



· 综述 ·

# 术前MRI标志物联合手术切缘预测HCC早期复发研究进展

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[摘要] 肝细胞癌 (hepatocellular carcinoma, HCC) 根治术后早期复发是患者预后生存不佳的重要危险因素。而术前磁共振成像 (magnetic resonance imaging, MRI) 相关影像标志物对HCC早期复发的预测作用得到广泛认可。同时, 手术切缘宽度作为HCC预后的术中指标, 与术前MRI标志物联合预测HCC预后情况可能较单独应用术前MRI标志物更有意义, 而后者可对切缘宽度的选择有一定的指导意义。本文就术前MRI标志物联合手术切缘预测HCC根治术后早期复发的研究进展进行综述。

[关键词] 肝细胞癌; 磁共振成像; 手术切缘; 早期复发

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**Research progress on preoperative MRI markers combined with surgical margins in predicting early recurrence of HCC** ZUO Liping<sup>1</sup>, DU Peng<sup>1</sup>, SONG Baoli<sup>1</sup>, TIAN Ziyu<sup>1</sup>, WANG Bowen<sup>1</sup>, YU Dexin<sup>1</sup>, CAO Yongquan<sup>2</sup>  
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[Abstract] Early recurrence of hepatocellular carcinoma (HCC) after resection is an important risk factor for patients with poor prognosis. The role of preoperative magnetic resonance imaging (MRI)-related imaging markers in predicting early recurrence of HCC has been widely recognized. And surgical margin width, as an intraoperative indicator of HCC prognosis, combined with preoperative MRI markers to predict the prognosis of HCC seems to be more meaningful than preoperative MRI markers alone. And the latter could provide guidance for the selection of margin width. This article reviewed the research progress of preoperative MRI markers combined with surgical margins in predicting early recurrence of HCC after radical surgery.

[Key words] Hepatocellular carcinoma; Magnetic resonance imaging; Surgical margin; Early recurrence

肝细胞癌 (hepatocellular carcinoma, HCC) 是全球第七大常见恶性肿瘤, 中国第四大常见癌症<sup>[1-2]</sup>。虽然手术切除被认为是可切除HCC的标准治疗方法<sup>[3]</sup>, 但术后复发率可高达70%<sup>[4]</sup>, 早期复发率 (即根治性切除术后2年内复发) 可高达50%<sup>[5-7]</sup>。在近期研究<sup>[8-11]</sup>中, 研究人员试图通过术前磁共振成像 (magnetic resonance imaging, MRI) 相关标志物识别可能导致HCC患者术后早期复发的一些危险因素, 如肿瘤大小、微血管侵犯 (microvascular invasion, MVI)、非光滑的肿瘤边缘、实质性坏死等, 旨在为治疗

提供额外的信息, 以延长术后生存期。此外, 成功的HCC根治术需要完全切除肿瘤并保留足够的残肝, 这两者都与手术切缘的宽度密切相关, 而其对长期预后的影响已被广泛评估<sup>[12]</sup>。2010年, 美国HCC相关专家共识<sup>[13]</sup>推荐1~2 cm作为手术切缘宽度。此外, 《原发性肝癌诊疗指南 (2022年版)》提出HCC根治切除术的术中判断标准为切缘距离肿瘤边界 $\geq 1$  cm; 若切缘 $< 1$  cm, 则切缘肝断面病理组织学检查无肿瘤细胞残留, 才视为根治性切除<sup>[14]</sup>。目前, 国内外指南或共识<sup>[13-14]</sup>对于HCC切除的手术切缘宽度

仍存在争议,术前MRI影像学相关标志物的出现联合手术切缘是否会影响早期复发尚未得到确切的结果,标志物的出现是否对切缘宽度的选择提供一定的指导意义仍不明确。本文就术前MRI标志物联合手术切缘预测HCC根治性术后早期复发的研究进展进行综述。

## 1 术前MRI标志物在预测早期复发中的价值

MRI以其高软组织分辨率和对背景肝组织特性的全面评估能力被广泛用于预测HCC的预后<sup>[15]</sup>。而术前MRI检查的目的是协助准确评估疾病状态并提供最佳治疗策略。据此,术前MRI检查的相关标志物<sup>[8-9]</sup>,如肿瘤大小、表观弥散系数(apparent diffusion coefficient, ADC)值、实质性坏死、不光滑的肿瘤边缘、瘤周动脉期强化、动脉期不规则边缘样强化、肿瘤包膜等均被用来评估HCC的侵袭程度并与术后预后相关联。

### 1.1 术前MRI定性参数预测HCC术后早期复发

在MRI定性参数中,众多研究<sup>[16-19]</sup>基于MRI肝脏影像报告和数据库系统提供的相关参数评估HCC预后情况,如瘤周动脉期强化、不规则的肿瘤边缘、包膜不完整等。既往研究<sup>[19-22]</sup>发现,瘤周动脉期强化是术前预测HCC患者早期复发的独立危险因素( $P < 0.05$ )。瘤周动脉期强化是指动脉晚期瘤周实质内静脉引流区域强化,由卫星肿瘤阻塞肝静脉所致,表明肿瘤细胞可能存在于表面正常的周围肝组织,手术无法完全清除<sup>[21]</sup>,最终引起术后早期复发。此外,不光滑的肿瘤边缘是与早期复发相关的重要变量<sup>[23-26]</sup>。Lee等<sup>[27]</sup>发现,出现不光滑的肿瘤边缘的HCC多为中、低分化,而较差的病理学分化程度与预后不佳密切相关。同样,HCC内存在实质性坏死( $P = 0.002$ )亦被证明与术后早期复发独立相关<sup>[9]</sup>。有研究<sup>[28]</sup>指出,坏死与肿瘤术后复发高度相关,且已被纳入原发性实体恶性肿瘤的病理学分型和预后指标中。而可清晰展现坏死的术前MRI对揭示HCC预后的价值不言而喻。

### 1.2 术前MRI定量参数预测HCC术后早期复发

在MRI定量参数中,肿瘤大小<sup>[23-24]</sup>及ADC值<sup>[29]</sup>作为研究重点而被广泛报道。通常HCC早期复发组肿瘤直径多 $> 5$  cm,且较大的HCC与

侵袭性指标(如MVI等)具备强相关性<sup>[30-31]</sup>。刘永倩等<sup>[32]</sup>的研究表明,HCC直径 $> 3.9$  cm是预测MVI 2级的MRI定量参数。由于HCC较大的患者通常伴有严重肝脏纤维化背景、较差的肝脏储备功能、血管及胆管的受压或侵犯,因此术后发生肝内转移和门/腔静脉侵犯概率较高,最终造成HCC术后复发率提升。此外,术前ADC值亦可用于评估HCC术后复发, Lee等<sup>[33]</sup>的研究发现,  $ADC_{min}$ 是HCC术后早期复发的独立危险因素; Muhi等<sup>[34]</sup>分析发现, ADC值是术后早期复发显著独立预测因子( $P = 0.000 2$ ),且最佳ADC预测界值为 $0.898 \times 10^{-3} \text{ mm}^2/\text{s}$ 。可能是因为较低的ADC值与较差的组织学分化等级相关,进而导致HCC术后早期复发。但ADC值受到 $b$ 值的选择及扫描技术差异的影响,各研究对ADC值的准确描述略有不同,使其在临床应用中存在一定的局限性<sup>[35]</sup>。但随着标准化扫描时代的到来,ADC值的临床应用与临床认可度将会逐步扩大。此外,一些功能影像技术,如磁共振波谱、 $R2^*$ 等在预测HCC术后早期复发中的应用价值也亟待探讨。

## 2 手术切缘宽度在预测早期复发中的价值

近年来,临床医师更倾向于通过术前影像学检查了解HCC相关不良预后因素,为患者制订精确且有益的手术策略。成功的肝切除术需要完全切除肿瘤并保留足够的残肝,这两者都与手术切缘宽度密切相关,手术切缘宽度也早已被广泛用来评估对HCC根治术后长期预后的影响<sup>[8, 36]</sup>。

在2010年,美国HCC手术治疗的专家共识<sup>[13]</sup>推荐1~2 cm手术切缘宽度;2012年,沙特阿拉伯的肝癌诊治指南<sup>[37]</sup>要求保留 $\geq 1$  cm的阴性切缘;2022年中国最新《原发性肝癌诊疗指南(2022年版)》<sup>[14]</sup>也推荐肝脏切缘距肿瘤边界 $\geq 1$  cm进行切除,但肝切除的手术切缘宽度仍存在争议。许多研究<sup>[38-39]</sup>指出,宽切缘( $\geq 1$  cm)的肝切除效果优于窄切缘( $< 1$  cm)的肝切除术。早年一项前瞻性随机试验<sup>[40]</sup>证实,在长期预后中,HCC宽切缘组( $> 1$  cm)的生存率明显优于窄切缘组( $\leq 1$  cm)( $P = 0.017$ )。但最近一项国际多中心研究的数据<sup>[41]</sup>表明,广泛切缘

(>1 cm)和窄切缘( $\leq 1$ cm)的HCC患者2年复发率相似,这意味着早期和远期预后在相同的肝切除宽度中出现不同。这些有争议的发现可能主要因为对手术切缘宽度的定义和纳入基线特征不同,这可能导致每项研究中HCC术后残肝中残留肿瘤细胞的概率不同。例如,对于伴有MVI的HCC患者,解剖性肝切除与非解剖性肝切除术相比总生存期无区别,但局部复发率更低<sup>[42-43]</sup>,且对于术前可预判存在MVI的患者,更加推荐肝脏切缘距肿瘤边界 $\geq 1$  cm进行切除<sup>[44]</sup>。此外,尽管众多研究<sup>[38-41]</sup>以1 cm作为手术切缘宽度分界点,但有研究者指出选择<1 cm的某一个数值作为切缘宽度分界点可以进一步细化和分层患者,以精确切缘宽度早期复发(2年内)的影响。Michelakos等<sup>[45]</sup>将切除边缘分为窄( $\leq 3.0$  mm)、中间(3.1~10.0 mm)和宽( $\geq 10.0$  mm),结果表明,3组之间总生存期差异无统计学意义( $P=0.87$ );Lazzara等<sup>[46]</sup>认为5~10 mm作为HCC肿瘤<5 cm的手术切缘宽度是安全的。上述研究表明,手术切缘宽度对评估HCC短期与长期预后争议重重,消除纳入混杂基线因素的影响(如倾向性评分)是必要的<sup>[47]</sup>,且需要更多的前瞻性研究或高质量meta分析对这一重要参数对HCC短期及长期预后影响进行探索。

### 3 术前MRI标志物联合手术切缘在预测早期复发中的价值

术前MRI相关标志物对预测早期复发的作用已得到广泛认可。而手术切缘宽度作为HCC预后的术中指标,与术前MRI标志物联合预测HCC预后情况可能较单独应用MRI标志物更有意义。

近年来,有许多关于MRI标志物联合临床因素和实验室指标对肿瘤术后复发风险进行分析的研究,但采用术前MRI标志物结合手术策略进行预后分析的研究较少。一些HCC早期复发危险因素往往只能在术后进行评估,杨浩然等<sup>[15]</sup>报道了一个基于术前MRI影像组学及临床因素(TNM分期、甲胎蛋白水平、 $\gamma$ -谷氨酰氨基转移酶、Child-Pugh分级)的联合模型用于预测HCC切除术后的早期复发,这有助于在术前确定患者的复发危险因素并选择合适的治疗策

略。Li等<sup>[47]</sup>的研究表示,在经导管动脉化疗栓塞术(transcatheter arterial chemoembolization, TACE)治疗的HCC患者中,治疗前血清血管内皮生长因子(vascular endothelial growth factor, VEGF)及C反应蛋白(C-reactive protein, CRP)水平较低、肿瘤直径较小、HCC病灶区ADC减低的HCC患者的生存率较高,因此MRI标志物ADC值与另外3个参数的组合可以作为评估TACE疗效和HCC预后的新方法。Chao等<sup>[48]</sup>证实,对于MRI示肿瘤大小>3 cm、肿瘤包膜不完整的患者,宽切缘(手术切缘 $\geq 5$  mm)组的总生存期优于短切缘(手术切缘<5 mm)组( $P=0.018$ )。肿瘤大小可作为确定可能受益于广泛切除边缘患者的分层因素之一,而MRI对于肿瘤大小可以精确评估,联合分析表明术前MRI的指标(至少肿瘤大小)可能可以指导手术切缘的选择。至于参数肿瘤包膜不完整是否可用于指导术前分层仍值得进一步探讨。由于不同的对比剂(肝胆特异性对比剂与细胞外对比剂)对于包膜检出灵敏度不同,需要更标准化的研究分别进行探讨。Romanzi等<sup>[49]</sup>的研究显示,在MRI示不光滑的肿瘤边缘组HCC患者中,肝部分切除术或较大肝切除术的5年无复发生存率( $P=0.0019$ )和总生存率( $P=0.0145$ )明显优于肝节段切除术或较小肝切除术,且在光滑的肿瘤边缘组的患者中,不同手术方式之间差异无统计学意义( $P>0.05$ )。由于非光滑的肿瘤边缘是与MVI密切相关的MRI标志物,因此对MRI示肿瘤边缘不光滑的HCC患者进行扩大切除的意义与指南<sup>[13-14, 37]</sup>中推荐的切缘宽度可以相互解释。总而言之,术前MRI众多指标中,如肿瘤大小、肿瘤包膜、不规则的肿瘤边缘、瘤周动脉期强化等,哪一个或几个参数单独或联合可指导手术切缘选择参与手术方案的制订仍处于探索阶段。

### 4 研究局限性与展望

目前术前MRI标志物联合手术切缘预测早期复发的相关研究基本为回顾性研究,且现有研究大多数仅探索MRI单一征象,例如肿瘤大小、不规则的肿瘤边缘等联合手术切缘宽度与预后之间的关系,且与HCC术后短期与长期预后的影响不

明确。此外,相关研究中纳入的HCC患者基线特征统一度不够,而不同基线特征的HCC患者手术切缘宽度尚无统一标准,如术前MRI预测可能为MVI、中/低病理学分级的患者<sup>[50-51]</sup>。因此,术前MRI标志物联合手术切缘在预测HCC早期复发中的价值仍需要大量的多中心前瞻性队列研究或真实世界研究来得到可靠结论,以期术前MRI标志物可以完成术前患者分层,并对确定手术切缘宽度及手术方式提供参考,最终提高患者生活质量并延长患者生存时间。

### 【参 考 文 献】

- [1] BRAY F, FERLAY J, SOERJOMATARAM I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. *CA Cancer J Clin*, 2018, 68(6): 394-424.
- [2] CHEN W Q, ZHENG R S, BAADE P D, et al. Cancer statistics in China, 2015 [J]. *CA A Cancer J Clin*, 2016, 66(2): 115-132.
- [3] HARTKE J, JOHNSON M, GHABRIL M. The diagnosis and treatment of hepatocellular carcinoma [J]. *Semin Diagn Pathol*, 2017, 34(2): 153-159.
- [4] KUMAR A M, FREDMAN E T, COPPA C, et al. Patterns of cancer recurrence in localized resected hepatocellular carcinoma [J]. *Hepatobiliary Pancreat Dis Int*, 2015, 14(3): 269-275.
- [5] ATTWA M H, EL-ETREBY S A. Guide for diagnosis and treatment of hepatocellular carcinoma [J]. *World J Hepatol*, 2015, 7(12): 1632-1651.
- [6] TABRIZIAN P, JIBARA G, SHRAGER B, et al. Recurrence of hepatocellular cancer after resection: patterns, treatments, and prognosis [J]. *Ann Surg*, 2015, 261(5): 947-955.
- [7] LEE J W, LEE Y J, PARK K M, et al. Anatomical resection but not surgical margin width influence survival following resection for HCC, a propensity score analysis [J]. *World J Surg*, 2016, 40(6): 1429-1439.
- [8] MARASCO G, COLECCHIA A, COLLI A, et al. Role of liver and spleen stiffness in predicting the recurrence of hepatocellular carcinoma after resection [J]. *J Hepatol*, 2019, 70(3): 440-448.
- [9] WEI T, ZHANG X F, BAGANTE F, et al. Early versus late recurrence of hepatocellular carcinoma after surgical resection based on post-recurrence survival: an international multi-institutional analysis [J]. *J Gastrointest Surg*, 2021, 25(1): 125-133.
- [10] KIM S S, LEE S, KIM M J. Prognostic factors of gadoteric acid-enhanced MRI for postsurgical outcomes in multicentric hepatocellular carcinoma [J]. *Eur Radiol*, 2021, 31(5): 3405-3416.
- [11] DONG S Y, WANG W T, CHEN X S, et al. Microvascular invasion of small hepatocellular carcinoma can be preoperatively predicted by the 3D quantification of MRI [J]. *Eur Radiol*, 2022, 32(6): 4198-4209.
- [12] LIU L H, SHUI Y J, YU Q Q, et al. Narrow-margin hepatectomy resulted in higher recurrence and lower overall survival for R0 resection hepatocellular carcinoma [J]. *Front Oncol*, 2020, 10: 610636.
- [13] JARNAGIN W, CHAPMAN W C, CURLEY S, et al. Surgical treatment of hepatocellular carcinoma: expert consensus statement [J]. *HPB (Oxford)*, 2010, 12(5): 302-310.
- [14] 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(2): 16-53.
- [15] 杨浩然, 张濬韬, 马密密, 等. 增强MR组学联合临床因素预测肝细胞癌根治性切除术后早期复发的价值研究 [J]. *磁共振成像*, 2022, 13(4): 49-55.
- [16] MIN J H, KIM S H, HWANG J A, et al. Prognostic value of LI-RADS category on gadoteric acid-enhanced MRI and <sup>18</sup>F-FDG PET-CT in patients with primary liver carcinomas [J]. *Eur Radiol*, 2021, 31(6): 3649-3660.
- [17] CHOI S H, LEE S S, PARK S H, et al. LI-RADS classification and prognosis of primary liver cancers at gadoteric acid-enhanced MRI [J]. *Radiology*, 2019, 290(2): 388-397.
- [18] TERZI E, GIAMPEROLI A, IAVARONE M, et al. Prognosis of single early-stage hepatocellular carcinoma (HCC) with CEUS inconclusive imaging (LI-RADS LR-3 and LR-4) is no better than typical HCC (LR-5) [J]. *Cancers (Basel)*, 2022, 14(2): 336.
- [19] LEE S, KIM K W, JEONG W K, et al. Liver imaging reporting and data system category on magnetic resonance imaging predicts recurrence of hepatocellular carcinoma after liver transplantation within the Milan criteria: a multicenter study [J]. *Ann Surg Oncol*, 2021, 28(11): 6782-6789.
- [20] ZHANG L Q, KUANG S C, CHEN J B, et al. The role of preoperative dynamic contrast-enhanced 3.0-T MR imaging in predicting early recurrence in patients with early-stage hepatocellular carcinomas after curative resection [J]. *Front Oncol*, 2019, 9: 1336.
- [21] WEI H, JIANG H Y, ZHENG T Y, et al. LI-RADS category 5 hepatocellular carcinoma: preoperative gadoteric acid-enhanced MRI for early recurrence risk stratification after curative resection [J]. *Eur Radiol*, 2021, 31(4): 2289-2302.
- [22] KANG H J, KIM H, LEE D H, et al. Gadoteric acid-enhanced MRI features of proliferative hepatocellular carcinoma are prognostic after surgery [J]. *Radiology*, 2021, 300(3): 572-582.
- [23] HUANG M Q, LIAO B, XU P, et al. Prediction of microvascular invasion in hepatocellular carcinoma: preoperative Gd-EOB-DTPA-dynamic enhanced MRI and histopathological correlation [J]. *Contrast Media Mol Imaging*, 2018, 2018: 9674565.
- [24] RYU T, TAKAMI Y, WADA Y, et al. A clinical scoring system for predicting microvascular invasion in patients with hepatocellular carcinoma within the Milan criteria [J]. *J*

- Gastrointest Surg, 2019, 23(4): 779–787.
- [ 25 ] KIM A Y, SINN D H, JEONG W K, et al. Hepatobiliary MRI as novel selection criteria in liver transplantation for hepatocellular carcinoma [ J ] . J Hepatol, 2018, 68(6): 1144–1152.
- [ 26 ] LEE S, KIM S H, LEE J E, et al. Preoperative gadoteric acid-enhanced MRI for predicting microvascular invasion in patients with single hepatocellular carcinoma [ J ] . J Hepatol, 2017, 67(3): 526–534.
- [ 27 ] LEE J H, LEE J M, KIM S J, et al. Enhancement patterns of hepatocellular carcinomas on multiphasic multidetector row CT: comparison with pathological differentiation [ J ] . Br J Radiol, 2012, 85(1017): e573–e583.
- [ 28 ] ATANASOV G, DIETEL C, FELDBRÜGGE L, et al. Tumor necrosis and infiltrating macrophages predict survival after curative resection for cholangiocarcinoma [ J ] . Oncoimmunology, 2017, 6(8): e1331806.
- [ 29 ] ZHAO W, LIU W G, LIU H P, et al. Preoperative prediction of microvascular invasion of hepatocellular carcinoma with IVIM diffusion-weighted MR imaging and Gd-EOB-DTPA-enhanced MR imaging [ J ] . PLoS One, 2018, 13(5): e0197488.
- [ 30 ] LI J D, XU X F, HAN J, et al. Preoperative prealbumin level as an independent predictor of long-term prognosis after liver resection for hepatocellular carcinoma: a multi-institutional study [ J ] . HPB (Oxford), 2019, 21(2): 157–166.
- [ 31 ] PAWLIK T M, DELMAN K A, VAUTHEY J N, et al. Tumor size predicts vascular invasion and histologic grade: implications for selection of surgical treatment for hepatocellular carcinoma [ J ] . Liver Transpl, 2005, 11(9): 1086–1092.
- [ 32 ] 刘永倩, 赵新湘. 原发性肝细胞肝癌微血管浸润分级的危险因素预测 [ J ] . 放射学实践, 2020, 35(11): 1453–1457.
- [ 33 ] LEE S, KIM S H, HWANG J A, et al. Pre-operative ADC predicts early recurrence of HCC after curative resection [ J ] . Eur Radiol, 2019, 29(2): 1003–1012.
- [ 34 ] MUHI A, ICHIKAWA T, MOTOSUGI U, et al. Diffusion-weighted imaging of hepatocellular carcinoma for predicting early recurrence and survival after hepatectomy [ J ] . Hepatol Int, 2013, 7(2): 662–668.
- [ 35 ] 王乐瑶, 马霄虹, 赵心明. 磁共振成像是预测肝细胞癌术后早期复发中的研究 [ J ] . 放射学实践, 2021, 36(6): 803–806.
- [ 36 ] SONG L, LI J, LUO Y. The importance of a nonsmooth tumor margin and incomplete tumor capsule in predicting HCC microvascular invasion on preoperative imaging examination: a systematic review and meta-analysis [ J ] . Clin Imaging, 2021, 76: 77–82.
- [ 37 ] ABDO A A, HASSANAIN M, ALJUMAH A, et al. Saudi guidelines for the diagnosis and management of hepatocellular carcinoma: technical review and practice guidelines [ J ] . Ann Saudi Med, 2012, 32(2): 174–199.
- [ 38 ] ZHONG F P, ZHANG Y J, LIU Y, et al. Prognostic impact of surgical margin in patients with hepatocellular carcinoma: a meta-analysis [ J ] . Medicine (Baltimore), 2017, 96(37): e8043.
- [ 39 ] ZHOU Z W, QI L N, MO Q Y, et al. Effect of surgical margin on postoperative prognosis in patients with solitary hepatocellular carcinoma: a propensity score matching analysis [ J ] . J Cancer, 2021, 12(15): 4455–4462.
- [ 40 ] SHI M, GUO R P, LIN X J, et al. Partial hepatectomy with wide versus narrow resection margin for solitary hepatocellular carcinoma: a prospective randomized trial [ J ] . Ann Surg, 2007, 245(1): 36–43.
- [ 41 ] TSILIMIGRAS D I, SAHARA K, MORIS D, et al. Effect of surgical margin width on patterns of recurrence among patients undergoing R0 hepatectomy for T<sub>1</sub> hepatocellular carcinoma: an international multi-institutional analysis [ J ] . J Gastrointest Surg, 2020, 24(7): 1552–1560.
- [ 42 ] 夏永祥, 张峰, 李相成, 等. 原发性肝癌10 966例外科治疗分析 [ J ] . 中华外科杂志, 2021, 59(1): 6–17.
- [ 43 ] KWON J H, LEE J W, LEE J W, et al. Effects of anatomical or non-anatomical resection of hepatocellular carcinoma on survival outcome [ J ] . J Clin Med, 2022, 11(5): 1369.
- [ 44 ] YANG P H, SI A F, YANG J, et al. A wide-margin liver resection improves long-term outcomes for patients with HBV-related hepatocellular carcinoma with microvascular invasion [ J ] . Surgery, 2019, 165(4): 721–730.
- [ 45 ] MICHELAKOS T, KONTOS F, SEKIGAMI Y, et al. Hepatectomy for solitary hepatocellular carcinoma: resection margin width does not predict survival [ J ] . J Gastrointest Surg, 2021, 25(7): 1727–1735.
- [ 46 ] LAZZARA C, NAVARRA G, LAZZARA S, et al. Does the margin width influence recurrence rate in liver surgery for hepatocellular carcinoma smaller than 5 cm? [ J ] . Eur Rev Med Pharmacol Sci, 2017, 21(3): 523–529.
- [ 47 ] LI Z, XUE T Q, CHEN X Y. Predictive values of serum VEGF and CRP levels combined with contrast enhanced MRI in hepatocellular carcinoma patients after TACE [ J ] . Am J Cancer Res, 2016, 6(10): 2375–2385.
- [ 48 ] CHAO J S, ZHU Q, CHEN D S, et al. Combined analysis of imaging tumor capsule with imaging tumor size guides the width of resection margin for solitary hepatocellular carcinoma [ J ] . Hepatobiliary Pancreat Dis Int, 2022, 21(6): 551–558.
- [ 49 ] ROMANZI A, AR II ZUMI S, KOTERA Y, et al. Hepatocellular carcinoma with a non-smooth tumor margin on hepatobiliary-phase gadoteric acid disodium-enhanced magnetic resonance imaging. Is sectionectomy the suitable treatment? [ J ] . J Hepatobiliary Pancreat Sci, 2020, 27(12): 922–930.
- [ 50 ] 中华医学会数字医学分会, 中国研究型医院学会数字智能化外科专业委员会, 中国医师协会肝癌专业委员会, 等. 计算机辅助联合吲哚菁绿分子荧光影像技术在肝脏肿瘤诊断和手术导航中应用指南 (2019版) [ J ] . 中国实用外科杂志, 2019, 39(7): 641–650.
- [ 51 ] YANG J, TAO H S, CAI W, et al. Accuracy of actual resected liver volume in anatomical liver resections guided by 3-dimensional parenchymal staining using fusion indocyanine green fluorescence imaging [ J ] . J Surg Oncol, 2018, 118(7): 1081–1087.