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综 述

基于 MRI 影像组学及深度学习预测肝细胞癌微血管侵犯的研究进展

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【摘 要】 微血管侵犯(MVI) 是肝细胞癌(HCC) 术后早期复发的独立预测因子,但现有诊断依赖术后病理,无法指导术前决策。磁共振(MRI) 与人工智能技术的融合为术前无创预测 MVI 提供了新途径。本文系统综述基于 MRI 影像组学及深度学习预测 HCC MVI 的研究进展,总结影像组学、影像基因组学及多模态模型的效能与挑战,讨论深度学习“黑箱”问题及可解释性解决方案。

【关键词】 肝细胞癌; 微血管侵犯; 影像组学; 深度学习; 磁共振成像

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【Abstract】 Microvascular invasion (MVI) is an independent predictor of early postoperative recurrence in hepatocellular carcinoma (HCC); however, current diagnosis relies entirely on postoperative pathology, limiting preoperative decision-making. The integration of magnetic resonance imaging (MRI) and artificial intelligence offers a new avenue for non-invasive preoperative prediction of MVI. This review systematically summarizes recent advances in MRI-based radiomics and deep learning for predicting MVI in HCC, outlines the efficacy and challenges of radiomics, radiogenomics, and multimodal models, discusses the "black-box" issue of deep learning and potential explainable solutions, and proposes relevant recommendations to facilitate clinical translation.

【Key words】 Hepatocellular carcinoma; Microvascular invasion; Radiomics; Deep learning; Magnetic resonance imaging

肝细胞癌(hepatocellular carcinoma, HCC) 是原发性肝癌的主要类型,由于早期诊断困难且治疗选择有限,患者 5 年生存率为 14.4%;根治性手术切除作为早期 HCC 的首选治疗方式,虽然能显著改善患者预后,但术后 5 年复发转移率仍高达 50%~88%^[1]。其中,微血管侵犯(microvascular invasion, MVI) 是导致术后早期复发的重要病理基础,也是反映 HCC 侵袭性的关键病理特征,因此已成为评估术后复发风险及指导辅助治疗的独立预后因子^[2]。然而,现有 MVI 诊断完全依赖术后病理,存在侵入性、选择偏倚及分析主观性等固有局限。近年来,磁共振(magnetic resonance imaging, MRI) 与人工智能(artificial intelligence, AI) 技术的深度融合,为术前无创预测 MVI 提供了新途径。文章系统综述基于 MRI 影像组学及深度学习预测 HCC

MVI 的研究进展,总结现有模型效能、识别主要挑战,并展望临床转化方向。

1 MVI 临床预后分层与分子机制

MVI 作为 HCC 侵袭性的组织学标志,特指镜下肿瘤细胞突破基底膜,侵入门静脉或肝静脉分支并形成癌栓^[3]。其发生率达 30%~50%,且与早期复发(<2 年) 显著相关($OR=3.82, P<0.001$)^[4-6]。《原发性肝癌诊疗指南(2026 年版) 》推荐 3 级分型标准^[7]: M0 为未检测到 MVI; M1 为近癌旁区域(≤ 1 cm) MVI 数量 ≤ 5 个; M2 为远癌旁区域(>1 cm) 出现 MVI 或数量 >5 个。该分型可有效区分不同预后人群,研究表明, M2 级患者术后复发率(80.9%) 显著高于 M1(57.8%) 和 M0(46.4%) , 5 年总生存率(overall survival, OS) (29.7%) 亦显著低于后两者^[8]。

从生物学基础来看,在炎症反应持续刺激下,HCC 细胞激活 PI3K/AKT、Wnt/ β -catenin 等信号通路获得侵袭能力,降解基底膜并破坏组织结构,最终在耐受血流剪切力与免疫攻击后侵入微血管腔形成癌栓^[1]。这一生物学转化在临床上则表现为循环肿瘤细胞(circulating tumor cells,CTC)计数升高(≥ 5 个/ml, $OR=3.227,P=0.025$)与术后 CTC 动态上升所预示的无复发生存期缩短^[2]。宏观预后层面,大规模队列研究已证实 MVI 阳性患者 5 年无病生存期与 OS 均显著劣于阴性组^[3],且 MVI 阳性组中肝功能储备较差者(Child-Pugh B/C 级)占比更高^[4]。这一分子-病理-临床的跨尺度关联,为基于 MVI 分级的个体化干预策略奠定了生物学基础。

2 MVI 传统影像学特征

在单一征象层面,不规则肿瘤边缘反映了肿瘤对周围组织的侵袭能力,是重度 MVI 分级的独立危险因素($OR=2.224,P=0.023$)^[1];动脉期瘤周强化提示肿瘤新生血管形成^[1];肿瘤包膜不完整则预示肿瘤已突破基质屏障^[1];瘤内异常动脉表明肿瘤血供丰富,利于癌细胞进入循环系统^[1];肝胆期瘤周低信号的病理机制更为复杂,涉及 MVI 导致的门静脉分支阻塞、局部肝实质灌注改变及肝细胞功能受损^[1]。在量化阈值方面,一项研究以 3.15 cm 为阈值可有效区分 MVI 高危与低危人群^[1],为临床快速筛查提供了简便依据。

然而,单一征象的预测效能有限,为此,孟存忠等^[1]基于肿瘤直径、肿瘤边缘形态、动脉期瘤周强化及肝胆期瘤周低信号构建了 MVI 预测模型。路志伟等^[3]的研究则揭示了肿瘤直径($AUC=0.763$)、马赛克结构($AUC=0.628$)及晕状强化($AUC=0.670$)预测效能的差异。磁共振弹性成像作为无创定量评估组织生物力学特性的新技术,联合肿瘤硬度与动脉期瘤周强化构建的列线图模型,一致性指数在训练集和验证集分别达 0.88 和 0.89^[1],表明单一征象向多参数联合建模的转变是提升传统影像学预测效能的关键路径。

3 基于影像学模型预测 MVI

影像学学的核心贡献在于将医学图像转化为高维定量特征,突破传统影像依赖肉眼判读的主观局限。围绕 MVI 预测模型的构建,现有研究面临 3 个关键技术选择:序列方面,非增强序列,如磁敏感加权成像与 T2 加权成像(T2-weighted imaging,T2WI),在验证队列中 AUC 达 0.888^[2],为对比剂禁忌人群提供了可行方案,但其与增强序列的效能差异尚缺乏头对头验证。区域方面,瘤周 3 mm 区域的环境特征与肿瘤直径均为独立预测因子^[2],生境分析进一步使训练集 AUC 提升至 0.961^[2],证实了瘤周信息的附加价值。策略方面,仅基于动脉期影像学特征构建的简约模型亦可取得 AUC 为 0.796 的效能^[3],提示简化方案与复杂建模的效能差距在特定临床场景下可能并不显著。

综合来看,影像学通过提供客观、定量的肿瘤异质性评估,显著拓展了传统影像学的预测边界,但其临床转化受制于数据异质性、特征提取缺乏统一标准及模型性能对感兴趣区(region of interest,ROI)勾画的高度依赖^[2]。

4 基于深度学习模型预测 MVI

深度学习通过构建含多个隐藏层的神经网络,能够从原始

图像中自动学习层次化特征,避免了传统影像组学中人工定义特征的局限性^[2]。张歌等^[2]基于平扫 MRI 构建深度迁移学习模型,发现基于 T2WI 的模型在训练集和外部测试集 AUC 分别为 0.779 和 0.741,均显著优于 T1WI 影像组学及临床模型,证实了该无创方法在规避对比剂风险方面的应用潜力。

多区域多尺度深度学习策略同样显示出独特优势。Zhang 等^[2]将不同尺度的瘤内区域及瘤周区域分别独立编码为 50 个生境,结合异质性定量特征与深度神经网络构建模型,在 3 个数据集中均表现较好。多序列融合策略方面,黄倩等^[2]基于动脉期、延迟期、脂肪抑制 T2WI 及扩散加权成像 4 个序列,采用 Swin Transformer 架构构建模型,延迟期 AUC 达 0.993,显著优于传统卷积神经网络及影像组学模型,梯度加权类激活映射(gradient-weighted class activation mapping,Grad-CAM)可视化显示模型有效聚焦于肿瘤相关区域。

然而,深度学习的“黑箱”特性仍是制约临床转化的关键瓶颈^[2]。可解释性 AI 方法如 Grad-CAM 已尝试用于揭示模型决策依据,通过热力图直观显示对预测结果贡献最大的区域,增强临床信任度^[2]。未来研究应推动多中心外部验证、发展可解释性技术、探索深度学习与影像组学的融合策略^[2]。

5 基于影像基因组学模型预测 MVI

鉴于传统基因检测因成本高、侵入性强及耗时长,影像基因组学以其无创、可视化特点,成为连接分子病理学与临床影像学的桥梁;该技术的流程包括影像数据采集与 ROI 分割、影像组学特征提取、基因组数据量化,以及通过 Pearson 相关性分析或加权基因共表达网络分析(weighted gene co-expression network analysis,WGCNA)等方法建立关联模型^[32-33]。与纯影像组学相比,影像基因组学通过关联影像特征与基因表达谱,为影像表型提供分子层面的生物学注释,两者互为补充^[34-35]。

自 Segal 等^[34]于 2007 年首次建立影像特征与肝癌基因表达谱的关联后,影像基因组学研究经历了 3 个递进式的技术突破。在数据层面,研究从基于组织块的批量转录组分析,至单细胞分辨率,使影像信号得以锚定于特定的免疫细胞亚群,解决了宏观与微观间的匹配问题^[37-38]。在建模层面,预测因子从单一模态的影像特征,拓展为影像组学评分与循环微小核糖核酸等分子标志物的联合,提升了多维度信息的整合利用效率^[34]。在机制阐释层面,进一步采用 WGCNA,使得影像组学特征能够关联至细胞周期调控、中性粒细胞外陷阱形成及过氧化物酶体增殖物激活受体信号通路等具体生物学通路^[34]。上述进展表明,影像基因组学正从相关性验证向多组学整合的系统性机制研究转变。

该领域仍面临多组学数据获取成本高、样本量小且缺乏外部验证、因果关系建立困难、成协协议差异影响可比性以及数据隐私伦理问题等挑战^[34,41-43]。

6 基于多模态影像模型预测 MVI

鉴于单一影像特征难以兼顾高敏感度与高特异度,多模态模型已成为提升预测效能的重要途径。根据融合发生的阶段,主流策略分为三类:早期融合在输入层直接拼接特征,但易受噪声干扰;晚期融合在各模态独立决策后整合,可能损失模态

间交互信息;中间融合在特征提取阶段引入跨模态交互机制,在效率与效果方面取得平衡^[44]。

影像组学框架下,一项基于四期相(平扫、动脉期、门脉期、肝胆期)特征融合的研究显示 AUC 达 0.889,显著优于单期相至三期相模型(AUC 0.789~0.848)^[43],证实多时相信息互补有助于全面评估肿瘤异质性。深度学习领域,多模态融合的方法学原理具有跨成像模态的普适性,因此无论输入数据为计算机断层扫描(computed tomography,CT)、MRI 序列还是两者组合,均可为基于 MRI 的相关建模研究提供方法论参考^[44]。深度学习层面,跨模态融合的探索集中于输入整合与架构优化 2 个方向:前者验证了 CT 与 MRI 联合输入的可行性(AUC=0.844) 及临床特征添加的增益空间(AUC=0.871)^[43];后者则证明高阶张量融合优于早期简单拼接^[43],表明融合方式的设计对模型性能影响显著。此外,针对巴塞罗那临床肝癌分期(BCLC) A 期小肝癌的前瞻性多参数 MRI 研究亦取得较理想结果(敏感度 0.818,特异度 0.900)^[43]。总体而言,现有证据已充分验证多源融合的预测价值,但跨模态整合(尤其 CT-MRI 融合)、自适应融合机制及大样本外部验证等方面仍为当前研究的薄弱环节,有待进一步突破。

多模态模型的临床转化仍面临数据获取成本增加、配准问题、参数规模大导致训练复杂、可解释性进一步下降及缺乏标准化融合策略评价体系等挑战^[4]。综上,多模态 MVI 预测模型虽展现出显著优势,但其数据获取、计算复杂性、可解释性及标准化等问题仍需深入探索。

7 总结与展望

本文系统综述了基于 MRI 影像组学及深度学习预测 HCC MVI 的研究进展,涵盖传统影像学特征、影像组学、深度学习、影像基因组学及多模态融合模型五大技术路径。影像组学通过高通量特征提取实现肿瘤异质性的定量评估,深度学习凭借自动特征提取与复杂模式识别提升预测精度,影像基因组学为影像表型提供分子注释,多模态融合整合互补信息突破单一模态效能瓶颈。然而,该领域仍面临四大核心挑战: 前瞻性研究缺乏,绝大多数为回顾性设计,泛化能力未经真实临床验证; 外部验证不足,多数模型仅依赖单中心数据,可迁移性存疑; 生物学可解释性较差,影像特征与 MVI 分子机制关联尚未阐明; 标准化缺失,ROI 勾画、特征提取、模型构建方法差异显著。针对上述问题,未来研究应聚焦以下方向: 一是开展前瞻性多中心研究,构建具有真实世界代表性的预测模型。二是建立标准化评价体系。建议: (1) ROI 采用全肿瘤逐层勾画和并行分析 3 mm、5 mm 及 10 mm 瘤周区域; (2) 特征提取遵循 IBSI 指南并使用 PyRadiomics; (3) 验证遵循 TRIPOD-AI 声明逐步推进验证。三是发展可解释性 AI,借助 Grad-CAM 等方法揭示决策依据,阐明影像特征与分子机制的关联。四是推动多模态数据融合,整合影像、基因组学、病理及临床信息,构建端到端个体化预测系统。

综上,MRI 影像组学及深度学习在 HCC MVI 术前预测中展现巨大潜力,但从前沿研究到临床应用的转化仍面临前瞻性验证不足、外部验证缺失、可解释性薄弱及标准化缺位等核心挑

战。建立统一的评价体系、发展可解释性 AI 方法、推进多中心前瞻性研究,将是推动 MVI 预测模型向临床应用转化、实现 HCC 个体化精准诊疗目标的重要方向。

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