

· 临床研究 ·

70 岁以上肝癌患者肝切除术安全性分析

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【摘要】 目的 分析 70 岁以上老龄肝癌患者肝切除术资料并探讨其安全性。方法 回顾性分析 2014 年 1 月至 2016 年 1 月南京医科大学附属淮安第一医院老年肝癌患者行肝切除术的资料。根据年龄将患者分为 ≥ 70 岁组 ($n = 68$) 和 < 70 岁组 ($n = 84$), 分析两组术前临床资料[乙型肝炎表面抗原 (HBsAg) 阳性率、合并症、实验室指标、吲哚菁绿 (ICG) 15 min 滞留率、Child-Pugh 肝功能分级、甲胎蛋白 (AFP) 异常比例、肿瘤病理情况]、选择腹腔镜肝切除比例、术中出血量、手术时间、术后并发症发生率和死亡率、术后重症监护室 (ICU) 入住率、术后住院时间等指标。组间比较采用独立样本 t 检验、卡方检验或确切概率法。结果 ≥ 70 岁组与 < 70 岁组比较, 术前 HBsAg 阳性率、血红蛋白 (Hb) 水平均较低 [29.4% vs 71.4%, (128.18 ± 15.26) vs (138.57 ± 16.67) g/L, $P < 0.05$], 高血压较多 (38.2% vs 14.3%), 差异均有统计学意义 ($P < 0.05$); 两组选择腹腔镜肝切除比例、术中出血量、手术时间差异无统计学意义 ($P > 0.05$); ≥ 70 岁组术后心血管事件发生率 (13.2% vs 2.4%) 及术后 ICU 入住率 (48.5% vs 17.9%) 与 < 70 岁组比较更高 ($P < 0.05$), 但术后其他并发症、死亡率及术后住院时间等两组之间差异无统计学意义 ($P > 0.05$)。结论 严格掌握适应证、重视围手术期处理, 70 岁以上肝癌患者行肝切除是可行的。

【关键词】 肝切除术; 手术后并发症; 老年人

【中图分类号】 R735.7; R592 **【文献标志码】** A **【DOI】** 10.11915/j.issn.1671-5403.2017.12.214

Clinical analysis on hepatectomy in ≥ 70 years patients with hepatocellular carcinoma

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【Abstract】 Objective To analyze the clinical data of the elderly undergoing hepatectomy and investigate the safety of the surgery. **Methods** Clinical data of the patients undergoing hepatectomy for hepatocellular carcinoma in our department from January 2014 to January 2016 were collected and retrospectively analyzed. According to their age, they were divided into the ≥ 70 years group ($n = 68$) and < 70 years group ($n = 84$). Their comorbidities, tumor differentiation, Child-Pugh classification, and pre-operative positive rate of hepatitis B surface antigen (HBsAg), ratio of abnormal alpha fetoprotein (AFP), other laboratory indices, and indocyanine green retention rate at 15 min (ICG 15 min), as well as operation-related indices, such as, ratio of laparoscopic hepatectomy, operation time, blood loss during operation, postoperative ratio of intensive care unit (ICU) stay, length of postoperative hospital stay, incidences of postoperative complications, and postoperative mortality, were analyzed and compared between the 2 groups. The inter-group comparison was carried out with independent sample t test, Chi-square test or exact probability test. **Results** Compared with the < 70 years group, the ≥ 70 years group had a significantly lower pre-operative positive rate of HBsAg (29.4% vs 71.4%), lower level of hemoglobin [Hb, (128.18 ± 15.26) vs (138.57 ± 16.67) g/L], but higher ratio of hypertension (38.2% vs 14.3%). There were no obvious differences in the ratio of laparoscopic hepatectomy, operation time, and peri-operative blood loss between the 2 groups ($P > 0.05$). The incidences of post-operative cardiovascular events (13.2% vs 2.4%) and ratio of ICU stay (48.5% vs 17.9%) were notably higher in the ≥ 70 years group than in < 70 years group ($P < 0.05$), though no significances were found in postoperative complications, mortality and length of hospital stay between the 2 groups ($P > 0.05$). **Conclusion** It is feasible to perform hepatectomy in the ≥ 70 years patients with hepatocellular carcinoma after strict indication and careful perioperative management.

【Key words】 hepatectomy; postoperative complications; aged

This work was supported by the Social Development of Huai'an (HAS2014011).

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肝切除术是治疗一些肝脏良恶性疾病的重要手段,随着近些年人们平均寿命的迅速增长,老年行肝切除术比例也在不断增加^[1,2]。然而高龄患者常合并有高血压、糖尿病、冠心病及肺部疾病等各种基础病,有可能对预后带来不利影响^[3]。关于高龄患者肝切除的报道很多,但结果一直存在争议^[4,5]。一些研究认为,高龄患者行肝切除会增加并发症的发生率及死亡率^[4,6],其他学者则认为年龄不是术后并发症及死亡率的危险因素^[7,8]。本文回顾性分析南京医科大学附属淮安第一医院 ≥ 70 岁老年肝癌患者行肝切除术的资料,探讨其安全性。

1 对象与方法

1.1 研究对象

收集本院 2014 年 1 月至 2016 年 1 月行肝癌根治性切除术患者 138 例,年龄(64.74 ± 11.29)岁,根据年龄将患者分为 ≥ 70 岁组($n=68$)和 <70 岁组($n=84$)。纳入标准:(1)肿瘤无肝外转移,无门静脉主干或下腔静脉癌栓;(2)肿瘤及卫星病灶局限于预计切除的范围内,剩余肝脏可以满足正常生理需求。排除标准:(1)术前接受过介入治疗、全身化疗或放疗;(2)肝癌复发。

1.2 方法

1.2.1 手术选择 基于肝脏功能、肿瘤数量及大小选择手术方式,其中肝功能的评估采用 Child-Pugh 分级及吲哚菁绿(indocyanine green, ICG)15 min 滞留率^[9]:Child A 和 B 级符合手术标准,Child C 级为肝切除的禁忌证;胆红素正常且无腹水的患者,ICG 15 min 滞留率是评估可切除性的重要手段。另外,术前通过 B 超、CT 及磁共振成像(magnetic resonance imaging, MRI)等影像学检查评估残留肝体积,从而决定肝切除是否可行。在整个研究过程中, ≥ 70 岁组与 <70 岁组的手术指征无差异。

1.2.2 临床资料 收集患者如下临床资料。(1)术前:包括乙型肝炎表面抗原(hepatitis B surface antigen, HBsAg)阳性率、合并症(高血压和糖尿病)、实验室指标[血红蛋白(hemoglobin, Hb)、凝血酶原时间(prothrombin time, PT)、白蛋白(albumin, ALB)、总胆固醇(total cholesterol, TC)、血肌酐(serum creatinine, SCr)和总胆红素(total bilirubin, TB)]、ICG 15 min 滞留率、Child 肝功能分级、甲胎蛋白(alpha-fetoproteins, AFP)水平异常比例(AFP 正常值: $0 \sim 8.78 \mu\text{g/L}$)、肿瘤分化程度、大小及数量;(2)术中:行腹腔镜肝切除术比例、术中出血量和手术时间;(3)术后:手术后患者并发症发生率、死亡

率、术后重症监护室(intensive care unit, ICU)入住率及术后住院时间。

1.2.3 术后并发症的评估 心血管事件:包括心力衰竭及心律失常。腹腔出血:需要介入治疗或手术治疗的出血。肝功能不全:包括肝功能衰竭、难治性胸水及需药物治疗的腹水。胆瘘:引流管内持续 5 d 以上有胆汁流出。感染:包括腹腔感染、肺部感染、泌尿系统感染及切口感染。胸腔积液:患者需要穿刺或引流来改善呼吸功能不全的情况。手术死亡率:术后 30 d 内发生的死亡。

1.3 统计学处理

采用 SPSS 16.0 统计软件进行分析。计量资料采用均数 $\pm$ 标准差($\bar{x} \pm s$)表示,进行方差齐性检验,方差齐资料进行独立样本 t 检验,方差不齐资料进行非参数检验。计数资料采用百分率 $[n(\%)]$ 表示,组间比较采用卡方检验或确切概率法。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者术前情况比较

两组患者年龄差异显著,有统计学意义($P < 0.05$);病因学上, ≥ 70 岁组 HBsAg 阳性率与 <70 岁组相比更低($P < 0.05$);在合并症中, ≥ 70 岁组与 <70 岁组比较高血压更多;实验室指标中 Hb 更低;肿瘤分化程度更高($P < 0.05$);在一些肝功能指标上,ICG 15 min 滞留率、Child-Pugh 分级两组差异无统计学意义($P > 0.05$), ≥ 70 岁组 AFP 异常率则低于 <70 岁组($P < 0.05$;表 1)。

2.2 两组患者术中及术后情况比较

两组患者手术时间及术中出血量比较,差异无统计学意义($P > 0.05$)。术后 ≥ 70 岁组心血管事件发生率高于 <70 岁组,差异有统计学意义($P < 0.05$),其他并发症发生率无显著差异($P > 0.05$); ≥ 70 岁组患者术后 ICU 入住率高于 <70 岁组,组间差异具有统计学意义($P < 0.05$),但两组患者在术后住院时间及死亡率差异无统计学意义($P > 0.05$;表 2)。

3 讨论

肝癌发病率居高不下,手术切除是治疗肝癌的有效手段,随着人口老龄化,越来越多的高龄肝癌患者开始接受手术治疗。研究表明,在评价肝功能储备能力上,高龄肝癌患者 ICG 15 min 滞留率与非高龄肝癌患者无明显差异^[9-12]。本文首先将 ≥ 70 岁患者基本特征与 <70 岁患者进行比较,发现两组 ICG 15 min 滞留率无显著差异,与之前研究相符,且

表 1 两组患者术前临床特征比较
Table 1 Comparison of preoperative clinical features between two groups

Item	≥70 years group (n = 68)	<70 years group (n = 84)	P value
Age (years, $\bar{x} \pm s$)	73.20 ± 2.78	54.43 ± 8.79	0.000
Male[n(%)]	42(61.8)	57(67.9)	0.433
HBsAg[n(%)]	20(29.4)	60(71.4)	0.000
Comorbidities[n(%)]			
Hypertension	26(38.2)	12(14.3)	0.001
Diabetes mellitus	10(14.7)	9(10.7)	0.459
Laboratory indices($\bar{x} \pm s$)			
Hb(g/L)	128.18 ± 15.26	138.57 ± 16.67	0.013
PT(s)	13.32 ± 1.13	13.49 ± 1.28	0.591
ALB(g/L)	40.52 ± 4.34	43.15 ± 7.18	0.08
TC(mmol/L)	5.60 ± 2.00	4.38 ± 0.74	0.584
SCr(umol/L)	66.97 ± 20.80	60.16 ± 26.02	0.256
TB(umol/L)	23.85 ± 32.91	18.17 ± 8.96	0.379
ICG 15 min(% , $\bar{x} \pm s$)	14.45 ± 14.93	13.90 ± 12.52	0.886
Child A[n(%)]	55(80.9)	69(82.1)	0.842
Abnormal AFP[n(%)]	42(61.8)	74(88.1)	0.000
Pathological index			
Poor differentiation[n(%)]	32(47.1)	58(69.0)	0.006
Tumor size(mm, $\bar{x} \pm s$)	27.11 ± 3.91	33.90 ± 4.52	0.290
Tumor number(n, $\bar{x} \pm s$)	1.11 ± 0.21	1.03 ± 0.19	0.716

HBsAg: hepatitis B surface antigen; Hb: hemoglobin; PT: prothrombin time; ALB: albumin; TC: total cholesterol; SCr: serum creatinine; TB: total bilirubin; AFP: alpha-fetoproteins; ICG: indocyanine green

表 2 两组患者术中及术后情况比较
Table 2 Comparison of intraoperative and postoperative data between two groups

Item	≥70 years group (n = 68)	<70 years group (n = 84)	P value
Laparoscopic hepatectomy[n(%)]	8(11.8)	9(10.7)	0.838
Operation time(min, $\bar{x} \pm s$)	140.28 ± 57.35	167.67 ± 62.61	0.068
Blood loss(ml, $\bar{x} \pm s$)	296.11 ± 228.73	380.00 ± 285.15	0.189
Complications[n(%)]	42(61.8)	40(47.6)	0.082
Cardiovascular events	9(13.2)	2(2.4)	0.024
Abdominal bleeding	3(4.4)	2(2.4)	0.810
Liver dysfunction	24(35.3)	23(27.4)	0.294
Bile leakage	2(2.9)	1(1.2)	0.853
Infection	6(8.8)	4(4.8)	0.499
Pleural effusion	12(17.6)	16(19.0)	0.869
ICU stay[n(%)]	33(48.5)	15(17.9)	0.000
Postoperative hospital stay(d, $\bar{x} \pm s$)	15.22 ± 5.66	13.33 ± 2.63	0.080
Death	1(1.47)	1(1.20)	1.000

ICU: intensive care unit

本文研究发现两组 Child-Pugh 肝功能分级亦无明显差异,具有可比性。在中国,73% 的肝细胞肝癌与乙型肝炎病毒(hepatitis B virus, HBV)相关,提示 HBV DNA 在肝细胞肝癌形成中具有重要作用^[13]。本研究发现,≥70 岁组 HBsAg 阳性率低于 <70 岁组,原因可能在于,随着年龄的增长 HBsAg 抗体滴度亦随之减少。在早些年报道中,高龄肝切除患者因比非高龄肝切除患者合并症多而被认为是肝切除的高风险人群^[7,14]。本研究显示,≥70 岁组比 <70 岁组

合并症(如高血压)更多,Hb 水平低($P < 0.05$),但术后两组增加并发症的总发生率差异无统计学意义($P > 0.05$),这可能与近些年手术技术水平提高、围手术期管理及麻醉水平的进步密切相关。众多研究表明,AFP 与肝细胞肝癌的分化和预后相关^[15,16],更有学者将 AFP 作为评判肿瘤分级的唯一变量,本研究发现≥70 岁组 AFP 异常比例低于 <70 岁组,病理结果显示,≥70 岁组肿瘤低分化程度低于 <70 岁组,提示≥70 岁组肿瘤恶性程度低于 <70 岁组,

这与上述文献结论一致。

关于术后并发症的特征,本研究发现术后 ≥ 70 岁组比 <70 岁组更容易发生心血管事件,包括心力衰竭、心律失常,该结果与一些研究结果相符^[17,18],这可能与年龄增长后心脏活力下降、动脉硬化程度较大相关。高龄患者入院时全身状况较差、存在轻度低蛋白血症、前白蛋白合成障碍等一定程度的营养不良表现,其术后 ICU 入住率明显高于 <70 岁组,说明高龄患者合并不同程度的基础病,术后需要加强辅助支持治疗。围手术期治疗是提高高龄患者术后短期效果的关键,本组患者通过积极的围手术期处理(术前合适的营养支持、采取积极的呼吸训练来提高肺通气能力),减少术中出血并保护脏器功能,术后加强监护治疗,使得 ≥ 70 岁组患者手术后获得了与 <70 岁组相当的临床近期结果,术后住院日及死亡率亦无明显差异。

可以预测,今后高龄肝切除患者还将会逐步增加,但在决定是否对高龄患者施行肝切除手术时,应从多方面评估高龄患者对肝切除的承受能力,做好围手术期处理,综合评估哪一种治疗方式能让患者受益。高龄不是肝切除术的禁忌证,在没有严重心肺疾病的基础上,经过充分的术前准备和掌握严格的手术指征,70 岁以上患者能够安全接受肝切除术。

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(编辑: 张美)