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腹腔镜肝癌切除术对肝细胞癌中的治疗效果及对血清 AFP、sEC、HGF、ICAM-1 的影响*

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摘要 目的:研究腹腔镜肝癌切除术对肝细胞癌中的治疗效果及对血清 AFP、sEC、HGF、ICAM-1 的影响。**方法:**选择 2012 年 3 月至 2017 年 3 月在我院接受治疗的肝细胞癌患者 196 例,根据治疗方案不同分为观察组和对照组,对照组给予开腹切除手术治疗,观察组给予腹腔镜切除手术治疗。观察并比较两组手术前后血清甲胎蛋白(AFP)、sEC、人类生长因子(HGF)、细胞间黏附分子-1(ICAM-1)及总胆红素(TBIL)、直接胆红素(DBIL)、谷丙转氨酶(ALT)及白蛋白(Alb)水平,术中出血量、术后绝对卧床时间、住院时间以及并发症发生率。**结果:**术后,观察组血清 AFP、sEC、HGF、ICAM-1 水平均明显低于对照组($P<0.05$);观察组 TBIL、DBIL、ALT 水平均显著低于对照组,Alb 则显著高于对照组($P<0.05$);观察组术中出血量、绝对卧床时间以及住院时间均明显低于对照组($P<0.05$);且观察组术后并发症发生率明显低于对照组($P<0.05$)。**结论:**使用腹腔镜肝癌切除术治疗肝细胞癌,可降低患者血清 AFP、sEC、HGF、ICAM-1 水平从而提高其治疗效果,且术后并发症发生率较低。

关键词:腹腔镜;肝细胞癌;AFP;sEC;HGF;ICAM-1

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Application of Laparoscopic Hepatectomy in Hepatocellular Carcinoma and Its Effects on Level of AFP, sEC, HGF, ICAM-1*

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ABSTRACT Objective: To study application of laparoscopic hepatectomy in hepatocellular carcinoma and its effects on levels of AFP, sEC, HGF and ICAM-1. **Methods:** 196 patients of hepatocellular carcinoma who received therapy from March 2012 to March 2012 in our hospital were selected as research objects, according to the different treatment is divided into observation group and control group. The control group was treated with open abdominal resection, while the observation group was treated with laparoscopic hepatectomy. Then AFP, sEC, HGF, ICAM-1 levels, liver function (TBIL, DBIL, ALT, Alb), Intraoperative blood loss, absolute bed time after surgery, length of stay, postoperative complications were compared. **Results:** After the operation, the serum AFP, sEC, HGF, ICAM-1 levels in observation group was less than the control ($P<0.05$); TBIL, DBIL and ALT levels in observation group was less than the control, while Alb in observation group was higher than the control ($P<0.05$); The blood volume, absolute bed time and hospitalization time in observation group was less than the control ($P<0.05$); The postoperative complications in observation group was less than the control ($P<0.05$). **Conclusion:** Using laparoscopic hepatocellular carcinoma treatment of hepatocellular carcinoma, it can reduce serum AFP, sEC, HGF, ICAM-1 level, and improve its therapeutic effect, and the incidence of complications is low.

Key words: Laparoscopy; Hepatocellular carcinoma; Alpha fetoprotein; Soluble E-cadherin; Hepatocyte growth factor; Intercellular cell adhesion molecule-1

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前言

肝细胞癌是一种全球范围常见的恶性肿瘤,具有较高的死亡率,其发病机制目前尚未明确,但通过临床研究发现其发病是一个多因素、多步骤的复杂过程,受到环境和遗传的双重因素影响^[1,2]。据相关研究表明,乙型肝炎病毒感染、丙型肝炎病毒感染、酒精性肝硬化为肝细胞癌的主要风险因素^[3]。肝细胞癌在

早期无典型的临床表现,因此多数患者在入院检查时多为中晚期。临床对于肝细胞癌的治疗主要通过开腹切除手术治疗,虽其治疗效果显著,但由于其暴露空间较大,易引发伤口感染,且术后并发症发生率较高。早在 1991 年则有学者通过研究报道了腹腔镜肝部分切除术,从而拉开了腹腔镜技术的序幕^[4]。随着医疗技术的不断发生与改,同时带动了微创技术的跨越一个新的高度,使的腹腔镜技术被广泛的运用于外科各个领域同时

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取得了较为满意的效果,且可减少术后并发症发生率。在各医院中对于肝细胞癌的治疗,腹腔镜切除术已逐渐占主导地位,且据国内外文献显示,开腹切除术与腹腔镜切除术对于肝细胞癌的根治性相差不异^[5,6]。但腹腔镜切除术对患者血清 AFP、sEC、HGF、ICAM-1 的影响相关文献较为罕见,本研究旨在观察腹腔镜肝癌切除术对肝细胞癌患者的治疗效果及对血清 AFP、sEC、HGF、ICAM-1 的影响。

1 资料与方法

1.1 一般资料

选择 2012 年 3 月至 2017 年 3 月在我院接受治疗的肝细胞癌患者 196 例,纳入标准:(1)病理检测符合《原发性肝癌诊

疗规范》中相关原发性肝细胞肝癌的诊断标准且确诊^[7];(2)术前未进行 TACE 等治疗;(3)预留的肝脏体积与标准肝脏体积比值大于 40%;(4)肝功能分级在 B 级及以上。排除标准:(1)存在肝内或远处转移病灶;(2)伴有严重的心脑血管疾病;(3)伴有凝血功能异常;(4)存在手术禁忌症;(5)合并其他恶性肿瘤。将入选患者根据治疗方案不同分为两组,观察组 98 例,其中男 43 例,女 55 例,年龄 30~64 岁,平均年龄(46.74±8.65)岁;肿瘤直径 1.8~7.6cm,平均直径(3.87±0.45)cm。对照组 98 例,其中男 47 例,女 51 例,年龄 29~65 岁,平均年龄(48.12±8.21)岁;肿瘤直径 2.1~8.9cm,平均直径(4.12±1.12)cm。两组患者性别、年龄、肿瘤直径、肿瘤位置等方面相比具有可比性,详见表 1。

表 1 两组患者的一般资料比较

Table 1 Comparison of general information between the two groups

Groups	n	M/F(n)	Age(year)	Tumor diameter(cm)	Single tumor/ Multiple tumor (n)	Tumor location(n)		
						II~III	IV	V~VI
Observation group	98	43/55	46.74±8.65	3.87±0.45	15/83	49(17.8)	33(55.6)	16(26.6)
Control group	98	47/51	48.12±8.21	4.12±1.12	18/80	52(22.2)	31(57.8)	15(20.0)

1.2 方法

所有患者经进行术前常规检测后,取仰卧位,给予气管插管下静脉全身麻醉。对照组患者给予开腹切除术,根据患者病灶位置确定切口,开腹后充分暴露肿物,对 1、2 肝门进行阻断,夹闭大血管与胆管,沿着病灶外缘 2 cm 处用电刀在肝脏表面划出拟切割线离断肝组织,用钳夹法离断肝脏。观察组给予腹腔镜切除术,将患者腹压控制为 12~15 mmHg,选脐下 2 cm 位置打孔置入腹腔镜,在腹腔镜下标记肿瘤的边缘,充分暴露肿瘤后使用解剖刀分离肿瘤,将肿瘤取出后进行常规止血,解除气腹,关闭穿刺口与切口。

1.3 观察指标

检测两组术前与术后 AFP、sEC、HGF、ICAM-1 水平以及肝功能(TBIL、DBIL、ALT、Alb),比较两组术中出血量、术后绝对卧床时间与住院时间;并观察术后两组并发症发生率。在

术前与术后第 2 天收集两组外周血 5 mL,离心处理后取上清液置于 -80℃ 环境中待检,采用放射免疫法检测 AFP 水平,采用酶联免疫吸附法检测 sEC、HGF、ICAM-1 水平。使用全自动生化分析仪检测 TBIL、DBIL、ALT、Alb 水平。

1.4 统计学分析

选择 spss18.0 进行数据统计,本研究数据比较计量资料采用 t 检验,计数资料采用 χ^2 检验,等级资料比较则用秩和检验,当 $P<0.05$ 时表示差异显著。

2 结果

2.1 两组血清 AFP、sEC、HGF、ICAM-1 水平比较

术前,两组血清 AFP、sEC、HGF、ICAM-1 水平无明显差异($P>0.05$);术后,患者血清 AFP、sEC、HGF、ICAM-1 水平均降低($P<0.05$);且观察组明显低于对照组($P<0.05$)。详见表 1。

表 2 两组治疗前后血清 AFP、sEC、HGF、ICAM-1 水平比较($\bar{x}\pm s$)

Table 2 Comparison of the serum AFP, sEC, HGF and ICAM-1 levels between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Time	AFP(ng/mL)	sEC(ng/mL)	HGF(μ g/L)	ICAM-1(ng/mL)
Observation group	98	Before operation	563.21±93.42	2664.45±420.43	2.11±0.34	987.32±125.43
		After operation	56.32±9.12 ^{ab}	2010.65±165.87 ^{ab}	0.38±0.06 ^{ab}	324.86±53.43 ^{ab}
Control group	98	Before operation	558.32±89.32	2631.64±417.32	2.08±0.32	974.43±113.17
		After operation	97.32±13.32 ^b	2156.42±167.32 ^b	0.43±0.07 ^b	415.75±68.32 ^b

Note: Compared with the control group, ^a $P<0.05$; Compared with before operation, ^b $P<0.05$.

2.2 两组肝功能比较

术前,两组患者肝功能比较未见差异($P>0.05$);术后,观察组 TBIL、DBIL、ALT 均明显低于对照组,Alb 则明显高于对照组($P<0.05$)。详见表 3。

2.3 两组术中出血量、绝对卧床时间与住院时间比较

观察组术中出血量、绝对卧床时间以及住院时间均明显低于对照组,差异具有统计学意义($P<0.05$),见表 2。

表 3 两组治疗前后肝功能指标比较($\bar{x} \pm s$)Table 3 Comparison of liver function indexes between the two groups before and after treatment($\bar{x} \pm s$)

Groups	n	Time	TBIL($\mu\text{mol/L}$)	DBIL($\mu\text{mol/L}$)	Alb(g/L)	ALT(U/L)
Observation group	98	Before operation	23.47 $\pm$ 3.42	5.71 $\pm$ 0.86	34.53 $\pm$ 5.21	40.92 $\pm$ 6.43
		After operation	32.14 $\pm$ 4.76 ^{ab}	7.94 $\pm$ 1.32 ^{ab}	31.23 $\pm$ 4.65 ^{ab}	95.53 $\pm$ 15.32 ^{ab}
Control group	98	Before operation	24.13 $\pm$ 4.02	5.68 $\pm$ 0.93	34.23 $\pm$ 5.15	39.76 $\pm$ 6.15
		After operation	36.04 $\pm$ 5.54 ^b	9.72 $\pm$ 1.28 ^b	29.76 $\pm$ 4.76 ^b	432.42 $\pm$ 71.43 ^b

Note: Compared with the control group, ^aP<0.05; Compared with before operation, ^bP<0.05.

表 4 两组术中出血量、绝对卧床时间与住院时间比较[(n)%]

Table 4 Comparison of efficacy between the two groups[(n)%]

Groups	n	Intraoperative blood loss(mL)	Absolute bed time(d)	Length of stay(d)
Observation group	98	137.53 $\pm$ 20.43 ^a	4.62 $\pm$ 0.73 ^a	7.21 $\pm$ 1.17 ^a
Control group	98	271.54 $\pm$ 37.43	6.83 $\pm$ 1.13	9.03 $\pm$ 1.43

Note: Compared with the control group, ^aP<0.05.

2.4 两组并发症比较

观察组胸腔积液、腹水、胆瘘、切口感染等并发症的发生率

低于对照组,差异具有统计学意义(P<0.05),两组接受保守治疗后均治愈,详见表 4。

表 5 两组并发症发生率比较[(n)%]

Table 5 Comparison of complication rate between the two groups[(n)%]

Groups	n	Pleural effusion	Hydrops abdominis	Subphrenic fluid	Biliary fistula	Incision infection	Total rate
Observation group	98	5(5.1)	8(8.2)	0(0.0)	5(5.1)	0(0.0)	18(18.4) ^a
Control group	98	7(7.1)	14(14.3)	2(2.0)	7(7.1)	5(5.1)	35(35.7)

Note: Compared with the control group, ^aP<0.05.

3 讨论

我国是肝细胞癌的高发区,此疾病死亡率极高,乙型肝炎病毒是致肝细胞癌病的一项主要因素,可通过降乙肝病的 DNA 整合至肝细胞的 DNA 中,从而导致肝细胞 DNA 发生病理变化引发癌病^[8-10]。目前临床对于肝细胞癌根治性的手段主要包括手术切除与肝移植^[11]。虽然肝移植术治疗其生存率较高,但由于此种手术难度较大、肝源较少,再加上拥有众多禁忌症等各种因素,导致此方法无法在临床上广泛使用。开腹切除术和腹腔镜切除术是目前临床较为常用的手术方式。与传统的开腹切除术相比,腹腔镜切除术具有术中出血量少、术后并发症少、住院时间短等优点^[12,13]。目前对于腹腔镜切除治疗肝细胞癌的直观疗效研究较多,但对机体相关血清指标的影响研究较少。

AFP 是一种糖蛋白,是通过新生的幼稚肝细胞所分泌,由于胎儿的肝细胞并没有发育完全,可大量分泌 AFP,导致孕妇血清 AFP 水平较高,但正常成人血清中 AFP 水平则极低^[14,15]。肝细胞癌是一种尚未分化的肝细胞发生癌变,机体会自动恢复生产 AFP 的功能,从而产生大量的 AFP,且随着病情的发展其在血清中的水平则急剧上升,因此目前临床已将高水平 AFP 作为肝细胞癌的主要标志物^[16]。sEC 是一种主要分布在上皮组织中的糖蛋白,其水平的表达在肝细胞癌的浸润与转移具有密切的关系^[17,18]。有研究表明,sEC 在肝细胞癌的发生发展中发挥重要作用,其可通过介导细胞以及细胞外基质的黏附活动,刺

激机体血管内皮细胞迁移,加速新生血管形成,从而促进肿瘤转移^[19-21]。

HGF 是一种重要的抗纤维化因子,具有广泛的生物活性,可刺激多种上皮细胞以及内皮细胞进行有丝分裂,促进肾小管形态生成;同时可促进肝脏受损后的组织修复、肝细胞增殖等作用^[22,23]。据相关研究显示,HGF 水平与肝细胞增殖、癌细胞侵袭以及转移有关^[24]。本研究中,患者在治疗前血清 HGF 水平显著升高,说明在肝细胞癌发生时,机体为保护肝脏组织,通过刺激肝脏组织生产大量的 HGF。此外,肝细胞癌的发生会释放出炎症因子,从而促进其他器官合成分泌 HGF,使患者血清 HGF 显著升高^[25]。ICAM-1 是免疫球蛋白超家族中的一员,可介导细胞与细胞间的相互作用^[26]。有研究发现,在正常的肝细胞中 ICAM-1 抗原是不存在的,而在肝癌细胞中其表达则明显加强^[27]。另有研究报道显示,肝细胞癌患者血清 ICAM-1 水平明显高于肝硬化患者^[28]。并且随着肿瘤生长,脱落于肿瘤细胞的 ICAM-1 会不断进入血液循环,形成一个保护肿瘤免遭机体免疫系统攻击的防御环境,从而不仅使血清 ICAM-1 水平升高,并且导致了病情逐渐恶化。

本研究结果显示,患者在进行切除术后,且血清 AFP、sEC、HGF、ICAM-1 均显著降低,相比与开腹切除术而言,腹腔镜切除术的效果更为显著。此外,无论是何种手术方式,均会对患者的肝脏造成不同程度的损害,但由于腹腔镜具有微创特性,相比之下,对肝脏的损害程度有所缓解。通过观察术后并发症发生情况发现,腹腔镜切除治疗后的患者其术后并发症发

生率显著降低,且无伤口感染病例出现。由此可见,使用腹腔镜肝癌切除术治疗肝细胞癌,可降低患者血清 AFP、sEC、HGF、ICAM-1 水平从而提高其治疗效果,且术后并发症发生率较低。

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