·指南与共识·

《原发性肝癌诊疗指南(2022 年版)》解读*

贺庆[1]　刘坤[2]　王超红[2]　张靖雨[1]

(1. 四川大学华西医院肿瘤中心，四川 成都 610041；2. 西藏自治区人民政府驻成都办事处医院肿瘤科，四川 成都 610041)

【摘要】 原发性肝癌是我国常见的肿瘤之一，近年来肝癌领域的研究有较多的突破性进展，这对肝癌的临床诊疗模式产生了深刻的影响。本文结合肝癌临床诊疗的现状以及研究领域的进展对《原发性肝癌诊疗指南(2022 版)》(以下简称指南)的要点进行解读，旨在推动肝癌临床诊疗模式更新，规范肝癌诊疗行为，提高肝癌的临床诊疗效果，早日实现本指南所提出的实现《"健康中国 2030"规划纲要》中总体癌症 5 年生存率提高 15%的目标。

【关键词】 肝癌；治疗；指南；解读

【中图分类号】 R735.7　【文献标志码】 A　DOI：10.3969/j.issn.1672-3511.2023.04.002

Interpretation on the key points of Guideline for the Diagnose and Treatment of Primary Liver Cancer (2022 Edition)

HE Qing[1], LIU Kun[2], WANG Chaohong[2], ZHANG Jingyu[1]

(1. *Oncology center, West China Hospital, Sichuan University, Chengdu* 610041, *China*;
2. *Onconolgy Department, Hospital of Chengdu Office of People's Government of Tibetan Autonomous Region, Chengdu* 610041, *China*)

【Abstract】 Primary liver cancer, one of the most common carcinomas of Chinese, is a huge burden to people's health and national medical insurance. To improve the treatment and diagnosis effectiveness of hepatocellular carcinoma, we interpret the key points of Guideline for the Diagnose and Treatment of Liver Cancer (2022 edition) and renew the mode of diagnose and treatment of primary liver carcinoma.

【Key words】 Primary liver cancer; Treatment; Guideline; Interpretation

肝癌在我国恶性肿瘤发病率及肿瘤致死病因位次中分居第四和第二，是一类高度恶性的肿瘤。原发性肝癌以肝细胞癌(Hepatocellular carcinoma，HCC)为主，占 75%～85%[1-2]。作为乙肝大国，高发病率、高死亡率的肝癌一直都是我国医疗卫生的重要负担[3]。近年来，随着消融技术的不断成熟以及靶向、免疫药物的相继问世，肝癌的治疗模式已经由原来以切除为主的综合治疗模式逐渐向介入为基础多种治疗手段干预的全周期综合治疗模式过渡。精细化、个体化已经成为肝癌治疗的必然趋势，这也在《原发性肝癌诊疗指南(2022 年版)》中得到了充分的体现，本文将对其进行解读。

1　筛查与诊断

1.1　筛查　研究表明肝癌总体 5 年生存率仅 18%，但符合米兰标准的早期肝癌不论是手术切除还是肝移植目前 5 年生存率都超过 60%[4-5]。早发现、早诊断、早治疗是肝癌提高疗效最重要、最有效的手段[6]。乙型肝炎病毒(Hepatitis B virus，HBV)和/或丙型肝炎病毒(Hepatitis C virus，HCV)感染者、过度饮酒、非酒精性脂肪性肝炎、其他原因引起的肝硬化以及肝癌家族史等人群都是肝癌高危人群，其中 40 岁以上的男性因风险更高需重点关注[7]。按照指南推荐，这类高危患者建议 6 个月一次超声加甲胎蛋白(AFP)检查，对于不能排除肿瘤的应该缩短复查时间至 2～3 个月或者考虑穿刺活检。

基金项目：(川大-泸州)科技创新平台建设项目(2020CDLZ-24)；湖北陈孝平科技发展基金会临床研究创新基金项目(CXPJJH12000001-2020202)；成都市技术创新研发项目(2021-YF05-01621-SN)

执行编委简介：贺庆，医学博士，副主任医师。成都市抗癌协会肿瘤介入治疗专委会副主任委员，国家分子影像介导精确诊断工作委员会、四川抗癌协会介入分会委员。从事介入诊断与治疗工作 20 余年，擅长肝癌、肺癌介入为主的综合治疗，静脉港植入及各种良恶性疾病的介入诊断与治疗。国内外期刊上发表专业论文数十篇。E-mail：tony-he11@sina.com

引用本文：贺庆，刘坤，王超红，等.《原发性肝癌诊疗指南(2022 年版)》解读[J].西部医学，2023，35(4)：474-479. DOI：10.3969/j.issn.1672-3511.2023.04.002

检查手段上，超声检查因无创、无辐射、方便、实时等优点依然是目前高危人群快速、便捷筛查的不二选择，其影像导航技术还可显示常规超声不能显影的隐匿肝癌，为消融、精准定位保驾护航[8-10]。

肿瘤标志物领域，临床上血清 AFP 依然是目前 HCC 最常用的诊断、疗效监测指标。除 AFP 外，异常凝血酶原（Protein induced by vitamin K absence/antagonist-Ⅱ，PIVKA Ⅱ；Des-gamma carboxyprothrombin，DCP）、血清甲胎蛋白异质体（Lens culinaris agglutinin-reactive fraction of AFP，AFP-L3）和 GALAD 模型（由性别、年龄、AFP、PIVKA Ⅱ、AFP-L3 构成）等，单个以及组合使用可以提高 AFP 阴性肝癌患者检出率，最高可达 77.7%[7,11-12]。除此之外，“液体活检”（Liquid biopsy）包括循环游离微 RNA（Circulating cell-free microRNA）、循环肿瘤细胞（Circulating tumor cell，CTC）、循环肿瘤 DNA（Circulating tumor DNA，ctDNA），虽然尚未应用于临床，但已经开始展现出在肿瘤早期诊断和疗效评价等方面的价值，值得期待[13]。

1.2 诊断 对于高度怀疑肝癌人群需要进一步明确诊断者，推荐动态增强 CT 或 MRI 多参数扫描。数字减影血管造影（Digital subtraction angiography，DSA）主要用于治疗，并不推荐作为筛查或者确诊的影像手段。但在治疗肝癌或肝癌破裂出血时，可同时提供肿瘤血管、血供、数量及大小情况相关信息[7]。正电子发射计算机断层成像（Positron emission tomography/CT，PETCT）以及断层磁共振成像（Positron emission tomography-MRI，PET-MRI）能够更全面评估淋巴结及远处转移，因不受解剖结构限制，在再分期中的应用中更有势，但对肿瘤预后和恶性程度评价特异性和敏感性较差且相对价格更高所以也不推荐为常规检查手段[14-21]。此外，肝细胞特异性磁共振对比剂钆塞酸二钠（Gd-EOB-DTPA）联合 MRI 检查，对直径小于 1 cm 原发性肝癌也有较高的敏感性；对甄别癌前病变，如高度异型增生结节（High-grade dysplastic nodules，HGDN），具有一定优势[22-24]。

虽然指南明确表述具有典型肝癌影像学特征的肝占位性病变，符合肝癌临床诊断标准的患者，通常不需要以诊断为目的的肝病灶穿刺活检。但也同时提出肝病灶穿刺活检可以明确病灶性质及肝癌分子分型，为明确肝病病因、指导治疗、判断预后和进行研究提供有价值的信息[7,25-27]。此外，按照影像学快进快出的诊断模式对于 1 cm 以上的肝癌结节诊断虽然特异性可以超过 90%但敏感性仅为 66%～82%。故对于可疑肝脏结节，为了能够尽早明确诊断，肝穿刺还是必要的[28-29]。

传统肝癌病理的主要临床价值是提供诊断以及对手术彻底性的评估，而随着肝癌的精准和个体化治疗进程的不断推进，其参与治疗策略的价值越来越受到重视，特别是基于肿瘤微环境的生物标志物更是目前研究的热点和重点，也是提高肝癌诊疗水平的重要突破方向。遗憾的是，由于肝癌的异质性，可用于指导治疗以及判断预后的病理指标依然处于探索阶段。目前推荐应用于临床的仅有微血管侵犯（Microvascularinvasion，MVI）这一指标。2022 版肝癌指南专门提出 MVI，既可以影像诊断也可以病理诊断。相对而言，影像诊断特异性高但敏感性较低。目前认为 MVI 是评估肝癌复发风险和选择治疗方案的重要参考依据，所以作为 A 级推荐指南认为 MVI 应纳入病理学常规检查[30-34]。除 MVI 之外，指南也在病理诊断报告部分专门提出：“可以附有与肝癌克隆起源检测、药物靶点检测、生物学行为评估以及预后判断等相关的分子病理学检查结果”以供临床参考。指南体现了肝癌的病理解读模式由单纯的诊断向诊断、治疗、预后更多功能和作用转化的趋势；同时，规范病理的检测既能兼顾诊疗的需要，也能减轻患者不必要的经济负担。

2 分期

肝癌分期直接关系到患者治疗方案的选择和预后。现有分期方案包括巴塞罗那（Barcelona Clinic Liver Cancer，BCLC）分期、TNM 和亚太肝脏研究学会（Asian-Pacific Association for the Study of the Liver，APASL）分期等。本指南根据肿瘤大小、数量、血管癌栓、肝外转移及患者体力活动状态（Performance status，PS）、肝功能 Child-Pugh 分级状况，建立并采用的是中国肝癌的分期方案（China liver cancer staging，CNLC）更贴近我国国情及实际[7]。

3 治疗

肝癌综合治疗体系的特点是多学科参与、多种治疗方法共存，不同时期乃至不同治疗方案的组合和先后顺序都是目前临床治疗策略中经常需要考虑的问题。故多学科诊疗团队（Multidisciplinary team，MDT）的诊疗模式是目前主流的诊疗模式，其中可治愈或者潜在可治愈患者的 MDT 目前依然是外科为主的综合治疗模式，而不可治愈患者则是以介入为基础的综合治疗模式。

3.1 外科手术切除和肝脏移植 完整的切除肿瘤并保留足够的正常肝组织是患者取得长期生存的重要治疗手段。为保证术后患者有足够的肝功能，指南指出手术必要条件，包括 Child-Pugh A 级，ICG 15min

滞留率(ICG-R15)<30%,有慢性肝病、肝损伤、肝硬化患者剩余肝脏体积应>40%,无肝硬化或肝纤维化者剩余肝脏体积应>30%[35-36]。技术上,采用入肝及出肝血流控制、术前三维可视化及腹腔镜可以有效地减少术中、术后并发症,有利于患者早期康复[37-40]。对于 CNLC Ⅱb、Ⅲa 期、Ⅲb 期(肝门淋巴结转移)以及肝功能差的患者并不首选推荐手术,但可通过转化治疗创造手术条件,在转化治疗中包括肝功能不足的转化治疗以及抗肿瘤的转化治疗;对肝储备功能不足,经门静脉栓塞(Portal vein embolization, PVE)肿瘤所在的半肝以及联合肝脏分隔和门静脉结扎的二步肝切除术(Associating liver partition and portal vein ligation for staged hepatectomy, ALPPS),可以短期内改善肝功能以获得手术机会[41]。其他局部抗肿瘤(消融、肝动脉灌注栓塞术)及系统抗肿瘤治疗(免疫治疗、靶向治疗)在围手术期的应用还在探索中,但均为降期治疗的重要手段。

肝移植是肝硬化失代偿不适宜手术或消融的患者获得长期生存的重要治疗手段,但因肝源有限,需严格把握指针,在国内众多的标准中,一致认为无血管侵犯、淋巴结及肝外转移是前提,但肿瘤大小及数目不一致,指南中采用的是美国加州大学旧金山分校(UCSF)标准;符合标准患者在等待肝源期间,可接受桥接治疗,成功降期治疗后接受肝移植的患者较未接受肝移植患者预后好,但降期治疗是否降低移植术后复发,证据有限[42-43]。

总体来说,虽然证据等级不高(证据等级 4,推荐 B),在非手术治疗方式取得长足进步的情况下,包括 TACE 以及靶向免疫治疗在内的各种非手术治疗手段控制肿瘤的良好效果为中晚期肝癌患者接受手术治疗提供可能[44]。因此,肝癌患者由之前的手术切除模式向手术、转化+手术以及手术+辅助治疗的综合模式转变。

3.2　消融治疗　指南主要讨论了射频消融(Radiofrequency ablation, RFA)、微波消融(Microwave ablation, MWA)、无水乙醇注射治疗(Percutaneous ethanol injection, PEI)并明确指出对于 CNLC Ⅰa、Ⅰb 期,无血管、胆管、临近器官侵犯且肝功能 Child-PughA/B 的患者可取得根治的效果,尤其是<2 cm 的肿块,手术和射频消融疗效疗效相当[45-47]。由于消融创伤小、疗效肯定、对肝功能影响较小,可以预见的是肝癌的消融治疗将必然会随着消融技术和设备的不断提升而更加广泛。此外,研究表明消融可以增强肝癌相关抗原 T 细胞应答,调节机体抗肿瘤自身免疫反应,极具前景,值得进一步探索[48-51]。

3.3　经动脉化疗栓塞　根据动脉插管、化疗与否及栓塞方式,可分为动脉灌注化疗(Hepaticarterial infusion chemotherapy, HAIC)、动脉栓塞(Transarterial embolization, TAE)、动脉化疗栓塞(ransarterial chemoembolization TACE)。目前,TACE 依然是肝癌治疗中最为重要且常用的方法,HAIC 在乏血供的患者中展现出了值得期待的疗效,而单纯的 TAE 在肝癌治疗中已经较少应用。指南推荐 TACE 可用于 CNLC Ⅰa-Ⅲb 期的治疗(虽然其中Ⅰa 患者是次选),这提示除了终末Ⅳ期肝癌,介入治疗是唯一涵盖了肝癌的几乎所有期别的治疗手段。而即便是Ⅳ期肝癌,介入治疗的诸多手段对于改善临床症状也能观察到积极的效果,可以说是目前肝癌治疗的基石也毫不为过[52-54]。虽然如此,但需要清晰认识到经皮穿刺血管(不论是静脉还是动脉)超选择治疗肝癌理论上并不是根治性手段,而现阶段的介入手段所获得的治疗效果已经到了一个瓶颈,介入特有的超选择局部治疗在操作技术上已经很难有突破性进展。因此,可以预见的是介入联合系统治疗,包括放化疗、靶向以及免疫治疗,将会是介入治疗肝癌相当长的一段时间的发展重点和方向[55]。因此,指南推荐 TACE 积极地联合消融、靶向、免疫治疗、外放射等手段争取更好的治疗效果[7,56]。

3.4　系统抗肿瘤治疗　系统治疗包括分子靶向治疗、免疫治疗、放化疗以及中医治疗等,其中免疫治疗联合抗血管治疗较单用免疫治疗效果好,因抗血管治疗可改善肿瘤微环境,增强 PD1/PD-L1 抗肿瘤疗效,两者起到协同作用。在一线系统抗肿瘤治疗中,阿替利珠单抗或信迪利单抗联合贝伐珠单抗类似物,疗效优于单用贝伐珠单抗[57-59]。伦伐替尼非劣效于索拉非尼,前者中位 PFS 显著优于后者[60]。FOLFOX4 方案全身化疗也是有效的一线治疗方案[61]。总体来说,系统治疗中索拉非尼的地位愈渐弱化,取而代之的是各种新型靶向药物以及以抗血管为主的靶向药物和以抗 PD-1 为代表的免疫药物的组合,这些新的组合和方案都显著地提高了晚期肝癌预后。可以预料的是,随着研究的深入,靶免治疗这种组合方式必将向中期以及早期肝癌患者推进,有望进一步整体提高肝癌的预后。

4　结语

新版指南对肝癌诊疗策略进行了梳理,继续强调了对于肝癌高危人群的筛查的重要性,规范了各种不同治疗手段的应用条件和范围,明确推荐肝癌 MDT 的诊疗模式以适应临床不同的状况,对于规范肝癌诊疗流程,提高我国诊疗效率和水平具有重要的意义。

但目前限于对肝癌的认识水平，仍需要继续深入研究以不断确立预后及疗效相关的生物标志物以及建立和完善成熟、可靠的治疗策略选择体系。

【参考文献】

[1] CHEN W, ZHENG R, BAADE P D, *et al*. Cancer statistics in china, 2015 [J]. CA Cancer J Clin, 2016,66(2):115-132.

[2] SUNG H, FERLAY J, SIEGEL R L, *et al*. Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. CA Cancer J Clin, 2021,71(3):209-249.

[3] YUE T, ZHANG Q, CAI T, *et al*. Trends in the disease burden of hbv and hcv infection in china from 1990-2019[J]. International Journal of Infectious Diseases, 2022,122:476-485.

[4] ISHIZAWA T, HASEGAWA K, AOKI T, *et al*. Neither multiple tumors nor portal hypertension are surgical contraindications forhepatocellular carcinoma[J]. Gastroenterology, 2008, 134:1908-1916.

[5] MAZZAFERRO V, SPOSITO C, ZHOU J, *et al*. Metroticket 2.0 model for analysis of competing risks of death after liver transplantation for hepatocellular carcinoma[J]. Gastroenterology, 2018,154(1):128-139.

[6] ZHANG B H, YANG B H, TANG Z Y. Randomized controlled trial of screening for hepatocellular carcinoma [J]. J Cancer Res Clin Oncol, 2004,130(7):417-422.

[7] 中华人民共和国国家卫生健康委员会. 原发性肝癌诊疗指南(2022 年版)[J]. 肿瘤综合治疗电子杂志, 2022,8:16-53.

[8] 王文平，季正标，董怡，等. 实时导航超声造影在小肝癌诊断中的应用研究[J]. 中华医学超声杂志(电子版), 2016,13: 56-60.

[9] DONG Y, WANG WP, MAO F, *et al*. Application of imaging fusion combining contrast-enhanced ultrasound and magnetic resonance imaging in detection of hepatic cellular carcinomas undetectable by conventional ultrasound [J]. J Gastroenterol Hepatol, 2016,31(4):822-828.

[10] DONG Y, WANG W P, XU Y, *et al*. Point shear wave speed measurement in differentiating benign and malignant focal liver lesions [J]. Med Ultrason, 2017,19(3):259-264.

[11] BEST J, BECHMANN L P, SOWA J P, *et al*. Galad score detects early hepatocellular carcinoma in an international cohort of patients with nonalcoholic steatohepatitis [J]. Clin Gastroenterol Hepatol, 2020,18(3):728-735.

[12] ZHOU J, YU L, GAO X, *et al*. Plasma microrna panel to diagnose hepatitis b virus-related hepatocellular carcinoma [J]. J Clin Oncol, 2011,29(36):4781-4788.

[13] ZHOU J, HUANG A, YANG X R. Liquid Biopsy and its Potential for Management of Hepatocellular Carcinoma[J]. J Gastrointest Cancer, 2016, 47(2): 157-167.

[14] NA S J, OH J K, HYUN S H, *et al*. 18f-fdg pet/ct can predict survival of advanced hepatocellular carcinoma patients: A multicenter retrospective cohort study [J]. Journal of Nuclear Medicine, 2017,58(5):730-736.

[15] LEE J W, OH J K, CHUNG Y A, *et al*. Prognostic significance of (1)(8)f-fdg uptake in hepatocellular carcinoma treated with transarterial chemoembolization or concurrent chemoradiotherapy: A multicenter retrospective cohort study [J]. J Nucl Med, 2016,57(4):509-516.

[16] HYUN S H, EO J S, LEE J W, *et al*. Prognostic value of 18f-fluorodeoxyglucose positron emission tomography/computed tomography in patients with barcelona clinic liver cancer stages 0 and a hepatocellular carcinomas: A multicenter retrospective cohort study [J]. European journal of nuclear medicine and molecular imaging, 2016,43(9):1638-1645.

[17] FERDA J, FERDOVA E, BAXA J, *et al*. The role of 18f-fdg accumulation and arterial enhancement as biomarkers in the assessment of typing, grading and staging of hepatocellular carcinoma using 18f-fdg-pet/ct with integrated dual-phase ct angiography [J]. Anticancer Research, 2015,35(4):2241-2246.

[18] BOELLAARD R, DELGADO-BOLTON R, OYEN W J, *et al*. Fdg pet/ct: Eanm procedure guidelines for tumour imaging: Version 2.0 [J]. Eur J Nucl Med Mol Imaging, 2015,42(2): 328-354.

[19] LIN C Y, CHEN J H, LIANG J A, *et al*. 18f-fdg pet or pet/ct for detecting extrahepatic metastases or recurrent hepatocellular carcinoma: A systematic review and meta-analysis [J]. Eur J Radiol, 2012,81(9):2417-2422.

[20] 伍发，蒋锐，杜飞舟，等. Pet/ct 与 mri 诊断原发性肝细胞癌介入治疗后边缘复发灶的对比研究 [J]. 西部医学, 2021,33(7): 1077-1080,1085.

[21] HECTORSSJ, WAGNERM, BESAC, *et al*. Multiparametric FDG-PET/MRI of Hepatocellular Carcinoma: Initial Experience [J]. Contrast Media Mol Imaging, 2018, 5638283. doi: 10.1155/2018/5638283 (2018).

[22] WANG W, YANG C, ZHU K, *et al*. Recurrence after curative resection of hepatitis b virus-related hepatocellular carcinoma: Diagnostic algorithms on gadoxetic acid-enhanced magnetic resonance imaging [J]. Liver Transplantation, 2020, 26(6): 751-763.

[23] ZENG M S, YE H Y, GUO L, *et al*. Gd-eob-dtpa-enhanced magnetic resonance imaging for focal liver lesions in chinese patients: A multicenter, open-label, phase iii study [J]. Hepatobiliary & Pancreatic Diseases International, 2013, 12(6): 607-616.

[24] RENZULLI M, BISELLI M, BROCCHI S, *et al*. New hallmark of hepatocellular carcinoma, early hepatocellular carcinoma and high-grade dysplastic nodules on gd-eob-dtpa mri in patients with cirrhosis: A new diagnostic algorithm [J]. Gut, 2018,67(9):1674-1682.

[25] VOGEL A, CERVANTES A, CHAU I, *et al*. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[J]. Annals of Oncology , 2018 , 29 (Suppl 4):iv238-iv255.

[26] ROBERTS L R, SIRLIN C B, ZAIEM F, *et al*. Imaging for the diagnosis of hepatocellular carcinoma: A systematic review and meta-analysis [J]. Hepatology, 2018,67(1):401-421.

[27] European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the

Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma[J]. J Hepatol, 2018, 69(1): 182-236.

[28] ROBERTS L R, SIRLIN C B, ZAIEM F, *et al*. Imaging for the diagnosis of hepatocellular carcinoma: A systematic review and meta-analysis [J]. Hepatology, 2018, 67(1): 401-421.

[29] VILLANUEVA A. Hepatocellular carcinoma [J]. N Engl J Med, 2019, 380(15): 1450-1462.

[30] CONG W M. Surgical pathology of hepatobiliary tumors [M]. Springer, 2017.

[31] CONG W M, BU H, CHEN J, *et al*. Practice guidelines for the pathological diagnosis of primary liver cancer: 2015 update [J]. World journal of gastroenterology, 2016, 22(42): 9279-9287.

[32] SHENG X, JI Y, REN G P, *et al*. A standardized pathological proposal for evaluating microvascular invasion of hepatocellular carcinoma: A multicenter study by lcpgc [J]. Hepatol Int, 2020, 14(6): 1034-1047.

[33] ISIK B, GONULTAS F, SAHIN T, *et al*. Microvascular venous invasion in hepatocellular carcinoma: Why do recurrences occur? [J]. J Gastrointest Cancer, 2020, 51(4): 1133-1136.

[34] ZHANG X, LI J, SHEN F, *et al*. Significance of presence of microvascular invasion in specimens obtained after surgical treatment of hepatocellular carcinoma [J]. Journal of gastroenterology and hepatology, 2018, 33(2): 347-354.

[35] SHEN Y, ZHOU C, ZHU G, *et al*. Liver stiffness assessed by shear wave elastography predicts postoperative liver failure in patients with hepatocellular carcinoma [J]. Journal of Gastrointestinal Surgery, 2017, 21(9): 1471-1479.

[36] RAJAKANNU M, CHERQUI D, CIACIO O, *et al*. Liver stiffness measurement by transient elastography predicts late posthepatectomy outcomes in patients undergoing resection for hepatocellular carcinoma [J]. Surgery, 2017, 162(4): 766-774.

[37] ZHONG J H, WU F X, LI H. Hepatic resection associated with good survival for selected patients with multinodular hepatocellular carcinoma[J]. Tumour Biol, 2014, 35(9): 8355-8358.

[38] 中国抗癌协会肝癌专业委员会转化治疗协作组. 肝癌转化治疗中国专家共识(2021 版)[J]. 中国实用外科杂志, 2021, 41(6): 618-632.

[39] WEI W, JIAN P E, LI S H, *et al*. Adjuvant transcatheter arterial chemoembolization after curative resection for hepatocellular carcinoma patients with solitary tumor and microvascular invasion: A randomized clinical trial of efficacy and safety [J]. Cancer Communications, 2018, 38(1): 1-12.

[40] CHEN Q, SHU C, LAURENCE A D, *et al*. Effect of huaier granule on recurrence after curative resection of hcc: A multicentre, randomised clinical trial [J]. Gut, 2018, 67(11): 2006-2016.

[41] HIDAKA M, EGUCHI S, OKUDA K, *et al*. Impact of anatomical resection for hepatocellular carcinoma with microportal invasion (vp1): A multi-institutional study by the kyushu study group of liver surgery [J]. Annals of Surgery, 2020, 271(2): 339-346.

[42] ZHU X D, HUANG C, SHEN Y H, *et al*. Downstaging and Resection of InitiallyUnresectable Hepatocellular Carcinoma with Tyrosine Kinase Inhibitor andAnti-PD-1 Antibody Combinations[J]. Liver Cancer, 2021, 10(4): 320-329.

[43] LEE S, KIM K W, SONG G W, *et al*. The real impact of bridging or downstaging on survival outcomes after liver transplantation for hepatocellular carcinoma [J]. Liver Cancer, 2020, 9(6): 721-733.

[44] MAZZAFERRO V, CITTERIO D, BHOORI S, *et al*. Liver transplantation in hepatocellular carcinoma after tumour downstaging (xxl): A randomised, controlled, phase 2b/3 trial [J]. The Lancet Oncology, 2020, 21(7): 947-956.

[45] LI L, ZHANG J, LIU X, *et al*. Clinical outcomes of radiofrequency ablation and surgical resection for small hepatocellular carcinoma: A meta-analysis [J]. Journal of gastroenterology and hepatology, 2012, 27(1): 51-58.

[46] FENG Q, CHI Y, LIU Y, *et al*. Efficacy and safety of percutaneous radiofrequency ablation versus surgical resection for small hepatocellular carcinoma: A meta-analysis of 23 studies [J]. Journal of cancer research and clinical oncology, 2015, 141(1): 1-9.

[47] PENG Z W, LIN X J, ZHANG Y J, *et al*. Radiofrequency ablation versus hepatic resection for the treatment of hepatocellular carcinomas 2 cm or smaller: A retrospective comparative study [J]. Radiology, 2012, 262(3): 1022-1033.

[48] WANG L, KE Q, LIN N, *et al*. The efficacy of transarterial chemoembolization combined with microwave ablation for unresectable hepatocellular carcinoma: A systematic review and meta-analysis [J]. International Journal of Hyperthermia, 2019, 36(1): 1287-1295.

[49] LI L, WANG W, PAN H, *et al*. Microwave ablation combined with ok-432 induces th1-type response and specific antitumor immunity in a murine model of breast cancer [J]. Journal of Translational Medicine, 2017, 15(1): 1-10.

[50] DUAN X, WANG M, HAN X, *et al*. Combined use of microwave ablation and cell immunotherapy induces nonspecific immunity of hepatocellular carcinoma model mice [J]. Cell Cycle, 2020, 19(24): 3595-3607.

[51] ROZEMAN E A, PREVOO W, MEIER M A, *et al*. Phase ib/ii trial testing combined radiofrequency ablation and ipilimumab in uveal melanoma (secira-um) [J]. Melanoma Research, 2020, 30(3): 252-260.

[52] HU H F, SANG Y F. A real-world study of chinese hepatocellular carcinoma patients treated with tace [J]. Eur Rev Med Pharmacol Sci, 2022, 26(9): 3091-3099.

[53] SI Z M, WANG G Z, QIAN S, *et al*. Combination therapies in the management of large (≥ 5 cm) hepatocellular carcinoma: Microwave ablation immediately followed by transarterial chemoembolization [J]. Journal of Vascular and Interventional Radiology, 2016, 27(10): 1577-1583.

[54] YANG M, FANG Z, YAN Z, *et al*. Transarterial chemoembolisation (TACE) combined with endovascular implantation of an iodine-125 seed strand for the treatment of hepatocellular carcinoma with portal vein tumour thrombosis versus tace alone: A

two-arm, randomised clinical trial [J]. J Cancer Res Clin Oncol, 2014, 140(2): 211-219.

[55] 魏军, 范习刚, 肖开美, 等. 卡瑞利珠单抗配合 tace 对伴微血管侵犯肝细胞癌患者肿瘤生长转移的影响 [J]. 西部医学, 2022, 34(7): 1031-1035.

[56] ZHANG Z H, ZHANG W, GU J Y, *et al*. Treatment of hepatocellular carcinoma with tumor thrombus with the use of iodine-125 seed strand implantation and transarterial chemoembolization: A propensity-score analysis [J]. Journal of Vascular and Interventional Radiology, 2018, 29(8): 1085-1093.

[57] FINN R S, QIN S, IKEDA M, *et al*. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma [J]. New England Journal of Medicine, 2020, 382(20): 1894-1905.

[58] FINN R S, QIN S, IKEDA M, *et al*. Imbrave150: Updated overall survival (os) data from a global, randomized, open-label phase iii study of atezolizumab (atezo) + bevacizumab (bev) versus sorafenib (sor) in patients (pts) with unresectable hepatocellular carcinoma (hcc). American Society of Clinical Oncology, 2021, 39(3suppl 3): 267. DOI: 10.1200/JCO.2021.39.3_suppl.267.

[59] REN Z, XU J, BAI Y, *et al*. Sintilimab plus a bevacizumab biosimilar (ibi305) versus sorafenib in unresectable hepatocellular carcinoma (orient-32): A randomised, open-label, phase 2-3 study [J]. The Lancet Oncology, 2021, 22(7): 977-990.

[60] KUDO M, FINN R S, QIN S, *et al*. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: A randomised phase 3 non-inferiority trial [J]. Lancet, 2018, 391(10126): 1163-1173.

[61] QIN S, BAI Y, LIM H Y, *et al*. Randomized, multicenter, open-label study of oxaliplatin plus fluorouracil/leucovorin versus doxorubicin as palliative chemotherapy in patients with advanced hepatocellular carcinoma from asia [J]. J Clin Oncol, 2013, 31(28): 3501-3508.

(收稿日期: 2022-09-01; 修回日期: 2023-02-10; 编辑: 黎仕娟)

(上接第 473 页)

[36] QU W, LIU Q, JIAO X, *et al*. Development and Validation of a Personalized Survival Prediction Model for Uterine Adenosarcoma: A Population-Based Deep Learning Study [J]. Front Oncol, 2021, 10: 623818.

[37] HU Y H, XIE C, YANG H, *et al*. Computed tomography-based deep-learning prediction of neoadjuvant chemoradiotherapy treatment response in esophageal squamous cell carcinoma [J]. Radiother Oncol, 2021, 154: 6-13.

[38] LI X, GAO H, ZHU J, *et al*. 3D Deep Learning Model for the Pretreatment Evaluation of Treatment Respons in Esophageal Carcinoma: A Prospective Study (ChiCTR2000039279) [J]. Int J Radiat Oncol Biol Phys, 2021, 111(4): 926-935.

[39] PAN Y, SUN Z, WANG W, *et al*. Automatic detection of squamous cell carcinoma metastasis in esophageal lymph nodes using semantic segmentation [J]. Clin Transl Med, 2020, 10(3): e129.

[40] WU L, YANG X, CAO W, *et al*. Multiple Level CT Radiomics Features Preoperatively Predict Lymph Node Metastasis in Esophageal Cancer: A Multicentre Retrospective Study [J]. Front Oncol, 2020, 9: 1548.

[41] LUO J, NING Z, ZHANG S, *et al*. Bag of deep features for preoperative prediction of sentinel lymph node metastasis in breast cancer [J]. Phys Med Biol, 2018, 63(24): 245014.

[42] KANN B H, ANEJA S, LOGANADANE G V, *et al*. Pretreatment Identification of Head and Neck Cancer Nodal Metastasis and Extranodal Extension Using Deep Learning Neural Networks [J]. Sci Rep, 2018, 8(1): 14036.

[43] LEE J H, BAEK J H, KIM J H, *et al*. Deep Learning-Based Computer-Aided Diagnosis System for Localization and Diagnosis of Metastatic Lymph Nodes on Ultrasound: A Pilot Study [J]. Thyroid, 2018, 28(10): 1332-1338.

[44] ERESEN A, LI Y, YANG J, *et al*. Preoperative assessment of lymph node metastasis in Colon Cancer patients using machine learning: a pilot study [J]. Cancer Imaging, 2020, 20(1): 30.

[45] WANG H, ZHOU Z, LI Y, *et al*. Comparison of machine learning methods for classifying mediastinal lymph node metastasis of non-small cell lung cancer from 18F-FDG PET/CT images [J]. EJNMMI Res, 2017, 7(1): 11.

(收稿日期: 2023-02-09; 修回日期: 2023-03-31; 编辑: 黎仕娟)