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解剖性肝叶切除与非解剖性肝叶切除治疗原发性肝癌的疗效对比研究 *

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摘要 目的：对比解剖性肝叶切除手术（AH）与非解剖性肝叶切除手术（NAH）治疗原发性肝癌（PHC）的疗效。**方法：**回顾性分析2015年1月~2018年3月期间我院收治的103例PHC患者的临床资料，根据手术方式的不同将患者分为对照组（n=54）和研究组（n=49），对照组给予NAH治疗，研究组给予AH治疗，比较两组围术期指标、黑色素瘤抗原-1（MAGE-1）mRNA、甲胎蛋白（AFP）mRNA阳性表达、肝功能指标、术后并发症及复发转移情况。**结果：**两组患者术后7d丙氨酸氨基转移酶（ALT）、天冬氨酸氨基转移酶（AST）、总胆红素（TBIL）均升高，但研究组低于对照组（*P*<0.05）。研究组住院时间短于对照组，术中出血量、术中输血量、术后引流量少于对照组（*P*<0.05），研究组手术时间长于对照组（*P*<0.05）。两组术后28d的MAGE-1 mRNA、AFP mRNA阳性表达率均有所降低，且研究组低于对照组（*P*<0.05）。研究组术后并发症发生率以及复发转移率均低于对照组（*P*<0.05）。**结论：**与NAH术式相比，AH治疗PHC患者可有效减轻肝功能损害，下调MAGE-1 mRNA、AFP mRNA阳性表达，降低术后并发症及复发转移发生率。

关键词：解剖性肝叶切除手术；非解剖性肝叶切除手术；肝切除术；原发性肝癌；疗效

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A Comparative Study of the Efficacy of Anatomical Hepatectomy and Non-anatomical Hepatectomy in the Treatment of Primary Hepatocellular Carcinoma*

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ABSTRACT Objective: To compare the efficacy of anatomical hepatectomy (AH) and non-anatomical hepatectomy (NAH) in the treatment of primary hepatocellular carcinoma (PHC). **Methods:** The clinical data of 103 patients with PHC who were admitted to our hospital from January 2015 to March 2018 were analyzed retrospectively. The patients were divided into control group (n=54) and study group (n=49) according to different surgical methods. The control group was treated with NAH, and the research group was treated with AH. Perioperative indicators, melanoma antigen-1 (MAGE-1) gene, alpha-fetoprotein (AFP) gene positive expression, liver function indicators, postoperative complications and recurrence and metastasis were compared between the two groups. **Results:** Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TBIL) were increased in both groups at 7 days after operation, but those in the study group were lower than those in the control group (*P*<0.05). The hospitalization time of the study group was shorter than that of the control group, and the intraoperative blood loss, intraoperative blood transfusion and postoperative drainage volume were less than those of the control group (*P*<0.05), while the operation time of the study group was longer than that of the control group (*P*<0.05). The positive expression rate of MAGE-1 mRNA and AFP mRNA in the study group were lower than those in the control group at 28 days after operation (*P*<0.05). The incidence of postoperative complications and recurrence and metastasis in the study group were lower than those in the control group (*P*<0.05). **Conclusion:** Compared with NAH operation, AH can effectively alleviate the damage of liver function, down-regulate the positive expression of MAGE-1 mRNA and AFP mRNA, reduce the incidence of complications and recurrence and metastasis.

Key words: Anatomical hepatectomy; Non-anatomical hepatectomy; Hepatectomy; Primary hepatocellular carcinoma; Efficacy

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前言

原发性肝癌（PHC）是由于肝细胞或肝内胆管上皮细胞发生癌变所致[1]。该病发病隐匿，恶性程度高，治疗难度大，极易导

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致患者死亡[2]。据统计[3],全球每年新发 PHC 人数约为 62 万人,而我国约占其中的 55%。肝叶切除术是治疗 PHC 的首选方式,根据解剖学原理可将其分为非解剖性肝叶切除手术(NAH)[4]与解剖性肝叶切除手术(AH)[5]。其中 NAH 为临床的常用术式,但存在切除范围不足的缺点,无法达到根治性切除肝细胞癌的目标[6,7]。AH 是近年来的临床研究热点,在切除病灶的同时,可最大程度的保留残余肝组织功能,有利于患者术后康复[8,9],但该术式对肝功能损伤较为严重的 PHC 患者的疗效有待加强,现临床有关这两种术式的疗效尚存在一定争议。本研究回顾性分析三六三医院分别经 NAH、AH 治疗的 PHC 患者的临床资料,并对比其临床疗效,以期为 PHC 患者术式的选择提供参考,现报道如下。

1 资料与方法

1.1 基线资料

回顾性分析 2015 年 1 月 ~2018 年 3 月期间我院收治的 103 例 PHC 患者的临床资料,此次研究经三六三医院伦理学委员会批准进行。纳入标准:(1)参考《原发性肝癌的临床诊断与分期标准》[10];(2)经影像学、实验室检查等确诊为 PHC;(3)均具备手术指征者;(4)预计生存期≥ 3 个月;(5)肝功能 Child-Pugh 分级[11]为 A 级或 B 级;(6)术前未行放化疗治疗者;(7)患者及其家属知情本次研究且已签署同意书。排除标准:(1)肝癌广泛转移者;(2)合并有精神疾病,依从性差者;(3)合并其他恶性肿瘤者;(4)合并感染性疾病、免疫性疾病者;(5)严重心肺肾等脏器功能不全者;(6)未能完成随访,中途失联者。根据手术方式的不同将患者分为对照组(n=54)和研究组(n=49),其中对照组男 32 例,女 22 例,年龄 43~71 岁,平均(54.28± 3.42)岁;Child-Pugh 分级:A 级 30 例,B 级 24 例;病灶直径 2.9~6.2 cm,平均(4.73± 0.26)cm。研究组男 28 例,女 21 例,年龄 40~68 岁,平均(53.92± 3.71)岁;Child-Pugh 分级:A 级 27 例,B 级 22 例;病灶直径 2.7~6.1 cm,平均(4.69± 0.33)cm。两组一般资料对比无差异(P>0.05)。

1.2 方法

研究组予以 AH 术式治疗,操作如下:全麻下气管插管,切口取双侧肋缘下,充分暴露肝脏后确认肿瘤位置。超声引导下明确即将切除的叶、肝段。跟踪门静脉与肝静脉,并确定肝脏的切除范围。于肝脏表面用电凝钩作出肝脏的切除范围,解剖第一肝门,选择性阻断半肝血流,继续解剖肝实质。解剖分离及切除肿瘤完成后,缝合切口,常规放置引流管。对照组患者给予 NAH 术式治疗,操作如下:操作如下:全麻下气管插管,切口取双侧肋缘下,充分暴露肝脏后确认肿瘤位置。超声引导下明确即将切除的叶、肝段。采用 Pringle 法阻断入肝血流,采用血管钳钳夹、电凝或刮吸法快速离断预备切除的肝组织。手术结束后清理手术野,将切口缝合,常规放置引流管。两组患者术后均给予常规护肝、预防感染、抗炎治疗。

1.3 观察指标

(1)抽取患者术前、术后 7d 的肘静脉血 4 mL,经 3600 r/min 离心 12 min,离心半径 8 cm,分离上清液,置于 -40℃冰箱中待测。采用美国贝克曼库尔特公司生产的 BEKMAN CX5 全自动生化检测仪检测肝功能指标:丙氨酸氨基转移酶(ALT)、天冬氨酸氨基转移酶(AST)、总胆红素(TBIL)。(2)于术前、术后 28d 抽取患者肘静脉血 4 mL,分离单个核细胞,提取 RNA,采用实时荧光定量 PCR 法检测黑色素瘤抗原 -1(MAGE-1)mRNA、甲胎蛋白(AFP)mRNA,严格遵守试剂盒(北京博奥森生物工程有限公司)的说明书进行操作,统计两组患者 MAGE-1 mRNA、AFP mRNA 阳性表达例数[12]。(3)记录两组患者术后并发症发生情况。(4)采用门诊复查的方式对术后患者进行为期 1 年的随访,统计复发及转移例数,随访终止指征为患者死亡。(5)记录两组围术期指标情况。

1.4 统计学方法

采用 SPSS20.0 进行数据分析。计数资料以例数及率的形式表示,组间比较行卡方检验。计量资料均为正态资料,以均值± 标准差的形式表示,组内治疗前后比较为配对 t 检验,组间比较行成组 t 检验。检验标准设置为 α=0.05。

2 结果

2.1 两组围术期指标比较

研究组住院时间短于对照组,术后引流量、术中出血量、术中输血量少于对照组(P<0.05);研究组手术时间长于对照组(P<0.05);详见表 1。

表 1 两组围术期指标比较($\bar{x}\pm s$)

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

Groups	Operation time(min)	Intraoperative bleeding volume(mL)	Hospitalization time(d)	Postoperative drainage volume(mL)	Intraoperative blood transfusion volume(mL)
Control group(n=54)	198.54± 58.64	519.07± 28.35	15.72± 1.89	255.35± 24.56	528.87± 22.87
Study group(n=49)	261.49± 60.93	424.10± 30.27	13.93± 1.43	186.41± 19.62	433.05± 20.31
t	5.341	16.441	5.378	15.635	22.390
P	0.000	0.000	0.000	0.000	0.000

2.2 肝功能指标比较

两组患者术前 ALT、AST、TBIL 比较无差异(P>0.05);两组患者术后 7d 的 ALT、AST、TBIL 均升高,但研究组低于对照组(P<0.05);详见表 2。

2.3 MAGE-1 mRNA、AFPmRNA 阳性表达率比较

两组术前 MAGE-1 mRNA、AFP mRNA 阳性表达率比较无差异(P>0.05);两组术后 28d 的 MAGE-1 mRNA、AFP mRNA 阳性表达率均有所降低,且研究组低于对照组(P<0.05);详见表 3。

2.4 术后并发症发生率比较

研究组术后并发症发生率为 12.24%(6/49),显著低于对照 组患者的 29.63%(16/54)(P<0.05);详见表 4。

表 2 两组肝功能指标比较($\bar{x}\pm s$)

Table 2 Comparison of liver function indexes between two groups($\bar{x}\pm s$)

Groups	ALT(U/L)		AST(U/L)		TBIL(μmol/L)	
	Preoperative	7d after operation	Preoperative	7d after operation	Preoperative	7d after operation
Control group (n=54)	54.24± 7.86	456.35± 33.48[a]	67.08± 13.86	432.99± 38.59[a]	17.65± 2.31	29.76± 2.49[a]
Study group(n=49)	54.19± 8.03	377.68± 32.39[a]	66.97± 15.31	351.16± 36.74[a]	17.73± 2.34	22.68± 2.81[a]
t	0.032	12.095	0.038	10.995	0.174	13.557
P	0.975	0.000	0.970	0.000	0.862	0.000

Note: Compared with preoperative, [a]P<0.05.

表 3 两组 MAGE-1 mRNA、AFPmRNA 阳性表达率比较($\bar{x}\pm s$)

Table 3 Comparison of positive expression of MAGE-1 mRNA and AFP mRNA in two groups ($\bar{x}\pm s$)

Groups	MAGE-1 mRNA		AFPmRNA	
	Preoperative	28d after operation	Preoperative	28d after operation
Control group(n=54)	28(51.85)	14(25.93)[a]	29(53.70)	21(38.89)[a]
Study group(n=49)	26(53.06)	5(10.20)[a]	27(55.10)	10(20.41)[a]
x^2	0.105	4.221	0.165	4.170
P	0.902	0.040	0.865	0.041

Note: Compared with preoperative, [a]P<0.05.

表 4 术后并发症发生率比较[n(%)]

Table 4 Comparisons of postoperative complications[n(%)]

Groups	Abdominal and thoracic infection	Pulmonary infection	Bile leakage	Liver failure	Total incidence
Control group(n=54)	4(7.41)	5(9.26)	3(5.56)	4(7.41)	16(29.63)
Study group(n=49)	1(2.04)	2(4.08)	1(2.04)	2(4.08)	6(12.24)
x^2					4.628
P					0.032

2.5 两组患者随访期间复发情况

随访期期间,对照组肝内复发 16 例,肝外转移 12 例,复发转移率为 51.85%(28/54); 研究组肝内复发 9 例, 肝外转移 3 例,复发转移率为 24.49%(12/49);研究组复发转移率低于对照组(x^2=8.097,P=0.004)。

3 讨论

PHC 作为常见的消化系统恶性肿瘤之一,占据我国恶性肿瘤死亡的第一位,已成为严重危害我国人民身体健康的恶性疾病。目前其发病机制尚不十分明确,既往认为与遗传、寄生虫感染、肝炎病史等因素相关[13]。多数 PHC 患者早期临床症状不典型,当典型症状出现时则已处于中晚期,预后较差[14]。PHC 的治疗方案多样,其中手术切除仍是其最基础、最有效的手段之一[15]。由于我国 PHC 具有其自身特点,绝大多数 PHC 患者常合并不同程度的肝硬化及肝功能损害,因此,以往传统的手术切除多以 NAH 为主,尤其针对小肝癌的治疗,疗效较佳[16],但由于 NAH 仅在手指触摸指导下完成, 肿瘤范围估算存在一定差异,极易造成切缘癌残留,增加术后残留切缘癌残复发风险[17]。以往患者及其临床工作者对手术质量的评价多局限于彻底清除病灶模式,随着医学模式的发展,该模式已逐渐发展成为最大脏器保护、最小伤害侵袭以及最佳术后康复的多维度综合模式[18,19]。在此背景下,AH 应运而生,伴随着术前肝功能检测技术的进步、手术器械的发展以及肝脏解剖学的深入了解,AH 日益受到临床重视,AH 是指预先切断病侧肝叶的入肝血流后,随后根据外科解剖的肝叶、肝段、半肝或肝三叶的范围切除肝组织[20,21]。

本研究结果中,研究组术后引流量、住院时间、术中出血量、术中输血量均优于对照组,可见 AH 可有效改善围术期部分指标, 这主要是因为 AH 手术步骤严格遵守 Couinaud 提出的 8 段分肝法,可行单独的肝段甚至亚肝段切除,可减少患者术中损伤,术后恢复快,减少住院时间,加之 AH 离断肝实质时对胆管和大血管的损害接近于无,可维持侧肝组织完整的血供运行,减少术中出血量、术中输血量[22-24]。而研究中研究组手术时间长于对照组, 这主要是因为 NAH 因阻断入肝血流必须在

一定时间内完成,而 AH 手术过程中的断肝过程又属于精细手术操作,致使 AH 手术时间较长。本研究结果显示,两组患者术后肝功能均有一定损伤,但研究组肝功能损伤程度较对照组减轻,表明 AH 术式可有效减轻肝功能损害。这与吕运海等人[25]研究基本一致,这可能与 AH 为选择性入肝血流阻断,肝断面出血减少,避免剩余肝脏缺血再灌注损伤,最大程度的保护剩余肝脏组织功能[26,27]。MAGE-1 属于 CT 抗原家族,其在肝癌组织中具有较高的表达率[28]。AFP 是一种血清单链糖蛋白,在健康群体中含量极低,然而当机体处于癌变状态时,AFP 合成基因被激活,其水平迅速升高[29]。本研究中两组患者 MAGE-1 mRNA、AFP mRNA 阳性表达率均有所改善,且研究组改善效果更佳。提示 AH 可更好的切除肝脏肿瘤,防止肿瘤扩散,究其原因,AH 术式中可将肝脏的门静脉及其分支切除,有效改善术后肿瘤扩散,同时还可确保切缘处无残留的肿瘤组织。本次研究结果还证实,研究组术后并发症及复发转移的发生率均低于对照组,充分说明 AH 在临床 PHC 治疗中的安全性和实用性更好,这与周超毅等人[30]的研究基本一致。

综上所述,与 NAH 术式相比,AH 治疗 PHC 可有效改善部分临床指标,减轻肝功能损害,降低 MAGE-1 mRNA、AFP mRNA 阳性表达率,减少术后并发症及复发转移,临床应用价值较高。

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(下转第 1527 页)

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