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论著

腹腔镜下胃癌D2根治术联合射频消融 应用于胃癌肝转移的临床疗效

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摘要: 目的 探讨腹腔镜下胃癌D2根治术联合射频消融肝转移瘤应用于胃癌肝转移的临床疗效。
方法 选取该院2017年1月—2020年1月收治的可切除胃癌肝转移需行胃癌D2根治术联合射频消融的患者62例, 随机分为对照组和观察组, 每组各31例。对照组采用开腹胃癌D2根治术联合射频消融治疗, 观察组采用腹腔镜下胃癌D2根治术联合射频消融治疗。比较两组患者手术指标、血清肿瘤标志物指标、免疫相关指标和并发症情况。**结果** 对照组术中出血量多于观察组, 肠功能恢复时间、住院时间明显长于观察组($P < 0.05$), 手术时间短于观察组($P < 0.05$); 术后两组患者血清甲胎蛋白(AFP)、癌胚抗原(CEA)水平降低($P < 0.05$), 观察组血清AFP、CEA水平均低于对照组($P < 0.05$); 术后两组患者CD4⁺、CD8⁺、CD4⁺/CD8⁺水平均较术前降低($P < 0.05$), 观察组CD4⁺、CD4⁺/CD8⁺水平明显高于对照组($P < 0.05$); 观察组并发症发生率12.90%低于对照组41.94%($P < 0.05$)。**结论** 腹腔镜下胃癌D2根治术联合射频消融治疗胃癌肝转移有利于患者术后康复, 可明显改善血清肿瘤标志物水平及机体免疫功能, 降低围术期并发症发生率。

关键词: 腹腔镜; 胃癌D2根治术; 射频消融; 胃癌肝转移

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Clinical effect of laparoscopic D2 radical gastrectomy combined with radiofrequency ablation for liver metastasis of gastric cancer

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Abstract: Objective To investigate the clinical effect of laparoscopic D2 radical gastrectomy combined with radiofrequency ablation for liver metastasis of gastric cancer. **Methods** 62 patients with liver metastasis of resectable gastric cancer treated from January 2017 to January 2020 were selected and randomly divided into control group and observation group with 31 cases in each group. The control group was treated with open D2 radical gastrectomy combined with radiofrequency ablation, and the observation group was treated with laparoscopic D2 radical gastrectomy combined with radiofrequency ablation. The operation indexes, serum tumor markers, immune related indexes and complications were compared between the two groups. **Results** The intraoperative blood loss in the control group was more than that in the observation group, the intestinal function recovery time and hospitalization time of the control group were significantly longer than those of the observation group ($P < 0.05$), and the operation time was shorter than that of the observation group ($P < 0.05$); the levels of serum alpha fetoprotein (AFP) and carcinoembryonic antigen (CEA) decreased in the two groups after operation ($P < 0.05$), and

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the serum AFP and CEA level of the observation group were lower than those of the control group ($P < 0.05$); the postoperative CD4⁺, CD8⁺, CD4⁺/CD8⁺ levels of the two groups were lower than those before operation, the levels of CD4⁺, CD4⁺/CD8⁺ in the observation group were significantly higher than those in the control group ($P < 0.05$); the incidence of complications in the observation group was 12.90%, which was lower than 41.94% in the control group ($P < 0.05$). **Conclusion** Laparoscopic D2 radical gastrectomy combined with radiofrequency ablation in treatment of liver metastasis of gastric cancer is conducive to postoperative rehabilitation, significantly improve serum tumor markers and immune function, and reduce the incidence of perioperative complications.

Keywords: laparoscopy; D2 radical gastrectomy; radiofrequency ablation; liver metastasis of gastric cancer

胃癌肝转移指胃癌患者肝脏中出现了源于胃癌的转移病灶，临床发生率约为4%~14%^[1]。胃癌肝转移的出现代表着疾病进入病程晚期，如不积极予以相关治疗，中位生存期低于半年，患者5年生存率不足10%，预后极差^[2]。目前，临床治疗胃癌肝转移缺乏标准治疗方案，胃癌肝转移根据胃原发灶和转移灶数目、大小、分布等分为可切除与不可切除两种情况。有研究^[3]指出，对可采用治愈性手术治疗的胃癌肝转移患者实施胃原发灶D2根除术联合肝转移灶干预可使患者肝脏功能代偿至正常水平。但传统开腹手术行胃癌D2根治术创伤较大、术后恢复较慢，随着腹腔镜技术的发展，腹腔镜下胃癌D2根治术已成为重要治疗手段^[4]。射频消融术是一种微创手术，用于治疗胃癌肝转移灶的局部疗效确切。故本研究对可切除胃癌肝转移患者行腹腔镜下胃癌D2根治术联合射频消融治疗并观察其疗效，旨在为临床工作提供参考依据。

1 资料与方法

1.1 一般资料

选取我院2017年1月—2020年1月收治的可切除胃癌肝转移需行胃癌D2根治术联合射频消融的患者62例，随机分为对照组31例和观察组31例。诊断标准：参照“胃癌肝转移规范化治疗”中的标准^[5]。纳入标准：①均为远端胃癌肝转移病例，且均行Billroth II式；②预计生存期≥3个月；③残余肝脏有足够的代偿储备者；④年龄≥18岁；⑤肝脏转移灶若为单发转移灶，则直径≤4 cm，若为多发转移灶，则局限于半肝内，若累及左右肝，则转移灶总数≤3个。排除标准：①合并上腹部手术史；②术前行放、化疗或免疫治疗者；③合并严重心、肾等脏器功能异常者；④合并血液、免疫疾病或严重感染者。对照组

中，男19例，女12例；年龄46~65岁，平均(58.20±4.39)岁；病理分型：腺癌21例，黏液腺癌10例；肝脏转移灶单发17例，多发14例；转移灶大小1~4 cm，平均转移灶大小(2.67±1.02)cm。观察组中，男20例，女11例；年龄43~64岁，平均(58.03±4.27)岁；病理分型：腺癌20例，黏液腺癌11例；肝脏转移灶单发19例，多发12例；转移灶大小1~4 cm，平均转移灶大小(2.61±1.05)cm。两组患者一般资料比较，差异无统计学意义($P > 0.05$)，具有可比性。患者均签署知情同意书。本研究经医院伦理委员会批准（批号20160306）。

1.2 方法

1.2.1 手术方法 对照组患者取仰卧位，行全身麻醉后，取上腹正中约20 cm长左绕脐切口，逐层切开网膜、游离皮下组织，暴露肿瘤，分离并结扎胃网膜右动脉后，行癌灶切除、D2淋巴结清扫并重建消化道。观察组患者采用腹腔镜下胃癌D2根治术，于脐下20 mm处穿刺Trocar作为观察孔，建立气腹，维持压力在15 mmHg左右，以左、右上腹穿刺Trocar为操作孔，腹腔镜下探查胃癌及周围组织解剖情况，采用超声刀切断胃网膜左右静脉及其根部，切除大网膜，游离并切断胃网膜右血管、肝总动脉、脾动脉、左右动静脉，行D2淋巴结清扫，确认清扫完毕后，在上腹部建立5 cm正中切口，进入腹腔，包埋时处理十二指肠残端，切除远端胃，行Billroth吻合重建消化道。两组患者术后常规冲洗、缝合、预防感染。

1.2.2 射频消融术 两组患者术后3或4周均给予射频消融治疗肝转移灶，使用GE彩色多普勒超声诊断仪作为引导装置，频率为4或5 MHz，采用RITA1500X射频消融系统治疗。在超声引导下，将探

头置于肿瘤部位, 根据制定的治疗方案实施消融治疗, 消融过程中要确保肿瘤完全消除, 此过程中应严密观察患者瘤体变化, 每次消融维持在15 min内。

1.3 评价指标

1.3.1 手术指标 包括术中出血量、手术时间及肠功能恢复时间和患者住院时间。

1.3.2 血清肿瘤标志物指标 于术前及术后采集患者外周静脉血3 mL, 以2 500 r/min离心10 min, 收集血清, 采用酶联免疫吸附法检测患者血清甲胎蛋白(alpha-fetal protein, AFP)和癌胚抗原(carcinoembryonic antigen, CEA)水平。

1.3.3 免疫相关指标 于术前及术后采集患者外周静脉血3 mL, 采用贝克曼流式细胞仪检测患者外周血中免疫细胞CD4⁺、CD8⁺和CD4⁺/CD8⁺水平。

1.3.4 并发症情况 比较两组患者围术期并发症发生情况, 并发症发生率=并发症发生例数/总例数×100%。

1.4 统计学方法

采用SPSS 20.0软件进行统计学分析, 计量资料以均数±标准差($\bar{x} \pm s$)表示, 采用t检验, 计数资料以例(%)表示, 采用 χ^2 检验。 $P < 0.05$ 表示差异

有统计学意义。

2 结果

2.1 两组患者手术指标比较

对照组术中出血量多于观察组, 肠功能恢复时间及住院时间长于观察组($P < 0.05$), 手术时间短于观察组($P < 0.05$)。见表1。

2.2 两组患者血清肿瘤标志物指标比较

术前两组患者血清AFP、CEA水平比较, 无明显差异($P > 0.05$), 术后两组患者血清AFP、CEA水平明显低于术前($P < 0.05$), 观察组血清AFP、CEA水平均明显低于对照组($P < 0.05$)。见表2。

2.3 两组患者免疫相关指标比较

术前两组患者CD4⁺、CD8⁺、CD4⁺/CD8⁺水平比较, 差异均无统计学意义($P > 0.05$), 术后两组患者CD4⁺、CD8⁺和CD4⁺/CD8⁺水平均较术前明显降低($P < 0.05$), 观察组CD4⁺和CD4⁺/CD8⁺水平明显高于对照组($P < 0.05$)。见表3。

2.4 两组患者并发症比较

观察组并发症发生率12.90%明显低于对照组41.94%($P < 0.05$)。见表4。

表1 两组患者手术指标比较 ($\bar{x} \pm s$)

Table 1 Comparison of operation indexes between the two groups ($\bar{x} \pm s$)

组别	术中出血量/mL	手术时间/min	肠功能恢复时间/d	住院时间/d
对照组(n=31)	467.03±41.60	172.60±20.60	4.22±0.65	14.90±2.78
观察组(n=31)	296.30±32.672	221.65±25.33	3.37±0.47	11.63±2.05
t值	17.97	8.37	5.90	5.27
P值	0.000	0.000	0.000	0.000

表2 两组患者血清肿瘤标志物指标比较 ($\bar{x} \pm s$)

Table 2 Comparison of serum tumor markers between the two groups ($\bar{x} \pm s$)

组别	AFP/(μg/L)		CEA/(ng/mL)	
	术前	术后	术前	术后
对照组(n=31)	202.36±17.62	175.62±14.33 [†]	1 525.11±60.97	296.31±20.60 [†]
观察组(n=31)	201.91±17.80	158.90±11.70 [†]	1 530.77±59.25	205.37±16.69 [†]
t值	0.10	5.03	0.37	19.10
P值	0.921	0.000	0.712	0.000

注:[†]与术前比较, 差异有统计学意义($P < 0.05$)

表3 两组患者免疫相关指标比较 ($\bar{x} \pm s$)
Table 3 Comparison of immune related indexes between the two groups ($\bar{x} \pm s$)

组别	CD4 ⁺ /%		CD8 ⁺ /%		CD4 ⁺ /CD8 ⁺	
	术前	术后	术前	术后	术前	术后
对照组(n=31)	42.06±3.50	25.69±2.43 [†]	28.10±2.73	23.06±2.09 [†]	1.52±0.26	1.09±0.15 [†]
观察组(n=31)	42.10±3.54	29.01±2.97 [†]	28.13±2.78	24.10±2.40 [†]	1.54±0.24	1.21±0.20 [†]
t值	0.05	4.82	0.04	1.82	0.31	2.67
P值	0.965	0.000	0.966	0.074	0.754	0.010

注: [†]与术前比较, 差异有统计学意义($P < 0.05$)

表4 两组患者并发症比较 例(%)
Table 4 Comparison of complications between the two groups n(%)

组别	切口感染	吻合口瘘	肠梗阻	发热	并发症发生率
对照组(n=31)	2(6.45)	3(9.68)	2(6.45)	6(19.35)	13(41.94)
观察组(n=31)	1(3.23)	0(0.00)	1(3.23)	2(6.45)	4(12.90)
χ^2 值					6.46
P值					0.011

3 讨论

胃癌是临床中常见的肿瘤疾病之一, 因胃癌疾病早期没有典型的临床症状表现, 不易引起重视, 确诊时多已处在疾病中晚期^[6]。随着肿瘤进展, 晚期胃癌病灶常伴随多途径转移, 以肝转移多见。射频消融术治疗胃癌肝转移的疗效已有报道^[7]。AFP是肝癌的重要标志物, 健康人群的肝细胞中不产生AFP蛋白分子, 而在肝癌细胞中出现高表达^[8]。本研究中, 两组患者均给予射频消融术治疗, 治疗后两组患者AFP水平均明显降低, 可见射频消融术对肝转移病灶疗效确切。既往认为, 胃癌肝转移常为多发病灶且涉及肝脏多叶, 部分患者甚至伴随远处转移, 难以通过治愈性手术达到根治目的^[9]。YOSHIDA等^[10]认为, IV期胃癌存在潜在可切除病灶, 如: 胃癌肝转移中孤立的肝转移灶或少量腹主动脉旁淋巴结转移等, 可通过胃癌D2根治术联合R0手术使患者生存获益。而对于IV期胃癌患者的原发病灶, 若采用传统的开腹D2根治术, 需大范围游离和切除腹内组织, 对患者造成的创伤较大^[11]。腹腔镜手术遵从微创理念, 借助腹腔镜的视野, 可有效清除癌灶^[12], 但目前对于潜在可切除原发病灶的胃癌肝转移患者, 采用何种方法更有利于生存, 报道仍较少。

本研究中, 观察组患者手术时间长于对照组, 分析与胃内原发病灶行D2根治术过程中胃部血管结构复杂、淋巴结清扫区域较广泛以及消化道重建相对困难有关^[13], 但观察组患者术中出血量、肠功能恢复时间、住院时间均明显少于对照组。因腹腔镜下胃癌D2根治术手术切口较小、患者出血较少, 术后可早起下床活动, 提示: 腹腔镜下胃癌D2根治术更有利于患者术后恢复。腹腔镜可放大影像, 使施术者能更精细地了解解剖结构, 进而按规范完成D2根治术^[14]。研究^[15]表明, 胃癌手术过程中对肿瘤部分牵拉和挤压, 可能导致癌细胞脱落并种植于腹膜上。CEA是灵敏度较高的肿瘤标志物, 在恶性肿瘤的诊断、评估中具有重要意义^[16]。本研究中, 术后两组患者血清CEA水平均降低, 观察组血清CEA水平明显低于对照组, 说明: 腹腔镜放大视野的作用有利于术中操作, 减少对肿瘤部位的挤压和牵拉, 进而减少术后癌细胞腹膜种植风险。报道^[17-18]显示, 胃癌患者随着病程进展, 免疫功能受到一定程度抑制, 其免疫细胞CD4⁺、CD8⁺和CD4⁺/CD8⁺较正常人群水平低, 因炎性因子影响, 还会对免疫功能产生进一步抑制。因此, 避免胃癌患者术后免疫抑制也是治疗中的重要环节。本研究中, 术后两组患者CD4⁺、CD8⁺、CD4⁺/CD8⁺水平均较术前降低, 但观察组CD4⁺、CD4⁺/CD8⁺水平明显高于

对照组, 表明观察组术后免疫功能优于对照组, 提示: 腹腔镜下胃癌D2根治术联合射频消融有助于改善患者免疫功能, 对术后恢复产生积极影响。从两组患者围术期并发症发生情况来看, 观察组切口感染、吻合口瘘、肠梗阻和发热等总并发症发生率12.90%低于对照组41.94%。开腹手术切口大、游离范围广, 切除腹内组织会对机体造成较大创伤, 引起机体剧烈应激反应, 进而导致一系列并发症^[19-20]。因此, 腹腔镜下胃癌D2根治术对胃癌肝转移患者恢复更有利。但本研究仍存在一定不足, 仅观察了患者近期疗效, 未对远期生存预后进行跟踪随访, 后续将针对以上不足进一步研究。

综上所述, 腹腔镜下胃癌D2根治术联合射频消融治疗胃癌肝转移有利于患者术后康复, 能改善血清肿瘤标志物水平及机体免疫功能, 降低围术期并发症发生率。

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