Advances in Clinical Medicine 临床医学进展, 2026, 16(3), 2320-2326
Published Online March 2026 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2026.1631027

Hans汉斯

前列腺癌诊断技术的研究进展

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收稿日期：2026年2月11日；录用日期：2026年3月4日；发布日期：2026年3月13日

摘　要

前列腺癌是全世界第二常见的男性恶性肿瘤疾病。前列腺癌早期多因无显著临床表现而很难被发现。目前对前列腺癌的诊断主要依赖于直肠指检、前列腺特异性抗原检测、经直肠超声检查、多参数磁共振成像、前列腺特异性膜抗原正电子发射断层扫描。早期、准确诊断前列腺癌并予以及时治疗，能够增加患者生存率。本综述对前列腺癌各种诊断方法研究进展进行综述，供临床参考。

关键词

前列腺癌，前列腺特异性膜抗原

Research Advances in Diagnostic Techniques for Prostate Cancer

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Received: February 11, 2026; accepted: March 4, 2026; published: March 13, 2026

Abstract

Prostate cancer is the second most common male malignant disease worldwide. Prostate cancer is difficult to detect in the early stage because of the lack of significant clinical manifestations. At present, the diagnosis of prostate cancer mainly relies on digital rectal examination, prostate specific antigen detection, transrectal ultrasonography, multi-parametric magnetic resonance imaging, and prostate specific membrane antigen positron emission tomography. Early and accurate diagnosis of prostate cancer and timely treatment can improve the survival rate of patients. This article reviews the research progress of various diagnostic methods for prostate cancer for clinical reference.

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文章引用: 李良宇, 徐光勇. 前列腺癌诊断技术的研究进展[J]. 临床医学进展, 2026, 16(3): 2320-2326.
DOI: 10.12677/acm.2026.1631027

Keywords

Prostate Cancer, Prostate-Specific Membrane Antigen

1. 引言

前列腺癌(prostate cancer, PCa)是仅次于肺癌的全球男性第二常见癌症，也是男性生殖系统常见的恶性肿瘤[1]。近年来，由于国内居民生活方式及饮食习惯改变、人口老龄化程度加剧等诸多因素的影响，前列腺癌的发病率呈逐年上升的趋势，且随着年龄增长显著升高[2]。前列腺癌早期多因无显著临床表现而很难被发现，早期诊断前列腺癌有助于改善患者预后。本文将从前列腺癌各种诊断方法现状进行综述，以期为前列腺癌患者尽早诊断提供参考价值。

2. 前列腺癌的诊断技术

2.1. 直肠指诊(DRE)

直肠指检(Digital Rectal Examination, DRE)是指检查者通过手指感知前列腺的质地、大小、有无硬结等，但其对局限于腺体内或体积较小的肿瘤敏感性很低，且结果高度依赖检查者的经验[3]。DRE 作为一个初步筛查方法，具有简便、无创伤和低廉的优点，对于早期发现前列腺癌有一定的价值[4]。

2.2. 血清前列腺特异性抗原(PSA)检测

PSA 是一种由前列腺上皮细胞产生的丝氨酸蛋白酶，主要分布在前列腺组织及精液中[5]。其血清学主要检测指标为总前列腺特异抗原(total PSA, tPSA)、游离前列腺特异抗原(free PSA, fPSA)和游离前列腺特异抗原与总前列腺特异抗原的比值(fPSA/tPSA)。目前临床一致观点是血清 tPSA 正常值为 0~4 ng/mL，如果 tPSA > 10 ng/mL，应高度怀疑恶性[6]。当血清 tPSA > 4 ng/mL 但≤10 ng/mL 时，应当参考 F/T (fPSA/tPSA)比值，F/T 比值越低，发生前列腺癌的可能性越大[7] [8]。

针对 PSA 灰区(4~10 ng/mL)的患者，我们参考欧洲泌尿外科学会关于前列腺癌的最新指南和最新证据，绘制了诊断流程图(见图 1)。

PSA 在血清中的浓度升高与前列腺组织异常(包括癌变、增生、炎症)相关。然而，PSA 最大的局限性在于其器官特异性而非癌症特异性。良性前列腺增生、前列腺炎等常见良性疾病均可导致 PSA 水平显著升高，这造成了较高的假阳性率。为优化 PSA 的诊断效能，如 PSA 密度(prostate specific antigen density, PSAD)、PSA 速率(prostate specific antigen velocity, PSAV)等衍生指标被开发和应用。一项回顾性研究表明，将 PSAD 指标纳入前列腺癌的评估中，能有效提高前列腺癌的诊断效能[9]。此外，近年来学者们综合 tPSA、fPSA 和 PSA 前体等指标开发出了前列腺健康指数(phi)，显示出比传统 PSA 更优的前列腺癌预测能力，正逐渐被纳入临床指南作为高级风险评估工具[10] [11]。

2.3. 经直肠超声检查

经直肠超声(TRUS)是实时观察前列腺形态、体积和回声结构的首选影像手段[12]。典型的前列腺癌在 TRUS 上可表现为低回声结节，许多 csPCa 在 TRUS 上呈等回声或难以辨认[13]。当前 TRUS 的核心

价值在于为前列腺穿刺活检提供实时引导。

近年来，发展出了超声造影(CEUS)、超声弹性成像(USE)、彩色多普勒血流成像(CDFI)等超声新技术。研究表明，CEUS 在检测前列腺癌方面优于传统经直肠超声[14] [15]。此外，这些新的超声引导技术已被证明在与系统活检结合时能提高前列腺癌的检测率[16]。

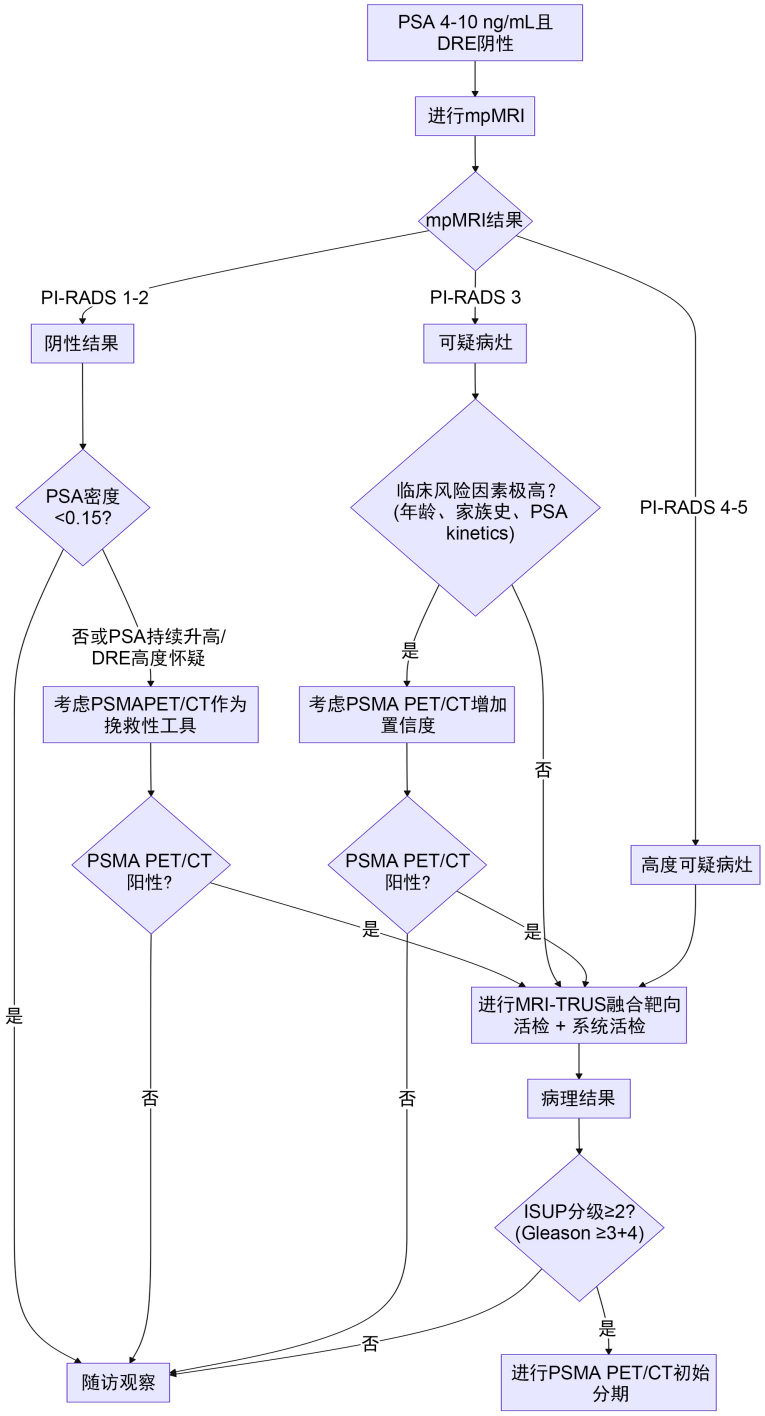

Figure 1. Flowchart for prostate cancer diagnosis in the PSA gray zone
图 1. PSA 灰区的前列腺癌诊断流程图

2.4. 多参数磁共振成像

多参数磁共振成像(multiparametric MRI, mpMRI)被广泛应用在前列腺癌的诊断中。它通过融合高分辨率的解剖成像(T2 加权成像, T2WI)和反映组织细胞密度、血流灌注的功能成像实现对前列腺内部结构的精细评估和肿瘤生物学特性的无创探测[17] [18]。

为了规范 mpMRI 的解读并减少观察者间差异，前列腺影像报告和数据系统(PI-RADS)应运而生，目前已更新至第二版(PI-RADS v2.1)。该系统为前列腺不同分区(外周带与移行带)的病灶设定了标准化的评分体系(1~5 分)，将影像发现与临床显著性癌症的风险等级直接关联：1~2 分考虑良性病灶可能性大，4~5 分考虑恶性病灶可能性大，3 分则为两者的中间值，良恶性可能差距不大。有研究证实，mpMRI 对 csPCa 具有出色的诊断性能[19] [20]。对于初诊患者，若 mpMRI 结果为阴性(PI-RADS ≤ 2)，可以考虑避免立即进行系统性活检，转而进行密切的主动监测，这使相当一部分男性免除了不必要的侵入性操作及其相关并发症[21]-[23]。此外，mpMRI 还可以融合 TRUS 指导靶向穿刺。在穿刺活检之前，先获取前列腺的 mpMRI 相关数据，如 T1WI、T2WI、动态增强 MRI、MR 波谱、MR 扩散加权成像、MR 扩散张量成像等；然后对正常前列腺组织与可疑前列腺癌病灶进行鉴别和描绘，并把描绘后的图像上传至融合软件中；将活检前 MRI 与实时 TRUS 融合，再进行定位穿刺。有研究表明，MRI-超声融合引导活检比单纯系统活检更能检测出临床显著性的前列腺癌[24]。

然而，基于前列腺影像报告与数据系统的 mpMRI 在前列腺癌的应用中仍面临挑战，如对 PI-RADS 3 分病灶的管理、观察者间差异以及移行带癌诊断的复杂性。同时，植入心脏起搏器的患者、髋关节置换术后患者及幽闭症患者等也是检查的绝对禁忌。

2.5. 前列腺特异性膜抗原正电子发射断层扫描

正电子发射断层扫描(PET)成像可提供有关肿瘤分子和代谢特征以及潜在远处转移部位的关键信息。PSMA 是一种谷氨酸羧肽酶II型非分泌性跨膜蛋白，被研究者们发现可在大多数 PCa 中表达，其表达量相比正常前列腺组织高 1000 倍[25]。PSMA 的表达水平与肿瘤的侵袭性正相关，是前列腺癌诊断和治疗的一个有前途的靶点。PSMA PET/CT 利用放射性核素(如 ^{68}Ga、^{18}F)标记的 PSMA 小分子抑制剂作为示踪剂，静脉注射后，示踪剂特异性地与肿瘤细胞表面的 PSMA 结合，通过 PET/CT 扫描即可实现病灶的高对比度、全身性显像[26]。一项荟萃分析显示，使用组织病理学作为参考标准，PSMA PET-CT 在临床怀疑患者中初次检测 PCa 的敏感性和特异度分别为 0.97 和 0.66 [27]。一项回顾性分析比较了 PSMA PET-CT 与 mpMRI 的 144 名患者，发现通过 PSMA PET-CT 对临床显著性 PCa 的敏感性高于 mpMRI (94.85% 对 86.03%；$p = 0.022$) [28]。另一项研究显示，PSMA PET-CT 在中等风险 PCa (国际泌尿病理学会分级 2 级和 3 级)中具有额外益处，显示其比单用 mpMRI 具有更高的敏感性、特异性、阳性预测值(PPV)和阴性预测值(NPV) [29]。

近年来，68Ga-PSMA PET/CT 作为 csPCa 的非侵入性诊断工具，已经受到广泛的关注。Emmett 等人进行的一项前瞻性多中心 II 期成像试验指出，将 mp-MRI 与 68Ga-PSMA PET/CT 相结合可大大提高诊断 csPCa 的灵敏度，降低假阴性率[30]。随后，Emmett 等人在 PRIMARY 试验的事后分析中提出了基于 68Ga PSMA PET/CT 的 5 分 Likert PRIMARY 评分，并将其引入到 PCa 分子成像标准化评价(PROMISE V2)标准中[31] [32]。PRIMARY 评分的引入标志着 PCa 初步诊断的进步，其使得 PSMA PET 结果的解读更加规范化和标准化。该评分结合了解剖定位(外周、中心或过渡区)、前列腺内 PSMA 活动模式(无、弥漫性或局灶性)和非常高的 SUVmax (>12)，以提高原发性肿瘤诊断的准确性[31]。

PRIMARY 评分最具潜力的应用场景之一，是对 mpMRI 结果为阴性(PI-RADS ≤ 2)或不确定(PI-RADS

3)的患者进行风险再分层。一项前瞻性研究显示，PRIMARY 评分对 PI-RADS 3 级病变的分类有很大潜力，有助于避免不必要的活检[33]。另一项回顾性研究显示，对于 PI-RADS 为 1~3 的男性而言，PRIMARY 评分具有良好的诊断价值，并能够使其安全地避免不必要的活检[34]。此外，Hatice 等人的研究指出，在低风险前列腺癌患者组中，无一人 PRIMARY 评分为 5 分，这提示，PRIMARY 评分未来可能辅助甄别适合主动监测的低危患者[35]。此外，研究表明 PRIMARY 评分在预测前列腺癌患者盆腔淋巴结转移可能性的方面同样具有良好效果[36]。

PRIMARY 评分是 PSMA PET/CT 技术在前列腺癌原发灶诊断领域走向标准化和成熟化的重要标志。它通过系统分析病灶的解剖、模式和功能信息，提供了与 mpMRI PI-RADS 互补且效能相当的诊断工具。现有证据充分支持其在提高 csPCa 检出率、优化活检决策、减少不必要的侵入性操作方面的临床价值。尽管在评估范围普适性和临床整合方面仍需完善，但随着前瞻性研究的推进和技术的迭代，PRIMARY 评分有望与 mpMRI 共同构成前列腺癌精准无创诊断的新双翼，推动诊疗模式向更加个体化、高效化的方向发展。未来的研究应致力于在更广泛的人群和示踪剂中验证并优化该评分系统，并积极探索其在疾病全程管理中的多元化应用。

3. 总结与展望

综上所述，前列腺癌的诊断已形成一个多层次、多技术协同的精密体系。通过持续推动技术创新与临床转化，未来有望实现对前列腺癌更早、更准、更个性化的诊断，最终转化为患者生存获益的切实提升。

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