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腹腔镜与开腹胃癌根治术治疗胃癌患者的疗效及对免疫功能和炎性因子的影响*

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摘要 目的：探讨不同手术方式治疗胃癌患者的疗效及对免疫功能和炎性因子的影响。**方法**：选择2015年1月-2018年4月我院收治的择期行根治性切除术胃癌患者236例，根据不同的手术方式分为对照组(n=107)和实验组(n=129)，对照组实施传统开腹胃癌根治术，实验组实施腹腔镜胃癌根治术。观察两组患者各项临床症状及并发症发生情况，比较两组患者术前、术后1 d、术后7 d免疫功能和炎性因子水平。**结果**：与对照组相比，实验组患者的手术时间明显升高，而其他临床症状指标以及并发症发生率显著下降(P<0.05)，两组淋巴结清除数目比较无统计学差异(P>0.05)。两组患者术后1 d的IL-6、TNF-α、CRP水平均明显高于术前，但实验组低于对照组(P<0.05)。术后7 d，对照组IL-6、TNF-α、CRP水平仍高于术前(P<0.05)，但实验组TNF-α、CRP水平与术前比较无统计学差异(P>0.05)，同时实验组IL-6、TNF-α、CRP水平均显著低于对照组(P<0.05)。术后1 d、7 d，两组$CD3^+$、$CD4^+$、$CD4^+/CD8^+$均低于术前，$CD8^+$高于术前，且实验组$CD3^+$、$CD4^+$、$CD4^+/CD8^+$高于对照组，$CD8^+$低于对照组(P<0.05)。**结论**：与传统开腹胃癌根治术比较，腹腔镜胃癌根治术治疗胃癌患者疗效更好，可减轻炎性反应，对患者的免疫功能影响较小，安全可靠。

关键词：胃癌；腹腔镜胃癌根治术；开腹胃癌根治术；免疫功能；炎性因子

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Effect of Laparoscopic and Open Radical Gastrectomy for Gastric Cancer in the Treatment of Gastric Cancer and its Effect on Immune Function and Inflammatory Factors*

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ABSTRACT Objective: The effect of different surgical methods in the treatment of gastric cancer patients and its effect on immune function and inflammatory factors. **Methods:** 236 gastric cancer patients underwent radical resection in our hospital from January 2015 to April 2018 were selected, they were divided into the control group (n=107) and the experimental group (n=129) according to the different surgical methods. The control group were treated with traditional open radical gastrectomy for gastric cancer, and the experimental group were treated with laparoscopic radical gastrectomy for gastric cancer. The clinical symptoms and complications between the two groups were observed. The immune function and the levels of inflammatory factors between the two groups were compared at preoperative, postoperative 1 d, postoperative 7 d. **Results:** Compared with the control group, the operative time of the experimental group increased significantly, while the levels of other clinical symptoms and complications incidence decreased significantly (P<0.05). There was no significant difference in the number of lymph node clearance between the two groups (P>0.05). Postoperative 1 d, the levels of IL-6,TNF-α, CRP in the two groups were significantly higher than that preoperative, but the experimental group were lower than that in the control group (P<0.05). Postoperative 7 d, the levels of IL-6, TNF-α, CRP in the control group were still higher than that preoperative (P<0.05), but in the experimental group there was no significant difference in the level of TNF-α, CRP compared with the preoperative (P>0.05), while the levels of IL-6, TNF-α, CRP in the experimental group were significantly lower than that in the control group (P<0.05). Postoperative 1 d, postoperative 7 d, the levels of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ in the two groups were lower than that preoperative, the level of $CD8^+$ was higher than that preoperative,and the levels of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ in the experimental group were higher than that in the control group, the $CD8^+$ level was lower than that in the control group (P<0.05). **Conclusion:** Compare with traditional open radical gastrectomy, laparoscopic radical gastrectomy is better in treating gastric cancer, it can reduce the inflammatory response, has little influence on the immune function of patients, and it is safe and reliable.

Key words: Gastric cancer; Laparoscopic radical gastrectomy for gastric cancer; Open radical gastrectomy for gastric cancer; Immune function; Inflammatory factors

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前言

胃癌是我国发病率最高的恶性肿瘤，在临床上，胃癌根治术是治疗胃癌的首选手术方式，胃癌根治术又分为传统开腹胃癌根治术和腹腔镜胃癌根治术[1-3]。腹腔镜胃癌根治术作为一种微创术式，在其应用中具有所有微创术式的优势，与开腹胃癌根治术比较，腹腔镜胃癌根治术具有切口小、创伤小、出血量少、并发症少等优点[4-6]。但是，两种手术均会对患者的免疫功能和炎症反应造成一定的影响，其中手术创伤越大其炎症反应就会越强烈，进而引发炎症介质的释放，如白细胞介素 -6（interleukin-6，IL-6）、C- 反应蛋白（C-reactive protein，CRP）、肿瘤坏死因子 -α（tumor necrosis factor-α，TNF-α）等，并且 T 细胞亚群可以直接反映胃癌患者术后的免疫功能[7-9]，本研究通过对比不同手术方式治疗胃癌的临床疗效以及对免疫功能和炎症反应的影响，为临床治疗提供数据支持，现作如下报道。

1 资料与方法

1.1 临床资料

选择我院于 2015 年 1 月 -2018 年 4 月收治的择期行根治性切除术胃癌患者 236 例，纳入标准：（1）患者经过影像学检查，并经组织病理学确诊为胃癌；（2）耐受手术者；（3）胃癌病灶并无其他位置的转移；（4）患者均签署知情同意书。排除标准：（1）重要脏器功能不全者；（2）认知功能障碍者、精神失常者；（3）癌肿已侵犯胃壁浆膜层者。根据不同的手术方式将其分为对照组（n=107）和实验组（n=129），其中对照组男 66 例，女 41 例；年龄 31-72 岁，平均（51.32± 12.39）岁；肿瘤部位：胃体部 28 例，胃窦部 48 例，胃体与胃窦交界处 17 例，贲门胃底部 14 例；TNM 分期：Ⅰ期 32 例，Ⅱa 期 46 例，Ⅱb 期 29 例。实验组男 82 例，女 47 例；年龄 29-70 岁，平均（52.19± 11.76）岁；肿瘤部位：胃体部 37 例，胃窦部 56 例，胃体与胃窦交界处 19 例，贲门胃底部 17 例；TNM 分期：Ⅰ期 39 例，Ⅱa 期 53 例，Ⅱb 期 37 例。比较两组患者各项基本资料无统计学差异（P>0.05），均衡可比。我院医学伦理委员会已批准此研究。

1.2 手术方法

患者取平卧位，行全身麻醉。对照组实施传统开腹胃癌根治术。实验组实施腹腔镜胃癌根治术，操作步骤：经脐孔穿刺，完成 CO_2 气腹，腹内压维持 13-14 mmHg 左右，置入套针管，并将腹腔镜头置入，在四个位置戳孔，分别为脐左 5 cm、右锁骨中线平脐偏上 12 mm、左侧腋前线肋缘下 12 mm、右侧腋前线肋缘下 5 mm，观察病灶及其周边脏器是否出现肿瘤转移，根据患者病情的不同，选择性使用根治性近端或远端胃大部切除术。术后实施常规消毒和抗感染治疗。

1.3 观察指标及检测方法

分别于术前、术后 1 d、术后 7 d 采集两组患者的空腹静脉血，低温离心 15 min，离心速度为 3000 r/min，分离血清，采用酶联免疫吸附测定法检测患者血清 IL-6、TNF-α 水平，同时采用免疫混悬计法测定血清 CRP 水平，相关试剂盒均购自赛默飞世尔科技有限公司。应用 FAC Scan 流式细胞仪（美国 BD 公司）测定 $CD3^+$、$CD4^+$、$CD8^+$，计算 $CD4^+/CD8^+$。观察两组患者临床症状改善情况及并发症发生率。

1.4 统计学方法

采用 SPSS20.0 对所有数据进行统计分析，淋巴结清除数目、$CD4^+$、CRP 水平等计量资料以（$\bar{x}$± s）表示，实施 t 检验，计数资料以[n(%)]表示，实施 x^2 检验，检验水准设置为 α=0.05。

2 结果

2.1 对比两组术中及术后情况

与对照组相比，实验组患者的手术时间明显升高，术中出血量、止痛药使用次数、住院时间、并发症发生率、术后肛门排气时间少于对照组（P<0.05），两组淋巴结清除数目比较无统计学差异（P>0.05）。具体见表 1。

表 1 两组患者术中及术后情况比较

Table 1 Comparison of intraoperative and postoperative conditions between the two groups

Groups	n	Operation time (min)	Intraoperative bleeding (mL)	Postoperative anus exhaust time(h)	Number of lymph node scavenging (one)	Use of painkillers (times)	Time of hospitalization (d)	Incidence of complications [n(%)]
Control group	107	179.56± 49.31	321.45± 69.82	28.69± 3.25	22.19± 5.62	5.13± 1.27	14.54± 2.19	26(24.30)
Experimental group	129	231.79± 46.87	187.13± 62.75	15.78± 2.79	21.78± 5.43	2.82± 0.96	11.18± 2.05	13(10.08)
t/x^2		8.323	15.553	32.883	0.568	15.898	12.152	8.575
P		0.000	0.000	0.000	0.570	0.000	0.000	0.003

2.2 对比两组术前及术后炎症因子水平

两组术前炎症因子水平比较无统计学差异（P>0.05）。术后 1 d，两组患者血清炎症因子水平均高于术前，但实验组低于对照组（P<0.05）。术后 7 d，对照组 IL-6、TNF-α、CRP 水平仍高于术前（P<0.05），实验组 IL-6 高于术前（P<0.05），TNF-α、CRP 水平与术前比较无统计学差异（P>0.05），且实验组 IL-6、TNF-α、CRP 等炎症因子水平均明显低于对照组（P<0.05）。具体见表2。

2.3 两组患者术前及术后免疫功能比较

术前两组免疫功能水平比较无统计学差异（P>0.05）。术后 1 d、7 d，两组 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 均低于术前，$CD8^+$ 高于术前，且实验组 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 高于对照组，$CD8^+$ 低于对照组（P<0.05）。具体见表 3。

表 2 两组患者术前及术后炎症因子水平比较($\bar{x}\pm s$)

Table 2 Comparison of preoperative and postoperative inflammatory factors between the two groups($\bar{x}\pm s$)

Groups	n	Times	IL-6(ng/L)	TNF-α(ng/L)	CRP(ng/L)
Control group	107	Preoperative	8.29± 2.05	8.25± 0.42	12.98± 2.35
		Postoperative 1 d	41.08± 6.57*	17.36± 0.59*	37.51± 5.18*
		Postoperative 7 d	12.51± 3.64*	11.23± 0.35*	18.65± 4.62*
Experimental group	129	Preoperative	8.36± 1.97	7.36± 0.23	11.82± 2.16
		Postoperative 1 d	19.36± 4.52*#	13.85± 0.17*#	27.58± 3.47*#
		Postoperative 7 d	0.98± 3.54*#	7.89± 0.32#	12.51± 2.19#

Note: Compared with preoperative, *P<0.05; Compared with control group, #P<0.05.

表 3 两组患者术前及术后免疫功能比较($\bar{x}\pm s$)

Table 3 Comparison of preoperative and postoperative immune function between the two groups($\bar{x}\pm s$)

Groups	n	Times	$CD3^+$(%)	$CD4^+$(%)	$CD8^+$(%)	$CD4^+/CD8^+$
Control group	107	Preoperative	56.86± 3.58	32.83± 2.79	27.01± 0.65	1.19± 0.12
		Postoperative 1 d	45.35± 3.32*	25.01± 2.27*	30.05± 0.52*	0.85± 0.07*
		Postoperative 7 d	47.69± 3.14*	27.25± 2.64*	29.19± 0.33*	0.96± 0.15*
Experimental group	129	Preoperative	56.25± 3.47	32.78± 2.84	26.98± 0.74	1.21± 0.13
		Postoperative 1 d	49.32± 3.87*#	26.47± 2.05*#	27.65± 0.25*#	0.93± 0.09*#
		Postoperative 7 d	53.26± 3.66*#	30.06± 2.68*#	27.32± 0.46*#	1.16± 0.11*#

Note: Compared with preoperative, *P<0.05; Compared with control group, #P<0.05.

3 讨论

近年来,随着人们饮食结构的变化,发生胃癌的几率也明显增加,因胃癌早期时无临床特异性表现,致使许多患者失去了早期诊断与治疗的机会,严重影响患者的生活质量和生命健康[10-12]。近年来,腹腔镜技术的不断发展与应用,在临床上治疗胃癌的应用越来越广,不仅安全有效,而且手术创伤小及预后效果好[13,14]。但是外科手术诱发的应激反应对机体的免疫功能及炎症反应产生不同影响,并且在一定程度上会增加术后感染和肿瘤发生的几率。T 淋巴细胞参与机体的肿瘤免疫应答反应,$CD3^+$是外周成熟 T 淋巴细胞,辅助 T 细胞受体识别抗原提呈细胞上的 MHC 分子 [15-17]。$CD4^+$能够辅助和诱导 T 淋巴细胞,一旦被激活导致大量细胞因子释放,增强机体的抗肿瘤作用,$CD8^+$能够发挥清除病毒的作用,$CD4^+/CD8^+$的比值用于表示机体的免疫反应平衡, 比值下降提示机体免疫功能低下,促进肿瘤增殖,比值显著下降被认为是疾病加重或预后效果差的指征[18-20]。

本研究结果表明,与对照组相比,实验组临床症状改善情况较好,且并发症发生率较低,但两组淋巴结清除数目比较差异不明显。说明实验组的手术方式可减少患者术后恢复时间,虽然手术操作较为复杂,花费了更多的手术时间,但是可以减少并发症发生率,这在 Wang H 的研究中也可以加以佐证[21]。手术创伤导致的应激反应诱发炎症反应, 从而释放炎性介质,并不利于临床治疗,CRP 是一种急性反应蛋白, 由 IL-6 诱导合成,作为重要的炎性介质,常用作研究机体的应激反应[22-24]。机体的应激反应受到免疫功能的影响,机体长期处于应激状态致使免疫抑制,另外术后恶性肿瘤的复发及转移也受到免疫功能的影响。本研究中,两组术后炎症因子水平均高于术前,但术后 7 d 实验组 TNF-α、CRP 水平已接近术前水平,说明两种手术方式均对机体产生创伤,导致上述指标明显升高,但与传统开腹胃癌根治术治疗的患者相比,行腹腔镜胃癌根治术治疗的患者术后炎症因子水平明显较低,同时恢复效果好,表明腹腔镜胃癌根治术的创伤小,应激反应较轻,有利于患者的预后[25-27]。并且该手术方式的创口及对组织的损伤小,可大大降低了其感染的几率,从而减小对机体生理功能的影响。腹腔镜胃癌根治术是一种微创手术,但是外科手术均会导致创伤,从而引起应激反应,进而对机体的免疫功能造成影响[28,29]。分析胃癌患者手术治疗前后免疫功能可间接反映出手术创伤抑制免疫功能的影响。本研究结果显示,术后实验组 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 高于对照组,$CD8^+$ 低于对照组(P<0.05),表明腹腔镜胃癌根治术并不会过度影响机体的免疫功能,预后效果好[30]。

综上所述, 腹腔镜胃癌根治术的疗效优于开腹胃癌根治术,对患者的免疫功能影响较小,能够减轻炎症反应,且并发症少,有利于患者的预后。

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