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·专题研究·

不同解剖部位肝内胆管癌患者淋巴结清扫范围与预后关系

谢伟选¹, 柏杨¹, 许怀生¹, 濮毅峰¹, 王林¹, 方征¹, 朱庆洲², 罗昆仑^{1,2}

(1. 中国人民解放军联勤保障部队第九〇四医院 肝胆外科, 江苏 无锡 214044; 2. 安徽医科大学无锡临床学院, 江苏 无锡 214044)

摘要

背景与目的:肝内胆管癌(ICC)发病率逐年升高,因起病隐匿、早期诊断率低,根治性切除仍是唯一可能治愈的手段。淋巴结转移是ICC预后不良的重要危险因素,但目前关于淋巴结清扫范围及其治疗价值仍存争议。有研究提示淋巴结清扫对中央型ICC的获益可能大于周围型ICC。临床主要依赖影像学评估淋巴结状态,但准确率有限。本研究旨在探讨淋巴结清扫对不同解剖部位ICC患者预后的影响,为手术策略选择提供依据。

方法:回顾性分析2016年5月—2021年5月在中国人民解放军联勤保障部队第九〇四医院行根治性切除的220例ICC患者的临床资料,其中男性126例、女性94例,平均年龄(56.76±13.15)岁。根据肿瘤解剖部位分为周围型(144例)和中央型(76例)。比较两组在临床特征、白蛋白-胆红素(ALBI)评分分级、术前淋巴结转移风险、淋巴结清扫数目、淋巴结转移情况及术后生存差异,并进一步分析淋巴结清扫数目在不同风险分层患者中的预后价值。

结果:周围型与中央型ICC患者在ALBI评分分级($\chi^2=9.952$, $P=0.002$)、术前淋巴结转移风险($\chi^2=6.166$, $P=0.014$)、清扫淋巴结数目($\chi^2=4.167$, $P=0.042$)及淋巴结转移率($\chi^2=7.331$, $P=0.007$)方面差异均有统计学意义。周围型ICC患者3年总生存率明显高于中央型ICC患者(31.94% vs. 15.79%, $\chi^2=13.890$, $P<0.001$)。在中央型ICC患者中,清扫淋巴结≥6枚者3年总生存率优于<6枚者(16.89% vs. 13.04%, $\chi^2=3.894$, $P=0.048$);尤其在术前淋巴结转移评估高风险的中央型患者中,清扫≥6枚组3年生存率(15.62%)亦优于<6枚组(11.11%)($\chi^2=3.962$, $P=0.047$)。而在周围型ICC患者及术前低风险人群中,清扫数目与预后差异无统计学意义($P>0.05$)。

结论:周围型ICC预后优于中央型ICC。对于术前淋巴结转移高风险的中央型ICC,行充分淋巴结清扫(≥6枚)可改善患者预后,并有助于提高病理分期准确性,提示应重视术前风险评估以优化手术策略。

关键词

胆管上皮癌; 淋巴结切除术; 治疗结果; 预后

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Impact of lymph node dissection extent on survival in intrahepatic cholangiocarcinoma at different anatomical sites

XIE Weixuan¹, BAI Yang¹, XU Huaisheng¹, PU Yifeng¹, WANG Lin¹, FANG Zheng¹, ZHU Qingzhou², LUO Kunlun^{1,2}

(1. Department of Hepatobiliary Surgery, the 904th Hospital of Joint Logistic Support Force of PLA, Wuxi, Jiangsu 214044, China;

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作者简介:谢伟选,中国人民解放军联勤保障部队第九〇四医院主治医师,主要从事普通外科肝胆方面的研究。

通信作者:罗昆仑,Email:lk197041@163.com

2. Wuxi Clinical School, Anhui Medical University, Wuxi, Jiangsu 214044, China)

Abstract

Background and Aims: The incidence of intrahepatic cholangiocarcinoma (ICC) has been increasing in recent years. Due to its insidious onset and low rate of early diagnosis, radical resection remains the only potential curative treatment. Lymph node metastasis is a major adverse prognostic factor in ICC, but the scope and therapeutic value of lymphadenectomy remain controversial. Previous studies suggest that patients with central ICC may derive greater survival benefit from lymphadenectomy than those with peripheral ICC. Preoperative assessment of lymph node status mainly relies on imaging, but its accuracy is limited. This study aimed to investigate the prognostic impact of lymphadenectomy in ICC patients at different anatomical sites to inform surgical decision-making.

Methods: A retrospective analysis was conducted on 220 ICC patients who underwent radical resection at the 904th Hospital of the Joint Logistic Support Force of the PLA from May 2016 to May 2021. The cohort included 126 males and 94 females, with a mean age of (56.76±13.15) years. Patients were categorized into peripheral ICC ($n=144$) and central ICC ($n=76$) groups. Clinical characteristics, albumin-bilirubin (ALBI) grade, preoperative risk of lymph node metastasis, number of lymph nodes dissected, lymph node metastasis status, and postoperative survival outcomes were compared. Subgroup analyses were conducted to assess the prognostic value of the number of lymph nodes dissected under different risk stratifications.

Results: Significant differences were observed between peripheral and central ICC in ALBI grade ($\chi^2=9.952, P=0.002$), preoperative lymph node metastasis risk ($\chi^2=6.166, P=0.014$), number of lymph nodes dissected ($\chi^2=4.167, P=0.042$), and lymph node metastasis rate ($\chi^2=7.331, P=0.007$). The 3-year overall survival (OS) rate was higher in peripheral ICC (31.94%) than in central ICC (15.79%) ($\chi^2=13.890, P<0.001$). Among central ICC patients, those with ≥ 6 lymph nodes dissected had better 3-year OS than those with <6 (16.89% vs. 13.04%, $\chi^2=3.894, P=0.048$). In the high-risk subgroup of central ICC, ≥ 6 lymph nodes dissected was also associated with improved 3-year OS compared with <6 (15.62% vs. 11.11%, $\chi^2=3.962, P=0.047$). In contrast, the number of lymph node dissections had no significant prognostic impact in peripheral ICC or in patients classified as low risk.

Conclusion: Patients with peripheral ICC had a better prognosis than those with central ICC. Adequate lymphadenectomy (≥ 6 nodes) improved survival and enhanced staging accuracy in central ICC patients at high risk of lymph node metastasis, highlighting the importance of preoperative risk assessment for optimizing surgical strategies.

Key words

Cholangiocarcinoma; Lymph Node Excision; Treatment Outcome; Prognosis

CLC number: R735.7

肝内胆管癌 (intrahepatic cholangiocarcinoma, ICC) 起源于肝内二级胆管及以上肝内胆管分支的上皮细胞,发病率约占肝脏恶性肿瘤的 10%~15%,仅次于肝细胞癌^[1-3]。淋巴结转移是公认的影响 ICC 预后的重要危险因素^[4-6]。但是目前对于 ICC 行淋巴结清扫的范围及其潜在的治疗作用存在矛盾^[7-9]。有研究^[10-11]显示,淋巴结清扫对 ICC 患者的生存获益受肿瘤解剖位置的影响,淋巴结根治性清扫对

中央型 ICC 患者的预后影响比周围型 ICC 患者更大。临床主要依靠术前影像检查评估淋巴结状态,但以往多项研究表明这种方法不精确^[12-16]。有研究^[17]显示,增强成像评分可以通过 ICC 患者术前特征来预测淋巴结转移,从而确定可能从淋巴结清扫中获得最大生存益处的 ICC 患者。本研究回顾性分析 220 例 ICC 行根治性切除术的患者的临床资料,探讨淋巴结清扫对不同位置 ICC 患者预后的影响。

1 资料与方法

1.1 一般资料

回顾性分析2016年5月—2021年5月于中国人民解放军联勤保障部队第九〇四医院因ICC行根治性切除术的220例患者的临床资料。其中男性126例,女性94例,年龄为(56.76±13.15)岁。纳入标准:(1)ICC根治性切除,术后病理为ICC;(2)行淋巴结清扫,且术后淋巴结病理资料完整;(3)无合并其他类型肿瘤;(4)临床资料及术后随访资料完整。排除标准:(1)未行淋巴结清扫;(2)合并有其他胆道系统疾病;(3)肿瘤侵及周围组织;(4)失访患者。本研究通过我院伦理委员会批准(批号:20211054)。

1.2 治疗方法及随访

术前行常规检查、CT或MRI检查,必要时行PET/CT检查,评估淋巴结状况。全麻后,开腹后首先探查,确定无明显转移灶后行手术治疗。标记肝切除范围,并行肝段、半肝或扩大肝切除术。区域淋巴结清扫范围为胆囊管周围及肝十二指肠韧带内淋巴结。扩大淋巴结清扫范围在区域淋巴结清扫基础上扩大清扫至胰头后、肝总动脉旁、腹腔干旁等部位淋巴结。随访采用电话及门诊随访,截至2024年3月30日,最长随访时间为36个月。

淋巴结清扫标准:《肝内胆管癌外科治疗中国专家共识2020版》^[18]建议:清扫范围基于肿瘤部位,起源于肝左叶者清扫范围包括肝十二指肠韧带、小网膜至胃小弯和贲门附近淋巴结,起源于肝右叶者清扫范围包括肝十二指肠韧带、门腔间隙和胰腺后方淋巴结。

1.3 观察指标和评价标准

观察指标:(1)ICC患者临床特征包括性别、年龄、肝功能Child-Pugh分级、术前CA19-9、HbsAg、白蛋白-胆红素(albumin-bilirubin, ALBI)评分分级、术前淋巴结转移风险评估、淋巴结清扫数目、淋巴结转移比较、被膜侵犯、脉管癌栓、肿瘤数目、肿瘤最大直径。(2)随访情况:生存状态、血生化、血常规、肿瘤标志物、全腹部CT/MRI扫描、胸部CT。

评价标准:根据肿瘤所在解剖位置将ICC分为周围型ICC和中央型ICC。肿瘤的解剖位置通过术前影像学检查,将与肝门部接触较多的ICC定义为

中央型,其他未与肝门部接触的ICC为周围型^[19]。

增强成像评分作为术前淋巴结转移风险评分按以下公式计算:1.23-0.016×年龄+0.146×肿瘤数目+(淋巴结影像学可疑或阳性,1.143)+(CA19-9>200 U/mL,0.514)+(ALBI 2/3级,0.345),增强成像评分≥0.886为术前淋巴结转移评估高风险,增强成像评分<0.886为术前淋巴结转移评估低风险^[16]。

1.4 统计学处理

应用SPSS 25.0,计数资料以绝对数或百分比表示,组间比较采用独立样本t检验,对于连续变量多组间比较采用方差分析进行比较。生存分析采用Kaplan-Meier法绘制生存曲线,Log-rank检验进行生存分析。P<0.05为差异有统计学意义。

2 结 果

2.1 患者基本临床特征

220例ICC患者中,周围型144例,中央型76例。两组患者的ALBI评分分级、术前淋巴结转移风险评估、淋巴结清扫数目、淋巴结转移方面差异均有统计学意义(均P<0.05);两组患者的性别、年龄、肝功能Child-Pugh分级、术前CA19-9、HbsAg、被膜侵犯、脉管癌栓、肿瘤数目、肿瘤最大直径差异均无统计学意义(均P>0.05)(表1)。

2.2 ICC患者术后生存情况

144例周围型ICC和76例中央型ICC患者3年生存率分别为31.94%和15.79%,周围型ICC患者3年总生存率明显高于中央型ICC患者($\chi^2=13.890$,P<0.001)(图1)。144例周围型ICC患者中,53例淋巴结清扫数目≥6枚患者和91例淋巴结清扫数目<6枚患者的3年总生存率分别为37.74%和28.57%,差异有统计学意义($\chi^2=7.815$,P=0.005)(图2A);76例中央型ICC患者中,53例淋巴结清扫数目≥6枚患者和23例淋巴结清扫数目<6枚患者3年总生存率分别为16.98%和13.04%,差异有统计学意义($\chi^2=3.894$,P=0.048)(图2B)。

144例周围型ICC患者中,37例术前淋巴结转移评估高风险,107例术前淋巴结转移评估低风险。37例术前淋巴结转移高风险患者中,18例淋巴结清扫数目≥6枚患者和19例<6枚患者3年总生存率分别为22.22%和26.31%,差异无统计学意义

($\chi^2=0.139$, $P=0.709$) (图3A)。107例术前淋巴结转移评估低风险患者中,35例淋巴结清扫数目 ≥ 6 枚和72例 <6 枚患者3年总生存率分别为34.29%和

34.72%,差异无统计学意义($\chi^2=0.174$, $P=0.677$) (图3B)。

表1 144例周围型ICC和76例中央型ICC患者临床特征比较[n(%)]

Table 1 Comparison of clinical characteristics between 144 patients with peripheral ICC and 76 patients with central ICC[n(%)]

特征	周围型(n=144)	中央型(n=76)	χ^2	P
性别				
男	82(56.94)	44(57.89)	0.075	0.784
女	62(43.06)	32(42.11)		
年龄(岁)				
≤ 50	69(47.92)	42(55.26)	0.875	0.351
>50	75(52.08)	34(44.74)		
肝功能Child-Pugh分级				
A	129(89.58)	69(90.79)	0.322	0.571
B	15(10.42)	7(9.21)		
术前CA19-9(U/mL)				
≤ 37	60(41.67)	35(46.05)	1.155	0.284
>37	84(58.33)	41(53.95)		
HbsAg				
阴性	98(68.06)	54(71.05)	0.870	0.352
阳性	46(31.94)	22(28.95)		
被膜侵犯				
是	46(31.94)	41(53.95)	0.117	0.732
否	68(47.22)	35(46.05)		
淋巴结转移				
是	29(20.14)	25(32.89)	7.331	0.007
否	115(79.86)	51(67.11)		
脉管癌栓				
阴性	109(75.69)	56(73.68)	0.415	0.520
阳性	35(24.31)	20(26.32)		
肿瘤数目				
单发	105(72.92)	53(69.74)	0.942	0.333
多发	39(27.08)	23(30.26)		
肿瘤最大直径(cm)				
≤ 5	99(68.75)	50(65.79)	0.749	0.388
>5	45(31.25)	26(34.21)		
淋巴结清扫数目(枚)				
<6	91(63.19)	23(30.26)	4.167	0.042
≥ 6	53(36.81)	53(69.74)		
术前淋巴结风险评估				
低风险	107(74.31)	26(34.21)	6.166	0.014
高风险	37(25.69)	50(65.79)		
ALBI分级				
1	98(68.06)	35(46.05)	9.952	0.002
2~3	46(31.94)	41(53.95)		

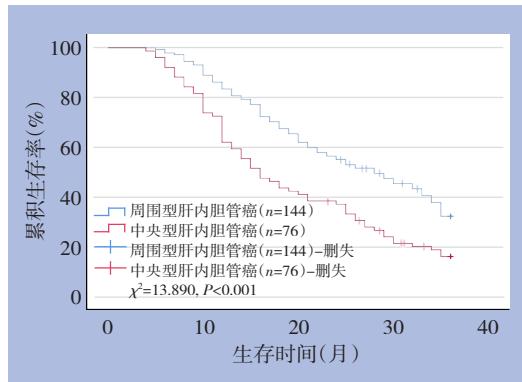


图1 144例周围型ICC患者和76例中央型ICC患者的生存曲线

Figure 1 Survival curves of 144 patients with peripheral ICC and 76 patients with central ICC

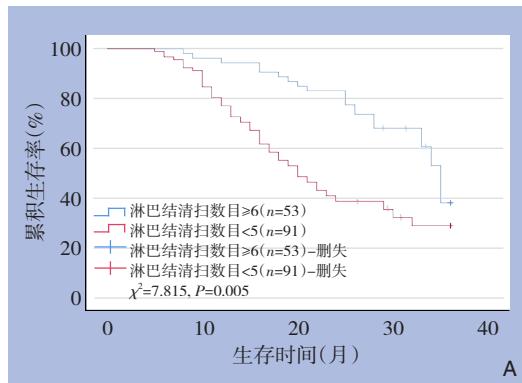


图2 不同淋巴结清扫数目ICC患者的生存曲线

Figure 2 Survival curves of ICC patients stratified by the number of lymph nodes dissected A: Peripheral ICC; B: Central ICC

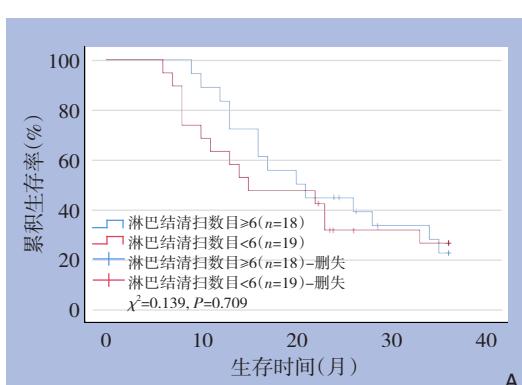
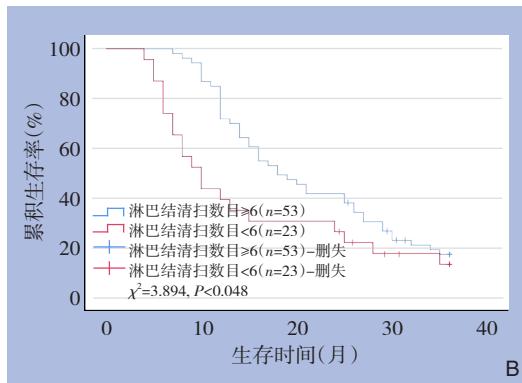
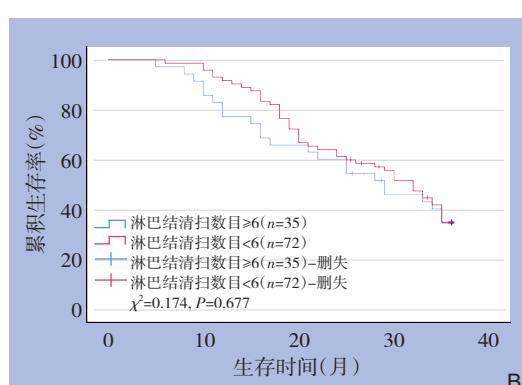


图3 不同淋巴结清扫数目的周围型ICC患者的生存曲线

Figure 3 Survival curves of peripheral ICC patients stratified by the number of lymph nodes dissected A: High preoperative risk of lymph node metastasis; B: Low preoperative risk of lymph node metastasis

76例中央型ICC患者中,50例术前淋巴结转移评估高风险,26例术前淋巴结转移评估低风险。50例术前淋巴结转移评估高风险患者中,32例淋巴结清扫数目≥6枚患者和18例淋巴结清扫数目<6枚患者3年总生存率分别为15.62%和11.11%,差异有统计学意义($\chi^2=3.962, P=0.047$) (图4A);26例术前淋巴结转移评估低风险患者中,21例淋巴结清扫数目≥6枚患者和5例<6枚患者3年总生存率分别为19.05%和20.00%,差异无统计学意义($\chi^2=0.295, P=0.587$) (图4B)。



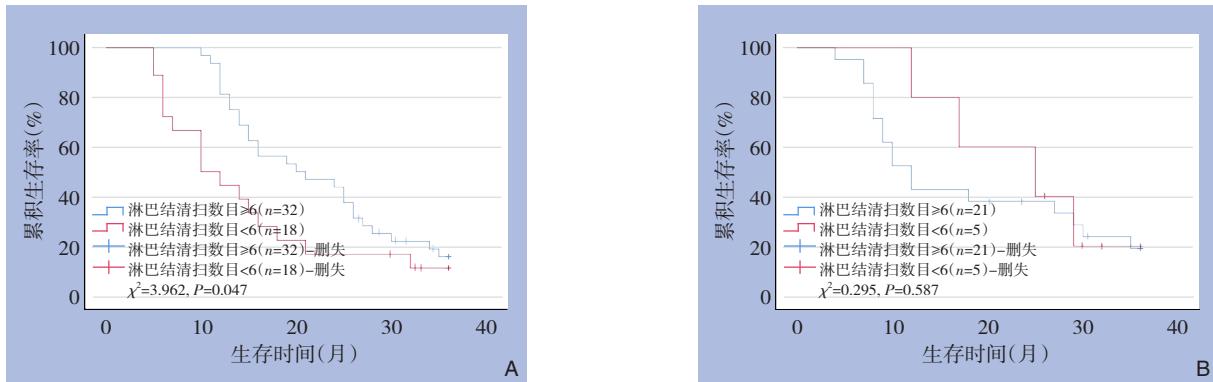


图4 不同淋巴结清扫数目的中央型ICC患者的生存曲线 A: 术前淋巴结转移评估高风险; B: 术前淋巴结转移评估低风险

Figure 4 Survival curves of central ICC patients stratified by the number of lymph nodes dissected A: High preoperative risk of lymph node metastasis; B: Low preoperative risk of lymph node metastasis

3 讨 论

目前,国内外学者多次报道了淋巴结清扫数目以及范围对ICC预后的影响,研究结果差异较大,推测原因可能与个体差异及疾病特征异质性有关^[8-9,20-22]。因此,评估淋巴结清扫数目的治疗价值应充分考虑到肿瘤特征,尤其是肿瘤原发位置^[23-26]。本研究结果显示,周围型ICC与中央型ICC的ALBI分级,术前淋巴结转移风险评估、淋巴结清扫数目、淋巴结转移方面有明显差异;周围型ICC患者术后3年生存情况明显优于中央型ICC患者。上述结果与既往研究结果一致^[27-30]。这提示周围型ICC整体术后预后优于中央型ICC。有研究者采用基因组分析揭示了位于不同部位的胆管癌存在的分子病理学差异^[31-32],提示基因表达异常或致瘤途径的改变会影响不同解剖位置ICC的生物学行为^[33]。

对于可能受益于淋巴结清扫的ICC适应证和应该清扫的淋巴结数目,既往研究结果不一致^[20,34]。Zhang等^[35]的研究结果显示,淋巴结清扫数目 ≥ 6 枚可更精确分期和延长术后生存时间,但也可能导致胆总管损伤或乳糜漏,导致术后并发症增加。本研究显示,在周围型ICC中,淋巴结清扫数目 ≥ 6 枚和<6枚患者的术后3年生存率,差异有统计学意义($\chi^2=7.815$, $P=0.005$)。进一步分析显示,术前淋巴结转移评估高风险与低风险中,淋巴结清扫数目 ≥ 6 枚和<6枚患者的术后3年生存率差异均无统计学意义。在中央型ICC中,淋巴结清扫数目 ≥ 6 枚和<6枚患者的术后3年生存率比较,差异有统计学意义($\chi^2=3.894$, $P=0.048$)。进一步分析

显示,对于术前淋巴结转移评估高风险的中央型ICC,淋巴结清扫数目 ≥ 6 枚患者的术后3年生存率显著优于淋巴结清扫数目<6枚患者($\chi^2=3.962$, $P=0.047$)。对于术前淋巴结转移评估低风险的中央型ICC,淋巴结清扫数目 ≥ 6 枚和<6枚患者的术后3年生存率差异无统计学意义($\chi^2=0.295$, $P=0.587$)。以上研究提示术前评估淋巴结转移风险对ICC术中淋巴结清扫方式的选择及术后预后有重要意义,对于术前评估为淋巴结转移高风险的中央型ICC,尤其需要行充分淋巴结清扫(≥ 6 枚)。

综上,周围型ICC的预后优于中央型ICC,对于术前淋巴结转移评估高风险的中央型ICC,充分的淋巴结清扫可改善ICC术后总体生存率,同时提高了术后病理分期的准确性,有利于根据制订更个体化的治疗方案。

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