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腹腔镜手术对结直肠癌根治术患者免疫功能及临床结局的影响*

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摘要 目的:探讨腹腔镜手术对结直肠癌根治术患者免疫功能和临床结局的影响。**方法:**选取我院 2015 年 2 月-2018 年 2 月收治的 50 例行手术治疗的结直肠癌患者,按照数字随机原则分成两组,对照组 25 例采用传统开腹手术,观察组 25 例采用腹腔镜手术,比较两组术前、术后外周血中 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 的变化和胃肠功能的改善情况,术后随访 1~3 年,记录两组患者的生存情况。**结果:**术前,两组外周血中 T 淋巴细胞亚群 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 比较差异无统计学意义($P>0.05$);术后 1 周、2 周,观察组 CD3⁺、CD4⁺、CD4⁺/CD8⁺ 比例均显著高于对照组,CD8⁺ 明显低于对照组($P<0.05$)。观察组术后肠鸣音恢复时间、肛门首次排气时间均显著短于对照组($P<0.05$),两组随访期并发症发生率、死亡率比较差异无统计学意义($P>0.05$)。**结论:**结直肠癌患者行腹腔镜手术治疗能够显著提升其免疫功能,术后胃肠功能恢复较快。

关键词:结直肠癌;腹腔镜;免疫功能;生存率

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Effect of Laparoscopic Surgery on the Immune Function and Clinical Outcome of Patients Undergoing Radical Resection of Colorectal Cancer*

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ABSTRACT Objective: To investigate the effect of laparoscopic surgery on the immune function and clinical outcome of patients undergoing radical resection of colorectal cancer. **Methods:** 50 patients with colorectal cancer who underwent surgery from February 2015 to February 2018 were enrolled in the study. They were divided into two groups according to the principle of numerical randomization, and 25 patients in the control group were treated with conventional open surgery. In the observation group, 25 patients underwent laparoscopic surgery. The changes of gastrointestinal function and CD3⁺, CD4⁺, CD4⁺/CD8⁺ in the peripheral blood of the two groups were compared. The patients were followed up for 1~3 years. The survival of patients were recorded. **Results:** There was no significant difference in the T lymphocyte subset including CD3⁺, CD4⁺, CD4⁺/CD8⁺ in the peripheral blood between the two groups before operation ($P>0.05$). The CD3⁺, CD4⁺, CD4⁺/CD8⁺ in the observation group were significantly higher than those in the control group at 1 week and 2 weeks after operation, and the CD8⁺ in the observation group was significantly lower than that in the control group ($P<0.05$). The postoperative recovery time of bowel sound and the exhaust time of first anus in the observation group was significantly shorter than that in the control group ($P<0.05$). There was no statistically significant difference between the two group in the incidence of complications and mortality during the follow-up period ($P>0.05$). **Conclusion:** Laparoscopic surgery can significantly improve the immune function and promote the recovery of postoperative gastrointestinal function for the patients with colorectal cancer.

Key words: Colorectal cancer; Laparoscopy; Immune function; Survival rate

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前言

结肠直肠癌(Carcinoma of colon and rectum)是胃肠道常见的恶性肿瘤,早期的检出率低,随着癌肿的增大,逐渐出现便血、腹泻与便秘交替、局部腹痛等^[1],晚期则表现贫血、体重下降等。随着人民饮食结构和习惯的改变,近年来结肠直肠癌的患

病率逐年攀升,仅次于胃癌和食管癌^[2,3]。结肠直肠癌多发于中年以上的男性,以 40~70 岁最为多见,但 20 世纪末发现 30 岁以下者亦不少见,男女两性发病比例约为 2:1^[4,5]。本病和其他恶性肿瘤一样,发病原因仍不清楚,可以发生在结肠或直肠的任何部位,但以直肠、乙状结肠最为多见,其余依次见于盲肠、升结肠、降结肠及横结肠^[6,7]。

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腹腔镜技术的成熟和普及给结直肠癌患者治疗提供了新的思路,有报道显示腹腔镜治疗结肠癌的近期疗效显著^[8,9]。由于结直肠癌的解剖结构位置较为特殊,其对腹腔镜手术操作要求极高,腹腔镜手术对患者术后胃肠功能、免疫功能影响仍不够明确。因此,本研究主要分析了腹腔镜手术对结直肠癌患者免疫功能、胃肠功能以及预后的影响。

1 资料与方法

1.1 一般资料

选取自 2015 年 2 月-2018 年 2 月收治的结直肠癌患者 50 例,按照数字随机原则分成两组。对照组 25 例,男性 14 例,女性 11 例,年龄 45-72 岁,平均(65.0± 2.7)岁,肿瘤直径 2.4~3.2 cm 间,平均(2.7± 0.2)cm,TNM- I 期 3 例、II 期 16 例、III 期 6 例;观察组 25 例,男性 16 例,女性 9 例,年龄在 43-70 岁间,平均(64.5± 2.5)岁,肿瘤直径 2.2~3.4 cm 间,平均(2.5± 0.3)cm,TNM- I 期 5 例、II 期 17 例、III 期 3 例。两组基本资料比较差异均无统计学意义($P>0.05$),具有可比性。

1.2 纳入和排除标准

纳入标准:确诊为结直肠癌患者,TNM 分期为 I~III 期患者^[10],首次进行手术治疗者,对实验知情且愿意签署研究授权书者,经医院伦理委员会批准。排除标准:合并其他部位肿瘤患者,伴血液系统疾病者,肝肾等重要脏器功能损伤者,传染性疾病患者等。

1.3 手术方法

开腹手术:患者行全身麻醉,按照常规结直肠癌根治手术,取患者腹部正中切口,切除肠系膜,结扎细胞膜根部动脉、静

脉,彻底清扫淋巴结。远端切除范围距边缘结肠大于 5 cm,直肠大于 2 cm。使用吻合器做肠管吻合。腹腔镜手术:患者同样行气管插管全麻,建立 CO₂ 气腹(压力为 12 mmHg),常规 5 孔操作^[11,12],于腹腔镜下行结直肠癌根治术,后续步骤同对照组。

1.4 观察指标

(1)外周血淋巴细胞亚群。分别在术前、术后 1 周、2 周时采集空腹状态下外周静脉血液 5 mL,使用流式细胞检测仪(美国 backman 公司,Coulter EpicsXL)测定其 T 淋巴细胞亚群 CD3⁺、CD4⁺、CD8⁺ 的水平情况,抗体应用鼠抗人 CD3⁺、CD4⁺、CD8⁺ 直标荧光抗体(法国 Immunotech 公司),计算 CD4⁺/CD8⁺。(2)术后胃肠功能恢复情况。记录两组术后肠鸣音恢复时间、肛门首次排气时间。(3)并发症和生存率。术后随访 1~3 年,记录两组并发症发生率,死亡率以及死亡患者的平均生存时间。

1.5 统计学方法

采用 SPSS20.0 软件进行数据分析,计数资料用%表示,组间采用 χ^2 检验,计量资料以($\bar{x} \pm s$)表示,组间数据比较采用 t 检验,以 $P<0.05$ 差异有统计学意义。

2 结果

2.1 两组手术前后免疫功能指标的变化比较

术前,两组 CD3⁺、CD4⁺、CD8⁺ 以及 CD4⁺/CD8⁺ 比较差异无统计学意义($P>0.05$),术后 3 d,观察组 CD3⁺、CD4⁺ 和 CD4⁺/CD8⁺ 略高于对照组,CD8⁺ 略低于对照组($P>0.05$);术后 1 周,观察组 CD3⁺、CD4⁺ 和 CD4⁺/CD8⁺ 显著高于对照组,CD8⁺ 明显低于对照组,差异有统计学意义($P<0.05$),见表 1。

表 1 两组手术前后免疫功能指标的变化比较

Table 1 Comparison of the changes in immune function indexes before and after operation between the two groups

Groups	Time	CD3 ⁺	CD4 ⁺	CD8 ⁺	CD4 ⁺ /CD8 ⁺
Control group(n=25)	Preoperative	61.32± 3.33	31.67± 2.32	26.42± 1.02	1.19± 0.17
	3 d after surgery	53.72± 3.15*	25.35± 2.09*	29.31± 0.37*	0.86± 0.10*
	1 week after surgery	52.70± 4.06*	27.60± 2.82*	28.47± 0.52*	0.97± 0.13*
Observation group (n=25)	Preoperative	60.82± 3.65	31.82± 2.24	26.35± 0.93	1.18± 0.15
	3 d after surgery	54.32± 2.95*	26.44± 2.51*	27.94± 0.74*	0.95± 0.12*
	1 week after surgery	55.40± 3.42**	30.43± 3.06**	27.03± 0.84**	1.13± 0.11**

Note:Compared with the same group before preoperative, * $P<0.05$; Compared with the control group at the same time, ** $P<0.05$.

2.2 两组术后胃肠功能恢复情况的比较

观察组术后肠鸣音恢复时间、肛门首次排气时间均显著短

于对照组($P<0.05$),见表 2。

表 2 两组术后胃肠功能改善情况的对比($\bar{x} \pm s$)

Table 2 Comparison of the postoperative gastrointestinal function improvement between the two groups($\bar{x} \pm s$)

Groups	Bowel sound recovery time(h)	Anal exhaust time(h)
Control group(n=25)	51.62± 6.45	70.35± 7.26
Observation group(n=25)	42.60± 5.84	57.32± 7.50
<i>t</i>	5.183	6.241
<i>P</i>	<0.05	<0.05

2.3 两组并发症发生情况和死亡情况的比较

所有患者随访 1~3 年,平均随访(15.6± 4.3)个月,观察组并发症的发生率为 16.0%,低于对照组的 36.0%,但两组对比差

异无统计学意义($P>0.05$)。随访期间,观察组死亡率为 12.0%,死亡患者平均生存时间为 20.4 个月;对照组死亡率为 8.0%,生存时间为 24.7 个月,两组对比均无显著差异($P>0.05$),见表 3。

表 3 两组并发症的发生情况和死亡情况对比

Table 3 Comparison of the incidence of complications and deaths between the two groups

Groups	n	Complication				Mortality rate
		Anastomotic fistula	Anastomotic bleeding	Incisional defect	Adhesive intestinal obstruction	
Control group	25	3(12.0)	1(4.0)	2(8.0)	3(12.0)	2(8.0)
Observation group	25	2(8.0)	1(4.0)	0	1(4.0)	3(12.0)
χ^2				0.857		0.222
P				0.355		0.637

3 讨论

腹腔镜是一种带有微型摄像头的医疗器械,腹腔镜手术是利用腹腔镜及其相关器械进行的手术^[13]。近年来,随着腹腔镜技术的不断成熟,其在各种结直肠癌手术中均得到广泛应用,但其优缺点也较为明显。相比于传统开腹手术,腹腔镜手术的手术耗时更长、对术者的要求更高,但对患者机体创伤小、术后恢复迅速^[14,15]。既往研究^[16,17]已经证实腹腔镜手术治疗直肠癌的近期效果令人满意。但是其对患者免疫功能、胃肠功能的影响尚不完全明确^[18,19]。

T 淋巴细胞是机体免疫系统内功能最重要的细胞群之一,健康人体 T 淋巴细胞亚群间相互作用,维持着正常的免疫功能。不同淋巴细胞亚群的数量、功能发生变化则表示机体免疫功能紊乱^[20,21]。血液中 T 淋巴细胞亚群水平能够准确反映机体免疫能力,本研究两组患者术后第 3 d CD3⁺、CD4⁺ 水平均较术前明显下降,对照组降幅明显高于观察组,提示开腹手术对机体免疫功能损伤更为严重;术后 1 周,观察组 CD3⁺、CD4⁺ 水平均略有回升,CD8⁺ 水平有所下降,但对对照组 CD3⁺、CD4⁺ 水平持续下降,CD8⁺ 则持续升高,提示在术后 1 周时观察组患者免疫功能逐渐恢复,而对对照组患者机体免疫功能受手术创伤的影响依然下降。由此可见,结直肠癌患者采用腹腔镜手术治疗对机体损伤小,术后免疫功能恢复较快。

结直肠癌手术治疗患者受麻醉、腹膜刺激以及手术中对胃肠组织的牵拉导致腹腔中解剖结构关系紊乱引发胃肠功能障碍^[22]。胃肠功能障碍导致术后早期无法正常进食,影响术后患者的恢复效果^[23]。研究结果显示观察组患者术后肛门排气时间和肠鸣音恢复时间均显著短于对照组,提示腹腔镜治疗方式对患者胃肠功能损伤小,术后恢复更快,这与相关研究^[24,25]等人的研究结果基本保持一致。原因可能是腹腔镜手术对患者机体创伤更小,组织炎性反应、机体应激反应均小于开腹手术,因此应激反应和神经纤维传导阻滞功能对胃肠蠕动、张力等的影响较小,术后恢复的时间也更快。手术安全性一直是肿瘤外科非常关注的问题之一,对于结直肠癌患者而言,需要吻合口瘘、吻合口出血、粘连性肠梗阻等都是较为严重的并发症^[26],必要时需要二次手术,实验结果显示观察组并发症发生率略低于对照组,可能是因为开腹手术导致腹腔组织暴露时间较长,容易引

发感染等情况^[27,28]。随访期间,两组的死亡率无明显统计学差异,与以往相关的研究结果有出入,造成该种差异的原因可能有两个方面,其一本研究收录患者数量较小,希望在之后的研究增加样本量以获取更为科学的数据^[29];此外,外科医生的综合素质也可能对整个治疗效果产生影响,所以必须加强医生综合能力的提升^[30]。

综上所述,结直肠癌患者行腹腔镜手术治疗能够显著提升其免疫功能,术后胃肠功能恢复较快,且安全性较高。

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