

多模影像在乳腺癌新辅助疗效中的应用

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摘 要

新辅助治疗(Neoadjuvant therapy, NAT)已成为局晚期乳腺癌的标准治疗方案,能够在术前缩小肿瘤体积,显著提高保乳率和患者生存率。近年来,随着影像组学技术的快速发展,多模态影像评估在新辅助治疗疗效监测和预后预测中发挥着越来越重要的作用,为临床决策提供了新思路与方法。本文就多模态影像组学在预测新辅助治疗后病理学完全缓解(Pathological Complete Response, pCR)中的价值,重点分析了各类影像学技术特征作为疗效预测的潜力,为乳腺癌患者提供更精准的个体化治疗策略提供依据。

关键词

乳腺癌, 新辅助治疗, 影像组学, 疗效评估, 病理学完全缓解率

Application of Multimodal Radiomics in Assessing Neoadjuvant Therapeutic Efficacy for Breast Cancer

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Abstract

Neoadjuvant therapy (NAT) has emerged as the standard treatment protocol for locally advanced breast cancer, effectively reducing tumor volume preoperatively and significantly enhancing both

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breast-conservation rates and patient survival outcomes. In recent years, the rapid advancement of radiomics technology has elevated the role of multimodal imaging evaluation in monitoring therapeutic efficacy and prognostic prediction during NAT, offering novel perspectives and methodologies for clinical decision-making. This article aims to explore the value of multimodal radiomics in predicting pathological complete response (Pathological Complete Response, pCR) following NAT, with a particular focus on analyzing the potential of various imaging technique characteristics as predictors of therapeutic efficacy, thereby facilitating more precise and individualized treatment strategies for breast cancer patients.

Keywords

Breast Cancer, Neoadjuvant Therapy, Radiomics, Therapeutic Effect Evaluation, Pathological Complete Response

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1. 引言

乳腺癌是全球女性中最常见的恶性肿瘤之一。据 2022 年统计数据,全球乳腺癌病例数约 230.9 万例,死亡病例达 66.6 万,严重威胁女性健康[1]。对于高危早期乳腺癌患者,治疗模式已从术后辅助化疗转变为术前全身治疗,显著提高了手术切除率和保乳率[2]。既往研究表明,新辅助化疗后达到 pCR 的患者有更长的无事件生存期(Event-Free Survival, EFS)和总生存期(Overall Survival, OS) [3] [4],尤其是三阴性乳腺癌和 HER2 阳性乳腺癌[5]。病理学完全缓解(Pathological Complete Response, pCR)定义为新辅助治疗后手术标本中乳腺原发灶及区域淋巴结均未发现残留浸润性癌细胞[6]。CTneoBC 汇总证实, pCR 可作为新辅助治疗后长期临床获益的可靠替代终点[4]。NSABP B-27 研究结果显示, 蒽环类联合紫杉类方案可提高 pCR 率[7]。KEYNOTE-522 研究表明,在化疗基础上联合免疫检查点抑制剂可显著提升 pCR 率[8]-[10]。然而,新辅助治疗的疗效存在显著异质性,对化疗不敏感的患者若接受无效治疗,不仅面临更高的毒性风险,还可能因治疗延误而影响手术时机。因此,如何实现早期、无创预测 pCR 成为当前研究热点。传统上,术后病理检查是评估新辅助治疗疗效的金标准[11],但其结果滞后性,无法实时指导治疗方案调整。影像学技术可在治疗过程中动态监测肿瘤变化,全面评估肿瘤负荷,早期预测治疗的反应,为临床决策提供重要依据。因此,建立基于影像学的早期疗效预测模型具有重要临床意义。本文旨在系统综述多模态影像技术在乳腺癌新辅助治疗中应用价值,探讨其在早期疗效预测中的可行性,为实现个体化精准治疗提供理论支持与实践指导。

新辅助治疗的有效实施依赖于贯穿全程的规范化影像与病理学评估体系[12]。目前国内外乳腺癌新辅助疗效评估的影像学方法包括乳腺 X 线摄影、超声检查、乳腺磁共振成像以及正电子发射断层扫描/计算机断层扫描(PET/CT) [13]。

2. 乳腺 X 线摄影(Mammography, MMG)

乳腺 X 线摄影是乳腺癌筛查与诊断的重要影像手段[14],其原理基于不同组织对 X 射线吸收程度的差异[15]。恶性病变常表现为高密度肿块、边缘不规则或呈毛刺状、簇状微钙化、结构扭曲及非对称性密度增高。然而,在致密型乳腺中,肿瘤显示效果较差,难以区分残余肿瘤与治疗相关纤维化改变,且对

微小残留病灶的检出敏感性较低[16][17]。因此,乳腺X线摄影在新辅助治疗疗效评估中应用价值有限,通常作为辅助手段与其他影像方法联合使用。

3. 超声检查(Ultrasonography, US)

超声成像主要通过评估肿块形态、方位、内部回声结构及多平面边缘特征进行诊断。Yang 等人研究了基于超声联合 KI-67%表达水平预测乳腺癌新辅助化疗疗效的可行性[18]。常规超声技术包括 B 型超声和多普勒超声。先进超声技术则涵盖弹性成像、对比增强超声、三维超声及自动乳腺全容积扫描 (ABVS) [19]。

3.1. 常规超声技术

B 型超声可清晰显示病灶的位置、大小、回声特性、边界情况及其与周围组织的关系[20]。多普勒超声在显示较大血管血流信息号方面具有优势,但在乳腺肿瘤微循环评估方面分辨率不足,有研究尝试将多普勒超声与高频超声结合,用于评估新辅助化疗疗效显示出一定潜力[21]。

3.2. 先进超声技术

超声弹性成像通过分析超声波传播过程中的组织形变信息,无创评估组织硬度,有助于良、恶性病变鉴别,但在伴有纤维增生或液化坏死的病灶中存在一定局限性[22]。对比增强超声通过静脉注射造影剂后观察肿瘤血管灌注特征。三维超声利用超声数据重建生成三维图像,可精确定位病变并准确测量肿瘤体积,在评估肿瘤与周围结构空间关系方面有一定优势[23]。自动乳腺全容积扫描(ABVS)是一种新型高分辨率三维乳腺超声成像技术,可减少操作者依赖性,提供传统手动超声难以获取的冠状面图像与容积信息[24][25],便于临床定位与直观地展示病灶。Wang 等人研究表明,ABVS 在评估新辅助化疗后 pCR 状态时具有较高的敏感性和特异性[26]。超声在新辅助治疗评估中的优势在于实时性、无辐射性及可重复性,并可用于评估腋窝淋巴结状态[27]。然而,单一超声模态在区分肿瘤残留与化疗诱导纤维化方面仍存在不足。合理整合多种超声技术的优势,有望提升乳腺癌新辅助治疗疗效评估的准确性[22]。目前关于超声在新辅助疗效评估中的研究相对较少,其临床价值需在更大样本、长期随访的研究中进一步验证。

4. 乳腺磁共振成像(Magnetic Resonance Imaging, MRI)

MRI 具有高软组织分辨率,支持多参数、多序列及功能成像[28],广泛应用于术前局部分期及治疗过程监测。既往研究证实,DCE-MRI、DWI 及 MRS 等多种成像标志物与 pCR 密切相关[29][30]。动态对比增强 MRI (Dynamic contrast-enhanced magnetic resonance imaging, DCE-MRI)通过静脉注射造影剂后连续采集 T1 加权图像,能够敏感反映组织微血管灌注与通透性变化,间接评估肿瘤血管生成情况[31]。Hou 等人构建了一种基于 DCE-MRI 的可解释影像组学模型,经多中心数据验证,证实该模型在预测乳腺癌患者新辅助化疗后 pCR 及无病生存期(DFS)分层方面具有潜在应用价值[32]。

弥散加权成像(Diffusion-weighted imaging magnetic resonance imaging, DWI-MRI)基于不同组织中水分子扩散运动特性,通过表观弥散系数(Apparent diffusion coefficient, ADC)进行定量评估,可反映细胞膜完整性及肿瘤细胞密度等生物学信息[33]。相较于 DCE-MRI 而言,DWI-MRI 采集无需注射造影剂即可完成扫描,具有更高的安全性与适用性。ACRIN 6698 临床研究证实,通过 DWI 测量 ADC 值的变化可用于预测新辅助治疗的疗效的反应[30]。

磁共振波谱(MRS)是目前唯一能够无创检测活体组织代谢物和生化变化的影像技术,在乳腺疾病诊断中具有重要价值[34]。乳腺 MRS 主要采用氢质子磁共振波谱(^1H -MRS)。研究表明,恶性乳腺病变通常表现为较高的水/脂肪(W-F)比例,且胆碱复合物(tCho)作为 ^1H -MRS 中的特征性代谢产物,已被广泛用

于乳腺癌的识别与评估。在新辅助治疗过程中, W-F 比值和 tCho 水平均被证实可作为治疗反应评估的潜在标志物[35]。然而, 该技术在乳腺应用中面临空间分辨率受限技术挑战。

为进一步提升乳腺癌新辅助治疗疗效的预测准确性, 近年来将多参数影像数据与临床病理信息整合的多模态分析成为研究热点。Liu 等人开展了一项回顾性研究, 整合患者临床资料、组织病理学特征及分析分型与多种影像特征相结合, 构建了一个结合多参数 MRI 与临床信息的放射组学模型, 并将其命名为 RMM, 结果显示该模型在预测乳腺癌患者 pCR 方面具有一定潜力[36]。I-SPY 2.2 研究通过整合 MRI 影像与空心针穿刺活检结果, 开发了用于预测 pCR 的算法模型, 并据此实施个体化降阶梯治疗策略, 在维持疗效的同时, 显著降低了治疗相关毒性[37]。TRAIN-3 研究显示, 基于 MRI 评估定义的放射组学完全缓解(rCR)与术后 pCR 高度一致(符合率达 87%) [38]。广东省人民医院王坤教授团队基于 MRI 影像, 纳入 1048 例完成新辅助化疗后接受手术切除的乳腺癌患者, 成功构建了针对不同乳腺癌分子亚型的人工智能预测系统, 可在治疗早期准确预测乳腺癌的残存肿瘤负荷(RCB)分级, 为个体化手术方案及术后随访策略优化提供了重要依据[39]。2025 年 ASCO 会议壁报展示的 CABIN 临床研究采用多模态评估三阴性乳腺癌新辅助治疗反应, 整合循环肿瘤 DNA(ctDNA)动态监测、MRI 肿瘤体积变化、PD-L1 表达状态及全外显子测序(Whole-exome sequencing, WES)数据, 构建 pCR 预测模型, 在训练集中, 该综合模型表现出优异的预测效能(AUC = 0.96), 显著优于单一生物标志物或影像指标。上述研究共同表明, 融合多参数 MRI 多功能成像与多组学数据的整合分析正突破传统影像学以结构为主的局限, 推动新辅助治疗疗效预测向动态化、精准化方向发展, 未来仍需更多大规模、前瞻性研究验证此类多模态预测模型的临床适用性。

5. PET/CT (Positron Emission Tomography/Computed Tomography, PET/CT)

PET/CT 是正电子发射断层(Positron Emission Tomography, PET)和 X 线计算机断层(Computer Tomography, CT)组合而成的多模式系统[40]。与未增殖的正常组织相比, 肿瘤对葡萄糖的消耗显著增加, 并显示与不良肿瘤预后相关[41]。最常见的示踪剂是氟-18 标记的氟代脱氧葡萄糖(18F-fluorodeoxyglucose, 18F-FDG)。一项荟萃分析表明, 在乳腺癌新辅助化疗后 1~2 周期后完善 PET/CT 检查, 通过摄取率变化可有效预测 pCR [34]。

除乳腺癌外, PET/CT 在其他实体肿瘤的新辅助治疗评估中亦有广泛应用。2025 年 ASCO 年会公布的 RATIONALE-213 研究, 针对食管癌新辅助治疗, 采用 PET/CT 动态监测诱导化疗后的代谢反应。所有患者在基线和第一周期化疗后完善 PET/CT 检查, 根据 Suvmax $\geq 35\%$ 定义为应答组和非应答组, 应答组采用“免疫 + 化疗”, 非应答组采用“同步放化疗 + 免疫”的治疗方案。结果显示, 两组 pCR 分别为 30%和 34.4%, 提示 PET/CT 可精准分层患者, 优化治疗策略。在非小细胞肺癌领域, 已有研究利用 PET/CT 评估非小细胞肺癌新辅助免疫治疗, 发现 PET/CT 的代谢参数(如 Δ Suvmax、 Δ Suvmean、 Δ Suvpeak)对术后病理完全缓解(pCR)的预测效能优于传统 CT 形态学评估[42]。Nchingolo R 等人探索了在直肠癌新辅助治疗中的应用。通过人工智能算法对 CT、MRI 及 PET/CT 影像进行深度分析, 提取医学数字成像与通信(DICOM)文件中的编码数据, 并将此类图像数值分析命名为“放射组学”, 结果表明, 放射组学在肿瘤诊断与预后预测中发挥关键作用[43]。这些临床研究为 PET/CT 在乳腺癌新辅助治疗中的应用提供了重要参考。

PHERGAIN 研究利用 18F-FDG PET/CT 评估 HER2 阳性乳腺癌新辅助治疗早期疗效以指导治疗决策。所有患者在基线和 2 个治疗周期后均接受 18F-FDG PET/CT 检查以评估疗效, 将经过 2 周期治疗后靶病灶的 Suvmax 较基线降低 40%定位为有反应者, 无反应者接受双靶联合化疗, 有反应者继续双靶治疗。最新研究数据显示, 约有三分之一的 HER2 阳性早期乳腺癌患者可通过 PET/CT 引导实现治疗降阶梯,

在保持良好疗效的同时显著降低治疗毒性[44]。此外,新型示踪剂如 18F-FES 和 68Ga-FAPI 在早期预测新辅助治疗反应方面展现出良好的应用前景[45][46]。多项临床研究初步表明,Suvmax 下降率与 pCR 显著相关[47][48],早期代谢反应可有效预测疗效:对于代谢应答明显的患者,可考虑降阶梯治疗以减少毒副作用;而对于无应答者应及时调整治疗方案以提高疗效,有望推动乳腺癌向更精准的个体化治疗模式迈进。

6. 讨论与展望

乳腺癌是全球女性中最常见的恶性肿瘤。流行病学数据显示,其发病率呈逐年上升趋势,使其成为中欧防治领域的重点研究方向之一[49]。新辅助治疗是指在术前进行全身治疗,不仅有助于缩小肿瘤体积、提高保乳率,还可实时评估肿瘤对药物的敏感性,为后续治疗方案的调整提供依据[50]。随着新辅助治疗的广泛应用,对新辅助治疗的疗效评估成为了临床医生值得深思的问题。探索更为精准、非侵入性的疗效评估方法成为当前研究热点。目前尚无公认的影像学标准能准确预测乳腺癌新辅助治疗后的 pCR [51]。传统乳腺 X 线摄影与超声检查主要依赖肿瘤大小或形态学改变进行疗效判断,存在明显局限性,尽管整合多种超声参数可能提升评估效能,但仍难以全面反映肿瘤生物学行为变化。相比而言,乳腺 MRI 可从功能层面提供治疗前后肿瘤微环境、血液灌注及细胞密度等多维度信息,现已成为乳腺癌新辅助治疗疗效评估中最常用的影像学手段[52][53]。既往研究表明,MRI 对残留病灶的评估准确性因乳腺癌分子亚型而异,尤其在三阴性乳腺癌、HER2 阳性型及高级别肿瘤中对治疗反应的预测更具优势[54]。PET/CT 作为一种功能性影像技术,在疗效监测中显示预测治疗疗效的阈值并未完全统一[55],且 18F-FDG 摄取易受血糖水平、胰岛素状态及炎症水平等因素干扰,影响结果稳定性[56]。2025 年 ESMO 会议公布了 BELLINI 临床研究的探索性结果,该研究评估两种影像方式预测 pCR,所有患者在基线和治疗 6 周后接受 PET/CT 和 MRI 检查[57],提示联合影像评估可能成为监测新辅助免疫治疗反应的有效工具,但仍需更大样本队列进一步验证。相较于单一影像模态,联合应用 PET/CT 与 MRI 可在更大程度上提高。

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