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Role of Gallium-68-Labeled Prostate-Specific Membrane Antigen Positron Emission Tomography to Detect Clinically Significant Prostate Cancer

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Abstract

Multiparametric Magnetic Resonance Imaging (mpMRI) interpreted using PI-RADS has become a cornerstone in the diagnostic workup of prostate cancer; however, its performance remains limited by inter-reader variability, equivocal lesions, and false-negative findings. Gallium-^{68}–labeled prostate-specific membrane antigen positron emission tomography/computed tomography (^{68}Ga-PSMA PET/CT) has emerged as a complementary imaging modality with potential relevance for primary tumor detection and surgical planning. This narrative review summarizes current evidence regarding the diagnostic accuracy of ^{68}Ga-PSMA PET/CT for Clinically Significant Prostate Cancer (csPCa) and its integration with mpMRI. A comprehensive literature search of PubMed (MEDLINE) and Embase was conducted for studies published up to September 30, 2025, focusing on the use of ^{68}Ga-PSMA PET/CT for primary prostate cancer detection or comparison with mpMRI. Evidence from prospective and retrospective studies, as well as meta-analyses, demonstrates that ^{68}Ga-PSMA PET/CT achieves high sensitivity and specificity for csPCa, with tracer uptake correlating with Gleason grade group, prostate-specific antigen levels, and tumor aggressiveness. When combined with mpMRI, ^{68}Ga-PSMA-PET/CT consistently improves sensitivity, negative predictive value, and intraprostatic lesion localization compared with either modality alone. This combined approach has shown particular benefit in patients with equivocal mpMRI findings or persistent clinical suspicion following negative biopsies, enabling more accurate targeting for biopsy and potentially informing surgical decision-making. Despite promising results, heterogeneity among studies and lack of standardized uptake thresholds limit widespread adoption. Large prospective trials are required to define its role in routine preoperative assessment and surgical planning for prostate cancer.

Keywords: Cspca; ^{68}Ga-PSMA-PET; Mpmri; Tumour Localisation

Introduction

Multiparametric Magnetic Resonance Imaging (mpMRI), interpreted according to the Prostate Imaging-Reporting and Data System (PI-RADS), has significantly transformed the diagnostic approach to prostate cancer (PCa) and reduced the frequency of unnecessary biopsies [1]. Compared with transrectal template biopsy, mpMRI demonstrates superior diagnostic accuracy, particularly by reducing false-negative findings [2,3]. mpMRI increases the detection of Clinically Significant Prostate Cancer (csPCa) from 26% to 38%, while also reducing the diagnosis of indolent disease from 22% to 9%. Despite these advances, the performance of mpMRI remains heterogeneous. Reported sensitivity ranges from 58% to 96%, specificity from 23% to 87%, Positive Predictive Value (PPV) from 38% to 93%, and Negative Predictive Value (NPV) from 63% to 98% [2-4]. Although the high NPV provides reassurance, mpMRI still misses up to 13% of clinically significant PCa (csPCa), cases, and false-positive rates may reach 60–80%, even among PI-RADS 4 or 5 lesions [5]. Equivocal PI-RADS 3 findings and inter-reader variability, influenced by protocol and scanner differences, further challenge its reliability [6]. In this context, positron emission tomography/computed tomography with Gallium-68–labeled prostate-specific membrane antigen ligands (^{68}Ga-PSMA PET/CT) has emerged as a promising complementary imaging tool [7]. Currently recommended for staging high-risk disease and detecting biochemical recurrence, its role in primary tumor localization remains uncertain [8,9]. While several studies have explored its capacity to identify intraprostatic lesions, methodological heterogeneity and inconsistent results have limited definitive conclusions [10,11]. This review summarizes current evidence on the diagnostic performance of ^{68}Ga-PSMA PET/CT in csPCa, with emphasis on its correlation with Gleason score, PSA levels, mpMRI findings, and potential clinical applications.

Materials and Methods

A comprehensive literature search was conducted across PubMed (MEDLINE) and Embase databases for articles published up to September 30, 2025. The search strategy incorporated a combination of controlled vocabulary and free-text terms, including “PSMA” or “prostate-specific membrane antigen positron emission tomography,” alongside keywords such as “magnetic resonance imaging,” “mp-MRI,” “multi-parametric MRI,” and “multi-parametric magnetic resonance imaging.” These terms were combined with phrases related to prostate cancer, specifically “prostate” paired with “cancer” or “adenocarcinoma.” Additionally, the search included the terms “PET” or “positron emission tomography” in conjunction with PSMA-related keywords to enhance the retrieval of relevant studies. To ensure a comprehensive review, all identified articles were scrutinized, and references from original studies were manually searched to include pertinent additional publications. The selection criteria focused on studies evaluating the diagnostic performance of PSMA PET/CT for the primary detection of prostate cancer or comparing its accuracy with multiparametric MRI (mp-MRI) in patients with clinical suspicion of prostate malignancy. Studies were excluded if they involved radiotracers other than [68Ga]PSMA and if they investigated ^{68}Ga-PSMA PET/CT for biochemical recurrence or staging high-risk prostate câncer. Non-English language publications, case reports, case series, conference abstracts, and letters to the editor were also excluded due to the increased risk of selection bias and limited data robustness.

Discussion

Prostate-specific membrane antigen (PSMA) is a type II transmembrane glycoprotein that demonstrates markedly elevated expression in prostate carcinoma cells compared with physiologic expression in tissues such as the kidney, proximal small intestine, and salivary glands [12,13,14]. Its structural characteristics, including a substantial extracellular domain, together with its intrinsic enzymatic activity, render PSMA a suitable target for the development of selective inhibitors capable of internalization upon ligand engagement [15]. These biological features position PSMA as a highly relevant biomarker for prostate cancer–specific molecular imaging and targeted therapeutic strategies. In that regard, ^{68}Ga-PSMA PET/CT has emerged as a promising method that can overcome these limitations. Afshar-Oromieh et al. conducted an investigation to characterize the biodistribution of a PSMA-targeted radioligand in normal tissues and to assess its diagnostic potential in prostate cancer. Tumor detection was evaluated through calculation of tumor-to-background uptake ratios. In their cohort, suspicious lesions consistent with malignancy were identified in 83.8% cases. The detection rate was stratified by Prostate-Specific Antigen (PSA) concentration, reaching 60% in patients with PSA <2.2 ng/mL and 100% in those with PSA >2.2 ng/mL. Median tumor-to-background ratios were reported as 18.8 (range, 2.4–158.3) on early-phase imaging and 28.3 (range, 2.9–224.0) on delayed acquisitions [16]. In patients with histopathologically confirmed primary prostate cancer, ^{68}Ga-HBED-CC-PSMA PET/CT findings were compared with ex-vivo CT and histopathology. After coregistration, voxel-wise analyses showed strong correlations between PSMA PET/CT and tumor distribution in eight of nine patients (R^2 42–82%, mean SUVmean: 5.6 vs. 3.3 for tumor vs. non-tumor tissue, $p = 0.012$). ROC analysis yielded an average AUC of 0.83, with SUV thresholds identified for ≥ 90% sensitivity. These results indicate that PSMA PET/CT can reliably detect and delineate prostate cancer, supporting its use for PET-guided focal therapies [17]. In addition to identifying clinically csPCa not apparent on mpMRI,

prostatic lesions demonstrating a high maximum standardized uptake value (SUVmax) on ^{68}Ga-PSMA PET/CT in conjunction with a PI-RADS score of 4 on MRI were associated with a high likelihood of csPCa [18]. Heetman et al. reported that all patients with SUVmax ≥16 exhibited Grade Group (GG) ≥2 disease, and 89% had GG ≥3. Furthermore, combining a PI-RADS score of 4 or 5 with SUVmax ≥8 corresponded to a GG ≥2 rate of 98%. These findings highlight that elevated PSMA uptake on PET/CT is strongly predictive of csPCa presence [19]. ^{68}Ga-PSMA PET/CT/ultrasound fusion biopsy may represent the most promising alternative to mpMRI/ ultrasound fusion biopsy for PCa diagnosis. Lopci et al. reported that ^{68}Ga-PSMA PET/CT/ultrasound fusion biopsy confirmed prostate cancer with Gleason scores ranging from 6 to 10. Clinically significant disease was identified in 25% of cases despite prior negative mpMRI, and PET/CT also detected cancer in patients with positive mpMRI but negative biopsy results. Malignant lesions exhibited markedly higher SUVmax and SUV ratios compared to benign findings ($p < 0.001$).

Using thresholds of SUVmax >5.4 and SUV ratio >2.2, the detection of clinically significant prostate cancer achieved accuracies of 81% and 90%, respectively [20]. Liu et al. conducted a prospective study evaluating the diagnostic accuracy of ^{68}Ga-PSMA PET/CT combined with PET/ultrasound-guided biopsy in men with persistently elevated PSA and prior negative biopsies. The authors found that for csPCa, ^{68}Ga-PSMA PET/CT demonstrated a sensitivity of 100%, specificity of 68.4%, PPV of 66.7%, and NPV of 100%, with an overall accuracy of 80.6%. These findings indicate that the method provides excellent sensitivity and negative predictive value, effectively ruling out csPCa in patients with negative scans (miPSMA-ES 0–1) while strongly correlating positive scans (miPSMA-ES 2–3) with malignancy. Thus, 68Ga-PSMA PET/CT, when combined with targeted biopsy, represents a highly valuable tool for improving csPCa detection and reducing unnecessary repeat biopsies [21]. Tracer uptake in primary prostate tumors correlated with Benign Prostate Disease (BPD), GG and PSA levels. Jiao et al. reported that an SUVmax cutoff of 5.30 optimally distinguished csPCa from BPD (AUC 0.893; sensitivity 85.9%; specificity 86.2%). In the prospective validation cohort, this threshold achieved 83.3% sensitivity, 81.3% specificity, 92.1% PPV, 65.0% NPV, and 82.8% accuracy [22]. High-risk patients showed significantly higher SUVmax than low-risk patients (18.9 ± 12.1 vs. 7.16 ± 6.2, $P < 0.001$). An SUVmax threshold of 9.1 identified high-risk disease with 78% sensitivity and 81% specificity.

Primary tumors also demonstrated greater uptake than normal prostate tissue (median SUVmax: 12.5 vs. 3.9), with Gleason scores >7 exhibiting higher SUVmax than 6–7b (21.2 vs. 5.9–8.3, $P < 0.001$). PSA ≥10 ng/ml was associated with increased tracer accumulation compared to PSA <10 ng/ml (17.6 vs. 7.7, $P < 0.001$) [23, 24]. Chan et al. reported that mean prostate SUVmax was significantly higher in PCa than in benign lesions (19.56 ± 18.11 vs. 4.21 ± 1.5, $P = 0.00001$), in patients with PSA >20 vs. <20 ng/mL (19.1 ± 20.6 vs. 6.01 ± 5.4, $P = 0.0052$), and in GS >7 vs. ≤7 (28.1 ± 20.3 vs. 10.2 ± 8.9, $P = 0.010$). An SUVmax cutoff of 5.6 on PSMA PET/CT yielded 95% sensitivity and 90.9% specificity (AUC 0.990, $P < 0.0001$) [25]. Recent evidence from systematic reviews and meta-analyses indicates that combining ^{68}Ga-PSMA PET/CT with mpMRI enhances the detection of csPCa. Mazzone et al. reported that for intraprostatic disease, PSMA PET had a sensitivity of 82% (95% CI, 73–90%), specificity of 67% (95% CI, 46–85%), positive predictive value of 77% (95% CI, 63–88%), and negative predictive value of 73% (95% CI, 56–87%) for clinically significant prostate cancer. Diagnostic accuracy was 84% based on the summary receiver operating characteristic curve and increased to 88% when combined with MRI [26].

Dhar et al. reported pooled sensitivity, specificity, and AUC of 64.7%, 86.4%, and 0.852 for mpMRI alone, 75.7%, 87.1%, and 0.889 for ^{68}Ga-PSMA-PET, and 70.3%, 81.9%, and 0.796 for the combined approach [27]. Similarly, Kawada et al. found that ^{68}Ga-PSMA PET/CT demonstrated a sensitivity of 0.89, specificity of 0.56, PPV of 0.69, NPV of 0.78, and AUC of 0.88 for csPCa detection. Pooled data from studies assessing the diagnostic performance of ^{68}Ga-PSMA PET/CT, mpMRI, and their combination indicated that mpMRI alone yielded a sensitivity of 0.84, specificity of 0.53, PPV of 0.70, and NPV of 0.76, whereas combined PSMA-PET/MRI achieved a sensitivity of 0.91, specificity of 0.64, PPV of 0.75, and NPV of 0.85 [28]. In a prospective multicenter study, Emmett et al. demonstrated sensitivity, specificity, PPV and NPV for mpMRI of 83%, 53%, 69% and 72% respectively and 90%, 50%, 69%, 80% for ^{68}Ga-PSMA-PET. ^{68}Ga-PSMA-PET/mpMRI improved sensitivity (97% vs. 83%) and NPV (91% vs. 72%) compared to mpMRI alone, although specificity decreased (40% vs. 53%) [29]. Likewise, Sonni et al. observed detection rates of 85% for ^{68}Ga-PSMA PET/CT, 83% for mpMRI, and 87% for the combined modality, with the combined imaging demonstrating superior diagnostic accuracy (AUC 0.77) [30]. Satapathy et al. in a systematic review and meta-analysis, reported pooled sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio for initial prostate cancer diagnosis using ^{68}Ga-PSMA PET/CT of 0.97 (95% CI, 0.90–0.99), 0.66 (95% CI, 0.52–0.78), 2.86 (95% CI, 1.95–4.20), and 0.05 (95% CI, 0.01–0.15), respectively, with high overall accuracy (AUC 0.91, 95% CI, 0.88–0.93) [31]. Jain et al. demonstrated in a prospective study that ^{68}Ga-PSMA PET/CT achieved a sensitivity of 84%, specificity of 80%, PPV of 72.2%, NPV of 88.9%, and overall accuracy of 81.5% (AUC 0.876, 95% CI: 0.799–0.953, $p < 0.001$) [32]. Similary, Rhee et al. reported that for mpMRI, sensitivity, specificity, PPV, and NPV were 44%, 94%, 81%, and 76%, respectively, whereas ^{68}Ga-PSMA

PET/CT demonstrated 49%, 95%, 85%, and 88% respectively, showing higher specificity and PPV [33].Retrospective studies further support these findings. Nuo et al. demonstrated that for distinguishing intermediate- to high-risk PCa from low-risk PCa or benign lesions, Biparametric Magnetic Resonance Imaging (bpMRI) showed 63% sensitivity and 88% specificity. 68Ga-PSMA PET/CT with SUVmax ≥12.9 showed 74% and 94%, and combined bpMRI/PET showed 80% and 88%. Overall, bpMRI/PET had 94% sensitivity and 81% specificity for diagnosing PCa [34]. Zhou et al. reported that in the high-risk prostate cancer cohort, 68Ga-PSMA PET/CT detected disease in 97.0% of patients, outperforming mpMRI, which was positive in 87.9% ($p < 0.05$). Conversely, mpMRI showed higher diagnostic confidence for low- and intermediate-risk prostate cancer, detecting 85.7% of cases compared with 60.0% for PET/CT ($p < 0.05$) [35]. Ylmaz et al. reported accurate tumor localization in 70.8% of cases using ^{68}Ga-PSMA PET/CT versus 54.2% with mpMRI [36]. Zhang et al. found ^{68}Ga-PSMA PET/CT sensitivity, specificity, PPV, and NPV of 91.67%, 81.82%, 89.19%, and 85.71%, respectively, with an AUC of 0.867 [37]. Li et al. reported that ^68Ga-PSMA-617 PET/CT demonstrated patient-based sensitivity, specificity, PPV, and NPV of 87.9%, 88.2%, 87.9%, and 88.2%, respectively, compared with 84.9%, 52.9%, 63.6%, and 78.3% for mpMRI. The AUC values were 0.881 for PET/CT and 0.689 for mpMRI [38]. Chandra et al. reported that PSMA PET/CT, evaluated using the PROMISE criteria, achieved 74% sensitivity, 92% specificity, 85% PPV, 86% NPV, and 86% accuracy for detecting prostate câncer [24]. Eiber et al. found that cancer detection rates were 66% with mpMRI 92% with PET, and 98% with combined PET/MRI.

For tumor localization, PET/MRI achieved the highest performance, with an AUC of 0.88, significantly outperforming mpMRI (0.73; $p<0.001$) and PET alone (0.83; $p=0.002$). PET was also superior to mpMRI (AUC 0.83 vs. 0.73; $p=0.003$) [39]. Sponh et al. observed similar lesion detection rates between mpMRI and ^{68}Ga-PSMA PET/CT; however, ^{68}Ga-PSMA PET/CT detected larger tumor volumes (median 4.9 mL vs. 2.8 mL) and more bilateral lesions (71 vs. 57, $p = 0.03$), with higher concordance of laterality in cases with bilateral biopsy-proven lesions ($p = 0.03$) [40]. Scheltema et al. reported sensitivities for identifying ISUP grade 2–3 tumors of 0.88 for ^{68}Ga-PSMA PET/Ct and 0.68 for mpMRI, with combined PSMA-PET/MRI achieving 92% sensitivity, 90% specificity, 96% NPV, and 81% PPV [41]. Berger et al. demonstrated that ^{68}Ga-PSMA PET/CT detected all 50 index lesions confirmed by histopathology (100%) compared with 94% detection by mpMRI, with secondary lesion detection rates of 93.5% versus 51.6%, respectively; ^{68}Ga-PSMA PET/CT showed higher sensitivity for index lesion localization (81.1% vs. 64.8%), while specificity was comparable (84.6% vs. 82.7%) [42]. In a retrospective cohort involving consecutive patients who underwent preoperative mpMRI and ^{68}Ga-PSMA PET/CT prior to radical prostatectomy, Donato et al. reported sensitivity and specificity values of 72.6% and 81% for mpMRI, compared with 71.4% and 90.5% for ^{68}Ga-PSMA PET/CT. Moreover, ^{68}Ga-PSMA PET/CT identified a greater proportion of tumor foci (78%, AUC 0.817) than mpMRI (69%, AUC 0.729). [43].

Chen et al. evaluated the diagnostic performance of imaging modalities for lesion-based detection of clinically significant prostate cancer (ISUP ≥ 2). mpMRI alone achieved a sensitivity of 66%, specificity of 92%, PPV of 95%, and NPV of 55%. When assessed independently, ^{68}Ga-PSMA-PET reached values of 76%, 89%, 94%, and 63%, respectively. The combined use of mpMRI with PET/CT improved sensitivity and NPV but resulted in lower specificity compared with either test individually, yielding values of 86%, 76%, 88%, and 73% for sensitivity, specificity, PPV, and NPV, respectively [44]. Cosar et al. reported that 68Ga-PSMA PET/MRI showed higher sensitivity and specificity than mpMRI (94.3% vs. 55.7% and 86.8% vs. 91.8%, respectively), though the difference was not statistically significant ($P = 0.464$). Combined imaging significantly improved diagnostic accuracy compared with either modality alone (AUC increase: 0.084 vs. mpMRI, $P < 0.001$; 0.046 vs. PET/MRI, $P = 0.028$), while no significant difference was observed between mpMRI and PET/MRI alone (AUC change: 0.038, $P = 0.246$) [45]. (Table 1) Summary of research studies included in this review

Author(s)	Year	No. of Patients	Study Design	Imaging Method	SUVmax Threshold	Detection Rate	Sensitivity	Specificity	PPV	NPV	AUC
Afshar-Oromieh et al.	2013	37	Prospective	68Ga-PSMA PET/CT	Not specified	83.80%	Not reported	Not reported	Not reported	Not reported	Not reported
Heetman et al.	2022	451	Retrospective	68Ga-PSMA PET/CT	6.9 (4.2 – 12.2)	Not specified	Not specified	Not specified	Not specified	Not specified	Not specified
Liu et al.	2020	31	Prospective	68Ga-PSMA PET/CT + Ultrasound	≥ 5.4	81%	100%	68,4%	66,7%	100%	Not reported
Jiao et al.	2021	135	Retrospective	68Ga-PSMA PET/CT	5.3	Not specified	85,14%	84,44%	94,74%	63,33%	0.893
Nuo et al.	2022	105	Retrospective	68Ga-PSMA PET/CT	≥12.9	Not specified	74%*	94%*	Not reported	Not reported	0.68
				bpMRI		Not specified	63%*	88%*			0.51
				bpMRI/PET		Not specified	94%	81%			0.75
Li et al.	2020	67	Retrospective	68Ga-PSMA PET/CT	Not specified	Not specified	87.88%	88.24%	87.88%	88.24%	0.881
				mpMRI	Not specified	Not specified	84,85%	52,94%	63,64%	78,26%	0.689
Kawada et al.	2022	497	Meta-Analysis/Systematic Review	68Ga-PSMA PET/CT	Not specified	Not specified	89%	56%	69%	78%	0.88
				mpMRI		Not specified	69%	73%	48%	86%	Not specified
				PSMA-PET/MRI		Not specified	91%	64%	75%	85%	Not specified
Emmett et al.	2021	291	Prospective	68Ga-PSMA PET/CT	5.6 (4.2–7.5)	Not specified	90%	50%	69%	80%	Not specified
				mpMRI		Not specified	83%	53%	69%	72%	Not specified
				PSMA-PET/MRI		Not specified	97%	40%	67%	91%	Not specified
Satapathy et al.	2021	389	Meta-Analysis/Systematic Review	68Ga-PSMA PET/CT	Not specified	Not specified	97%	66%	Not specified	Not specified	0.91
Jain et al.	2021	81	Prospective	68Ga-PSMA PET/CT	6,15	Not specified	84%	80%	72.20%	88.90%	0.876
Rhee et al.	2016	20	Prospective	68Ga-PSMA PET/CT	Not specified	Not specified	49%	95%	85%	88%	Not specified
				mpMRI		Not specified	44%	94%	81%	76%	Not specified
Zhou et al.	2022	101	Retrospective	68Ga-PSMA PET/CT	5.6 (3.7-7.8)	97%	Not specified	Not specified	Not specified	Not specified	Not specified
				mpMRI		87.90%	Not specified	Not specified	Not specified	Not specified	Not specified
Ylmaz et al.	2022	24	Retrospective	68Ga-PSMA PET/CT	16.7 ±15.0	Not specified	Not specified	Not specified	Not specified	Not specified	Not specified
Zhang et al.	2019	58	Retrospective	68Ga-PSMA PET/CT	Not specified	Not specified	91.67%	81.82%	89.19%	85.71%	0.867
Chandra et al.	2020	64	Retrospective	68Ga-PSMA PET/CT	5.6	Not specified	74%	92%	85%	86%	Not reported
Mazzone et al.	2025	1533	Meta-Analysis/Systematic Review	68Ga-PSMA PET/CT	Not specified	Not specified	82%	67%	77%	73%	0.84
Dhar et al.	2025	Not specified	Meta-Analysis/Systematic Review	68Ga-PSMA PET/CT	Not specified	Not specified	75,7%	87,1%	Not specified	Not specified	0.889
				mpMRI		Not specified	64,7%	86,4%	Not specified	Not specified	0.852
				68Ga-PSMA PET/MRI		Not specified	70,3%	81,9%	Not specified	Not specified	0.796
Eiber et al.	2016	53	Retrospective	68Ga-PSMA PET/CT	12.0 (6.9-18.8)	92%	64%	94%	Not specified	Not specified	0.83
				mpMRI		96%	43%	98%	Not specified	Not specified	0.73
				68Ga-PSMA PET/MRI		98%	76%	97%	Not specified	Not specified	0.88
Sponh et al.	2020	101	Retrospective	68Ga-PSMA PET/CT	10.9 (9.4-13.0)	Not specified	Not specified	Not specified	Not specified	Not specified	Not specified
				mpMRI		Not specified	Not specified	Not specified	Not specified	Not specified	Not specified
Scheltema et al.	2019	56	Retrospective	68Ga-PSMA PET/CT	3.95	Not specified	88%	93%	85%	95%	0.91
				mpMRI		Not specified	68%	91%	75%	87%	0.79
Berger et al.	2018	50	Retrospective	68Ga-PSMA PET/CT	9.27 ± 6.41	100%	81.10%	84.60%	93%	28.60%	Not specified
				mpMRI		94%	64.80%	64.80%	14.30%	6.90%	Not specified
Donato et al.	2019	58	Retrospective	68Ga-PSMA PET/CT	9.5 (6.3-4.3)	Not specified	71.40%	90.50%	Not specified	Not specified	0.817
				mpMRI		Not specified	72.60%	81%	Not specified	Not specified	0.729
Chen et al.	2019	54	Retrospective	68Ga-PSMA PET/CT mpMRI	Not specified	Not specified	97%	67%	Not specified	Not specified	0.87
					Not specified	Not specified	89%	71%	Not specified	Not specified	0.9
Cosar et al.	2021	64	Retrospective	68Ga-PSMA PET/mpMRI	7.1 (2.7-78)	Not specified	60.80%	94.30%	86.80%	79.80%	Not specified
				mpMRI	-	Not specified	55.70%	91.80%	80.60%	77.20%	

*Intermediate- to high-risk PCa versus low-risk PCa or benign lesions (Yi et al.).

In summary, ^{68}Ga-PSMA-PET provides superior sensitivity, predictive value, and lesion localization compared with mpMRI alone, particularly for high-risk and clinically significant disease. Combining ^{68}Ga-PSMA-PET with mpMRI further enhances detection, guides targeted biopsies, and informs personalized treatment strategies.Despite promising results, several limitations exist. Study heterogeneity, small sample sizes, and single-center designs limit generalizability. Variability in PI-RADS interpretation and lack of standardized SUVmax thresholds contribute to inconsistent reporting. False-positive uptake can occur in benign conditions such as prostatitis, benign prostatic hyperplasia, and granulomatous disease, while ~5% of prostate cancers lack PSMA expression. Evidence remains limited in low-risk populations, and cost and availability may restrict widespread implementation [46,47,48]. Future research should prioritize large, multicenter, prospective studies with standardized imaging protocols. Comparative studies evaluating added value over mpMRI in diverse patient populations, including low- and intermediate-risk cohorts, are needed. Integrating PET metrics with mpMRI-based risk stratification may refine patient selection for targeted biopsy or focal therapy, optimizing individualized management strategies. Such studies are essential to establish the clinical utility and cost-effectiveness of ^{68}Ga-PSMA PET/CT.

Conclusion

Emerging evidence underscores the diagnostic value of ^{68}Ga-PSMA PET/CT in the detection of clinically significant prostate cancer (csPCa), particularly in patients with equivocal mpMRI findings or persistent clinical suspicion despite prior negative biopsies. The combination of high SUVmax values with PI-RADS ≥4 lesions has shown strong predictive value for csPCa, reinforcing the utility of integrating molecular imaging with conventional multiparametric MRI. Notably, the synergistic application of ^{68}Ga-PSMA PET/CT and mpMRI has been associated with improved sensitivity for intraprostatic tumor localization, while also offering the potential to reduce unnecessary biopsies. This complementary diagnostic approach may represent a paradigm shift in the workup of suspected prostate cancer, especially in challenging clinical scenarios. While current data support the selective implementation of ^{68}Ga-PSMA PET/CT in conjunction with mpMRI, its widespread adoption requires further validation. Ongoing and future large-scale prospective randomized studies are essential to confirm its diagnostic superiority over mpMRI alone and to refine its role in personalized risk stratification and targeted biopsy guidance.

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