Results:** The operative time of the observation group was significantly higher than that of the control group, and the intraoperative blood loss, hospital stay, postoperative exhaust time and incision length were significantly lower than those of the control group, with significant differences ($P<0.05$). Before treatment, there was no significant difference in serum levels of BGF, MTL and gdf-15 between the two groups. After treatment, serum levels of BGF, MTL and gdf-15 in the two groups were significantly reduced, and the above indicators in the observation group were lower than those in the control group ($P<0.05$). Before treatment, there was no significant difference in stress response between the two groups. After treatment, serum CRP and MDA levels in the two groups were significantly increased, and the above indexes in the observation group were lower than those in the control group, while SOD levels in the two groups were significantly decreased, while those in the observation group were higher than those in the control group ($P<0.05$). Before treatment, there was no significant difference in gastrointestinal hormone levels between the two groups. After treatment, vasoactive intestinal peptides were significantly increased in both groups, lower in the observation group than in the control group, and gastrin levels were significantly reduced in the observation group, and higher in the observation group than in the control group ($P<0.05$). The total incidence of complications in the two groups was 5.56% and 26.00%, and the difference was statistically significant ($P<0.05$). **Conclusion:** Laparoscopic radical resection of rectal cancer in patients with rectal cancer has a significant effect, which can effectively improve the patients' serum serum b FGF, MTL and df -15, with fewer complications.

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作者简介：马聪（1981-），男，本科，主治医师，研究方向：消化道肿瘤，肝胆胰腺常见疾病，

E-mail: diaoyunhui006@163.com，电话：13855461739

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前言

直肠癌是消化道最常见的恶性肿瘤之一，是一种发生于齿状线至乙状结肠交界处的恶性肿瘤，与生活习惯、饮食结构等因素相关，其发病率较高，仅次于胃癌和食管癌，近年来，发病率呈现出逐年增加的趋势[1,2]。临床表现为消瘦、排便梗阻，常侵犯尿道、膀胱等器官，严重者甚至会诱发下肢水肿、尿路刺激等症状，危及患者生命安全[3]。直肠癌患者常使用根治性手术切除治疗，可有效切除癌变组织，控制病情恶化，有研究显示，b FGF、MTL 及 GDF-15 在直肠癌中表达异常[4]。b FGF 由内皮细胞、平滑肌细胞、巨噬细胞分泌，能促进内皮细胞的游走，不能使平滑肌细胞游走，促进新血管形成，修复损害的内皮细胞；MTL 分布在全部小肠，能促进和影响胃肠运动，促进胃强力收缩和小肠分节运动；GDF-15 参与调控骨细胞形成及造成功能，多项研究发生其与多种肿瘤的发生过程中表达异常，且与肿瘤转移、分化等有关[5-8]。三种指标与肿瘤的关系密切，参与了肿瘤的转移及分期，因此 bFGF、MTL 及 GDF-15 可作为治疗直肠癌的重要指标，本研究在直肠癌患者中使用直肠癌根治术治疗，并观察其对 bFGF、MTL 及 GDF-15 的影响，现报道如下。

1 资料与方法

1.1 一般资料

选择 2016 年 01 月 -2019 年 12 月在我院接受治疗的 104 例直肠癌患者。采用抽签法分为 2 组，观察组 54 例：男 29 例，女 25 例，年龄 24-83 岁，平均(61.37± 12.87)岁，病理分型：低分化 18 例，中分化 25 例，高分化 11 例；对照组 50 例，男 32 例，女 18 例，年龄 41-84 岁，平均(65.71± 9.43)岁，病理分型：低分化 15 例，中分化 26 例，高分化 9 例。两组基线资料无明显差异，可比较。

参照《直肠癌诊治指南》[9]，(1)伴有腹痛、腹胀；(2)便意频繁；(3)病理检查证实。

纳入标准：(1)符合上述诊断标准；(2)年龄＞18 岁；(3)肠旁淋巴结未见肿大；(4) 近期影像学证实肿瘤未侵犯肠壁外组织；(5)患者知情且签署知情同意书。排除标准：(1)严重肝肾疾病者；(2)患有意识障碍、精神障碍者；(3)肿瘤远处转移者；(4)妊娠、围产、哺乳期妇女的患者；(5)严重脑血管疾病；(6)既往腹部手术者；(7)晕针者。

1.2 方法

对照组给予传统直肠癌根治术：患者麻醉后，下腹部正中切口，进入腹腔，分离肠段、系膜等，夹闭血管，清除肿瘤病灶及淋巴结。常规放置引流管，逐层缝合。观察组采用腹腔镜直肠癌根治术：麻醉后，建立人工气腹，脐下切口，穿刺主操作孔，确定肿瘤情况后，游离肠段及系膜，夹闭血管，超声刀分离，游离病变肠段，清扫肿瘤病灶、淋巴结等。常规放置引流管，冲洗缝合。

1.3 观察指标

采集空腹静脉血 5 mL，以 3000 r·min^{-1} 的速度进行离心，时间 10 min，提取上层血清后，置于零下 20℃的冷冻箱内存储以备检测，送外单位检测，采用双抗体夹心酶联免疫吸附法测定 b FGF、MTL、GDF-15、CRP、SOD、MDA 水平；检测记录胃激素水平；记录手术情况及并发症发生情况。

1.4 统计学分析

以 SPSS18.0 软件包处理，符合正态分布计量资料用均数± 标准差($\bar{x}$± s)表示，组间比较使用独立样本 t 检验，计数资料以率表示，x^2 检验，P＜0.05 表示差异具有统计学意义。

2 结果

2.1 两组手术情况比较

观察组手术时间显著高于对照组，术中出血量、住院时间、术后排气时间及切口长度均显著低于对照组，差异显著(P<0.05)见表 1。

表 1 两组手术情况比较($\bar{x}$± s)

Table 1 Comparison between the two groups($\bar{x}$± s)

Groups	n	Operation time (min)	Intraoperative hemorrhage(mL)	Length of stay(d)	Postoperative exhaust time(h)	Cut length(cm)
Observation group	54	147.52± 34.63	80.65± 8.74	9.91± 1.78	36.54± 18.41	4.25± 1.41
Control group	50	115.96± 41.38	162.24± 15.46	12.87± 2.05	77.26± 15.76	17.16± 4.23
t value		4.229	33.444	7.878	12.071	21.199
P value		0.000	0.000	0.000	0.000	0.000

2.2 两组 b FGF、MTL 及 GDF-15 水平比较

治疗前，两组血清 b FGF、MTLT 及 GDF-15 水平无明显差异；治疗后，两组血清 b FGF、MTL 及 GDF-15 水平均显著降低，且观察组上述指标均低于对照组(P<0.05)，见表 2。

2.3 两组应激反应比较

治疗前，两组应激反应水平无明显差异；治疗后，两组血清 CRP、MDA 水平均显著升高，且观察组上述指标均低于对照组，两组 SOD 均显著下降，观察组高于对照组(P<0.05)，见表 3。

2.4 两组胃肠激素水平比较

治疗前，两组胃肠激素水平无明显差异；治疗后，两组血管活性肠肽均显著升高，且观察组低于对照组，胃泌素水平均显著降低，且观察组均高于对照组(P<0.05)，见表 4。

表 2 两组 b FGF、MTL 及 GDF-15 水平比较($\bar{x}\pm s$)

Table 2 Comparison of B FGF, MTL and GDF-15 levels in two groups($\bar{x}\pm s$)

Groups	n	b FGF(pg/L)		MTL(ng/L)		GDF-15(ng/L)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	54	46.39± 1.18	7.25± 0.78	875.64± 127.45	401.23± 57.61	1642.15± 471.25	752.63± 87.46
Control group	50	46.11± 1.42	13.12± 1.65	874.58± 128.63	648.52± 72.34	1647.25± 469.58	1052.36± 121.25
t value		1.097	23.469	0.042	19.354	0.055	14.537
P value		0.275	0.000	0.966	0.000	0.956	0.000

表 3 两组应激反应比较($\bar{x}\pm s$)

Table 3 Comparison of stress response between the two groups($\bar{x}\pm s$)

Groups	n	CRP(mg/L)		SOD(U/mL)		MDA(mmol/L)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	54	6.36± 0.67	37.53± 3.16	94.63± 9.26	63.55± 5.13	5.31± 0.52	7.98± 0.72
Control group	50	6.42± 0.73	64.42± 6.24	94.83± 9.14	40.52± 4.03	5.41± 0.59	12.46± 1.49
t value		0.437	28.029	0.111	25.321	0.919	19.749
P value		0.663	0.000	0.912	0.000	0.361	0.000

表 4 两组胃肠激素水平比较($\bar{x}\pm s$)

Table 4 Comparison of gastrointestinal hormone levels between the two groups($\bar{x}\pm s$)

Groups	n	Vasoactive intestinal peptide(ng/L)		Gastrin(pg/mL)	
		Before the treatment	After treatment	Before the treatment	After treatment
Observation group	54	242.28± 25.79	298.15± 14.63	154.26± 13.51	151.21± 18.15
Control group	50	239.26± 29.28	330.25± 16.35	149.96± 13.28	104.25± 10.26
t value		0.559	10.566	1.635	16.068
P value		0.577	0.000	0.105	0.000

3 讨论

直肠癌是指从齿状线至直肠乙状结肠交界处之间的癌，发病隐匿，早期无明显症状，多数患者确证时已是中晚期，近年来随着人们生活习惯及饮食结构的改变，直肠癌的发生率呈逐年上升趋势，且逐渐呈年轻化，已成为威胁人们健康的恶性肿瘤之一[10,11]。相关数据显示，直肠癌发病率仅次于胃癌和食管癌，居所有恶性肿瘤的第三位，死亡率为第五位，严重威胁人们的生命安全[12]。因此对直肠癌早期及时有效治疗具有重要意义。

目前治疗直肠癌最常用的方式是通过使用手术切除病灶组织，传统手术为开腹切除，能准确清扫淋巴结，但该术术中出血量较多，给患者的手术创伤较大，且该手术是将腹腔环境暴露在外界中，易发生术后感染，不利于预后[13-16]。近年来随着医疗技术的不断进步，腹腔镜技术在临床中得到广泛运用[17]。腹腔镜直肠癌根治术能准确地对血管进行结扎，手术过程是在完全直视状态下开展的，根据全直肠系膜切除的原则达到开腹手术的效果，且伤口较小，所引发的疼痛感轻，利于伤口恢复[18,19]。国外研究证实，对直肠癌患者进行微创手术具有开放手术同样的治疗效果，且创伤小、恢复快，对患者胃肠功能基自身免疫功能所造成的影响较小，有利于患者恢复[20]。本研究结果显示，使用腹腔镜直肠癌根治术治疗的患者术中出血量、住院时间、术后排气时间及切口长度均显著低于对照组，且并发症总发生率为 5.56%，也低于对照组患者，结果提示，腹腔镜直肠癌根治术对直肠癌的治疗是可行且有效的，对患者机体损伤较小，可减少患者术中出血量，降低并发症发生率。分析其原因可能是因为腹腔镜手术术野清晰，操作精确，对患者的创伤性和刺激性均较小，且直视下可迅速发现病变组织，减少对周围组织的损伤，降低术后并发症发生风险，促进患者术后机体的恢复。

b FGF 是与肿瘤血管生成相关的碱性蛋白质，可促进神经内胚层细胞有丝分裂及血管内皮细胞生成，相关研究报道，b FGF 是重要的促血管生长因子，在多种肿瘤组织中表达较高，与肿瘤的生长关系密切[21,22]。国外研究显示，bFGF 在直肠癌中表达较高，且促进了的血管生成，在直肠癌的生长侵袭转移过程中起重要作用[23,24]。有研究显示，腹腔镜手术对直肠癌患者胃肠功能影响小[25]。胃肠激素由内分泌细胞与胰腺胰岛细胞分泌且分布于胃肠道管壁的调节消化道器官功能的关键激素，能抑制对

胃肠功能的兴奋,其中 MTL 是最常见的胃肠激素指标,能促进小肠运动。GDF-15 被称为巨噬细胞抑制细胞因子 -1,在正常情况下其水平较低,在缺氧、炎症或恶性肿瘤进展期间细胞应激后其水平增加,其在肿瘤发展的不同阶段发挥作用不同,在肿瘤早期,其能通过抑制肿瘤生长起到抑制癌细胞扩散的作用,而在晚期,GDF-15 可通过促进增殖、迁移等促进肿瘤的发展。有研究显示,GDF-15 在多种肿瘤患者中表达升高,可作为肿瘤的血清物标志物。本研究结果显示,治疗后,两组血清 b FGF、MTL 及 GDF-15 水平均显著降低,且采用腹腔镜直肠癌根治术的患者上述指标均低于使用传统开腹患者,M. A. Pereira 等研究也显示,腹腔镜直肠癌根治术对患者 b FGF、MTL 水平影响较小[26]。分析其原因可能是因为腹腔镜直肠癌根治术对患者机体影响小,从一定程度上减少肿瘤组织释放的细胞因子进入血液循环,抑制细胞肿瘤扩散,所以术后 bFGF、MTL 及 GDF-15 水平低于对照组。

胃肠道蠕动功能受机体神经内分泌因素影响,包括胃泌素、血管活性肠肽,手术过程中,由于手术牵拉及应激反应的共同作用,机体胃泌素等分泌异常,影响患者胃肠道正常功能。本研究结果还显示,治疗后,两组血清 CRP、MDA 水平均显著升高,且观察组上述指标均低于对照组,两组 SOD 均显著下降,观察组高于对照组,结果提示,治疗后患者应激反应明显,而观察组患者应激反应较对照组患者低,结果还显示,治疗后,两组血管活性肠肽均显著升高,且观察组低于对照组,胃泌素水平均显著降低,且观察组均高于对照组,分析其原因可能是因为腹部手术后患者交感神经兴奋,可抑制胃肠道神经丛兴奋神经元,影响胃肌电活动,而腹腔镜直肠癌根治术避免了脏器长时间暴露,减少脏器损伤,进而使胃肠道应激反应下降,最终促进术后胃肠道功能恢复。

综上所述,在直肠癌患者中应用腹腔镜直肠癌根治术效果显著,可有效改善患者血清 b FGF、MTL 及 GDF-15,且并发症较少,值得临床推广与运用。

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