doi: 10.13241/j.cnki.pmb.2020.16.036

不同肝血流阻断方式肝切除手术对原发性肝癌合并肝硬化患者肝功能及肠黏膜屏障的影响 *

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摘要 目的：探讨肝切除手术运用 Pringle 法阻断、半肝血流阻断（HVC）后对原发性肝癌合并肝硬化患者肝功能及肠黏膜屏障的影响。**方法：**选取 2016 年 4 月 ~2019 年 9 月期间我院收治的原发性肝癌合并肝硬化患者 93 例，根据随机数字表法将患者分为 A 组（n=46，Pringle 法阻断）和 B 组（n=47，HVC），比较两组患者围术期指标、肝功能指标[谷丙转氨酶（ALT）、谷草转氨酶（AST）以及总胆红素（TBIL）]、肠黏膜屏障指标[D- 乳酸，内毒素]及并发症发生情况。**结果：**两组阻断时间、术中失血量、手术时间比较无差异（*P*>0.05）；B 组住院时间短于 A 组（*P*<0.05）。两组术前、术后 3 d、术后 7 d ALT、AST、TBIL 呈升高后降低趋势，且 B 组低于 A 组（*P*<0.05）。两组患者术后并发症发生率比较无差异（*P*>0.05）。两组术前、术后 3 d、术后 7dD- 乳酸、内毒素呈升高后降低趋势，且 B 组低于 A 组（*P*<0.05）。**结论：**与 Pringle 法阻断相比，原发性肝癌合并肝硬化患者在肝切除手术中运用 HVC，可有效缩短住院时间，减轻肝功能及肠黏膜屏障损害，且不增加并发症发生率，临床应用价值较高。

关键词：Pringle 法阻断；半肝血流阻断；原发性肝癌；肝硬化；肝功能；肠黏膜屏障

中图分类号：R735.7 **文献标识码：**A **文章编号：**1673-6273(2020)16-3164-04

Effect of Hepatectomy with Different Hepatic Blood Flow Blocking Methods on Liver Function and Intestinal Mucosal Barrier in Patients with Primary Liver Cancer and Cirrhosis*

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ABSTRACT Objective: To investigate the effect of different hepatic blood flow blocking methods of hepatectomy on liver function and intestinal mucosal barrier in patients with primary liver cancer and cirrhosis. **Methods:** 93 patients with primary liver cancer and cirrhosis who were treated in our hospital from April 2016 to September 2019 were selected, they were divided into group A (n=46, Pringle method) and group B (n=47, HVC) according to the random number table method. Perioperative indexes, liver function indexes [alanine aminotransferase (ALT), transglutaminase (AST), total bilirubin (TBIL)], intestinal mucosal barrier indexes [D-lactate, endotoxin] and complications were compared between the two groups. **Results:** There was no significant difference in intraoperative block time, blood lossand operation time between the two groups (*P*>0.05), the hospitalization time of group B was shorter than that of group A (*P*<0.05). The ALT, AST and TBIL in the two groups were increased and decreased 3 d and 7 d after operation, and the level in group B was lower than that in group A (*P*<0.05). There was no difference in the incidence of postoperative complications between the two groups (*P*>0.05). The levels of D-lactate and endotoxin in group B were lower than those in group A(*P*<0.05). **Conclusion:** Compared with Pringle method, HVC can effectively shorten the hospitalization time, reduce the damage of liver function and intestinal mucosa barrier, and do not increase the incidence of complications, so it has a higher clinical application value.

Key words: Pringle block; Hemihepatic Blood flow block; Primary liver cancer; Liver cirrhosis; Liver function; Intestinal mucosal barrier

Chinese Library Classification(CLC): R735.7 Document code: A

Article ID: 1673-6273(2020)16-3164-04

前言

原发性肝癌是临床常见的消化道恶性肿瘤，我国每年新增肝癌病例数约占全球每年新增肝癌病例数的一半[1]。该病早期

* 基金项目：国家自然科学基金面上项目（31571184）；广西壮族自治区卫生和计划生育委员会自筹经费科研项目（Z20170117）

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（收稿日期：2020-02-27 接受日期：2020-03-24）

发病隐匿,无特异性症状,不少患者确诊时已处于中晚期,死亡率高[2,3]。根据最新流行病学调查研究可知[4],超过 90%的原发性肝癌患者伴有病毒性肝炎且存在不同程度的肝硬化。肝切除手术是治疗该病的主要方法,可有效改善患者预后,但因为肝脏血流丰富,术中出血量的大小可直接影响患者手术疗效[5,6]。Pringle 法阻断[7]、半肝血流阻断(Hemihepatic vascular occlusion,HVC)[8]均是临床常见的血流阻断方式,但关于两种阻断方式的具体疗效孰优孰劣尚存在一定的争议。鉴于此,本研究通过探讨肝切除手术运用 Pringle 法阻断、半肝血流阻断(HVC)后对原发性肝癌合并肝硬化患者的影响,以期为临床原发性肝癌合并肝硬化患者行肝切除术时血流阻断方式的选择提供数据支持,现报道如下。

1 资料与方法

1.1 一般资料

选取 2016 年 4 月 ~2019 年 9 月期间我院收治的原发性肝癌合并肝硬化患者 93 例,纳入标准:纳入标准:(1)术前超声、CT、MRI 证实肝占位、肝硬化;(2)术后病理检查证实原发性肝癌合并肝硬化;(3)术前未接受放疗、化疗及介入治疗者;(4)患者及其(或被委托)家属知情本研究且签署了同意书;(5)均符合手术指征者。排除标准:(1)术前存在肝内 / 肝外转移、肿瘤侵及腔静脉以及伴门脉及肝静脉癌栓;(2) 合并其他恶性肿瘤者;(3)术后严重并发症甚至行二次手术者;(4)合并心肝肾等脏器功能不全者;(5)合并凝血功能障碍者。根据随机数字表法将患者分为 A 组 (n=46,Pringle 法阻断) 和 B 组(n=47,HVC),其中 A 组男 38 例,女 8 例;年龄 46~71 岁,平均(59.82± 5.41)岁;肝功能 Child 分级 A 级 32 例,B 级 14 例;肿瘤大小 1~8 cm,平均(4.34± 0.86)cm;体质量指数 20.4~26.8 kg/m^2,平均(23.29± 0.88)kg/m^2。B 组男 39 例,女 8 例;年龄 45~73 岁,平均(60.18± 4.97)岁;肝功能 Child 分级 A 级 33 例,B 级 14 例;肿瘤大小 2~8 cm,平均(4.17± 0.98)cm;体质量指数 20.8~26.3 kg/m^2,平均(23.51± 0.74)kg/m^2。两组一般资料对比未见统计学差异(P>0.05),具有可比性。本次研究已获取我院医学伦理学委员会批准进行。

1.2 方法

A 组给予 Pringle 法阻断,游离肝脏后经文氏孔绕过肝十二指肠韧带乳胶管,定位切除范围后,将十二指肠韧带扎紧,阻断全部肝蒂血供,切除肝肿瘤。一次阻断时间不超过 20 min,若超过 20 min,则给予间歇性阻断,最多阻断 2 次,间隔时间 >5 min。B 组给予 HVC,游离肝脏,暴露十二指肠韧带,采用组织剪等游离肝左右动脉,随后采用血管夹阻断病侧半肝动脉。肝固有动脉深面使用一根乳胶管经文氏孔连接肝十二指肠韧带,切除肝脏肿瘤。

1.3 观察指标

(1)记录两组阻断时间、术中失血量、住院时间、手术时间。(2)记录术后并发症发生情况。(3)分别采集两组患者术前、术后 3 d、术后 7 d 晨起空腹静脉血 5 mL,经 3200 r/min 离心 16 min,离心半径 12 cm,取上清液,冻存于 -40℃冰箱中。采用罗氏 Modular 全自动生化分析仪检测肝功能指标:谷丙转氨酶(Alanine aminotransferase,ALT)、谷草转氨酶(Glutamic oxaloacetylase,AST)、以及总胆红素(Total bilirubin,TBIL)。采用酶学分光光度法检测 D- 乳酸,采用偶氮显色法鲎试验定量测定内毒素浓度,均严格遵守说明书进行操作(试剂盒购自深圳芬德生物技术有限公司)。

1.4 统计学方法

采用 SPSS25.0 软件进行统计分析,计数资料以比或率的形式表示,采用 χ^2 检验,计量资料以($\bar{x}\pm s$)的形式表示,采用 t 检验。以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组围术期指标比较

两组阻断时间、术中失血量、手术时间比较无差异(P>0.05);B 组住院时间短于 A 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 the two groups($\bar{x}\pm s$)

Groups	Intraoperative blood loss (mL)	Blocking time(min)	Operative time(min)	Length of stay(d)
Group A(n=46)	414.58± 23.41	21.46± 1.44	150.84± 10.57	12.32± 1.25
Group B(n=47)	413.97± 22.39	20.98± 1.63	152.92± 9.51	8.41± 0.97
t	0.128	1.504	0.998	16.874
P	0.898	0.136	0.321	0.000

2.2 两组肝功能指标比较

两组术前 ALT、AST、TBIL 比较无差异(P>0.05);两组术前、术后 3 d、术后 7 d ALT、AST、TBIL 呈升高后降低趋势,且 B 组低于 A 组(P<0.05);详见表 2。

2.3 两组肠粘膜屏障功能指标比较

两组术前 D- 乳酸、内毒素比较差异无统计学意义(P>0.05);两组术前、术后 3 d、术后 7 d D- 乳酸、内毒素呈升高后降低趋势,且 B 组低于 A 组(P<0.05);详见表 3。

2.4 两组并发症发生率比较

A 组术后出现肺部感染 2 例、胆漏 1 例、腹腔积液 3 例,并发症发生率为 13.04%(6/46);B 组术后出现肺部感染 1 例、胆漏 1 例、腹腔积液 2 例,并发症发生率为 8.51%(4/47);两组患者术后并发症发生率比较无差异(χ^2=0.498,P=0.480)。

3 讨论

肝脏表面包括肝十二指肠韧带以及肝胃韧带,解剖结构复

表 2 两组肝功能指标比较($\bar{x}\pm s$)

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

Groups	ALT(U/L)			AST(U/L)			TBIL(μmol/L)		
	Before operation	3 d after operation	7 d after operation	Before operation	3 d after operation	7 d after operation	Before operation	3 d after operation	7 d after operation
Group A (n=46)	52.64± 6.33	482.96± 29.13[a]	366.90± 22.78[ab]	17.65± 2.29	45.63± 3.49[a]	36.28± 4.48[ab]	20.85± 2.43	48.54± 2.64[a]	33.07± 3.35[ab]
Group B (n=47)	51.98± 7.47	375.82± 29.28[a]	241.69± 18.16[ab]	17.92± 2.32	37.32± 4.82[a]	21.34± 4.51[ab]	19.93± 2.38	36.49± 2.93[a]	26.10± 3.27[ab]
t	0.459	17.688	26.841	0.565	21.538	26.726	1.845	20.822	10.154
P	0.647	0.000	0.000	0.574	0.000	0.000	0.068	0.000	0.000

Notes: compared with before operation, [a]*P*<0.05; compared with 3 d after operation , [b]*P*<0.05.

表 3 两组肠粘膜屏障功能指标比较($\bar{x}\pm s$)

Table 3 Comparison of intestinal barrier function between the two groups($\bar{x}\pm s$)

Groups	D- lactic acid(μg/mL)			Endotoxin(μg/mL)		
	Before operation	3 d after operation	7 d after operation	Before operation	3 d after operation	7 d after operation
Group A(n=46)	0.47± 0.08	17.66± 2.53[a]	12.65± 2.67[ab]	0.06± 0.01	0.19± 0.03[a]	0.14± 0.02[ab]
Group B(n=47)	0.49± 0.09	13.95± 3.24[a]	7.82± 1.39[ab]	0.07± 0.01	0.15± 0.02[a]	0.09± 0.01[ab]
t	1.132	6.146	10.976	4.822	7.581	15.298
P	0.261	0.000	0.000	0.000	0.000	0.000

Notes: compared with before operation, [a]*P*<0.05; compared with 3d after operation, [b]*P*<0.05.

杂,血液供给丰富[9-11]。我国作为原发性肝癌多发大国,原发性肝癌一直是影响我国人民生命健康的重要公共卫生问题。肝切除手术是治疗肝癌的主要方法,但以往研究表明[12,13],原发性肝癌患者多合并乙肝或肝硬化,肝功能储备能力较差。此时,合理的控制入肝血流可为肝切除手术的顺利进行提供便利,但入肝血流的截断也会造成不同程度的肝功能损伤。Pringle 法阻断技术始于 1908 年,此类阻断技术可完全阻断肝动脉及门动脉入肝血流,可避免长时间缺血导致的继发损伤,止血迅速[14,15]。但不少临床实践发现 Pringle 法几乎阻断了所有的入肝血流,一定程度上影响肝脏功能失去代偿能力,严重者甚至可影响肠粘膜屏障功能[16,17]。HVC 则于 1987 年问世,此类阻断技术可保留健侧半肝正常血流,选择性的切断患侧半肝静脉和动脉入肝血流,为精细手术的操作争取更多时间[18-20]。

本次研究结果显示,两组术中失血量、阻断时间、手术时间比较无差异,但 B 组住院时间短于 A 组。可见 HVC 与 Pringle 法阻断手术操作难度大致相当,同时 HVC 可促进患者术后恢复。这可能是因为 HVC 可为正常健侧肝脏组织提供正常的血液供应,减少对肝脏的缺血再灌注损伤,加快患者术后恢复[21,22]。进一步检测肝功能指标发现,两组患者术后均有不同程度的肝功能损伤,但 HVC 的肝功能损伤程度明显更轻。究其原因,HVC 在减少出血的同时还可减少对肝脏的缺血再灌注损伤,不造成内脏充血及血液动力学重大改变,可避免肝功能的进一步损害,使肝脏功能继续代偿[23-25]。肠道作为外科应激反应的中心器官,机体应激过度或失调均可累及肠粘膜屏障[26]。既往动物实验证实进行门静脉阻断等肝胆外科操作时会导致细菌易位,且肠道细菌易位与阻断时间、肠道淤血程度等息息相关[27]。本研究结果显示 HVC 可有效减轻肠黏膜屏障损害。究其原因,Pringle 法可导致门静脉完全阻断,影响肠道血液回流,导致肠黏膜绒毛出现缺血、缺氧状况,引起肠粘膜屏障损害,加之 Pringle 法无法一次性完成肝切除手术,需多次、交替阻断,肝脏的缺血再灌注损伤又进一步加重黏膜机械性损伤[28,29]。而 HVC 可使肠黏膜的血流通过健侧肝脏回流入体循环,避免出现肝脏失代偿后造成的肠黏膜损伤现象[30]。另两组术后并发症发生率比较无差异,可见 Pringle 法阻断、HVC 均安全可靠。此外,HVC 需要分离肝门,并且在阻断肝血流时,未阻断半肝平面会持续性出血,对术者具有较高的操作要求。术者应根据视患者具体情况灵活运用肝血流阻断术,尽可能减少术中损伤,促进患者术后恢复。

综上所述,与 Pringle 法阻断相比,原发性肝癌合并肝硬化患者在肝切除手术中运用 HVC,可有效缩短住院时间,减轻肝功能及肠黏膜屏障损害,且不增加并发症发生率,临床应用价值较高。

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