

MRI表观扩散系数值和血清炎症指标(SII、PLR、NLR)在膀胱癌浸润性评估中的应用价值

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摘要

膀胱癌在男性泌尿系统肿瘤中发病率最高, 目前研究发现有多种危险的致病因素。临床上根据其病理金标准将其分为尿路上皮癌、鳞状细胞癌、腺癌及其他特殊类型癌; 其中常见为尿路上皮癌, 根据其是否侵犯肌层分为浸润性癌和非浸润性癌两大类, 两者分型在治疗方案及预后方面均存在差异。目前, 经尿道的膀胱镜活检仍然是诊断膀胱癌精确诊断的金标准, 但由于侵入性操作, 过度依赖操作人员的经验, 有时存在误报率较高的情况。为突破传统膀胱癌分型对病理学的依赖, 提高早期患者诊断率, 降低侵入性检查对患者的创伤, 现为了早期发现病灶, 识别病灶的良恶性, 为临床医师诊断及治疗方案提出可靠依据, 将影像技术与检验技术结合, 该体系通过整合高分辨率影像特征与特异性血清分子标记, 旨在实现对非浸润性与浸润性膀胱癌的精准鉴别。本文就目前血清学及影像学指标在膀胱癌患者中的临床应用的现状及其未来发展做一综述。

关键词

膀胱癌浸润性, MRI表观扩散系数, 血清炎症指标

The Value of MRI Apparent Diffusion Coefficient and Serum Inflammatory Markers (SII, PLR, NLR) in the Assessment of Bladder Cancer Invasiveness

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Abstract

Bladder cancer has the highest incidence among male urological system tumors. Current research has identified multiple risk factors. Clinically, based on the pathological gold standard, bladder cancer is classified into urothelial carcinoma, squamous cell carcinoma, adenocarcinoma, and other special types, among which urothelial carcinoma is the most common. According to whether it invades the muscle layer, it is divided into invasive and non-invasive cancer, with differences in treatment approaches and prognosis between the two types. Currently, transurethral cystoscopic biopsy remains the gold standard for the accurate diagnosis of bladder cancer; however, due to its invasive nature and heavy dependence on the operator's experience, there is sometimes a relatively high rate of misreporting. To overcome the dependence of traditional bladder cancer typing on pathology, improve early diagnosis rates, and reduce the trauma of invasive examinations for patients, imaging technology combined with laboratory testing has been proposed to enable early detection of lesions, distinguish between benign and malignant lesions, and provide clinicians with reliable bases for diagnosis and treatment. This system integrates high-resolution imaging features with specific serum molecular markers to achieve precise differentiation between non-invasive and invasive bladder cancer. This article reviews the current clinical application and future development of serum and imaging indicators in bladder cancer patients.

Keywords

Bladder Cancer Invasiveness, MRI Apparent Diffusion Coefficient, Serum Inflammatory Markers

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1. 引言

1.1. 膀胱癌流行病学及研究背景

膀胱癌是泌尿系统最常见的恶性肿瘤，在中国，膀胱癌是男性泌尿系统发病率最高的肿瘤，随着目前老龄化趋势上升，老年发病率也随之上升。由于与膀胱癌(BC)相关的主要风险因素——吸烟和化学品暴露，它被认为是一种在很大程度上可以预防和避免的癌症[1]。国家和地区之间的发病率和死亡率存在差异，这些差异取决于暴露于不同风险因素和治疗方法的几个人群之间的变量，包括流行病学数据、社会和文化特征以及经济状况[2]。起源于膀胱的任何肿瘤，尿路上皮癌是其最普遍的组织学亚型，其包括浸润性膀胱癌及非浸润性膀胱癌。临床表现常以肉眼或镜下血尿常见，使用膀胱镜检查、尿液分析和其他专业检查进行评估病情。膀胱癌是一个国际性的公共卫生问题。它是全球第九大最常见的癌症和第十三大癌症死亡原因[3]。

目前根据病理分型，将尿路上皮癌根据病理结果分为亚型。非浸润性膀胱癌是指癌细胞还局限在膀胱的表层，比如粘膜层，未侵袭到肌层；浸润性膀胱癌指癌细胞已经穿透粘膜层，侵入到更深的组织层，甚至是穿透肌层达到周围器官组织。尿路上皮膀胱癌因侵犯位置不同，其治疗、诊断及其预后率均不相

同；治疗方面，非浸润性膀胱癌目前通过经尿道膀胱肿瘤切除术(TURBT)加上术后灌注化疗或免疫治疗来控制；浸润性需要更激进的手术，比如膀胱全切，加上后期化疗或放疗，因为容易复发和转移，且其恶性程度高，预后较差。但是仍存在两者界限争议点：T1 期肿瘤虽然未达到肌层，但侵犯黏膜下层结缔组织，部分指南将其划为 NMIBC，但若合并高级别或广泛原位癌，可能需按浸润性癌处理；TIS 虽属非浸润性，但若为高级别，易发展为浸润性癌，故需密切监测，进展后按浸润性处理。虽然非浸润性及浸润性膀胱癌的界限在病理分期中明确(以肌层侵犯为界)，但实际临床决策需考虑肿瘤分级、分子特征及患者个体情况。T1 期和高级别原位癌的治疗和诊断是主要争议点，需通过多学科诊疗后制定个性化方案。

1.2. MRI 表观扩散系数研究进展及其在膀胱癌浸润性中的应用

为突破传统膀胱癌分型对组织病理学的依赖，降低侵入性检查对患者的创伤风险，近年来基于多模态影像学联合血清生物标志物的无创分型评估体系逐渐成为研究热点。该体系通过整合高分辨率影像特征与特异性血清分子标记，旨在实现对非浸润性与浸润性膀胱癌的精准鉴别，尤其为高级别非肌层浸润性膀胱癌(high-risk NMIBC)的早期风险分层提供客观依据。基于扩散模型的扩散加权成像(diffusion weighted imaging, DWI)获得的表观扩散系数(apparent diffusion coefficient, ADC)可以为膀胱肿瘤的分级和分期提供有用的诊断信息。此外，峰度指标在区分 MIBC 和 NMIBC 方面表现良好。弥散加权磁共振成像(DW MRI)可以提供与肿瘤特征和对化疗反应相关的功能信息。

越来越多的证据探索了 DW-MRI 中表观扩散系数(ADC)值测量值的作用，作为预测和监测不同肿瘤类型对化疗反应的有前途的成像标志物[4]-[10]。表观扩散系数(ADC)是弥散加权成像(DWI)的定量参数，反映组织内水分子扩散受限程度。低 ADC 值与肿瘤细胞密度高、侵袭性强相关，可能作为影像学预后标志物。目前，基于 CT 或 MRI 的影像学模型已在膀胱癌预后预测中展现出潜力。通过无创影像诊断，不仅可以提高诊断效率，而且为患者提供了更加合理且有益的方案。

1.3. 血清炎症指标(SII、PLR、NLR)在肿瘤中的评估重要性及其在膀胱癌浸润性中的应用

癌症和炎症就像一对“坏朋友”。长期慢性炎症会破坏细胞 DNA，让正常细胞“黑化”成癌细胞。炎症分为急性、慢性两种，前者是物理、化学或急性感染情况中发生，是机体早期防御措施，通常会自愈。后者主要是发生慢性感染或自身免疫疾病中，机体正常反馈调节无法终止炎症，导致炎症慢性化。慢性炎症对肿瘤的起始、生长和恶化都起到了促进作用。促炎因子的大量分泌导致机体的免疫系统变化，促进炎症细胞恶化且发生肿瘤。炎症因子可能导致癌症的发病率、肿瘤分期和进展。在确诊为癌症的患者中，肿瘤浸润淋巴细胞是患者分层的重要临床生物标志物，可补充传统的预后指标，如分期和分级。事实上，肿瘤中免疫细胞浸润的局部增加以及全身炎症反应的升高可能是癌症进展和预后的重要指标。此外，以炎症细胞和促炎介质持续增加为特征的低度慢性炎症通常在癌症诊断之前升高，并可能促进癌症[11]-[15]。全身性炎症可使用常见血液检查中常规测量的各种生化或血液学标志物或根据这些测量得出的比率来评估。具体来说，以前的研究强调了四个与发病率和死亡率相关的比率，包括中性粒细胞与淋巴细胞比值(NLR)、血小板与淋巴细胞比值(PLR)、淋巴细胞与单核细胞比值(LMR)和基于外周淋巴细胞、中性粒细胞、单核细胞和血小板计数的全身免疫炎症指数(SII)。全身炎症标志物与几种癌症风险之间的关联。诊断前最后一年的风险增加可能反映了对已经存在但临床上未被发现的癌症的全身免疫反应。血细胞比值可以作为癌症发病风险的生物标志物，有可能在临床诊断前的最后一年早期识别疾病。中性粒细胞、血小板和淋巴细胞的血清水平已被认为是许多实体瘤(包括膀胱癌(BC))预后不良的相关因素。根据常规全身炎症标志物的测量定义了一个风险评分(SIM 评分)。该评分可以识别未侵犯肌肉层且更易发生肿瘤复发和进展的高级别膀胱癌患者。因此，该评分可用于选择可能受益于早期膀胱摘除的患者[16]-[21]。 $SII(\text{系统性免疫炎症指数}) = \text{血小板} \times \text{中性粒细胞/淋巴细胞}$ ； $NLR(\text{中性粒细胞/淋巴细胞比值})$ ；

PLR (血小板/淋巴细胞比值)。在膀胱癌中: SII (血小板 \times 中性粒细胞/淋巴细胞)可综合反映炎症与免疫状态, 高 SII (如 ≥ 385)是 MIBC 术后复发和生存的独立危险因素。NLR 和 PLR 升高与肿瘤微环境中的促炎反应相关, 高 NLR (如 ≥ 2.40)和高 PLR (如 ≥ 159.3)显著降低无复发生存率(RFS)和总生存率(OS)。

1.4. 结合影像和血清指标的协同作用

以往在诊断膀胱癌患者时常依赖单一的检查影像或者是血液特异性指标, 未将两者结合。所以针对目前临床需求将整合影像参数(ADC)与炎症指标(SII、NLR、PLR), 构建多模态预测模型, 可弥补单一指标的局限性, 为膀胱癌高级别非浸润性癌及浸润性癌患者的个体化治疗和动态随访提供依据。目前临床诊断膀胱癌分化主要依靠病理组织活检, 但其不仅为有创检查, 还具有取材的片面性和局限性, 不能反映肿瘤组织者全面情况, 因此常出现假阴性或假阳性。因此本研究旨在探讨多参数 MRI 影像参数及 ADC 直方图参数分析与膀胱癌是否伴有病理亚型之间的关系, 以期鉴别尿路上皮癌是否伴有分化提供一种新的简便的辅助诊断方法。比较两组间膀胱癌患者的临床、病理及影像参数差异, 计算受试者工作特征曲线(ROC)的曲线下面积(AUC)评估各参数鉴别膀胱癌有无分化的诊断效能。采用多因素 logistic 回归筛选独立危险因素, 以此构建临床模型。结论提示多参数磁共振成像联合 ADC 直方图分析可准确预测膀胱癌患者是否合并其他病理分化, 可协助临床制定更个体化的治疗方案[22]-[26]。病灶的标化 ADC 值与 HER2 表达水平呈负相关, 标化 ADC 值是预测 HER2 表达水平的潜在工具。

2. 结论

分析影像与炎症指标的协同作用是否显著提升术前诊断和预后预测的准确性。构建基于多模态特征的预后列线图模型, 辅助临床风险分层。构建多模态预测模型, 可在影像中提取深层次的肿瘤异质性图像信息, 结合患者术前的血液指标检验结果, 将影像学特征与临床血液炎症风险因子相结合, 建立影像学-临床列线图预测 BCa 患者的无复发生存期(recurrence-free survival, RFS)。并探索这种联合模型的综合应用方法在 BCa 复发风险中的增量预后预测价值。综上, 多参数 MRI 定性征象联合定量指标可准确预测膀胱癌患者是否合并其他病理亚型的出现, 有利于临床医生对膀胱癌患者全面评估, 从而制定更加个体化的治疗方案, 改善患者预后。DC 值反映肿瘤细胞密度和微观结构, 膀胱癌通常表现为 ADC 值降低。结合血清指标如癌胚抗原(CEA)、细胞角蛋白 19 片段(CYFRA 21-1)等, 可综合评估肿瘤的生物特性。例如, ADC 值低且血清肿瘤标志物升高时, 更倾向于诊断为膀胱癌, 减少误诊率。有研究通过构建联合模型, 将 ADC 直方图特征与血清指标结合, 预测膀胱癌病理分化类型, AUC 值可达 0.91, 显著高于单一指标评估[27]。其不仅能在术前客观全面地无创性预测膀胱癌复发风险分层, 帮助医师提高诊断准确率; 而且实现了膀胱癌患者早期的复发风险可视化预测, 帮助临床医生借助一种无创性预测工具实现患者个体化、精准化的复发评估。多模态预测模型方法的应用为无创评估肿瘤异质性和智能诊疗体系的发展提供了一种新思路。

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