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Research Progress of Multiparametric Magnetic Resonance Imaging in Predicting Extraprostatic Extension of Prostate Cancer

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Abstract: Extraprostatic extension (EPE) of prostate cancer is a key pathological feature that affects patient prognosis and the choice of treatment strategy. Accurate prediction of EPE is of significant clinical value in developing individualized treatment plans. Multiparametric magnetic resonance imaging (mpMRI), with its non-invasiveness, high spatial resolution, and multi-sequence imaging capabilities, has become a core imaging method for preoperative assessment of EPE. However, current imaging diagnosis of EPE still faces challenges such as high subjectivity, lack of standardized diagnostic criteria, and relatively low sensitivity in detecting minor extensions. In recent years, continuous breakthroughs in radiomics and artificial intelligence technologies are expected to significantly enhance the diagnostic performance of mpMRI. This article systematically reviews the optimization strategies of mpMRI imaging technology in the assessment of EPE in prostate cancer, explores the development from empirical interpretation to precise quantitative analysis of mpMRI features, focuses on the current application of radiomics in mpMRI-based prediction of EPE, and deeply analyzes the limitations of mpMRI in evaluating minor EPE. By integrating existing research evidence, it aims to provide clinicians with precise diagnostic strategies for EPE based on mpMRI, thereby contributing to the advancement of individualized diagnosis and treatment of prostate cancer.

Keywords: Multiparametric magnetic resonance imaging; Prostate cancer; Extraprostatic extension

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1. Introduction

Prostate cancer ranks second in incidence and fifth in mortality among cancers in men [1]. The clinical staging, pathological grading, and prognostic risk stratification of prostate cancer are important bases for guiding treatment plan selection. Based on clinical staging and pathological grading, non-metastatic prostate cancer can be divided into organ-confined (T1-2N0M0) and locally advanced (T3-4N0M0) types. Radical prostatectomy is one of the effective methods for treating organ-confined and locally advanced prostate cancer [2]. However, a retrospective study pointed out that, compared with other treatment methods, patients who underwent this surgery performed worse in terms of postoperative urinary incontinence incidence and preservation of sexual function [3]. Radical prostatectomy requires finding a balance between tumor control, urinary continence, and preservation of sexual function, and whether to preserve the neurovascular bundles

(NVB) is a key factor affecting postoperative tumor control, urinary continence, and recovery of sexual function [4]. For patients with low- to intermediate-risk localized prostate cancer, bilateral NVB should be preserved as much as possible; however, for patients with established extraprostatic extension (EPE), preserving the NVB is contraindicated in radical prostatectomy, as it significantly increases the positive surgical margin rate and the risk of postoperative biochemical recurrence. If it is unclear during surgery or there is a high suspicion of residual tumor, NVB preservation should be abandoned. EPE is a common pathological finding after radical prostatectomy, with previous studies reporting an incidence ranging from 23% to 67% [5].

In recent years, multiparametric magnetic resonance imaging (mpMRI), by integrating T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE) sequences, can provide morphological and functional information of the prostate, helping to identify the extent of tumor invasion. A previous study reported that mpMRI has a sensitivity of approximately 65–75% and a specificity of approximately 65–85% for EPE, with a certain risk of missed diagnoses and misdiagnoses [6]. Studies show that mpMRI has high specificity in the diagnosis of EPE, but its sensitivity still has considerable limitations, especially for tiny EPE lesions, where its ability to detect is limited [7]. Based on mpMRI images, the Prostate Imaging-Reporting and Data System (PI-RADS) v2.1 score shows that the higher the score, the higher the malignancy of prostate cancer [8]. The length of contact between the prostate tumor and the capsule (LCC) and the maximum diameter of the tumor measured on mpMRI images are positively correlated with EPE [6]. Some scholars have combined various relevant indicators in mpMRI images with clinical and pathological indicators to construct predictive models, and the results show that it can significantly improve the accuracy of EPE prediction [9]. Multiparametric magnetic resonance imaging technology plays a crucial role in the preoperative diagnosis, assessment, treatment decision-making, and postoperative follow-up of patients with prostate cancer. This study aims to review the research progress of multiparametric magnetic resonance imaging technology in predicting EPE in prostate cancer.

2. Optimization of mpMRI imaging technology in the assessment of extraprostatic extension in prostate cancer

The core advantage of multiparametric magnetic resonance imaging lies in integrating multiple functional imaging sequences to assess the pathophysiological characteristics of EPE from different dimensions. T2-weighted imaging is the fundamental sequence for evaluating prostate anatomical structures and tumor morphology and plays a central role in the diagnosis of EPE. The normal prostate capsule appears as a thin low-signal structure on T2WI. Tumor tissue shows low-signal nodules, and this difference can help us check if the capsule is intact [10]. Research shows that multiple signs on T2WI together can predict EPE better than one clinical parameter. Also, we build multivariable model combining MRI features. It can get an AUC of 0.81, and this is better than the model with only clinical parameters (AUC = 0.69) [10].

Diffusion-weighted imaging can show tumor cell density and cell membrane integrity by detecting water molecule movement in tissues, and in the EPE region, the high density of tumor cells and reduced extracellular space can restrict water diffusion, which makes the ADC value decrease. Research shows that ADC values are related to prostate cancer aggressiveness, and low ADC values often mean higher Gleason scores and worse prognosis [11]. Also, ADC values can help us distinguish between low-risk and high-risk prostate cancer, and it is worth noting that the AUC is up to 0.87 when we diagnose high-grade prostate cancer [12].

DCE-MRI can assess microvascular perfusion and permeability in tumor tissue. We inject contrast agent intravenously and continuously acquire images. In fact, prostate cancer, especially aggressive types, can have neovascularization. This leads to increased vascular permeability and blood flow. Semi-quantitative parameters such as the volume transfer constant (Ktrans) can reflect the rate at which contrast agent diffuses from vasculature into extravascular extracellular space, and can be related to microvessel density and permeability. It is worth noting that multiple studies confirmed that elevated Ktrans values are associated with increased risk of EPE, and this suggests that tumors with high Ktrans values can have greater invasiveness [13]. We can combine DCE-MRI with T2WI and DWI, and this combination can help improve diagnostic accuracy, and one study showed that the AUC for the combined diagnosis of clinically significant prostate cancer with Gleason ≥ 4+3 was 0.87, which is better than any single sequence [14].

3. mpMRI imaging features: From empirical interpretation to precise quantification

3.1. Experience-based judgment

In the past, radiologists assessed the likelihood of EPE through a series of visual signs, mainly including capsular disruption and tumor protrusion. Capsular disruption is the most direct MRI sign of EPE. On T2WI, a normal prostate capsule appears as a continuous, smooth low-signal line. When a tumor breaks through the capsule, the continuity of this low-signal line is interrupted, showing focal defects or breaks, with tumor tissue directly extending into the surrounding high-signal fat tissue [15]. Its specificity is extremely high, and once observed, the presence of EPE can almost be confirmed.

Tumor protrusion is also a direct sign, which means the tumor tissue extends beyond the normal contour of the prostate and forms soft tissue shadows in surrounding fat, and these shadows can be nodular or cord-like with irregular shapes, so we can observe them in clinical images. Also, previous studies show that when the tumor protrusion length is ≥1 mm, the specificity for diagnosing EPE can reach more than 90% [16,17].

3.2. Precise quantification: Tumor size, tumor-to-capsule contact length, PI-RADS scoring system

We find that larger prostate tumors can have higher EPE risk [10]. In fact, when the tumor diameter reaches or exceeds 15 mm, or the volume is more than 0.5 cm^3, the EPE risk can be higher, especially when the tumor is in the peripheral zone, as the capsule there is relatively thin and lacks surrounding tissue support, making the capsule more prone to involvement [18]. This can help clinicians choose treatment plans, and tumor contact length with capsule (TCL) is a quantifiable indicator for predicting EPE. Studies indicate that when TCL reaches or exceeds 10 mm, the positive predictive value for EPE can exceed 80%, which can be used as a reference for preoperative assessment of tumor local invasion [11] .

PI-RADS v2.1 is mainly used for detecting prostate cancer. But its imaging features, especially the assessment of capsule integrity on T2WI, can help estimate the risk of EPE. Studies show that PI-RADS score and EPE occurrence are correlated. When the score is higher, the likelihood of extraprostatic extension in prostate cancer [19]. Different observers may give different correlations between PI-RADS scores and EPE. So if we only use PI-RADS scores to predict EPE, there can be some limitations [20].

4. Integrated model of radiomics and clinical parameters

The integrated model significantly improves the prediction of EPE in prostate cancer by jointly modeling radiomic features with clinical variables such as PSA levels, Gleason score, age, and others. Clinical parameters themselves are independent predictors of EPE; for example, PSA density, tumor percentage, and maximum tumor length have all been shown to be significantly associated with EPE [16]. Studies have shown that after integrating radiomics features with clinical parameters, the model's AUC can be improved to 0.85–0.92, significantly outperforming a single model [21]. For example, an integrated model constructed by a multicenter study (combining clinical features, tumor microenvironment heterogeneity, and radiomics features) achieved an AUC of 0.853 in an external validation set [22]. This integrated model not only enhances predictive accuracy but also improves the clinical applicability of the model.

5. The detection challenge of micro EPE

Extraprostatic extension (micro EPE) under the microscope is the main source of missed diagnosis of mpMRI in prostate cancer staging. Micro EPE is pathologically defined as tumor cells penetrating the prostate capsule but with a very short radial distance (usually less than 1 mm). Due to the lack of significant morphological changes, conventional mpMRI sequences are difficult to detect these microscopic changes. Studies have shown that while mpMRI has acceptable overall diagnostic performance for EPE, its sensitivity to micro-invasion is significantly insufficient; for example, one study showed that the sensitivity of MRI for detecting ECE was only 56.2%, with a specificity of 82.6% [23]. In addition, different MRI interpretation criteria (such as EPE grading and the Likert scale) have AUC values mostly between 0.77 and 0.81 in predicting EPE, but none can reliably identify small EPE [24]. The consistency among observers was only moderate (weighted κ value 0.47), further highlighting the limitations of subjective interpretation [20]. At present, there is no single imaging biomarker that can accurately identify microscopic EPE, mainly due to tumor heterogeneity and the physical limitations of imaging resolution.

6. Future research directions and emerging technologies

6.1. Artificial intelligence (AI)-assisted diagnosis

Recently, AI technology, especially deep learning models, has shown good potential in imaging diagnosis of EPE in prostate cancer. Some results can even surpass human experts. A study with 849 patients from two centers shows that deep learning-based AI models (such as PAGNet) achieved an area under the curve (AUC) of 0.807 in the internal validation set and 0.728 in the external validation set, and the performance is better than two radiology experts (0.632–0.741) [25]. This indicates AI models can extract subtle features from complex mpMRI images that are difficult for the human eye to discern, and the accuracy of EPE prediction can be improved. When radiology experts use AI predictions together with their own interpretation, the diagnostic performance is improved [26]. This human-machine collaboration model can help reduce interpretation differences among different radiologists, and it works well for less experienced doctors, and diagnostic consistency is improved [27]. These findings indicate that AI-assisted diagnosis can improve the accuracy of detecting EPE. Also, it can overcome the limitations of high subjectivity and poor reproducibility in traditional imaging assessments. The results can be used as a reference for clinical decision-making.

6.2. Multimodal fusion and molecular imaging

Multimodal fusion and molecular imaging are now key directions to improve the diagnosis accuracy of EPE in prostate cancer. When we combine mpMRI with prostate-specific membrane antigen positron emission tomography (PSMA PET), we can get anatomical information with high resolution and molecular-targeted signals at the same time, and this can avoid the limits of using only one imaging modality. In fact, studies show that PSMA PET/mpMRI fusion imaging has good performance in EPE diagnosis. One systematic review and meta-analysis reported that when using 68Ga-PSMA PET/MRI to detect EPE, the natural logarithm of the pooled diagnostic odds ratio (lnDOR) was 2.27, which means the diagnostic efficacy is high [28]. Another study compared the performance of mpMRI and 68Ga-PSMA PET/MRI in staging of primary prostate cancer, found that both have similar accuracy in detecting ≥T3 stage (i.e., EPE), but PET/MRI is better for assessing lymph node metastasis [29]. These results suggest that PSMA PET/mpMRI fusion imaging, because it combines molecular and anatomical information, can better identify EPE, with diagnostic performance (AUC up to 0.92) better than single mpMRI or PET/CT modalities [23,30]. The integration of multimodal and molecular imaging technologies is building a more complete and accurate EPE diagnostic system, and it is expected to help achieve better risk stratification and treatment decision-making in future clinical practice.

7. Conclusion

Multiparametric magnetic resonance imaging (mpMRI), with its multi-sequence imaging capability, has upgraded from an auxiliary tool to a core pillar in the preoperative diagnosis of EPE of prostate cancer. Through the combined use of T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced MRI (DCE-MRI), it provides rich biological information across multiple dimensions such as tumor morphology, cell density, and microvascular perfusion. Direct signs (such as capsular disruption) and indirect signs (such as capsular contact length ≥10 mm) demonstrate indispensable localization value in clinical practice, but the limitations of single signs require us to interpret imaging data with an integrated approach. The introduction of radiomics and artificial intelligence techniques, utilizing high-throughput feature extraction and nonlinear modeling, has elevated predictive performance to an AUC > 0.85, marking a paradigm shift from "empirical interpretation" to "data-driven decision-making." However, it must be recognized that the superiority of these models mostly comes from single-center retrospective data, and their generalizability is constrained by factors such as detection blind spots for small EPE, interobserver variability, and lack of data standardization. In addition, PSMA PET/mpMRI multimodal integration is expected to overcome the detection bottleneck for small EPE through the complementary effects of molecular and morphological information. Ultimately, efforts should be made to establish standardized diagnostic pathways based on mpMRI, translating technological innovation into reproducible clinical benefits, and enabling precision medicine to extend from concept to every aspect of prostate cancer management.

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Disclosure statement

The author declares no conflict of interest.

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