编者导读：为了提高临床医生手术技能，并及时了解和掌握国外新进展，本刊与 AME Publishing Company 合作，建立“国际在线”系列栏目，旨在丰富杂志内容，更好地为临床服务。

胆管癌是相对少见的消化系统恶性肿瘤，但近年来其发病率有逐年升高的趋势。胆管癌可发生在肝外胆管的各个部位，其中以肝门部胆管最多见。肝门部胆管癌尤其是高位肝门部胆管癌根治性切除术难度大、手术风险高、患者预后差，如何提高该病早期诊断与治疗水平，依然是一项巨大的挑战。本期国际在线栏目向读者推荐的是为美国学者撰写的有关方肝门部胆管癌诊治现状的述评类文章，该文对肝门部胆管癌的流行病学与病因、临床表现与诊断、治疗选择与策略等方面进行了系统的阐述。

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肝门部胆管癌的诊断、治疗选择与处理策略

Hilar cholangiocarcinoma: diagnosis, treatment options, and management

Kevin C. Soares[1], Ihab Kamel[2], David P. Cosgrove[3], Joseph M. Herman[4], Timothy M. Pawlik[1]

（*1. Department of Surgery, Division of Surgical Oncology 2. Department of Radiology 3. Department of Oncology 4. Department of Radiation Oncology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA*/ 美国霍普金斯大学医学院 1. 肿瘤外科 2. 放射科 3. 肿瘤科 4 . 肿瘤放疗科）

Corresponding author: *Timothy M. Pawlik, Email: tpawlik1@jhmi.edu*

摘　要　肝门部胆管癌（HC）是一种少见的疾病，通常在 60 岁左右发病，预后较差；在美国，每年约有 3 000 例患者被诊断为该病，但仅有不到一半的人可以行手术治疗；有多种因素与 HC 的发病有关，最常见的有原发性硬化性胆管炎（PSC），胆石症以及寄生虫肝病。患者通常表现为腹痛、瘙痒、体质量减轻和黄疸。CT、MRI 及超声可以用来发现胆道病损；逆行性胰胆管造影术（ERCP）及经皮肝胆管造影术（PTC）在评估肿块位置、长度的同时还可以行治疗性的胆汁引流。MRCP 在辨别肿瘤延伸范围时同 PTC 及 ERCP 有相同的准确性，并且并发症较前两者少。HC 的治疗方式主要为手术切除、放射治疗、化疗及光动力学治疗。残余肝脏胆汁引流有助于降低胆红素水平，进而促进残肝的生长；标准的治疗包括切缘为阴性切除（R_0），范围为肝外胆管切除、肝切除及周围的淋巴结清扫术；局部的切除术是不适当的；淋巴结侵犯的程度、肿瘤的级别以及切缘的性质是重要的预后指标；如果无法行肿瘤切除，那么在经反复选择后的患者中实施肝移植术也是种可行的方式；尽管数据有限，化疗对于不可切除的患者来说仍有一定的作用；经手术切除的 HC 患者 5 年生存率约为 10%~40%，然而即使为 R_0 切除，复发率也高达 50%~70%。由于这种疾病的复杂性，多种学科的综合治疗是较为理想的治疗方式。

[中国普通外科杂志，2014, 23(8):1011-1023]

关键词　胆管肿瘤 / 诊断；胆管肿瘤 / 治疗；Klatskin 肿瘤

中图分类号：R735.8

大约 50 年前，Altemeier 和 Klatskin 等[1-3]第一次描述肝门部胆管癌（HC），这种肿瘤约占全部胆管癌（CC）的 60%。这是一种复杂及侵袭性强的疾病，预后较差；我们检索相关文献重点在于总结关于 HC 适当的管理方式。检索数据库包括 PubMed/MEDLINE，实施检索的关键词为肝门部胆管癌及 Klatskin's 瘤。另外，在 Mesh 数据库中，以胆道肿瘤为标题并结合上述的关键词通过 AND 或 OR 进行搜索。其他的限制包围英文文章、研究对象为人类（图 1）。

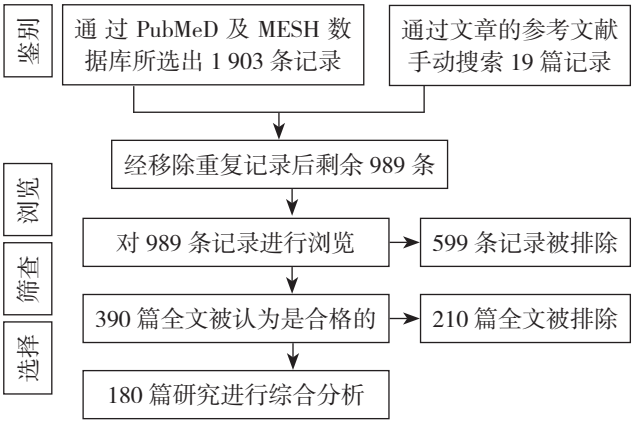

图 1 PRISMA 系统在本文中排除及选择方案

Figure 1 PRISMA diagram demonstrating inclusion and exclusion methodology for articles in this review

1 发病率及流行病学

胆道肿瘤占人类全部恶性肿瘤的 2%，但是在原发性肝癌中是第二常见的肿瘤 [4-5]。在西方国家中较罕见，亚洲国家中较为常见，发病率在男性中约为 0.113%，女性中约为 0.050%[6]。胆道肿瘤根据肿瘤的国际分类法可分为肝内型（ICC）及肝外型（ECC），在美国每年仅 ECC 新增患者约 3 000 例 [5, 7-8]，ICC 的发病率在过去 20 年中有所升高，相较而言，ECC 的发病率一直较为平稳 [9-10]，然而造成这种现象的原因可能由于肿瘤的国际分类法将 HC 错误分类所致 [8]。

与 HC 发病相关的高危因素包括：高龄、男性、肝硬化、炎性肠病以及慢性胰腺炎 [7]。寄生虫性肝病（如胆道蛔虫病、肝吸虫病、肝血吸虫病等）合并胆石症是造成 HC 的重要病因 [4, 7]，同样原发性硬化性胆管炎（PSC）也是 HC 最重要的致病因素，PSC 患者在一生中胆道肿瘤的发病率约为 6%~36%，并且大部分患者在诊断 PSC 后的 2 年中即可发病 [6-7, 11]，因 PSC 可累计肝内及肝外胆道，因此，PSC 相关的胆道肿瘤可以为 ICC 或 ECC，两者的发病风险相同 [12]。

2 临床表现及诊断评估

HC 大约在患者 60 岁左右发病 [13-16]，患者通常表现为黄疸、腹痛以及体质量减轻 [14-16]，另外还可以出现疲劳、瘙痒、恶心、深色尿液及陶土样便等症状 [16]。同时患者常合并胆石症、炎性肠病、PSC 以及病毒性肝炎 [16-17]。

超过 80% 的胆道梗阻间接提示 HC[18-20]，其他疾病可能为炎症性疾病、硬化性胆管炎、胆石症、抑或为胆囊癌侵犯肝十二指肠韧带 [19, 21-24]。良性与恶性的胆管狭窄有相似的临床表现 [19-21]，同时，胆红素及血清肿瘤标志物也不是鉴别两者的可靠手段 [21, 23]，故术前的鉴别是不准确的，手术切除仍是最佳的方式 [19-21, 23]。

血清肿瘤标志物尤其是癌胚抗原（CEA）和 CA19-9 结合其他的诊断方法对于 HC 的诊断、治疗及监测测敏感性可达到 89%，特异性为 86%[25]。需要说明的是，肿瘤标志物的水平同肿瘤的阶段相关，肿瘤的阶段越高代表其切除率越低，同时代表其预后越差 [25-27]。

2.1 影像学表现

可以手术切除的 HC 患者不到一半 [28-29]，准确的放射学评估这些病灶是困难的，如肝门区的复杂性，周围相邻近的大血管及小肿瘤的大小 [30]。计算机成像技术（CT），磁共振成像（MRI）以及超声（US）可以用来描述这些可疑的胆道病灶。由于腹部超声的费用低廉及其可操作性强等原因，使之成为影像学检查中最初的评估。US 对胆管扩张的敏感度较好，但对局部的胆道狭窄敏感度较差 [31-32]。典型的 HC 肿块在超声中表现为较周围的肝实质呈现为低回声（图 2）。超声不能准确的评估狭窄的类型及肿瘤浸润的程度 [33]。另外超声在鉴别淋巴结、肝，以及腹膜的有无侵犯的敏感度较差，因此进一步的检查是需要的 [22, 34]。

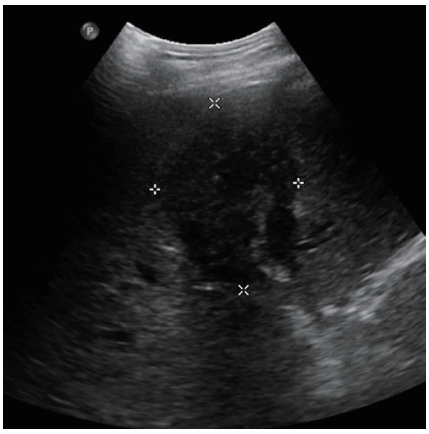

图 2 男性 79 岁，因右上腹部疼痛就诊，行超声发现肝门部巨大低回声肿块

Figure 2 Right upper quadrant ultrasound on a 79-year-old male with right upper quadrant pain. Note the presence of a large hilar hypoechoic mass

CT 可以准确的预测 60%~90%HC 患者的是否存在可切除性，同时也是评估胆道肿瘤可切除性最常用的影像学方法[35-38]。CT 可以帮助区分良性及恶性狭窄同时可以描绘胆道梗阻的水平（图 3）。动脉期及门静脉期的 CT 可以帮助描述狭窄处胆管对血管的侵犯程度[28, 29]。通过手术及病理发现薄层（2~5 mm）CT 扫描（MDCT）在评估局部肿块范围方面具有更好的优势，准确率 >90%[36]。在一篇关于 HC 影像学系统性的综述中，CT 被认为是最适当的影像学检查方式，在评估相关胆道、门静脉、肝动脉的准确性 >80%，但其无法准确评估相关淋巴结[29]，同时对腹膜的转移通常估计不足[28, 37]，因此，尽管根据文献所知 CT 对于 HC 可切除性的判断有较高的敏感性及特异性，但手术中仍可能发现转移及肿瘤侵犯周围组织及器官。

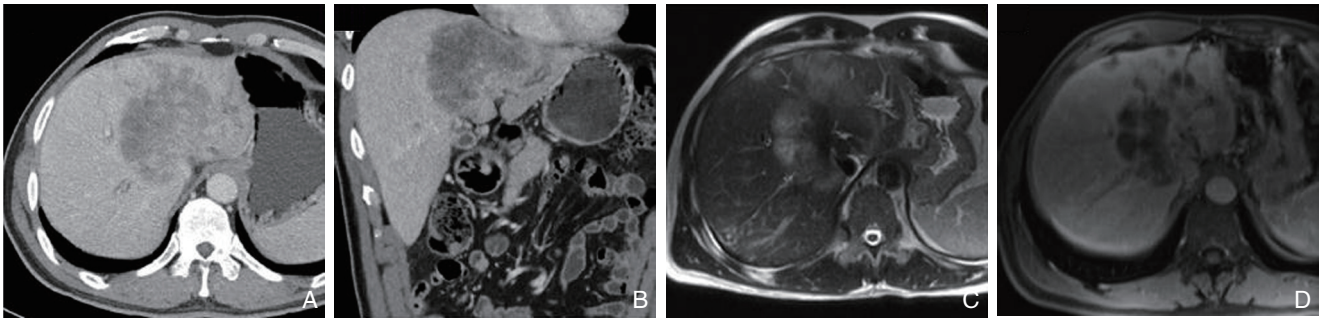

图 3　A，B 为肝静脉期 CT 示肝脏巨大不均质肿块；C 为 T_2 像及对比门静脉期增强核磁；D 示由于巨大的肿块而引起胆管扩张

Figure 3　Axial (A) and coronal (B) CT of the liver in the portal venous phase showing a large heterogeneous mass in both lobes; Axial T_2 (C) and contrast enhanced portal venous phase (D) MR shows ductal dilatation resulting from the large central mass

MRI 在评估胆道肿瘤方面的作用受到越来越多的关注。HC 在 T_1 加权像表现为低信号，在 T_2 像中表现为高信号（图 4）。肿瘤与临近肝组织相比通常是乏血供的，同时可以显示出胆管壁的不规则增厚及上段的肝内胆管扩张（图 5）[40]。将 MRI 结合 MRCP 预测 HC 的可切除性的准确率可达到 80%[41-43]。然而，Park 等[44] 发现 MRI 结合 MRCP 同 MDCT 结合直接的胆道造影术相比较，在预测可切除性的判断上无明显差别。当前而言，MRCP 结合 CT 检查优于直接的胆管造影，不过 MRCP 无法进行有创性操作：如行活检，胆汁引流及放入支架，因此直接胆管造影仍有存在的必要性。

PET/CT 在 HC 诊疗中的作用仍然不太明确。有报道称 PET/CT 检测淋巴结及远处转移的特异性可超过 80%，但在评估可切除性方面就没那么实用了[45-47]。PET/CT 的案例研究其在 HC 中的作用是有限的，需要更多的研究去评估这种影像学检查的优势。当前，PET 有助于评估转移性疾病，但在评估局部切除性方面的作用仍需要研究。

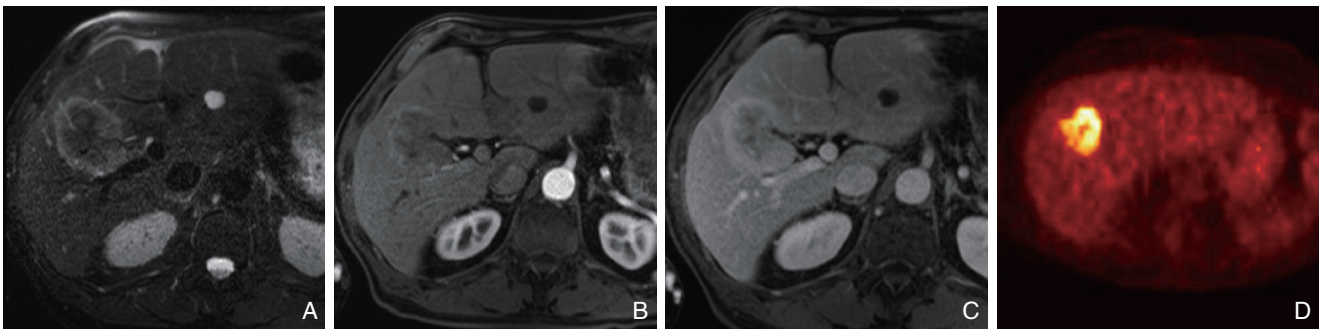

图 4　A 为 T_2 像；B 为肝动脉期对比增强；C 为门静脉期；在 T_2 像中肿块呈轻微增强，而在肝动脉期肿块边缘强化，在门静脉期表现为中央部的坏死；D 为 FDG PET 显示中央部的坏死

Figure 4　T_2 (A) and contrast enhanced hepatic arterial phase (B) and portal venous phase (C) MR images of the liver demonstrate illdefined slightly hyperintense mass on T_2 with peripheral rim enhancement on the hepatic arterial phase, and central necrosis on the portal venous phase; (D) FDG PET shows increased uptake and central photopenic zone indicating necrosis

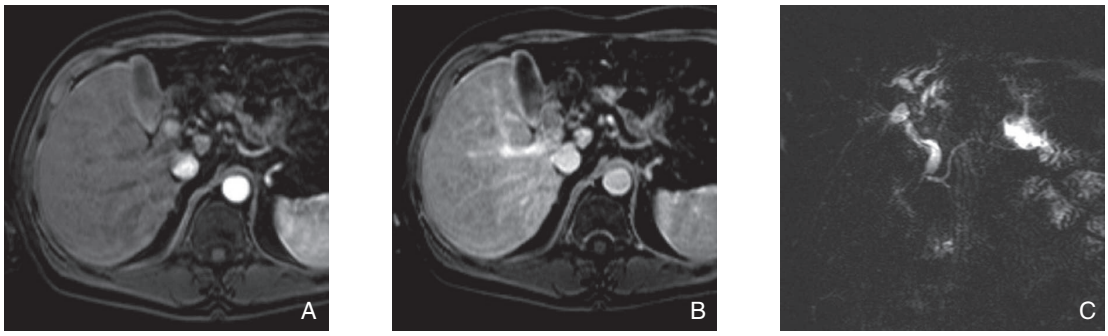

图5 A为肝动脉期的平扫增强MRI及门静脉期；B为小的管腔内多血管肿块，在门静脉期减弱；C为冠状位的MRCP示在左右肝管回合部的肿块引起肝内胆管扩张

Figure 5 Axial contrast enhanced MRI in the hepatic arterial phase (A) and portal venous phase (B) showing a small intraductal hypervascular mass with washout on the portal venous phase. Coronal MRCP image (C) showing intraductal mass at the confluence of the right and left hepatic ducts causing moderate intrahepatic ductal dilatation

2.2 直接胆道造影

逆行性胰胆管造影术（ERCP）及经皮肝穿刺造影术（PTC）在评估肿瘤大小范围的同时，可以允许治疗性的胆汁引流，尽管这种术前的胆道引流（PBD）在HC治疗中的作用仍存在争议。Liu等[48]通过对术前行PBD及未行PBD者进行比较，未发现患者从PBD中明显获益，尽管文章有一定的局限性。多重回顾性分析表明虽然在HC黄疸的患者中应用PBD无法改善预后，但可以减少术后的并发症[14, 49-52]。再者多重研究[53-56]表明对出现黄疸的患者行肝切除术，术后增加肝衰及并发症的发生率，术前行PBD有助于增加手术的可切除术性。Kennedy等[57]发现对于残存肝体积<30%的患者行PBD可提高围手术期的安全性。尽管需要更多的随机研究去证实PBD在HC患者中的作用，但文献[58]表明在出现黄疸的HC患者中对残存肝的PBD应作为常规。

在ERCP及PTC取活检的应用方面，两者拥有相似的敏感性（75%~85%）和特异性（70%~75%），然而，需要说明的是阴性的活检结果不能完全排除HC，并且跟据临床表现可以忽略活检结果[59-63]。直接比较而言，PTC的操作相关并发症较少，不过约有2%~5%的患者需重复插管[64-65]。目前两项检查均可以提供满意的检查结果，具体选择与各个机构相关。

超声内镜在帮助肿瘤分期方面其敏感性是可以接受的，尽管这项技术与操作者的水平有一定的相关性，故其准确性也存在差异[38, 66-67]。有限的数据表明在超声内镜引导下的HC及周围淋巴结细针穿刺活检是可行的，但仍需更多的研究证实其实际作用[68-71]。经腹膜的细针穿刺活检有潜在较高的腹膜转移发生率，故在考虑可切除的患者中应避免选择该项检查[72]。

MRCP在辨认肿瘤在解剖学上的侵犯范围时，其效果与PTC及ERCP相当[31, 60, 73]。胆道的分段评估最好应用MRCP，而评估肿瘤的血管及远处转移最好应用MDCT或对比增强MRI[31]。术前所行的胆道支架或经皮的肝穿刺影流可能导致胆管壁炎症及创造出影响影像学结果的伪影。因此在行这些侵入性操作之前要先获得分段及评估可切除性的影像学资料，这是很重要的[32-33, 41]。

2.3 分期规则

不同的HC分期规则目前都在使用。Bismuth-Corlette分型提供了术前肿瘤范围的评估，同时也用来确定手术范围（图6）[74-75]。但是并没有涉及有关血管及转移方面的信息，并存在判断预后方面的局限性[7, 76]，纪念Sloan Kettering癌症中心（MSKCC）罗列出有关肿瘤范围的相关细节，同时也评估涉及的门静脉及萎缩的肝叶情况（表1）。同样的MSKCC系统也没有涉及肿瘤转移情况的评价，主要适合于局部切除的分类[77-79]。

美国癌症联合会（AJCC）对于CC的分期系统最为常用[80]，在第7版的AJCC分期系统中，肝外的胆管肿瘤有独立的分期，并进一步分为肝门部胆管肿瘤及远端胆管肿瘤。同Bismuth-Corlette及MSKCC分期系统不同的是，AJCC分期将血管（包括门静脉及肝动脉），相关淋巴结及远处转移均做为分期指标，但其对术前可切除性的评估作用较小，主要应用术后的肿瘤分期。多项文献[81-84]表明AJCC系统对于生存期的评估是不准确的，可能是由于其未将肿瘤侵袭深度作为分期指标。实际上，回顾性分析表明MSKCC分期系统对整体

生存率的评估较 AJCC 系统更为准确 [85-86]。通过对各个机构对不同分期系统的研究，Deoliveira 等 [87] 建议以肿瘤的大小、侵及范围、涉及的血管、淋巴结、远处转移情况及术后的残肝体积的指标重新确立分期系统。

图 6　肝门部胆管癌的 Bismuth-Corlette 分型　I 型为肿瘤位于肝胆管汇合部（HDC）的远端；II 型为肿瘤延伸至 HC；III 型肿瘤侵犯汇合部同时分为侵及右肝管的 IIIA 型及侵及左肝管的 IIIB 型；IV 型为肿瘤延伸至双侧肝管 [74]　缩写：RHD，右肝管；LHD，左肝管；HDC 左右肝管汇合处

Figure 6　The Bismuth-Corlette classification of hilar cholangiocarcinoma　Type I tumors are distal to the hepatic duct confluence (HDC) while type II neoplasms extend to and involve the HDC; Type III tumors involve the HDC and either the proximal right hepatic duct (type IIIA) or proximal left hepatic duct (type IIIB); Type IV tumors extend into the bilateral proximal hepatic ducts up to the segmental bile ducts [74]　Abbreviations: RHD, right hepatic duct, LHD, left hepatic duct, HDC hepatic duct confluence

表 1　Sloan Kettering 癌症中心肝门部胆管癌分期 [77]

Table 1　Memorial sloan kettering cancer center hilar cholangiocarcinoma classification[77]

分期	标准			
	侵及胆管汇合处	侵犯 2 级胆管	侵及门静脉	肝萎缩
T_1	是	+/– 单侧	否	否
T_2	是	+/– 单侧	肿瘤同侧	+/– 肿瘤同侧
T_3	是	双侧	是 / 否	是 / 否
	是	单侧	肿瘤对侧	是 / 否
	是	单侧	是 / 否	对侧
	是	+/– 单侧	双侧	是 / 否

3　病理学特征

大体而言，HC 被分为 3 种类型：乳头型，结节型和硬化型。结节型和乳头型典型表现为向管壁内突出。硬化型 HC 常利用肉眼可见的黏膜突起广泛的侵犯胆管壁 [88]。硬化型 HC 是最常见的病理类型；乳头型的 HC 因其侵袭性低的生长模式通常情况下较易切除并有较好的预后 [88-90]。然而，许多 HC 肿瘤都包括两种以上的病理类型。

超过 90% 的肝外上皮胆管肿瘤为腺癌，其根据腺组织在肿瘤中所占百分比分为高、中、低分化类型 [91-92]。直接侵犯肝组织，周围淋巴管及神经是常见的现象。尽管胞质的 CEA 及 MUC1 通常良性胆道上皮细胞表面有所表达，但在 HC 中也可以被发现，并在肿瘤转移中起到一定的作用 [88]。基因表达在胆管腺癌中有不同的起源，这可能有预后的意义。例如，在 HC 中周期依赖的激酶抑制剂 P-27 的表达较胆囊癌及远端胆管肿瘤更为常见，同时其低表达，常提示预后不良 [93]。在胆管肿瘤中的 K-ras 突变常预示整体生存率的下降，相比于 HC，在远端胆管肿瘤中其突变频率更高 [94-95]。

癌前病变包括胆管上皮内瘤（BiIN）和胆管内的乳头状赘生物（IPN-B）。这些病变被认为与胰腺的上皮内瘤（PanIN）及胰腺的管内的黏液素瘤（IPMN-P) 相对应 [88, 91]。与 PanIN 相似，BiIN 可以进展为管内腺癌，并可根据其非典型增生的程度进行判定。BiIN-3 代表原位癌，可以在 10%~75% 的肝外胆管癌中发现 [88]。伴随胆管上皮的表面播散也可在 10%~18% 肝外胆管癌患者中发现，通常有较好的预后 [96-97]。

4　治疗措施

4.1　术前肝功能的改良

许多 HC 的患者均存在黄疸并可能行肝切除术，这些均可能增加术后并发症的发生率 [54]。残余肝（FLR）胆道引流可以帮助降低胆红素水平并便于残肝的生长 [53]。如果 FLR<30%~40%，门静脉栓塞可以考虑应用 [53, 98-99]。尽管没有随机试验证实其在 HC 中的作用，但 PVE 可以使术前 FLR 增加从而减少术后肝衰及并发症的发生。通常在行胆道引流或 PVE 后 4~6 周可考虑行手术治疗 [53, 98]。

4.2　手术切除

不可切除的指证包括：肿瘤侵犯双侧胆管的

二级分支，侵犯门静脉主干，侵犯肝动脉或门静脉分叉处，单侧的肝动脉受累并有证据表明对侧脉管的广泛播散[100]。肝动脉及门静脉的受累情况，腹膜转移，影像学中可疑的淋巴结均是重要的判断能否切除的指标[37-38, 101]。尽管有各种不同的检查方法的应用，仍有40%~50%的HC患者在剖腹探查中发现无法行根治性手术[13, 102]。许多人提倡应用分段腹腔镜探查来避免不必要的剖腹探查，有一些研究[102-105]显示利用此项技术可避免45%的患者不必要的剖腹探查，如果可以结合超声内镜检查，其准确度及获益会更大[106]，而腹膜细胞刷并没有显示出获益[107]。尽管A级的证据是缺乏的，分段腹腔镜检查对于一些患者是有利的，尤其是那些CA19-9高或怀疑肝外胆管疾病的患者。

R_0切除仍是唯一有可能延长生存期的治疗方式[13-15, 17, 77, 108-110]。由于HC性质及位置，外科手术切除有时仍是一种挑战。发病率及病死率分别波动在40%~70%和5%~15%之间（表2）[13-15, 17, 113, 119]。仅仅是肝外胆管的局部切除是应该避免的，因为这种方式很有可能是R_1（切缘微观阳性）切除甚至是R_2（切缘肉眼阳性）切除，并且遗留了可疑的淋巴结及预后不良[14, 110, 120-124]。肝切除结合肝外胆管的切除可以增加R_0切除的几率并有助于生存期的延长，故应被认为是标准治疗方式[17, 77, 118, 120, 125]。一般而言Bismuth-Corlette I、II、IIIa的病变一般需要额外的右肝切除，而Bismuth-Corlette IIIb型则可能行相应的左肝切除。有资料[100, 126-128]表明完整的尾状叶切除可改善复发率及提高远期生存率，所以尾状叶应常规切除。淋巴结及周围神经的受侵发生较早，并提示较差的生存期[88, 129]。尽管淋巴结清扫术不能延长生存期，但其可以有助于局部肿瘤的控制，并且研究发现拥有5年生存期的患者其阳性淋巴结率仅为15%[130-132]。

表2 近期肝门部胆管癌的病例分析

Table 2 Recent hilar cholangiocarcinoma case series

作者	手术切除（*n*）	肝切除（%）	R_0切除（%）	中位随访时间（月）	发病率（%）	病死率（%）	生存率
Cho, et al. 2012[13]	105	72	70.50	25	—	14.3	34.1%[1)]
Nuzzo, et al. 2012[14]	440	85.5	77.3	—	47.5	8.6	25.5%[1)]
Cannon, et al. 2012[15]	59	83.1	62.7	—	39	5.1	17.7%[1)]
Zheng-Rong, et al. 2011[17]	71	25	69	—	—	6.4	10.6%[1)]
Chauhan, et al. 2011[111]	51	67	73	19	68	10	19%[1)]
van Gulik, et al. 2011[112]	99	38	31	60	68	10	20%[1)]（1988—1993年）；33%[1)]（1998—2003年）
Regimbeau, et al. 2011[113]	39	100	77	—	72	8	—
Shimizu, et al. 2010[114]	163	100	63.8	—	44	6.4	R_0右肝切除42.2%；R_0左肝切除36.7%
Unno, et al. 2010[115]	125	100	63.2	18.5	48.7	8	34.7%[1)]
Miyazaki, et al. 2010[116]	107	91	59	—	—	1.9	R_0 33%
Lee et, al. 2010[117]	302	88.7	71	—	43	1.7	R_0 47.3%, R_1 7.5%[1)]
Rocha, et al. 2010[109]	60	80	80	18	28	5	R_0 24%, R_1 0%[1)]
Ito, et al. 2008[118]	38	20	63	29	26	3	55个月（切除患者）*vs.* 4个月（未切除患者）

注：1）5年生存率

Note: 1) 5-year survival

大多数外科手术的基本方式包括肝切除合并肝外胆管切除，从而获得R_0切除，R_0切除率约占60%~80%[13-14, 17, 113, 116, 120]。尽管术中切缘需行冷冻快速切片分析，但其不能帮助改善R_0切除率[20-21]。虽然R_1切除较非手术治疗有较好的生存获益，但R_0切除仍应作为主要目标[133-135]。

常规的血管切除现有较多的争议性。在一个Meta分析[136]中，门静脉切除（PVR）与较高的病死率联系在一起，尽管在更有经验的中心中没有发现这一关系[136]。重要的是PVR组同非血管切除组比较，其5年生存率无明显差别，尽管PVR组的肿瘤恶性程度较高。整体而言，PVR对于恶性程度较高的HC而言可以使患者的长期生存获益，而不应将这类患者列为手术的禁忌[120, 137]。相反，肝血管切除可以增加患者的病死率及并发症的发生率，且长期生存未得到明显改善，故不应作为常规切除手段[138-139]。1999年Neuhaus等[140]提出“无瘤”技术应用于HC患者行整块的右三叶切除术并结合常规的PVR。在最近的回顾分析中，Neuhaus等[141]发现应用无瘤技术组5年生存率（58%）高于常规肝切除组（29%），并且两组之间的手术病死率无显著性差别。尽管这些结果是令人振奋的，

但这些结果可能存在干扰及回顾时的选择性偏倚，所以，在采取无瘤技术作为 HC 切除的标准之前，需要做进一步的研究。

最小侵害性的 HC 手术作用仍是不明确的，尽管有很多相关的病例报道。有数据表明这种技术的可用性，但适当的评估仍需要大量的临床研究及长期的随访 [142-144]。

有人推荐对于对剖腹探查发现肿瘤已不可切除的患者行姑息性手术 [145]。HC 的姑息性手术包括胆囊切除及胆肠引流。尽管其可以增加其通畅率，但会增加发病率（17%~51%）和病死率（6%~12%），同时与未行手术组相比，整体的生存并无改善 [146-148]。其中，这种术式最常见的并发症为胆肠吻合瘘（6%~21%）[147]。所以外科的引流术不常规推荐，并且如患者胆汁排泄通畅，这种手术是不必要的 [147, 149]。

一般而言，HC 术后的 5 年生存率约为 10%~40%[13-14, 150]，而且即使是 R_0 切除，复发率仍高达 50%~70%[151-152]，其主要原因可能同淋巴结转移，淋巴管侵犯，阳性切缘，肿瘤 T 分期较高有关 [13-15, 111, 117, 153-155]。

4.3 移植

在过去的 10 年中，对不可切除的 HC 患者而言，原位肝移植术（OLT）可以作为一种治疗方式。早期多个评估 OLT 对不可切除的 HC 效果显示其 5 年生存率仅为 20%~30%[156-158]。早期的研究结果来自 Mayo 临床中心，然而，他们建立出一套成功的多形式的 HC OLT 规则，并在高度选择的患者中，其 5 年生存率达到 60%[27, 159]。经腔内穿刺活检、细胞刷、胆道狭窄加 FISH 染色体，横断面的大块病灶及狭窄的病灶结合升高的 CA19-9 或 FISH 染色体等检查诊断为 HC 者，可考虑行 OLT[160]。患者应有足够的身体条件以便耐受新辅助治疗及肝移植术。其排除标准由肿块在胆囊管水平以下，肿块 >3 cm，有证据考虑肝内外转移或存在经腹膜活检史。治疗的程序包括外放射治疗（40~50 Gy），通过 ERCP 或 PTC 的介入放射治疗（20~30 Gy），同时应用 5-FU 及口服卡培他滨，直至移植术当天 [160]。在移植术前，患者应行分段手术如淋巴结清除评估，及彻底的排除腹腔转移。在 2009 年美国器官分享中心（UNOS）将 HC 列入 OLT 的手术指证中 [27, 161]，所以其他中心也越来越多的开始为不可切除的 HC 患者实施 OLT。Darwish 等 [27] 发现按照 UNOS 的程序对 HC 患者实施 OLT 的 12 个美国主要的移植中心中，其 5 年无瘤生存率达 65%，对比临床中心，其结果无明显差异。最后，与无标准的中心比较，UNOS 的标准与无瘤生存率紧密联系在一起 [27]。

因 PSC 所致的 HC 患者在手术后其 3 年生存率不超过 20%[162-163]。再者与 PSC 相关的 CC 恶性程度较高并且为多灶性，无法手术切除 [162]。Rea 等 [164] 在 PSC 相关的 HC 患者中实施 OLT 者较常规手术切除的患者有生存期的改善。Darwish Murad 等 [27] 在 12 个多中心的分析中发现，对 PSC 相关的 HC 患者实施肝移植术较非 PSC 相关者无瘤生存率有明显的改善（62% *vs*. 51%，P=0.06）。OLT 术后结合新辅助治疗，这类患者的 5 年生存率可超过 70%，因此这种治疗模式成为其标准的治疗方式 [164]。相反，对于非 PSC 相关的 HC 患者实施 OLT 仍存在争议。未来的 OLT 在 HC 患者中的应用应严格按照标准实施并且需要进一步的评价。

4.4 放射治疗

对于不可切除的 HC 患者，研究是结合传统的 5-FU 化疗及放射治疗进行的，故效果也是混杂的。其数据是由小的单一的机构并结合不同位置的胆道肿瘤（如胆囊癌，肝内外胆管癌）得出的。预期的 HC 试验被肿瘤发病率，侵袭性及发现较晚期等因素所限制。在辅助治疗中，放射治疗的目标在于控制肿瘤的生长，减缓疾病的进展以及延长生命。HC 术后的的局部控制是关键的，因为在胆管局部进展的的发生率较高。放化疗可以帮助阻止或减缓未经控制的进展症状。

在一项回顾性研究中，Todoroki 等 [165] 对 1976—1999 年行 Klatskin 瘤的 63 名患者作为研究对象，全部 29/49 患者行辅助治疗如术中放射治疗（IORT），体外放射治疗（EBRT），或两者结合治疗。行辅助治疗组对比未行辅助治疗组 5 年生存率有所改善（33.9% *vs*. 13.5%，P<0.01）。局部复发在接受辅助放疗组下降：20% 对比 69%。Gerhards 等 [166] 以 91 例 HC 手术患者作为研究对象，其中有 86% 的患者切缘为阳性；有 71 名切缘阳性的患者接受 EBRT、内部放射或两者结合的治疗。研究发现这些接受放射治疗的患者中位生存期为 24 个月，而仅仅行观察者其中位生存期仅 8 个月（P<0.01）。所以这些研究者认为辅助的放射治疗可以帮助切缘阳性的患者控制肿瘤进展及延长生存期。

传统上的放疗需 5~6 周，并且被限制在 54 Gy，原因在于可能造成器官的放射性损伤（OARs），尤其是周围的肠管及胃。当了解引起 OARs 的剂量

后，改进了治疗模式包括调强放射治疗（IMRT）及立体放射治疗（SBRT），所以目前放射治疗被越来越广泛的应用[167]。不可切除的患者应用标准放射治疗或化疗，传统上而言结果仍不理想。SBRT可以在短期（2周内）应用较大剂量并显示出一定的对控制复发的作用。然而，远期复发率仍然较高，需要进一步更有效的方式。

4.5 化疗

目前对于不可切除的HC患者标准的化疗方案仍是吉西他滨加铂剂。这些治疗在随机临床试验及小的回顾性研究中对生存期有小的改善[168-171]。尽管数据有限，化疗对于不可切除的患者而言仍有一定的作用[172]。需要更多的随机试验证明其效果，并可以考虑根据患者情况的不同选择不同的治疗方案，包括增加新的药物、靶向制剂及传统的细胞毒性药物[173]。

新辅助化疗对于HC而言仍疗效不佳，只是在移植方向的文献中显示出比较好的效果[27]。很少有文献说明其可以使肿瘤降期并可是肿瘤达到R_0切除[174]。需要更多的研究来证实其作用，但目前没有指证对延迟切除的患者应用新辅助化疗。

4.6 光动力疗法

光动力疗法（PDT）需要静脉注射光敏剂并使之在肿瘤细胞累积，当被光激发时，将导致纯态氧的释放并对临近的细胞造成破坏。皮肤的光损伤见于30%的患者中[175]。多种预期试验及回顾性研究[176-179]表明常规治疗并辅助PDT可增加生存期2~3个月。在Wiedmann等[180]评估的II期随机试验中，作为新辅助治疗的一种形式，PDT后患者的1年生存率为83%。尽管多证据不足并需要进一步研究，这项治疗仍显示出一定的实用性[180]。

5 结 论

HC是一种罕见但恶性程度较高的疾病，远期预后不良。淋巴结受侵、肿瘤的分期及阴性的切缘是重要的预后指标。R_0切除仍是使患者获得长时间生存的唯一机会。局部切除应该被否定。标准的手术治疗包括肝外胆管切除、肝切除及整块的淋巴结清除。在经高度选择后的患者中实施OLT是可行的。放化疗可以改善整体的生存率但仍需进一步的随机试验。由于这种疾病的复杂性，推荐应用多学科及多种模式的综合治疗。

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