

·指南与共识·

肝细胞癌伴微血管侵犯诊断和治疗 中国专家共识(2024 版)

中国医师协会肝癌专业委员会

通信作者:沈锋,海军军医大学第三附属医院,上海 200438, Email: shenfenghehbh@sina.com;程树群,海军军医大学第三附属医院,上海 200438, Email: chengshuqun@aliyun.com

【摘要】 肝细胞癌(以下简称肝癌)是我国常见的恶性肿瘤之一,手术切除是首选的治疗方法,但术后复发转移率高。目前证据表明微血管侵犯(MVI)是导致肝癌复发转移的独立危险因素,但是目前国际上对于MVI的诊断、分型、预测和治疗仍存在较多争议。为更好地指导肝癌伴MVI的诊断和治疗,中国医师协会肝癌专业委员会组织国内相关领域专家,经过多次讨论和修改,形成《肝细胞癌伴微血管侵犯诊断和治疗中国专家共识(2024 版)》,以供国内同行参考。

【关键词】 肝细胞癌; 微血管侵犯; 诊断; 治疗; 共识

基金项目:国家重点研发计划(2022YFC2503705);国家自然科学基金(82072618);上海市卫健委“重中之重”项目(2023ZZ02005)

Chinese expert consensus on the diagnosis and treatment of hepatocellular carcinoma with microvascular invasion (2024 edition)

Chinese Association of Liver Cancer of Chinese Medical Doctor Association

Corresponding authors: Shen Feng, the Third Affiliated Hospital of Naval Medical University, Shanghai 200438, China, Email: shenfenghehbh@sina.com; Cheng Shuqun, the Third Affiliated Hospital of Naval Medical University, Shanghai 200438, China, Email: chengshuqun@aliyun.com

【Abstract】 Hepatocellular carcinoma (hereinafter referred to as liver cancer) is one of the most common malignant tumors in China. Surgical resection is the preferred treatment for liver cancer, but the postoperative recurrence and metastasis rates are quite high. Current evidence shows that microvascular invasion (MVI) is an independent risk factor for postoperative recurrence and metastasis of liver cancer, but there are still many controversies about the diagnosis, classification, prediction and treatment of MVI over the world. The Chinese Association of Liver Cancer of Chinese Medical Doctor Association organizes domestic experts in related fields to form the *Chinese Expert Consensus on the Diagnosis and Treatment of Hepatocellular Carcinoma with Microvascular Invasion (2024 Edition)* after many discussions and revisions, in order to better guide the diagnosis and treatment of Liver Cancer with MVI and for reference by domestic peers.

【Key words】 Hepatocellular carcinoma; Microvascular invasion; Diagnosis; Treatment; Consensus

Fund programs: National Key Research and Development Program (2022YFC2503705); National Natural Science Foundation of China (82072618); Shanghai Municipal Health Commission "Top Priority" Project (2023ZZ02005)

肝细胞癌(以下简称肝癌)是我国第5种最常见的恶性肿瘤,每年新发病例约为40万例,死亡率仅次于肺癌,居全部恶性肿瘤死亡原因的第2位^[1]。

手术切除仍是我国肝癌的首选治疗方法,但术后5年总体复发率高达70%^[2-3];肝移植术后5年复发率为4.3%~57.8%^[4-7]。肝癌极易侵犯血管造成血行

DOI: 10.3760/cma.j.cn115610-20240125-00041

收稿日期 2024-01-25

引用本文:中国医师协会肝癌专业委员会.肝细胞癌伴微血管侵犯诊断和治疗中国专家共识(2024 版)[J].

中华消化外科杂志, 2024, 23(2): 153-164. DOI: 10.3760/cma.j.cn115610-20240125-00041.



转移,可能是造成肝癌复发转移的主要原因。微血管侵犯(microvascular invasion, MVI)主要指仅能在显微镜下观察到、在覆衬有内皮细胞的微小血管腔内存在的癌细胞巢团,多见于肿瘤包膜内和癌旁肝组织内的门静脉微小分支。MVI是导致肝癌复发转移的独立危险因素,其生物学特性和预后作用日益受到重视,但目前国际上对于MVI的诊断、分型、预测和治疗仍存在较多争议。为此,中国医师协会肝癌专业委员会基于现有的循证医学证据,尤其是我国学者在肝癌伴MVI领域取得的研究成果,组织共识委员会的多学科专家进行多次讨论,形成《肝细胞癌伴微血管侵犯诊断和治疗中国专家共识(2024版)》(以下简称共识)。随着新的循证医学证据不断出现,本共识将随之进行更新和完善。

本共识中循证医学证据等级评估参照证据评价与推荐意见分级、制定和评价(grading of recommendations, assessment, development and evaluation, GRADE)^[8-9],见表1。证据评价分级的指导原则法(<http://www.gradeworkinggroup.org/>)和《牛津循证医学中心2011版》。专家推荐的强度参照GRADE对推荐意见分级的指导原则。本共识已在国际实践指南注册与透明化平台(<http://www.guidelines-registry.cn/>)注册,注册号:PREPARE-2024CN185。

表1 证据评价与推荐意见分级、制定和评价证据质量与推荐强度分级

Table 1 Grading of recommendations assessment, development and evaluation

类别	具体描述
证据质量分级	
高(A)	非常有把握观察值接近真实值
中(B)	对观察值有中等把握:观察值有可能接近真实值,但也有可能差别很大
低(C)	对观察值的把握有限:观察值可能与真实值有很大差别
极低(D)	对观察值几乎没有把握:观察值与真实值可能有极大差别
推荐强度分级	
强(1)	明确显示干预措施利大于弊或弊大于利
弱(2)	利弊不确定或无论质量高低的证据均显示利弊相当
GPS(Good practice statement)	基于非直接证据或专家意见/经验形成的推荐

一、MVI的诊断和分型

(一)发生率、病理诊断和分型

已有研究结果显示:肝癌MVI的发生率为17.0%~

93.4%^[10-21]。MVI发生率与肿瘤长径呈正相关,长径<3 cm的肝癌MVI发生率为17.0%~40.6%^[16,18,21-26];长径为3~5 cm的肝癌为31.0%~42.5%^[22-23,27-28];长径>5 cm的肝癌为46.2%~93.4%^[23,27,29-33];多发性肝癌为9.9%~81.3%^[4,13,17,23,34-37];符合米兰标准的肝癌为9.9%~54.0%^[4,13,38-39]。

已有研究结果显示:MVI的部分病理特征,例如侵犯微血管的数量^[40-43]、分布情况^[43-45]、巢团内癌细胞计数^[40,43,46]、侵袭性分型^[42]和侵犯具有肌层的微血管^[44]等,均显著影响肝癌预后。Roayaie等^[44]将MVI定义为显微镜下微血管可见肿瘤细胞,并依据侵犯的微血管是否存在肌层,以及距肿瘤≥1 cm 2个危险因素将MVI分为B1型:存在MVI但无其他危险因素;B2型:MVI合并1个危险因素;B3:MVI合并2个危险因素。也有学者将MVI定义为镜下发现肝癌侵犯门静脉、肝静脉、微动脉及淋巴管中的一个或多个^[38,46]。Iguchi等^[46]依据巢团内癌细胞计数及MVI数量将MVI分为低危型:存在MVI但无其他危险因素;高危型:MVI数量≥2个或巢团内癌细胞计数≥50个。Feng等^[42]将MVI区分为非侵袭性(游离型和粘连型)和侵袭性(侵袭型和突破型),并结合MVI数量将MVI分为:I型,非侵袭性MVI且数量<5个;II型,侵袭性MVI或数量>5个;III型:侵袭性MVI且数量>5个。但是,目前MVI分型均基于非客观指标,尚需要多中心大样本研究加以验证。

本共识推荐使用《原发性肝癌病理诊断指南》的MVI病理分级标准:M0级:未发现MVI;M1级:≤5个MVI,且发生于近癌旁肝组织区域(≤1 cm);M2级:>5个MVI,或MVI发生于远癌旁肝组织区域(>1 cm)^[10]。已有研究结果显示:按照该标准区分MVI可以更准确地评估早期肝癌患者的预后,M0级、M1级、M2级患者肝切除术后的中位总生存时间(overall survival, OS)分别为61.1、52.7、27.4个月($P<0.001$),中位无瘤生存时间(disease-free survival, DFS)分别为43.0、29.1、13.1个月($P<0.001$)^[20,47]。

推荐意见1:建议使用《原发性肝癌病理诊断指南》推荐的MVI病理分级标准:M0级:未发现MVI;M1级:≤5个MVI,且发生于近癌旁肝组织区域(≤1 cm);M2级:>5个MVI,或MVI发生于远癌旁肝组织区域(>1 cm)(证据等级:B;推荐级别:强烈推荐)。

(二)标本取材法

目前肝癌切除标本的常用取材方法有3点法、

7点法、13点法和肝癌影像-数字化大体病理(image-matching digital macro-slide, IDS)等(图1)。海军军医大学第三附属医院团队的研究结果显示:“7点法”对于 MVI 的诊断率与“13点”相当(47.1%比51.3%, $P=0.517$),均显著优于“3点法”的34.5%($P=0.048$)),但“7点法”较“13点法”更为简便和实用^[20]。

已有研究结果显示:为了提高 MVI 的检出率,癌旁组织取材点的个数不应固定不变,应与肿瘤长径和数目呈正相关,长径为1~3 cm、3~5 cm、>5 cm 和多发肿瘤的癌旁组织内,取材数应至少达到4个、6个、8个和8个,但该建议仍需更多研究予以验证^[45]。IDS是指对整个肝癌切除标本进行切片固定,再进一步借助全切片扫描(whole slide imaging, WSI)技术获得优质的可视化数字图像,最后根据扫描仪相匹配的软件对图像进行分析和诊断,包括 MVI 在内的肝癌病理学特征。IDS 相较于传统的“7点法”可以显著提高 MVI 的检出率^[48]。但是 IDS 对于设备要求高且读片工作量大,在目前人工智能诊断尚不成熟的情况下,其大范围应用受到限制^[49]。

推荐意见 2:推荐使用“7点法”对肝癌标本进行取材(证据等级:B;推荐级别:强推荐),有条件的医学中心可使用 IDS(证据等级:C;推荐级别:强推荐)。

(三)临床分型

结合病理分型和临床特征的临床分型不仅能更准确地预测肝癌伴 MVI 的预后,也可以细化肝癌伴 MVI 的临床治疗。Zhang 等^[50]将 AFP、肿瘤包膜、肿瘤长径、HBeAg、乙型病毒性肝炎(以下简称乙肝)病毒脱氧核糖核酸(hepatitis B virus deoxyribonucleic acid, HBV-DNA)肿瘤个数和食管/胃底静脉曲张等变量构建为列线图,可将肝癌伴 MVI 患者进行临床预后分型。海军军医大学第三附属医院团队的研究结果显示:肝癌患者的预后与 AFP、是否存在肝硬化、肿瘤个数、肿瘤长径、MVI 个数及分布显著相关,用这些因素建立的列线图通过计算得分可将患者分为3型,此临床分型可以准确预测预后,

且仅有 C 型患者能从术后辅助性 TACE 治疗中获益^[51]。但上述临床分型的可推广性尚需进一步验证。

二、MVI 预测

MVI 是目前可指导肝癌复发防治的最重要的病理学特征。MVI 诊断依赖于对术后切除标本的组织病理学检查,而非对术前穿刺活组织病理学检查。但术后病理学检查的结果具有滞后性,不利于将 MVI 信息用于指导术前和术中治疗决策,由此,凸显术前预测 MVI 的必要性和重要性。目前可用于预测 MVI 的因素包括临床特征^[52-54]、影像学特征^[55-56]、影像组^[57-59]、蛋白组^[60]和基因组^[61-62]等各种组学研究提供的 MVI 相关特征。将影像组学特征应用于 MVI 预测的报道较多,但此类研究均存在样本量较小、缺乏外部验证、纳入患者的标准不统一等问题。总体而言,目前利用单一因素预测 MVI 的准确性均不理想,尤其是特异性较差。此外,报道的结果仍需多中心大样本资料加以验证。

多因素联合较单一因素可提高 MVI 预测的准确性。Lei 等^[63]提出了 MVI 预测模型-EHBH 列线图,该研究纳入 1 004 例早期肝癌患者,列线图模型包括肿瘤长径、肿瘤个数、肿瘤包膜、AFP 水平、PLT 计数、HBV-DNA 水平和影像学典型增强特征等 7 个因素,在最佳临界值为 200 时受试者工作特征曲线下面积(area under the receiver operating characteristic curve, AUC)灵敏度和特异度分别为 0.81、73.5% 和 76.6%。Lee 等^[64]报道用 AFP 水平、异常凝血酶原(des-gamma-carboxyprothrombin, DCP)水平、瘤周强化和瘤周低密度等 4 个因素联合预测 <3 cm 肝癌的 MVI 的发生概率,共纳入了 2 家医学中心 377 例患者,其 AUC、灵敏度和特异度分别为 0.87、65.2% 和 85.9%。四川大学华西医院团队报道纳入 2 160 例患者的 MVI 预测研究,结果显示:AFP 水平、DCP 水平、肿瘤长径、卫星结节、AST 及 AST/ALT 比值联合预测 MVI 的 AUC 为 0.80^[65]。Sun 等^[66]比较了上述预测方法,结果显示:EHBH 列线图在目前所有预测方法中稳定性与可靠性最佳。

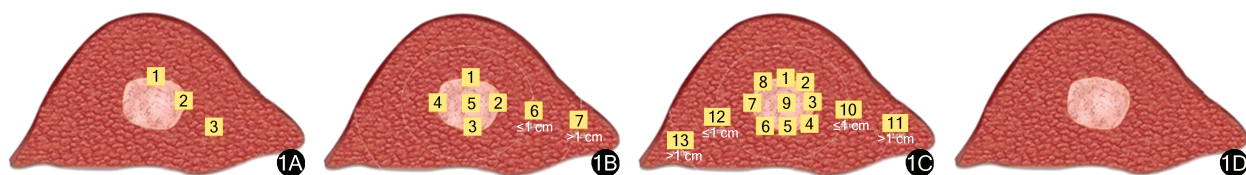


图1 常见的病理学检查标本取材方法 1A:3点法;1B:7点法;1C:13点法;1D:肝癌影像-数字化大体病理

Figure 1 Common pathological examination on specimen collection 1A: 3-points method; 1B: 7-points method; 1C: 13-points method; 1D: liver cancer imaging-image matching digital macro slide pathology

推荐意见 3: 建议肝癌患者术前进行 MVI 预测, 推荐使用 EHBH 列线图预测 MVI (证据等级: B; 推荐级别: 强推荐)。

三、MVI 指导治疗选择

肝癌伴 MVI 的治疗遵循保障安全性和改善肿瘤学预后 2 个主要原则。在保障治疗安全的前提下, 根据肿瘤情况和 MVI 信息, 首次治疗应选择对原发病灶及 MVI 根治性较佳的方法, 并强调多学科综合治疗, 以降低复发率, 延长生存时间, 改善生命质量。

(一) 首次根治性治疗

对于肝癌伴 MVI 的首次治疗, 比较不同治疗方法疗效的报道较少, 且缺乏前瞻性研究。已有研究结果显示: 术前预测为 MVI 高危的小肝癌 (长径 ≤ 3 cm) 患者, 肝切除术尤其是解剖性肝切除术 5 年 DFS 及 OS 显著优于经皮肝穿刺肝癌射频/微波消融术 (percutaneous radiofrequency ablation, PRFA/percutaneous microwave coagulation therapy, PMCT), 而低危患者的肝切除术与 PRFA/PMCT 疗效相似^[16,26,67-68]。对于符合米兰标准的肝癌患者, MVI 阳性患者的肝移植远期预后优于肝切除术, 而在阴性患者中解剖性肝切除术与肝移植的预后无显著性差异^[69-70]。但也有研究结果显示: 与肝切除术比较, 肝移植并不能使可切除肝癌伴 MVI 患者生存获益, 只能使 MVI 阴性患者获益^[71]。MVI 预测研究起步不久, 尚需更多临床试验充实其准确指导早期肝癌治疗决策的证据。

推荐意见 4: 对于肝癌可切除的患者建议首选手术切除 (证据等级: B; 推荐级别: 强推荐); 对于长径 ≤ 3 cm 且 MVI 预测为低危的患者可以选择手术或 PRFA/PMCT (证据等级: C; 推荐级别: 弱推荐)。

(二) 术后复发防治

1. 新辅助治疗

已有研究结果显示: 新辅助 TACE 导致的肿瘤坏死程度与术后病理学检查中的 MVI 检出率呈负相关^[72-73]。海军军医大学第三附属医院团队的研究结果显示: 在 TACE 后坏死面积 $>90\%$ 的肿瘤切除标本中, MVI 的检出率低于术前未行 TACE 的对照组 (8.1% 比 34.2%, $P < 0.05$), 坏死面积为 60%~90% 两组检出率相似 (47.1% 比 43.3%, $P > 0.05$), 坏死面积 $<60\%$ TACE 组的检出率显著高于对照组 (88.0% 比 48.0%, $P < 0.05$)^[73]; 总体而言, 肝切除术前新辅助 TACE 不能降低 MVI 总体发生率及改善预后^[73-74]。Kim 等^[75]对符合米兰标准的肝移植患者

给予新辅助 TACE, 结果显示: 该治疗不能降低 MVI 的发生率及改善远期生存。目前尚缺乏新辅助 TACE 对术前预测 MVI 高危患者的疗效报道。海军军医大学第三附属医院团队的 1 项随机对照研究结果显示: 术前放疗不能降低 MVI 高危者肝切除术后复发率和延长总体生存时间, 但该研究样本量较小, 其结果仍需大样本前瞻性研究验证^[76]。

推荐意见 5: 暂不建议对 MVI 预测高危肝癌患者单独使用 TACE 或放疗作为新辅助治疗 (证据等级: C; 推荐级别: 弱推荐); 为降低术后复发率, 鼓励在此类患者中开展新辅助治疗临床试验 (GPS)。

2. 术中治疗

解剖性肝切除术对病理 MVI 阳性肝癌患者的远期疗效优于非解剖性肝切除术^[26,77-89], 且腹腔镜肝切除术与开腹肝切除术的疗效相似^[90], 而 MVI 阴性患者则不能从解剖性肝切除术中获益^[83,87-88]。在肝切除术患者中, 除手术方式之外, 切缘的宽度也与预后密切相关。宽切缘 (切缘距离 ≥ 1 cm) 切除显著延长 MVI 阳性患者的 DFS 和 OS^[81,89,91-94]; 其预后价值甚至比解剖性肝切除术更重要^[95-99]; 但 MVI 阴性患者能否从宽切缘切除获益仍存在争议^[93-94,99-100]。此外, 1 项前瞻性 II 期临床试验报道术中放疗显著改善窄切缘的中央型伴 MVI 阳性肝癌患者的术后 DFS 及 OS, 但对 MVI 阴性患者无此作用。MVI 所致肿瘤肝内播散转移是患者死亡的主要原因^[101]。在保证手术安全的前提下, 术中宜减少、减轻对肝脏及肿瘤的挤压、翻转, 行原位切除可减少和避免肝内播散转移的风险。先行离断或阻断相应的流域血管也有利于减少此风险。

推荐意见 6: 建议对 MVI 预测高危肝癌患者行解剖性肝切除术或保证切缘距离 ≥ 1 cm (证据等级: B; 推荐级别: 强推荐); 如果不能行解剖性肝切除术或不能保证切缘距离 ≥ 1 cm, 有条件的医学中心可行术中放疗 (证据等级: C; 推荐级别: 弱推荐)。

3. 术后辅助治疗

肝癌伴 MVI 患者的术后辅助治疗主要包括以下措施:

(1) 抗病毒治疗。对于有乙肝背景的肝癌伴 MVI 患者, 规范化的抗病毒治疗既可保护肝功能, 又可降低复发率并改善远期生存。已有研究结果显示: 术前抗病毒治疗可显著降低 MVI 发生率^[102-104], 术后持续抗病毒治疗可显著延长 DFS 和 OS^[89,105-109]。目前常用的抗 HBV 核苷类似物/核苷酸类似物药物包括恩替卡韦、富马酸替诺福韦和丙酚替诺福

韦等。

(2)辅助性 TACE。TACE 是国内最常用的肝癌切除术后辅助治疗手段,治疗周期短且安全性较高。较多研究结果显示:TACE 降低肝癌伴 MVI 患者的复发率并延长生存时间^[89,110-114],但对 MVI 阴性者无此作用^[115-116]。已有研究结果显示:术后 2 次辅助性 TACE 的疗效优于 1 次,但该结果的可靠性仍需进一步证实^[117]。此外,东方肝胆 MVI 临床分型中仅有 C 型能从辅助性 TACE 获益,A 型和 B 型能否获益仍需进一步研究^[51]。

(3)辅助性放疗。2 项前瞻性研究结果均显示:肝切除术后辅助性放疗显著延长肝癌伴 MVI 患者的 DFS 及 OS^[118-119],对窄切缘者更具有优势。另有回顾性研究结果显示:术后辅助性放疗优于辅助性 TACE,但此方面的研究证据尚少^[120-121]。肝癌伴 MVI 的术后放疗技术推荐采用常规分割调强放射治疗,总剂量 50~60Gy,靶区建议包括手术切缘旁开 1.0~2.0 cm 的肝实质。

(4)辅助性肝动脉灌注化疗 (hepatic arterial infusion chemotherapy, HAIC)。国内 1 项纳入 315 例肝癌伴 MVI 患者的多中心随机对照研究结果显示:基于 FOLFOX 化疗方案的术后辅助性 HAIC 较对照组显著降低复发率^[122]。另 1 项纳入 11 项研究共 1 290 例患者的荟萃分析结果显示:术后辅助性 HAIC 可使肝癌伴 MVI 亚组患者生存获益^[123]。

(5)术后靶向治疗或靶向联合免疫治疗。虽然 STORM 试验^[124]未能证实索拉非尼可降低肝癌术后复发,但其他文献报道术后索拉非尼^[125-127]或仑伐替尼^[128-129]可以使肝癌伴 MVI 者获益。阿替利珠单抗联合贝伐珠单抗联合免疫治疗 (T+A) 方案辅助治疗研究 (IMbrave050 研究) 中期分析已达到了 DFS 的主要终点,该治疗使高复发风险者的复发/远处转移或死亡风险下降 28% (DFS 的 $HR=0.72$),提示 T+A 方案可作为肝癌伴 MVI 患者的有效辅助治疗^[130]。海军军医大学第三附属医院 1 项纳入 198 例肝癌伴 MVI 患者的前瞻性随机对照研究已达预设终点^[131],与主动监测比较,信迪利单抗联合免疫治疗可显著延长 DFS (27.7 个月比 15.5 个月, $P<0.001$),但还需进一步随访以确认 OS 的差异。此外,尚有多项 II 期或 III 期的靶向免疫治疗预防肝癌术后复发的临床研究结果有待公布。在选择靶向免疫治疗前需评估患者的一般体力状态、肝功能状态和治疗风险等,基线评估及不良反应处理等建议参照中国医师协会肝癌专业委员会发布的《肝细胞癌免疫治疗中

国专家共识(2021)》^[132]及《肝细胞癌分子靶向药物临床应用中国专家共识(2022)》^[133]。

(6)术后局部治疗联合系统治疗。术后联合辅助治疗可能优于单一辅助治疗,例如 TACE 联合抗病毒治疗^[105]优于单用抗病毒治疗或 TACE, TACE 联合索拉非尼^[134]优于单用索拉非尼或 TACE 等,但上述均为回顾性研究,未来仍需更多证据加以明确。

(7)肝移植术后辅助治疗。对于 MVI 阳性肝癌行肝移植者,除常规的早期调整免疫抑制剂方案外,文献报道针对预防肝癌伴 MVI 移植后复发的治疗手段还包括系统化疗^[135]和血浆置换^[136]等,但仍需前瞻性研究进一步明确疗效。

推荐意见 7: 建议对乙肝背景肝癌患者术后常规进行抗病毒治疗 (证据等级:A; 推荐级别:强推荐),对于术后病理学检查诊断 MVI 阳性患者还应依据实际情况推荐以下至少 1 种辅助治疗: T+A (证据等级:A; 推荐级别:强推荐),信迪利单抗联合免疫治疗 (证据等级:A; 推荐级别:强推荐), TACE (证据等级:B; 推荐级别:强推荐),放疗 (证据等级:B; 推荐级别:强推荐), HAIC (证据等级:A; 推荐级别:强推荐),仑伐替尼或索拉非尼 (证据等级:C; 推荐级别:弱推荐)。

(三)复发后治疗

文献报道 MVI 阳性肝癌较 MVI 阴性肝癌有复发率高、易于肝外转移和进展快等特点^[137-142]。已有研究结果显示: MVI 阳性肝癌复发且处于 BCLC 0/A 期者,再切除和 RFA 的疗效优于 TACE,但 BCLC B/C 期者 3 种治疗的疗效相似^[143]。参考《肝细胞癌术后复发和转移的多学科管理:国际专家共识》^[144],结合共识委员会讨论意见,本共识建议:即使 MVI 阳性肝癌复发后预后较差,但如果符合 PRFA/PMCT 指征则首选该治疗;如果复发灶为单发、无门静脉主干癌栓且至复发时间 (time to recurrence, TTR) ≥ 1 年,可考虑手术切除。同时,复发灶行综合治疗的效果优于单一治疗,如前次 MVI 阳性的复发性小肝癌患者行 TACE 联合 RFA^[145-146]或索拉非尼联合 RFA^[147]的疗效优于单用 RFA;前次 MVI 阳性的复发性不可切除肝癌行 TACE 联合索拉非尼的效果优于单用 TACE^[148]等。因此, MVI 阳性肝癌复发后的治疗需谨慎对待,需结合肿瘤复发的位置、TTR、复发病灶的数量及分布等综合考虑,建议经多学科团队 (multidisciplinary team, MDT) 讨论后决定相应的治疗方案。

推荐意见 8: 建议 MDT 讨论后决定 MVI 阳性

肝癌复发防治方案:复发灶 ≤ 3 个且最大肿瘤长径 ≤ 3 cm 则首选 PRFA/PMCT;如果复发灶为单发、无门静脉主干癌栓且 TTR ≥ 1 年,可考虑手术切除;对于复发灶不可切除,或早期复发(TTR ≤ 1 年)且无法行 PMCT/PRFA 的患者可行 TACE(证据等级:B;推荐级别:强推荐)。

四、多学科诊断与治疗流程

MDT 通过多学科协同诊断与治疗,最大程度发挥各学科的专业优势,让患者获益最大化,肝癌伴 MVI 的诊断与治疗更需要通过 MDT 制订诊断与治疗方案。首先需要对可切除肝癌进行 MVI 预测,对高危患者首选手术切除且尽可能行解剖性肝切除术或保证切缘 ≥ 1 cm,有条件的医学中心可以对窄切缘患者术中放疗;如为 MVI 低危者,对于长径 ≤ 3 cm 的肝癌可选切除或 PRFA/PMCT,对于长径 > 3 cm 的肝癌首选手术切除。其次,对于术后病理 MVI 阳性且有乙肝背景者术后常规行抗病毒治疗,并依据患者情况选择至少 1 项术后辅助治疗,包括 T+A、信迪利单抗克隆抗体、TACE、放疗、HAIC、仑伐替尼或索拉非尼等。最后,肝癌伴 MVI 患者复发后需要行 MDT 讨论后决定相应的治疗方案。

五、展望

近年来,肝癌伴 MVI 的诊断、预测和治疗取得了长足的进步,但仍有诸多问题亟需解决,例如:(1)预测 MVI 的准确性仍需提升,既往大量的文献已证实单一临床指标难以准确预测 MVI,将来引入组学数据等新变量可能提高预测准确性。(2)MVI 的病理学检查尚需不断完善,目前最常用的病理学检查标本取材“7 点法”对于 MVI 的检出率显著低于 IDS,但 IDS 的推广难度较大,因此,现阶段如何平衡取材、检出率和推广应用尚需进一步探索。(3)我国肝癌伴 MVI 患者数量众多,现有的共识推荐意见循证级别还较低,今后应充分利用我国的病例资源,结合最新的治疗进展如靶免治疗、双免治疗等,通过开展更多的随机对照研究以建立更为有效的肝癌伴 MVI 的治疗方法和方案。(4)肝癌发生 MVI 的分子机制研究尚需进一步研究,为治疗提供新靶点和新疗法。

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 夏 勇 海军军医大学第三附属医院

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