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手术切除与介入栓塞治疗肝癌术后复发患者的临床对比研究

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摘要 目的:比较手术切除与介入栓塞治疗肝癌术后复发患者的临床疗效。**方法:**选择 2010 年 6 月到 2011 年 6 月本院收治的 92 例肝癌手术切除术后复发患者,按随机数字表法分为手术切除组和介入栓塞组,各 46 例。手术切除组患者给予再次切除治疗,介入栓塞组患者给予介入栓塞治疗。记录并比较两组患者治疗后 1 年、3 年及 5 年的生存率。检测并比较两组患者治疗前后血清肝纤维化指标,包括血清透明质酸(HA)、层黏蛋白(LN)、人 III 型前胶原(HPC-III)及 IV 型胶原(IV-C)水平。检测并比较两组患者治疗前后血清白细胞(WBC)、甲胎蛋白(AFP)及癌胚抗原(CEA)水平。**结果:**手术切除组患者治疗后 1 年、3 年、5 年的生存率均明显高于介入栓塞组,差异均具有统计学意义(P<0.05)。治疗后,介入栓塞组血清 HA、LN、HPC-III 及 IV-C 明显高于治疗前,且均明显高于手术切除组,差异均具有统计学意义(P<0.05)。两组患者治疗后血清 WBC、AFP 及 CEA 水平均明显低于治疗前,且手术切除组患者血清 WBC 明显高于介入栓塞组,而血清 AFP、CEA 水平明显低于介入栓塞组,差异均具有统计学意义(P<0.05)。**结论:**手术切除治疗肝癌术后复发能够明显提高患者生存率,降低肝纤维化程度,改善血清 AFP 及 CEA 水平,值得在临床上推广应用。

关键词:手术切除;介入栓塞;肝癌术后复发;疗效

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Effect of Surgical Resection and Interventional Embolization on Patients with Recurrent Liver Cancer

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ABSTRACT Objective: To study the effect of surgical resection and interventional embolization on patients with recurrent liver cancer. **Methods:** A total of 92 patients with recurrent liver cancer in our hospital from June 2010 to June 2011 were enrolled in this study. The subjects were divided into the surgical resection group (n=46) and the interventional embolization group (n=46) according to the random number table method. The surgical resection group were treated with surgical resection once again, the interventional embolization group were treated with interventional embolization. The survival rates of the two groups at 1 year, 3 years and 5 years after treatment were recorded and compared. The serum hyaluronic acid (HA), laminin (LN), human procollagen type-III (HPC-III), and type IV collagen (IV-C) of the two groups before and after treatment were compared. The serum white blood cell (WBC), alpha fetal protein (AFP) and carcino embryonic antigen (CEA) of the two groups before and after treatment were compared. **Results:** The survival rates of 1 year, 3 years and 5 years after treatment of the surgical resection group were significantly higher than that of the interventional embolization group (P<0.05). After treatment, the serum HA, LN, HPC-III and IV-C of the interventional embolization group were significantly higher than before treatment (P<0.05), and that of the interventional embolization group were significantly higher than the surgical resection group (P<0.05). The serum WBC, AFP and CEA of the two groups after treatment were significantly lower than before treatment (P<0.05), and the serum WBC of the surgical resection group was significantly higher than the interventional embolization group, the serum AFP and CEA was significantly lower than the interventional embolization group (P<0.05). **Conclusion:** Surgical resection can significantly improve the survival rates of patients with recurrent liver cancer,reduce the degree of liver fibrosis, improve the serum levels of WBC, AFP and CEA, and it was worthy clinical application.

Key words: Surgical resection; Interventional embolization; Recurrent liver cancer; Efficacy

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前言

肝癌是临床常见的一种恶性肿瘤,在我国具有较高的发病率和病死率,其发病率居于各类恶性肿瘤的第三位,严重威胁着人们的身体健康[1]。肝癌在发病早期并没有典型的临床特征,因此大多数患者在临床确诊时往往已处于肝癌晚期,大多患者都错过了最佳的治疗时机,故临床治疗肝癌多采用肝部分切除的手段[2,3]。有研究表明[4],肝癌切除术后患者 5 年内的复发率高

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达 70%,导致患者术后生存期较短。因此,如何能够有效降低肝癌切除术后患者的复发率、延长患者生存期,是目前广大医学工作者研究的焦点。再次手术切除和介入栓塞治疗是临床上广泛应用的两种治疗手段,然而选用哪种手段仍旧存在较大的争议。再次手术切除能够彻底清除复发病灶,但对患者的二次创伤较为严重;介入栓塞治疗对患者创伤轻,但其所用化疗药物对正常细胞影响较大[5,6]。基于此,本研究探讨比较手术切除与介入栓塞治疗肝癌术后复发患者的临床疗效,研究结果如下。

1 资料与方法

1.1 一般资料

选择 2010 年 6 月到 2011 年 6 月我院收治的 92 例肝癌手术切除术后复发患者作为研究对象。病例纳入标准:(1)经病理学确诊为肝癌术后复发患者;(2) 未有远处转移或肝内弥散性转移;(3)肿瘤体积占肝体积少于一半以上。病例排除标准:(1)合并有其他恶性肿瘤患者;(2)不配合治疗患者;(3)肾功能不全患者;(4)有严重感染性疾病患者;(5)无可测量病灶患者。将 92 例所有入选患者按随机数字表法分为手术切除组和介入栓塞组,各 46 例。手术切除组患者,男 28 例,女 18 例;年龄 40-74 岁, 平均年龄 (63.35± 5.72) 岁; 体重 43-75 kg, 平均体重 (51.46± 4.82)kg;术后 1 年复发者 7 例、术后 2-3 年复发者 19 例、术后 3 年多复发者 20 例;复发肝癌分期:Ia 期 16 例、Ib 期 15 例、IIa 期 8 例、IIb 期 7 例。介入栓塞组患者,男 27 例,女 19 例;年龄 41-76 岁,平均年龄(64.29± 5.45)岁;体重 44-76kg,平均体重(53.64± 5.22)kg;术后 1 年复发者 6 例、术后 2-3 年复发者 16 例、术后 3 年多复发者 24 例;复发肝癌分期:Ia 期 17 例、Ib 期 16 例、IIa 期 7 例、IIb 期 6 例。两组患者性别、年龄、体重、复发情况、复发肝癌分期比较差异均无统计学意义(P>0.05),具有可比性。所有患者均知情同意且自愿加入本研究,并经医院伦理委员会批准。

1.2 实验方法

手术切除组患者于全身麻醉后给予再次切除治疗,切除范围为病灶以外 1cm,病灶范围较大需行不规则肝叶切除。介入栓塞组患者给予介入栓塞治疗,具体为:经皮穿刺患者一侧股动脉,将 5FRH 导管插入肝固有动脉造影,确定肿瘤功血动脉,行超声引导下插管于肝左动脉和肝右动脉,注入栓塞剂于复发病灶部位,栓塞剂组成为:表阿霉素(购自辉瑞制药(无锡)有限公司,规格 10 mg/ 瓶,国药准字 H20000496)60 mg、顺铂(购自齐鲁制药有限公司,规格 10 mg/ 瓶,国药准字 H37021358)100 mg 及 40%的碘化油 (购自上海旭东海普药业有限公司, 规格 10 mL/ 支,国药准字 H31021603)20 mL。两组患者均给予适当抗生素以防止感染。

1.3 检测指标

记录并比较两组患者治疗后 1 年、3 年及 5 年的生存率。两组患者均于治疗前后清晨空腹采集静脉血 5 mL, 以 3000 rpm 离心 10 min 以分离血清,检测并比较治疗前后血清白细胞(white blood cell,WBC)、甲胎蛋白(alpha fetal protein,AFP)及癌胚抗原(carcinoembryonic antigen,CEA)水平;检测并比较两组患者治疗前后血清肝纤维化指标,包括透明质酸(hyaluronic acid,HA)、层黏蛋白(laminin,LN)、人 III 型前胶原(human pro-collagen type-III,HPC-III)及 IV 型胶原(type IV collagen,IV-C)水平。

血清 WBC 水平的检测采用 XE-5000 全自动血液分析仪(购自 Sysmex 公司);血清 AFP、HA、LN、HPC-III 及 IV-C 水平的检测均采用双抗夹心酶联免疫(ELISA)法检测。ELISA 检测试剂盒均购自上海恪敏生物科技有限公司,具体操作严格按照试剂盒说明书进行;采用电化学发光微粒子免疫分析法检测血清 CEA 水平,所用仪器为购自美国贝克曼公司的 AIA-1800 型全自动酶免疫分析仪。

1.4 数据处理

使用 SPSS19.0 统计学软件,计数资料以百分率(%)表示,采用 x^2 检验,计量资料以均数± 标准差($\bar{x}$± s)表示,采用 t 检验,P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组患者治疗后不同时期生存率比较

手术切除组患者治疗后 1 年、3 年、5 年的生存率均明显高于介入栓塞组,差异均具有统计学意义(P<0.05)。见表 1。

表 1 两组患者治疗后不同时期生存率比较

Table 1 Comparison of the survival rates in two groups of different times after treatment

Groups	n	1 year after treatment	3 years after treatment	5 years after treatment
Surgical resection group	46	35(76.09)	22(47.83)	12(26.09)
Interventional embolization group	46	24(52.17)	10(21.74)	4(8.70)
x^2 value		5.718	6.900	4.842
P value		0.017	0.009	0.028

2.2 两组患者治疗前后肝纤维化指标比较

治疗前, 两组患者血清 HA、LN、HPC-III 及 IV-C 比较,差异无统计学意义(P>0.05);治疗后,介入栓塞组血清 HA、LN、HPC-III 及 IV-C 明显高于治疗前, 且均明显高于手术切除组,差异均具有统计学意义(P<0.05)。见表 2。

2.3 两组患者治疗前后血清 WBC、AFP 及 CEA 水平比较

治疗前, 两组患者血清 WBC、AFP 及 CEA 水平比较差异无统计学意义(P>0.05);治疗后,两组患者血清 WBC、AFP 及 CEA 水平均明显低于治疗前,且手术切除组患者血清 WBC 明显高于介入栓塞组,而血清 AFP、CEA 水平明显低于介入栓塞组,差异均具有统计学意义(P<0.05)。见表 3。

3 讨论

肝癌术后复发多是由于手术切除不彻底或术前患者已有的转移病灶受到手术影响而引发扩散[7]。肝癌术后复发率较高,严重影响手术治疗效果,缩短了患者术后的生存时间[8,9]。再次

手术切除和介入动脉栓塞治疗是临床上治疗肝癌术后复发的两种主要手段。再次手术切除能够彻底的清除患者病灶,虽然对患者的创伤较大,但治疗效果明显[10]。介入动脉栓塞是一种非根治性的治疗措施,阻断供应肝癌细胞的动脉血流,并注入高浓度的化疗药物来发挥杀灭癌细胞的作用[11-13]。有研究表明[14],介入动脉栓塞有引发或加重肝硬化的风险。另外,介入动脉栓塞还有阻断动脉不彻底,癌细胞从新的侧支循环扩散的危险,最终导致治疗的失败[15]。因此,选用哪种治疗手段用于肝癌术后复发患者的治疗,一直以来都是医学工作者研究的重点。本研究通过比较手术切除与介入栓塞治疗肝癌术后复发患者的临床疗效,并进一步分析对肝纤维化指标和血清 WBC、AFP 及 CEA 水平的影响,以期为临床治疗肝癌术后复发患者提供一定的思路。

表2 两组患者治疗前后肝纤维化指标比较

Table 2 Comparison of hepatic fibrosis indicators in the two groups before and after treatment

Groups	n	Times	HA(μg/L)	LN(μg/L)	HPC-III(μg/L)	IV-C(μg/L)
Surgical resection group	46	Before treatment	271.47± 40.52	113.42± 25.60	212.26± 42.93	108.43± 17.60
		After treatment	284.37± 55.60	118.76± 30.42	214.08± 46.13	109.61± 27.42
Interventional embolization group	46	Before treatment	273.55± 42.38	115.93± 26.45	213.55± 39.72	107.77± 16.84
		After treatment	359.84± 61.25*#	157.69± 21.45*#	282.59± 51.57*#	155.74± 20.05*#

Note: Compared with before treatment,*P<0.05; Compared with the surgical resection group, #P<0.05.

表 3 两组患者治疗前后血清 WBC、AFP 及 CEA 水平比较

Table 3 Comparison of the serum WBC, AFP and CEA levels in two groups before and after treatment

Groups	n	Times	WBC(× 109/L)	AFP (ug/L)	CEA(ug/L)
Surgical resection group	46	Before treatment	5.88± 1.12	893.46± 72.68	496.37± 45.46
		After treatment	5.25± 0.94*#	212.28± 50.38*#	173.36± 11.15*#
Interventional embolization group	46	Before treatment	5.90± 1.15	896.67± 73.41	489.95± 50.32
		After treatment	3.11± 0.51*	425.79± 68.49*	264.60± 17.43*

Note: Compared with before treatment, *P<0.05; Compared with the interventional embolization group, #P<0.05.

本研究结果显示,手术切除组患者治疗后 1 年、3 年、5 年的生存率均明显高于介入栓塞组,差异均具有统计学意义(P<0.05)。提示手术切除治疗肝癌术后复发能够明显提高患者的远期生存率。这可能是由于再次手术切除能够更加彻底的清除患者肝内复发病灶部位,治疗效果明显。而介入动脉栓塞治疗则有阻断动脉血管不彻底的风险,癌细胞很可能通过侧支循环进入到肝其他部位,导致治疗效果不理想[16,17]。本研究结果显示,治疗后,手术切除组患者各肝纤维化指标,包括 HA、LN、HPC-III 及 IV-C,均明显低于介入栓塞组,差异均具有统计学意义(P<0.05)。提示手术切除相比于介入动脉栓塞治疗能够明显降低肝癌术后复发患者的肝纤维化程度。这可能是由于介入动脉栓塞治疗在栓塞动脉部位注入高浓度的化疗药物和碘化油,而化疗药物和碘化油有可能进入到周边肝正常组织,从而损伤正常肝组织,引起肝纤维化[18,19]。另外本研究结果显示,治疗后,两组患者血清 WBC、AFP 及 CEA 水平均明显低于治疗前,且手术切除组患者血清 WBC 明显高于介入栓塞组,手术切除组患者血清 AFP、CEA 水平明显低于介入栓塞组,差异均具有统计学意义(P<0.05)。提示手术切除能够明显改善肝癌术后复发患者血清 AFP 及 CEA 水平。这可能是由于手术切除能够彻底清除病灶部位,从而相比于介入动脉栓塞治疗能够明显降低血清 AFP、CEA 水平,而手术切除相比于介入动脉栓塞治疗对患者的创口较大,导致患者血清 WBC 水平较高,针对此点,可以给予一定的抗炎治疗[20]。

综上所述,手术切除治疗肝癌术后复发能够明显提高患者生存率,降低肝纤维化程度,改善血清 AFP 及 CEA 水平,值得在临床上推广应用。

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