

肝门胆管癌外科手术及相关问题的研究进展

梅永, 彭慈军, 李伟男, 李雄雄, 谢万桃, 舒德军, 张金刚

梅永, 彭慈军, 李伟男, 李雄雄, 谢万桃, 舒德军, 遵义医学院附属医院肝胆外科 贵州省遵义市 563003

张金刚, 德江县民族中医院肝胆外科 贵州省铜仁市 565200
梅永, 在读硕士, 主要从事肝胆外科方面的研究。

作者贡献分布: 此课题由梅永与彭慈军设计; 论文写作主要由梅永完成, 张金刚参与写作; 李伟男、李雄雄、谢万桃及舒德军共同参与文献检索; 由彭慈军审校。

通讯作者: 彭慈军, 教授, 主任医师, 563003, 贵州省遵义市大连路149号, 遵义医学院附属医院肝胆外科。

doctorpengcijun@163.com

电话: 0851-28608244

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Surgical treatment of hilar cholangiocarcinoma: New advances

Yong Mei, Ci-Jun Peng, Wei-Nan Li, Xiong-Xiong Li, Wan-Tao Xie, De-Jun Shu, Jin-Gang Zhang

Yong Mei, Ci-Jun Peng, Wei-Nan Li, Xiong-Xiong Li, Wan-Tao Xie, De-Jun Shu, Department of Hepatobiliary Surgery, Affiliated Hospital of Zunyi Medical University, Zunyi 563003, Guizhou Province, China

Jin-Gang Zhang, Department of Hepatobiliary Surgery, Hospital of Traditional Chinese Medicine of Dejiang County, Tongren 565200, Guizhou Province, China

Correspondence to: Ci-Jun Peng, Professor, Chief Physician, Department of Hepatobiliary Surgery, Affiliated Hospital of Zunyi Medical University, 149 Dalian Road, Zunyi 563003, Guizhou Province, China. doctorpengcijun@163.com

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Abstract

Hilar cholangiocarcinoma, a malignant tumor that occurs in the left and right hepatic duct, is the most common form of bile duct carcinoma. Early diagnosis of hilar cholangiocarcinoma is difficult, and the majority of patients are diagnosed in advanced stages. Therefore,

surgery for this malignancy is difficult, has high risk, and is associated with a poor prognosis. In recent years, with the development of imaging technology and extended radical surgery, the preoperative diagnosis and surgical treatment of hilar cholangiocarcinoma have been improved. However, hilar cholangiocarcinoma still has a low cure rate, high complication rate, and poor prognosis. Therefore, we should strengthen the research on the susceptible factors and biological characteristics of hilar cholangiocarcinoma, and improve early diagnosis. Currently, although there has been no unified standard for the resectability of the tumor, surgery combined with partial hepatectomy is strongly recommended in patients without surgical contraindication. This paper reviews the recent progress in surgical treatment of hilar cholangiocarcinoma.

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Key Words: Hilar cholangiocarcinoma; Classification; Biliary drainage; Portal vein embolization; Surgery; Hepatectomy

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摘要

肝门胆管癌(hilar cholangiocarcinoma, HCCA)是指发生在左、右肝管及肝总管的恶性肿瘤,是最常见的胆管癌。因其早期发病隐匿,临床症状出现较晚,多数患者诊断

背景资料

肝门胆管癌(hilar cholangiocarcinoma, HCCA)是最常见的胆管癌,因肿瘤解剖位置在肝门部,常常容易侵犯其临近的肝组织、门静脉及肝动脉,导致外科手术风险和难度较大。因为HCCA对放疗均不敏感,所以外科手术仍然是目前唯一可能获得治愈希望的治疗方法。

同行评议者

刘超, 教授, 主任医师, 中山大学孙逸仙纪念医院(附属第二医院)肝胆胰外科

■ 研发前沿

虽然HCCA的诊断方法及外科手术技术日益改进, 但外科手术方式及相关问题仍然存在争议, HCCA的治疗仍然面临巨大的挑战。

时往往处于中晚期阶段, 导致手术难度及风险大, 预后较差。近年来, 随着影像学技术的发展、扩大根治术式的广泛开展, 对于HCCA的术前诊断及手术疗效得到逐渐提高。但是, HCCA根治率低、并发症多、预后不良等问题仍然很严峻, 我们应加强对HCCA的易感因素及生物学特性的研究, 力争早期诊断。判断肿瘤能否切除尚无统一标准, 对无明显禁忌证的确诊病例应积极手术, 力争通过联合部分肝切除根治HCCA。本文就HCCA的外科手术及相关问题的研究进展作一综述。

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关键词: 肝门胆管癌; 分型; 胆道引流; 门静脉栓塞; 外科手术; 肝叶切除

核心提示: 肝门胆管癌(hilar cholangiocarcinoma)仍然存在根治率低、并发症多、预后不良等一系列问题。判断肿瘤能否切除尚无统一标准, 对无明显手术禁忌证的确诊病例应积极手术, 力争通过联合部分肝切除达到根治。

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0 引言

肝门胆管癌(hilar cholangiocarcinoma, HCCA)是指发生在左、右肝管及肝总管的恶性肿瘤, 首先由Klatskin描述(1965年), 亦称为Klatskin肿瘤, 其仍然是最常见的胆管癌, 约占胆管癌总体的60%-70%^[1]。其病因目前尚不清楚。该病早期缺乏特异性的临床表现, 多数患者就诊时已属于中晚期, 并且肿瘤解剖位置在肝门部, 常常容易侵犯其临近的肝组织、门静脉及肝动脉, 导致外科手术风险和难度较大。因为HCCA对放疗及化疗均不敏感, 所以外科手术治疗仍然是目前唯一可能获得治愈希望的治疗方法^[2]。虽然近年来诊断方法已逐渐改进, 且肝胆管切除术的技术积极进步, 但是HCCA的治疗仍然面临巨大的挑战。本文就HCCA当前的外科治疗方法进行综述。

1 HCCA的肿瘤分型及可切除性评估

根据肿瘤发生的解剖部位为依据, 由Bismuth

等^[3]于1975年提出的Bismuth-Corlette分型, 是目前临床上最常用的HCCA分型方法, 他包括四型: I型, 肿瘤位于肝总管内, 未侵犯左右肝管汇合部; II型, 肿瘤侵犯左右肝管汇合部, 尚未侵犯左或右肝管; III型, 肿瘤侵犯左右胆管, 又分为IIIa型和IIIb型两种亚型, IIIa型是指肿瘤侵犯右肝管, IIIb型是指肿瘤侵犯左肝管; IV型, 肿瘤同时侵犯左、右肝管。但是该分型方法只能了解肝外胆管的肿瘤, 不能明确肿瘤的脉管侵犯及远处转移情况。因此近年来Deoliveira等^[4]提出了新的分期方法, 更全面的描述了肿瘤的大小、病灶累及胆管、肝动脉及门静脉的情况、淋巴结和远处转移情况及推荐的预留肝体积。但该分期法的实际指导价值有待进一步临床实践中的运用及观察。关于HCCA的检查方法包括腹部B超、计算机断层扫描(computed tomography, CT)、磁共振成像(magnetic resonance imaging, MRI)、磁共振胆胰管成像(magnetic resonance cholangiopancreatography, MRCP)、内镜逆行胆胰管造影(endoscopic retrograde cholangiopancreatography, ERCP)等。因为CT可以观察到肿瘤的大小、形态、肝脏萎缩情况及肝体积等, 所以常常作为HCCA的评估标准^[5]。HCCA的早期诊断和术前全面而准确的可切除性评估是制定正确的治疗方案和提高患者根治率的关键所在^[6]。因此, 必须结合多种影像学方法, 术前对肿瘤在胆管系统的位置及形态、血管侵犯程度、淋巴结受累情况、远处转移及肝萎缩情况进行充分的评估, 明确肿瘤的分型, 制定合理手术方案。

2 术前胆道引流

预留肝脏肝功能储备是实施联合肝切除术根治HCCA术前准备的首要问题, 直接关系到手术的成败及患者的存亡。为了改善患者的预后而追求HCCA的R0切除, 多数HCCA患者都需要行右半肝或超右半肝切除、左半干或超左半肝切除、中肝切除等大部分肝切除术, 导致剩余的肝脏体积不够, 术后容易出现小肝综合征、肝功能衰竭等凶险性并发症。术前实施预留肝脏的胆道引流可以降低胆红素水平, 有助于预留肝脏的肥大, 代偿术后肝功能。但是针对HCCA是否应采用术前胆道引流, 目前尚存在争议, 国际上也缺少随机对照实验。有研究^[7]认为, 术前胆道引流并不能改善可切除的

HCCA患者的临床结局。众多的研究发现, 术前胆道引流虽然不能改善黄疸性HCCA患者术后死亡率及生存情况, 但可以降低其术后的并发症发生率^[8-10]。Belghiti等^[11]研究认为术前胆道引流能改善黄疸患者的肝功能, 从而降低术后死亡率及并发症。Kennedy等^[12]研究认为术前胆道引流能改善预留肝体积不足30%的患者的围手术期结局。

3 门静脉栓塞

选择性门静脉栓塞(portal vein embolization, PVE)是术前增加剩余肝脏体积和肝脏储备功能的重要方法, 他通过选择性栓塞拟切除侧肝叶的门静脉分支, 从而使对侧肝组织代偿性增生, 以达到降低肝切除术后肝功能衰竭的风险。Ebata等^[13]对353例胆管癌患者术前行PVE后行联合肝脏切除术, 术后因并发症死亡率只有38%, 5年生存率达到39%, 远高于未行术前PVE患者。文献^[11,14,15]报道, 如果预留肝体积不足30%-40%, 则应考虑行PVE。并指出一般行PVE术4-6 wk后手术比较合理^[11,14]。虽然目前尚未发现关于HCCA患者行PVE疗效的随机试验文献报道, 但可以适当的选择性行PVE术来促进预留肝肥大, 预防根治性切除术后肝功能衰竭。早期手术及充分的术前准备是取得HCCA根治手术成功最为重要的两个因素。但是这两个因素本身就是相互矛盾的, 不能最大限度的追求某一方面的效果, 只能探索两者的平衡点。

4 根治性手术

4.1 局部切除术 局部切除术主要是针对肝外胆管的局部肿瘤切除, 有时会联合少量的临近肝组织的切除。此种手术方式主要适合于肿瘤局限于胆管壁、肿瘤体积较小及Bismuth I型HCCA患者^[16]。从理论上说, 针对Bismuth I型和II型HCCA行肿瘤局部切除术可以获得R0切除, 因此有部分同行主张行非联合肝切除的单纯胆管切除术适合于Bismuth I型及II型HCCA患者^[17,18]。但有研究^[19]报道, HCCA尾叶胆管和肝实质侵犯率为40%-50%, 仅仅骨骼化处理肝十二指肠韧带是不够的, 必须同时切除包括肝尾叶在内的受侵犯的肝叶或肝段。并且有研究^[20,21]表明, 单纯的局部肿瘤切除术后肿瘤的局部复发率高达52.6%-74.2%。局部切除术的优点是手术创伤小, 最大限度地保留了剩余

肝体积, 且肿瘤切除后可以直接行肝管空肠吻合术, 技术难度不大。但缺点是术后肿瘤复发率高, 术后生存率比扩大根治术低。因此, 我们建议针对确诊的HCCA患者尽可能实施联合部分肝切除的根治手术。若患者一般状况不佳, 不能耐受手术, 且诊断早、肿瘤局限者, 可谨慎选择局部切除术。

4.2 联合部分肝切除术 联合部分肝切除术既能直接切除HCCA侵犯肝实质的病灶, 也能切除HCCA沿着胆管分支跳跃式生长的病灶, 有助于获得横向及纵向的R0切缘, 提高根治性切除率, 减少肿瘤复发率, 延长术后生存时间。HCCA易通过胆管累及肝实质, 为保证根治率及提高生存率, 需考虑联合肝叶切除^[21-29]。完整的尾状叶切除能降低术后肿瘤的局部复发率, 并提高长期生存率^[30-32]。因此, 针对HCCA的根治性治疗应常规行完整的尾状叶切除。

针对Bismuth分型法的各型推荐术式尚存在争议, 主要集中在Bismuth I型和II型HCCA的术式。Ikeyama等^[33]通过对54例Bismuth I、II型HCCA术式研究, 认为应根据HCCA的大体形态来决定具体的手术方式, 对于结节状癌及浸润性癌应联合右半肝切除; 而对于乳头状癌, 联合或非联合局部肝切除的肝外胆管切除即可。越来越多的最新研究^[20,34]表明, 联合肝部分肝切除能改善Bismuth I型和II型HCCA术后生存率。从解剖学结构来看, 由于右肝动脉行走于肝总管的后方, 容易受到癌细胞的浸润, 因此Bismuth I、II型HCCA应联合部分右肝或中肝切除术。Seyama等^[35]研究也证实了联合右半肝及尾状叶切除的此类患者预后更好。Bismuth IIIa型HCCA推荐行右半肝切除; Bismuth IIIb型HCCA推荐左半肝切除; Bismuth IV型HCCA推荐行中肝切除或左右三叶切除^[5]。**4.3 联合门静脉切除** 由于肝门的解剖结构特殊及HCCA的生物学特异性, 造成癌细胞容易侵犯门静脉, 为完整切除肿瘤, 有时需联合门静脉切除。传统观点认为, 肿瘤侵犯门静脉是不可根治性切除的标志。随着肝胆外科技术的不断发展, 联合门静脉切除根治HCCA已逐渐报道^[26]。但是联合门静脉切除的安全性及疗效尚存在争议。最新的一篇Meta分析^[36]报道, 通过纳入13篇文献对1921例HCCA患者进行分析, 与非联合门静脉切除术相比较, 联合门静脉切除术后生存情况更差, 淋巴结转移率更高, 根

■ 相关报道

目前针对HCCA的研究热点是早期诊断和手术治疗方法。相关的文献报道指出该肿瘤具有独特的生物学特性, 早期诊断困难; 尽管外科手术方式较多, 但各种术式也都存在各自的局限性, 不同术式的选择尚存在争议。

■ 创新盘点

HCCA的外科治疗是同道们关注的焦点,但是众多的文献集中于研究某种术式或比较几种方式之间的疗效。本研究通过综述近年来关于HCCA的外科治疗研究进展,系统的阐述各种外科手术及相关问题。

治性切除率更低;术后并发症发生率及死亡率无统计学差异。可见联合门静脉切除术安全性尚可,但根治效果及患者预后不理想。因此该术式在临床实践中的应用务必谨慎,其具体疗效尚有待进一步研究证实。

4.4 联合肝脏离断和门静脉结扎的二步肝切除术 2007年德国Schlitt教授完成了首例联合肝脏离断和门静脉结扎的二步肝切除术(associating liver partition and portal vein ligation for staged hepatectomy, ALPPS),并于2012年由de Santibañes等^[37]将该技术正式命名为ALPPS,此后即获得国内外学术界广泛关注。文献报道,ALPPS能有效降低大范围肝切除术后肝功能衰竭风险^[38]。目前,ALPPS大多应用于结肠癌肝转移和肿瘤发展相对较缓慢的神经内分泌肿瘤肝转移的病例,这类患者一般无基础肝病,转移瘤发展相对缓慢,残肝再生幅度大,手术易于成功^[39]。也有文献报道^[40]ALPPS对于原发性肝癌、胆管细胞癌等同样适用。虽然ALPPS被认为是近年来最具创新突破性的肝胆外科技术之一^[37],但施行ALPPS的患者围手术期并发症发生率和病死率相对较高,该手术围手术期死亡的主要原因是术后胆汁漏合并感染^[41,42],而且ALPPS需要两次手术,手术周期延长,有可能增加癌细胞扩散的风险^[43]。针对ALPPS应用于HCCA患者的疗效研究报道较少,该技术可能会增加晚期HCCA患者获得手术治疗的机会,但其具体的疗效和手术的安全性有待进一步的临床实践研究证实。

4.5 肝移植 对于无法切除的HCCA,肝移植是可能获得治愈希望的唯一方法。近年来,Schüle等^[44]研究发现针对无法切除的胆管癌行肝移植术,总体5年生存率可达到27%,在无淋巴结转移的患者中,肝移植术后5年生存率可高达50%。Rea等^[45]研究报道对无法切除的无肝外转移的Bismuth I型和II型HCCA,特别是合并原发性硬化性胆管炎的患者,肝移植术后的5年生存率达72%。但也有文献报道早期HCCA的肝移植结果尚不满意,其早期复发率达50%,5年生存率仅为10%-20%^[46,47]。肝移植术的缺点是术后的免疫抑制,容易导致残余肿瘤组织的扩散^[48]。同时也面临着供体缺乏等诸多的现实问题有待解决,其临床应用前景仍然十分严峻。

5 姑息性手术

若肿瘤涉及的范围广或发生远处转移而失去

根治手术治疗机会,为解除HCCA导致的胆道梗阻,预防因胆道内压异常升高所引起的肝功能损害及其他脏器功能的损害,延长患者生命及提高生活质量,有时需要行姑息性引流手术。但姑息手术疗效一直不理想,Vladov等^[49]报道姑息性手术的术后平均生存时间为7 mo,术后1年及3年的生存率仅仅只有60%及14.3%,无患者存活5年^[27]。而且,手术的打击可能会导致肿瘤的扩散或转移,加速患者死亡。有资料显示手术非根治切除组与介入引流组两者平均生存时间无明显差别,但手术引流创伤大,恢复慢,并发症多,因此术前应充分分析影像学检查结果,尤其是对III、IV型患者尤应慎重,估计切除可能性不大者应尽量减少手术探查,而采用介入治疗^[50]。经皮肝穿刺胆道引流术(percutaneous transhepatic cholangial drainage, PTCD)或胆道内支架放置能够减轻黄疸,改善肝功能,延长生存期,而且成功率高,并发症少。因此,对于HCCA患者应积极手术根治,若经术前评估失去根治手术机会的患者,应首先介入引流治疗,谨慎选择姑息手术治疗。

6 结论

HCCA仍然存在根治率低、并发症多、预后不良等一系列问题,我们应加强对HCCA易感因素及生物学特性的研究,力争早期诊断。判断肿瘤能否切除尚无统一标准,对无明显手术禁忌证的确诊病例应积极手术,力争通过联合部分肝切除根治HCCA。

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应用要点

本文系统的阐明了针对HCCA的各种外科手术方法及相关问题,为HCCA的临床实践中个体化治疗方案的选择提供依据。

同行评价

本文总结了肝门胆管癌的分型及手术治疗方式, 观点准确, 内容较全面, 具有一定的临床实践指导意义。

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