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RESEARCH

Joint survey by AIMN, AIOM, AIRO, SIU, SIUrO, and Meet-URO about the use of PSMA PET imaging in prostate cancer in Italy: PSA persistence, biochemical recurrence, hormone-sensitive and castration-resistant metastatic settings

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Abstract

Background Prostate-specific membrane antigen (PSMA) PET/CT has transformed prostate cancer (PCa) management by improving lesion detection and guiding treatment decisions across disease stages. Following the first paper of the Italian PSMA Survey focused on technical aspects and primary staging, this second analysis explores its clinical use in PSA persistence after radical prostatectomy, biochemical recurrence (BCR), hormone-sensitive metastatic (mHSPC), and castration-resistant metastatic (mCRPC) settings.

Methods A national cross-sectional survey was conducted jointly by five Italian scientific societies involving nuclear medicine physicians, medical oncologists, radiation oncologists, and urologists (AIMN, AIOM, AIRO, SIU, SIUrO) and the Meet-URO cooperative group. Dedicated sections addressed the adoption, timing, and perceived clinical impact of PSMA PET/CT in PSA persistence after radical prostatectomy, BCR, mHSPC, and mCRPC. Responses were analysed descriptively and stratified by medical competences (clinicians versus nuclear medicine physicians).

Results PSMA PET/CT emerged as the preferred imaging modality in all clinical scenarios. In PSA persistence and BCR, 87–95% of respondents selected PSMA PET as first-line imaging, most often performed at PSA levels of 0.2–0.5 ng/mL. When negative, more than two-thirds recommended repeating PSMA PET/CT after PSA further rise. In mHSPC, over 80% of clinicians applied the CHAARTED criteria directly to PSMA PET findings, while PSMA PET/CT was also widely used for restaging and therapy monitoring. In mCRPC, PSMA PET/CT was routinely used for baseline and follow-up imaging. Most clinicians considered the low-dose CT component sufficient for radioligand therapy (RLT) eligibility, while [^{18}F]Fluorodeoxyglucose (FDG) PET was reserved for selected high-risk or discordant cases.

Conclusion PSMA PET/CT has become the central imaging modality in the management of advanced PCa in Italy. Its adoption has progressed faster than supporting evidence, underscoring the need for prospective validation, implementation of harmonised interpretation criteria, and unified national recommendations.

Keywords Prostate-specific membrane antigen · Positron emission tomography · Prostate cancer · PSA persistence · Biochemical recurrence · HSPC · CRPC · Radioligand therapy · Survey · Italy

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This article is a companion paper to the previously published analysis on technical aspects and primary staging from the Italian PSMA PET Survey.

The affiliations of the indexed collaborators are provided in the Supplementary Materials.

Introduction

The advent of prostate-specific membrane antigen positron emission tomography (PSMA PET) has reshaped the diagnostic and therapeutic landscape of prostate cancer (PCa). Compared with conventional imaging, PSMA PET offers higher sensitivity and specificity, enabling more accurate disease staging and restaging. The technology has rapidly transitioned from research to clinical practice, has

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been incorporated into international and national guidelines [1–3], and has influenced patient management at every disease stage—from primary staging to biochemical recurrence (BCR), metastatic hormone-sensitive prostate cancer (mHSPC), and castration-resistant prostate cancer (mCRPC).

Nonetheless, real-world implementation remains heterogeneous across institutions and specialties, with variations in tracer selection, accessibility, PSA thresholds for imaging, and interpretation of findings—particularly in complex scenarios such as PET-only progression or PSMA-targeted radioligand therapy (RLT) eligibility.

To capture the diversity of clinical practice in Italy, five major scientific societies involved in PCa management—the Italian Association of Nuclear Medicine (AIMN), the Italian Association of Medical Oncology (AIOM), the Italian Association of Radiotherapy and Clinical Oncology (AIRO), the Italian Society of Urology (SIU), and the Italian Society of Uro-Oncology (SIUrO)—in collaboration with the Meet-URO cooperative group, jointly developed a comprehensive national survey on PSMA PET use in PCa. The first paper from this initiative [4] focused on technical aspects, tracer selection, and clinical indications related to primary staging.

The present manuscript expands on those findings, examining the use of PSMA PET in four critical disease settings: PSA persistence after radical prostatectomy (RP), BCR, mHSPC, and mCRPC. The objectives of this analysis were to (1) describe real-world use of imaging tools and decision-making processes involving PSMA PET/CT; (2) explore inter-specialty differences and multidisciplinary interactions; and (3) identify areas of consensus and controversy to support the development of national recommendations for PSMA PET integration into clinical pathways.

Materials and methods

Survey structure and distribution

The questionnaire design and distribution are described in detail in the previous publication [4]. In brief, it consisted of 93 items (multiple-choice and open-ended). It was launched on November 4, 2024, via the official mailing lists and newsletters of AIMN, AIOM, AIRO, SIU, SIUrO, and Meet-URO, remaining open until November 29, 2024. Participation was anonymous, voluntary, and without financial compensation, with electronic informed consent obtained before completion. Responses were collected in XLS format for subsequent analysis. The survey comprised two sections: Section A for clinicians (urologists, oncologists, radiation oncologists) and Section B for nuclear medicine physicians. Both included general questions on PSMA PET adoption, as well as subsections on primary staging, PSA persistence after RP, biochemical recurrence (BCR), metastatic hormone-sensitive prostate cancer (mHSPC), and metastatic castration-resistant prostate cancer (mCRPC). The present manuscript focuses on the PSA persistence, BCR, mHSPC, and mCRPC items, detailed in the Supplementary Materials.

Data collection, analysis, and consensus process

A total of 339 responses were received. When multiple entries originated from the same institution and professional category, only one response was retained to avoid overrepresentation. In these cases, the response from the most experienced participant was selected. Experience was defined based on self-reported professional seniority and expertise in PSMA PET imaging, prioritising respondents with the longest clinical practice and the highest reported exposure to PSMA PET interpretation or clinical management of prostate cancer. Incomplete questionnaires were excluded from the final analysis. After removal of duplicate institutional entries and incomplete surveys, 238 fully completed responses were included in the final dataset. Data were summarised using descriptive statistics (categorical variables reported as percentages), and qualitative responses were grouped into recurring themes.

Result interpretation and discussion followed a structured, multidisciplinary consensus process endorsed by AIMN, AIOM, AIRO, SIU, SIUrO, and Meet-URO. Each society appointed representatives to four thematic working groups—(i) Technical Aspects, (ii) Primary Staging, (iii) BCR/PSA Persistence/mHSPC, and (iv) mCRPC—comprising specialists in nuclear medicine, oncology, urology, and radiation oncology. Discussions were conducted through online meetings guided by pre-organised slide decks summarising survey results. Insights from these sessions informed the manuscript draft, which underwent internal review and society approval. Details of the working groups are provided in the Supplementary Materials.

Results

General data about survey responders

General characteristics of the survey respondents were previously reported in detail [4]. Briefly, 238 complete surveys were analysed, including 29% nuclear medicine physicians and 71% clinicians. Participants were affiliated with academic or research institutions (41%), public hospitals (48%), and private facilities (11%). Most respondents were

experienced professionals, with 44% having more than 15 years of practice. Among clinicians, the distribution was balanced across urologists (22%), radiation oncologists (34%), and medical oncologists (44%). Within nuclear medicine departments, PET scanners were available in 99% of centres and RLT units in 69.6%. The majority (54%) had interpreted more than 300 PSMA PET scans, confirming a high level of expertise.

PSA persistence after RP and BCR

In the context of PSA persistence after RP and BCR, PSMA PET/CT clearly emerged as the preferred imaging modality across both clinicians and nuclear medicine physicians (Figs. 1, 2). Among clinicians (Fig. 1), 46% reported performing restaging with PSMA PET in patients showing PSA persistence after RP (PSA≥0.1 ng/mL at 4–8 weeks), whereas 23% opted for early salvage treatments without imaging and 22% chose observation. Only 2–3% selected conventional or choline-based imaging. When asked to indicate their first-line imaging method for BCR, 87% of clinicians selected PSMA PET, compared with 6% for conventional imaging and 2% each for pelvic MRI or choline PET. A similar trend was observed among nuclear medicine physicians (Fig. 2), with 95% identifying PSMA PET as their preferred restaging technique after local therapy and only 3% still relying on choline PET. Most respondents across both groups initiated PSMA PET at a PSA level between 0.2 and 0.5 ng/mL (approximately 70–75%), whereas very few used thresholds < 0.2 ng/mL or > 1 ng/mL. In cases where PSMA PET results were negative, the majority (64% of clinicians and 73% of nuclear medicine physicians) preferred to repeat PSMA PET once PSA levels further increased, while a small proportion would repeat the scan using a different PSMA-targeted agent or switch to alternative imaging such as whole-body MRI or choline PET.

mHSPC

In the mHSPC setting, survey responses confirmed the widespread integration of PSMA PET/CT in both staging and disease monitoring (Figs. 3, 4, 5). Across all cases, PSMA PET was the predominant choice from both the clinician's (Fig. 3, 4) and nuclear medicine's perspectives (Fig. 5). When defining disease volume in de novo mHSPC already staged with PSMA PET (Fig. 3), 84% of clinicians reported applying the CHAARTED criteria directly to PSMA PET images, whereas 13% preferred to rely on conventional imaging, and only 3% declared uncertainty. In cases of discordance between PSMA PET and conventional imaging, 70% prioritised PSMA PET findings, 16% conventional imaging, and 10% prescribed additional examinations such

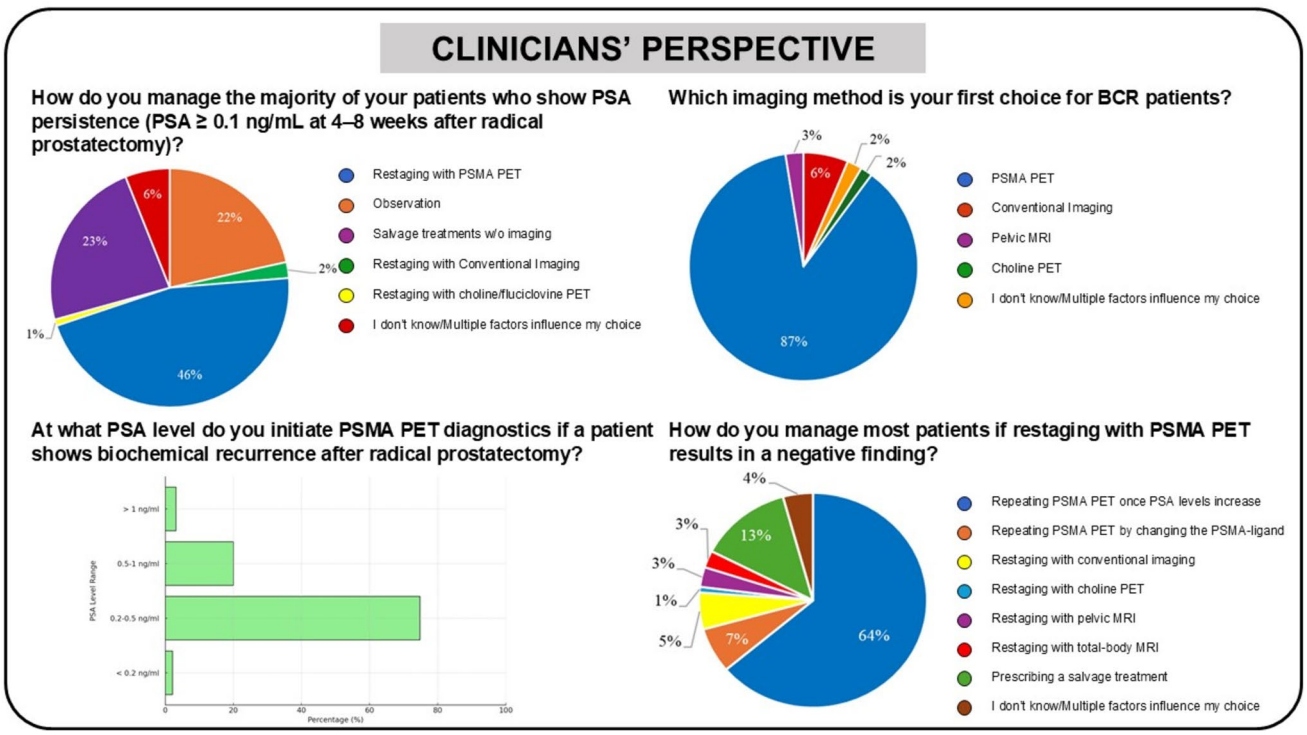

Fig. 1 Clinicians' responses on PSMA PET use in PSA persistence and BCR. Distribution of responses from clinicians regarding imaging strategy in PSA persistence after radical prostatectomy and in biochemical recurrence after local therapy. PSMA PET/CT was overwhelmingly identified as the preferred imaging modality, typically initiated at low PSA levels, and most clinicians repeated PSMA PET after a PSA increase when initial findings were negative

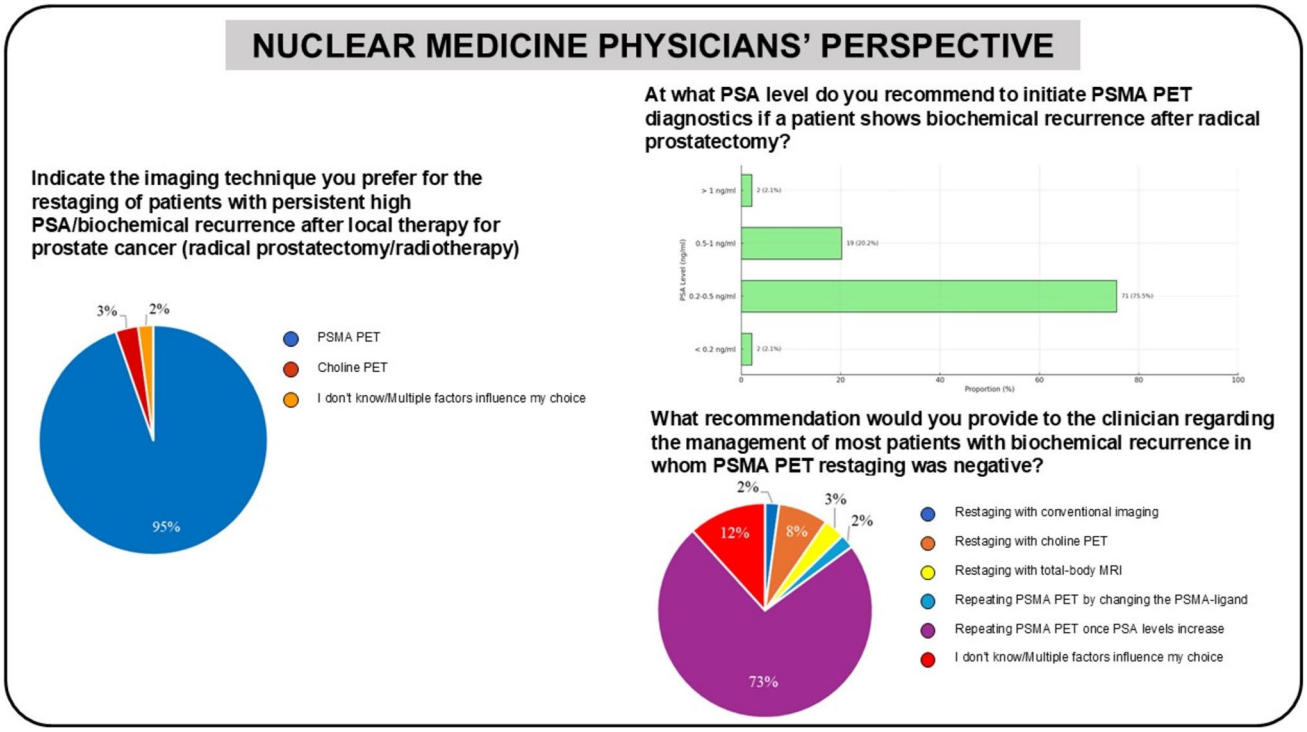

Fig. 2 Nuclear medicine physicians' responses on PSMA PET use in BCR. Summary of nuclear medicine physicians' preferences regarding imaging in BCR, PSA thresholds for PSMA PET indication, and management following negative findings. Nearly all respondents selected PSMA PET/CT as first-line restaging and recommended repeating the examination after PSA progression

as choline PET. For oligorecurrent HSPC, 83% identified PSMA PET as the preferred modality to guide metastasis-directed therapies (MDT), while 11% favoured conventional imaging and 4% total-body MRI. Similarly, PSMA PET was the first-choice restaging tool in patients with biochemical progression under systemic therapy (64%, compared with 22% for conventional imaging and 10% for choline PET). Regarding treatment response assessment (Fig. 4), clinicians mainly relied on PSA monitoring (≈90%) and clinical evaluation (≈80%), but a relevant proportion (≈45%) also incorporated PSMA PET into follow-up. When confronted with PSMA PET-only progression, in the absence of biochemical or clinical progression, 62% would treat oligometastatic cases with MDT (e.g., SBRT) or adapt systemic therapy if polymetastatic, while 20% sought confirmation with conventional imaging and 10% preferred to await biochemical or clinical evidence. Nuclear medicine physicians reported consistent attitudes (Fig. 5): 80–83% selected PSMA PET as the imaging modality of choice for both oligorecurrent and biochemically progressive mHSPC, with conventional imaging and MRI rarely used (< 10%). For therapy monitoring, biochemical (33%) and PSMA PET (27%) assessments predominated, with limited reliance on conventional imaging (12%).

mCRPC

In the mCRPC setting, survey responses revealed widespread adoption of PSMA PET/CT as the primary imaging tool for disease assessment and therapeutic decision-making, both at the onset of castration resistance and throughout subsequent management (Figs. 6, 7, 8, 9, 10).

Among clinicians, 60% reported using PSMA PET/CT as their preferred staging modality, while 30% still relied on conventional imaging, and smaller proportions selected choline PET or total-body MRI (Fig. 6, left). In patients classified as non-metastatic on conventional imaging (nmCRPC), when next-generation imaging identified new lesions consistent with mCRPC, 77% of respondents stated they would manage the patient as metastatic (Fig. 6, right), underscoring the diagnostic authority of PSMA PET findings.

In cases of biochemical progression under systemic therapy, 61% of clinicians preferred PSMA PET for restaging, whereas 28% continued to use conventional imaging and fewer than 10% chose choline PET or MRI (Fig. 6, bottom). Regarding RLT eligibility, 58% considered the low-dose CT component of PSMA PET/CT sufficient, while 37% recommended additional CT plus bone scan (Fig. 7, left).

Opinions on FDG PET were divided: 67% believed it may be useful only in selected cases, 9.5% supported systematic FDG PET for all PSMA RLT candidates, and 23%

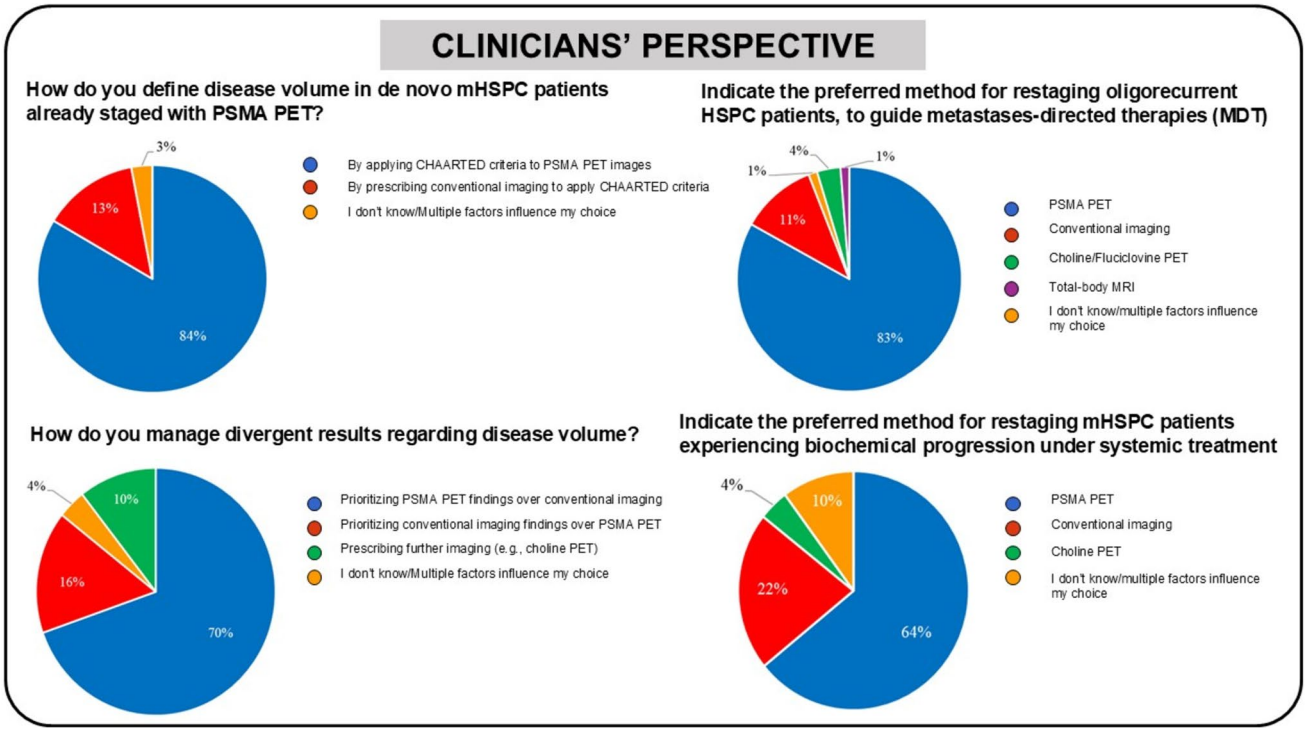

Fig. 3 Application of CHAARTED criteria and management of imaging discordance in mHSPC. Clinicians' approaches to defining disease volume and resolving discrepancies between PSMA PET and conventional imaging in metastatic hormone-sensitive prostate cancer. Most participants directly applied CHAARTED criteria to PSMA PET findings and prioritised molecular imaging when results were discordant

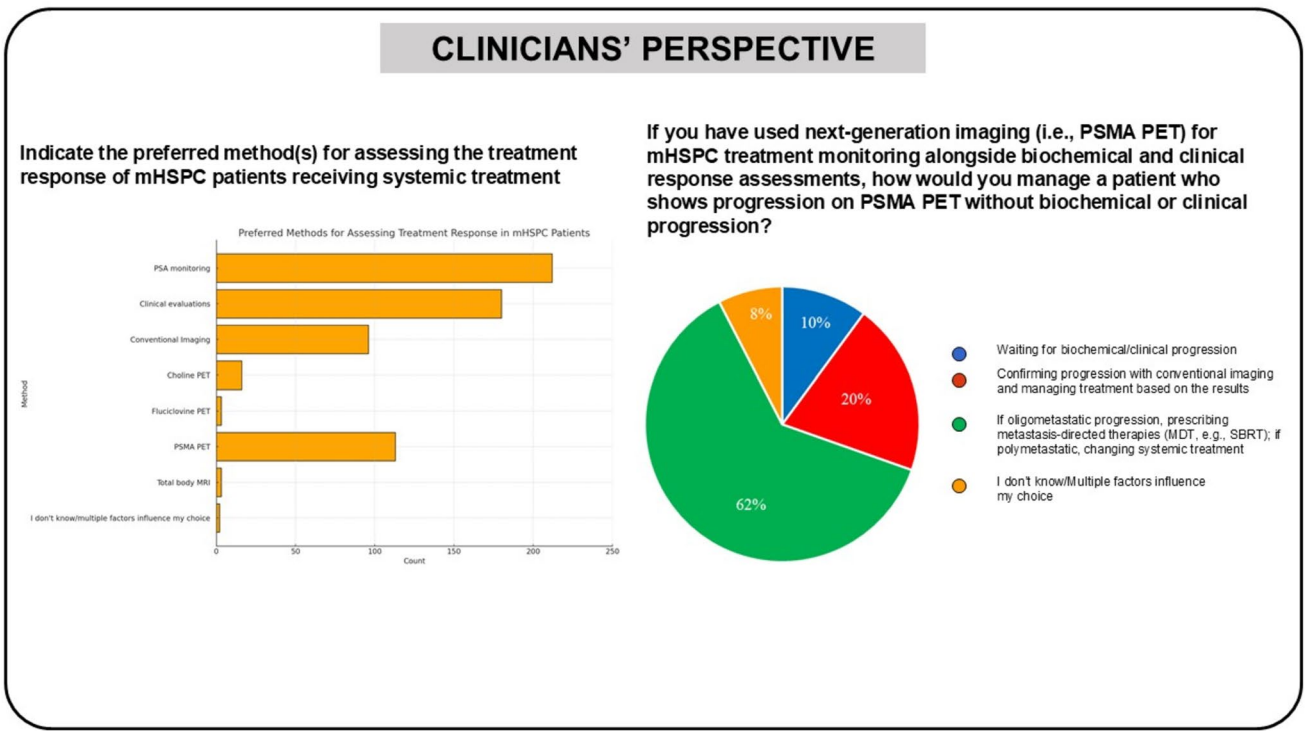

Fig. 4 Role of PSMA PET in oligorecurrent and biochemically progressive mHSPC. Reported imaging preferences for guiding metastasis-directed therapy in oligorecurrent disease and for restaging patients with biochemical progression under systemic treatment. PSMA PET/CT was consistently indicated as the imaging tool of choice

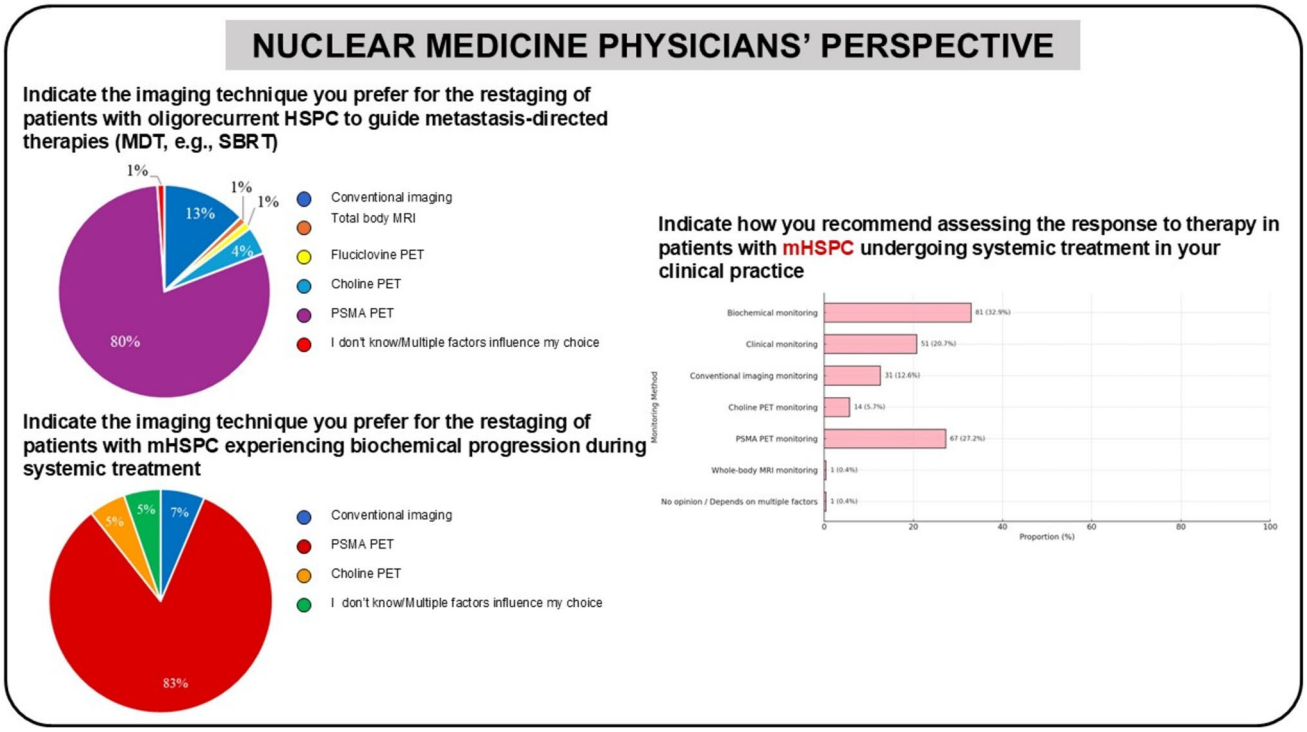

Fig. 5 Treatment-response assessment and management of PSMA PET-only progression in mHSPC. Clinicians' strategies for monitoring treatment response and addressing PSMA PET-only progression. PSA and clinical evaluation remained the most common tools, with PSMA PET increasingly integrated into follow-up and used to guide management of limited progression

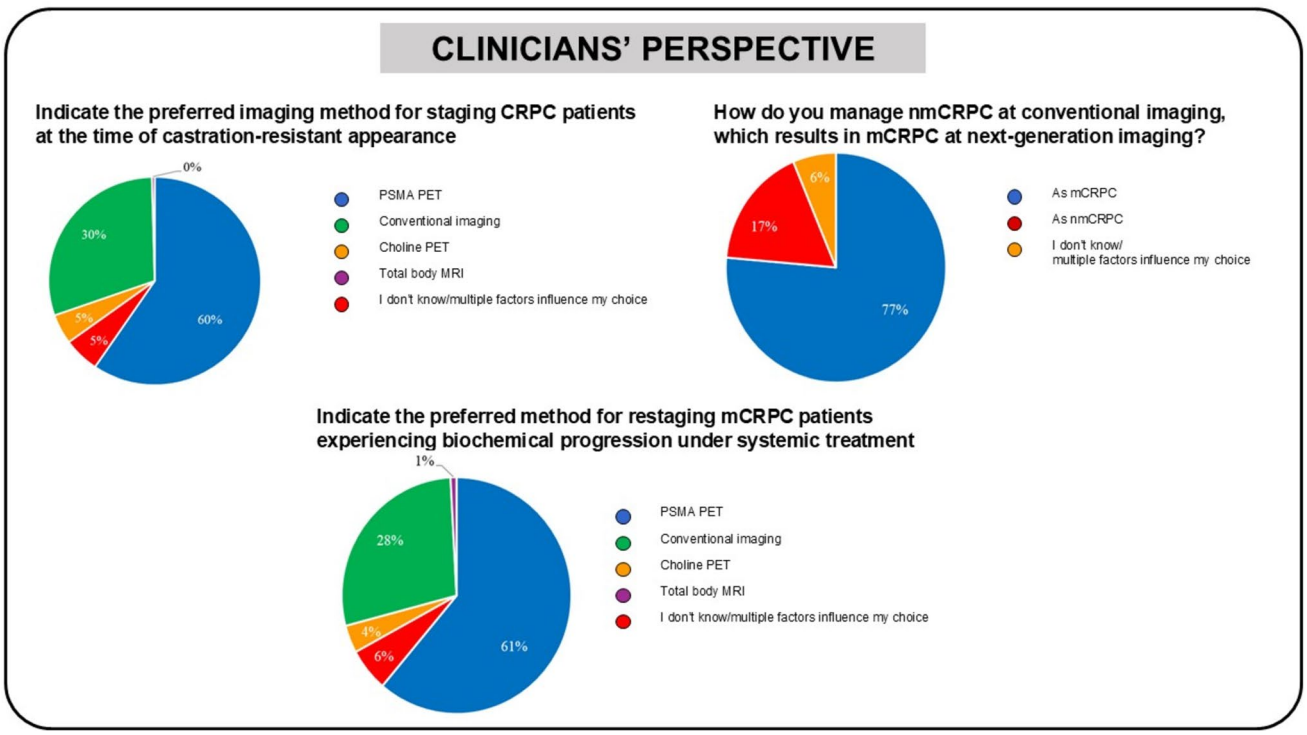

Fig. 6 Clinicians' imaging preferences at the onset of mCRPC. Preferred imaging methods used to confirm castration-resistant progression and to resolve discrepancies between molecular and conventional imaging. PSMA PET/CT was the dominant choice for staging and restaging in this setting

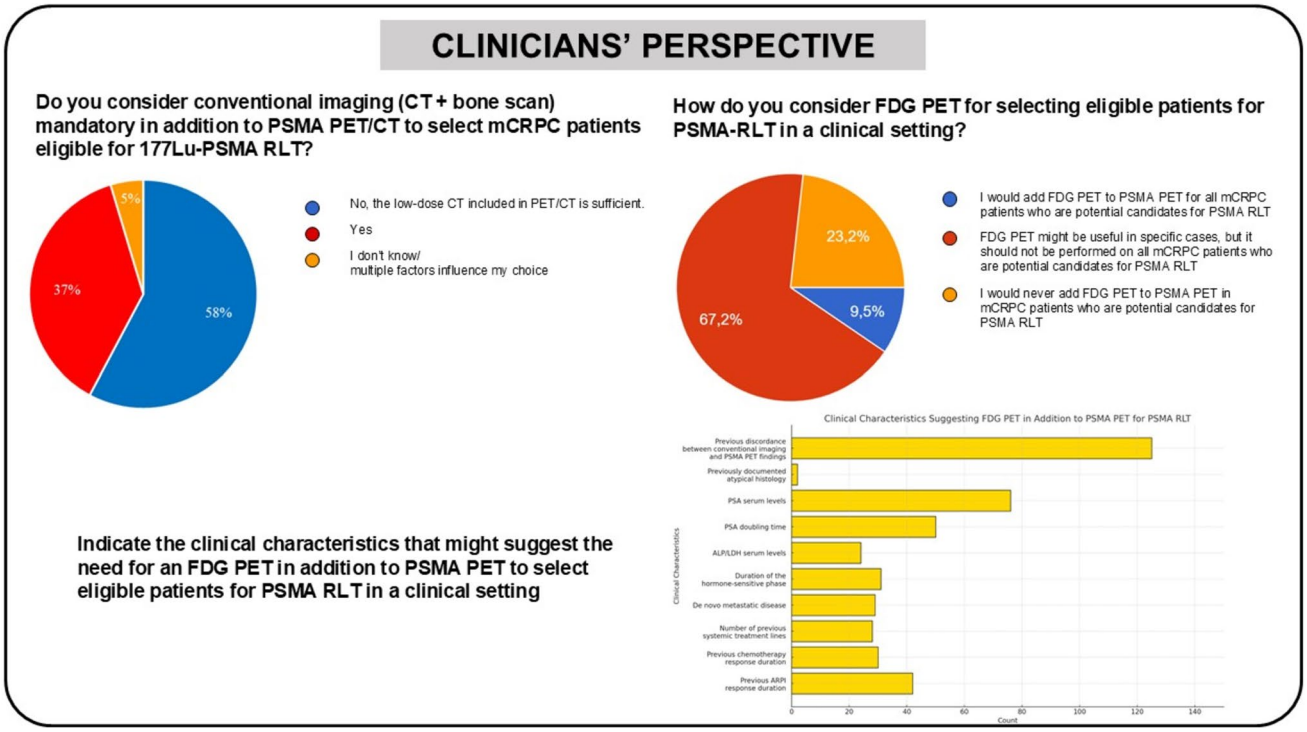

Fig. 7 Clinicians' perspectives on imaging requirements and FDG PET before PSMA RLT. Reported opinions on the need for conventional imaging in addition to PSMA PET/CT for RLT eligibility and on the role of FDG PET. Most respondents considered PSMA PET/CT with low-dose CT sufficient, reserving FDG PET for selected high-risk or discordant cases

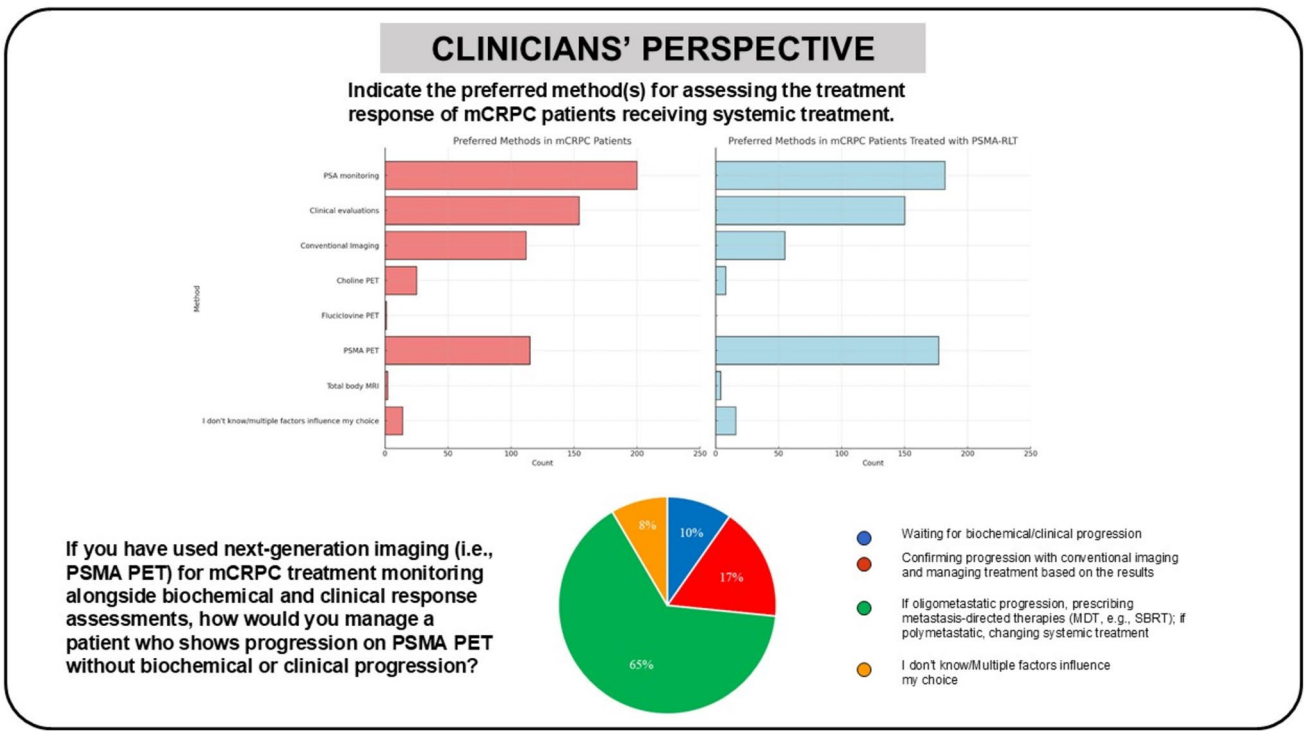

Fig. 8 Clinicians' evaluation of treatment response and management of PSMA PET-only progression in mCRPC. Approaches used to monitor therapy and interpret PSMA PET-only progression in the absence of biochemical or clinical worsening. Most clinicians adopted a multimodal strategy and relied on PSMA PET findings to guide systemic- or metastasis-directed treatment

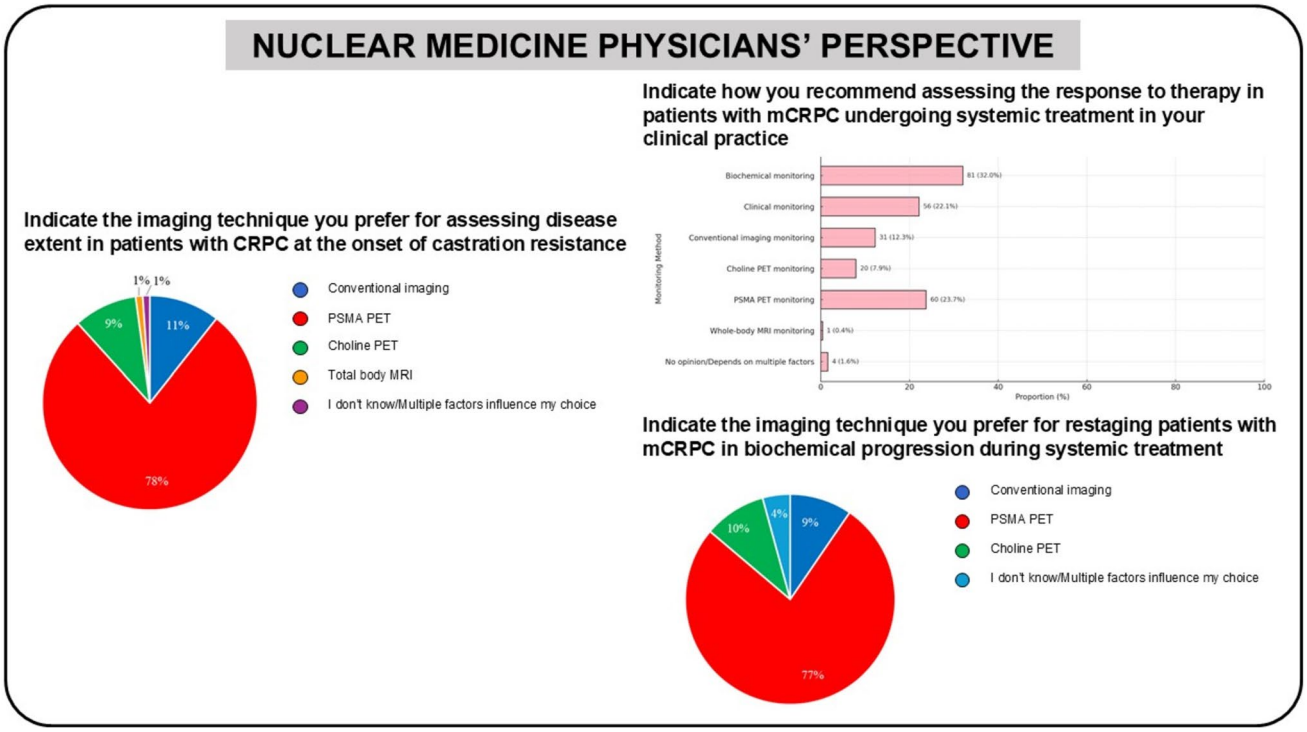

Fig. 9 Nuclear medicine physicians' imaging preferences for staging, restaging, and follow-up in mCRPC. Imaging modalities most frequently used by nuclear medicine physicians across the mCRPC continuum. PSMA PET/CT was consistently prioritised over choline PET and conventional imaging for both disease assessment and therapy monitoring

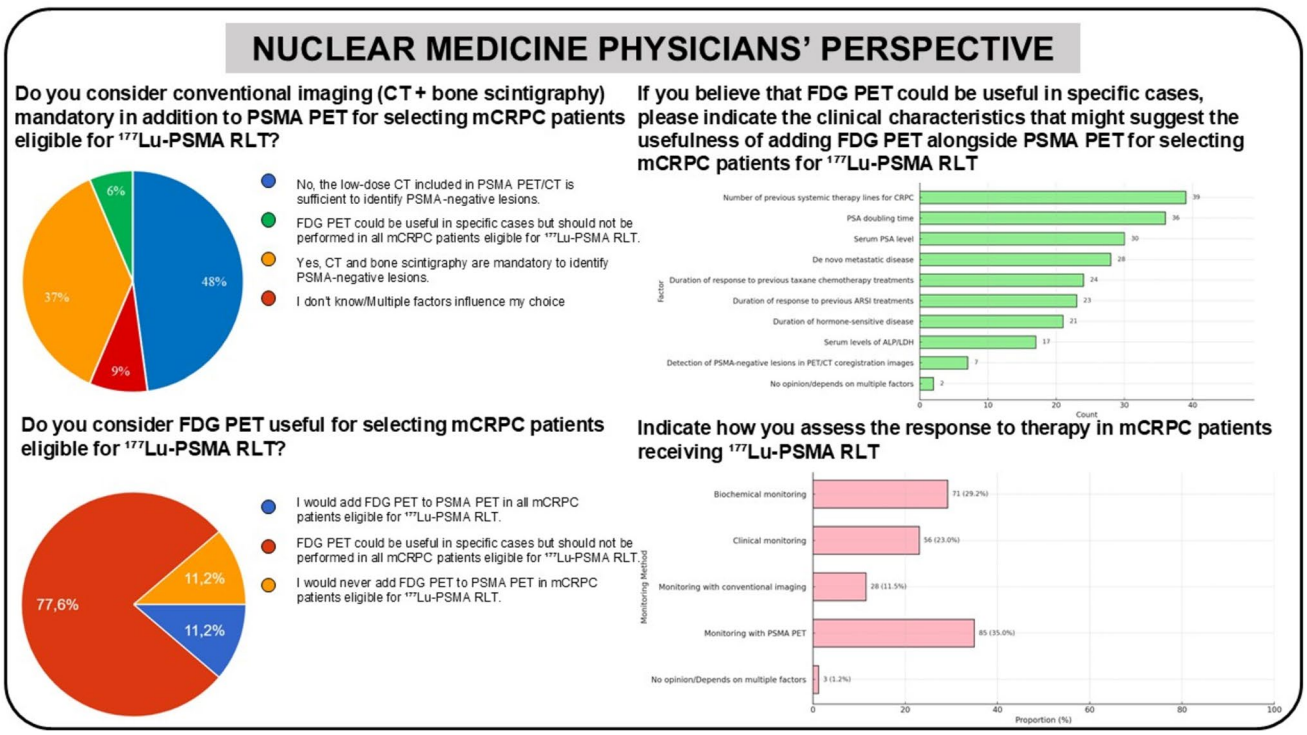

Fig. 10 Nuclear medicine physicians' perspectives on patient selection and monitoring during PSMA RLT. Reported practices concerning the adequacy of low-dose CT within PSMA PET/CT, the selective use of FDG PET before therapy, clinical triggers for dual-tracer imaging, and preferred modalities for treatment monitoring. The responses confirm PSMA PET/CT as the cornerstone for both selection and follow-up of patients undergoing PSMA-targeted RLT

would exclude it altogether (Fig. 7, right). The main indications for FDG PET were discordant lesions between PSMA PET and conventional imaging (lesions resulting low PSMA-expressing but positive at conventional imaging), aggressive histologic or biochemical features (rapid PSA doubling, high PSA, elevated ALP/LDH), short response to ARSI or taxane therapy, and high metastatic burden (Fig. 7, bottom).

A multimodal strategy was the preferred approach for treatment-response assessment, combining PSA monitoring, clinical evaluation, and PSMA PET (Fig. 8, upper panels). PSMA PET was more frequently selected for response assessment in patients receiving RLT than in those receiving other systemic treatments. When PSMA PET suggested disease progression in the absence of biochemical or clinical deterioration, 65% of respondents indicated they would manage oligometastatic cases with MDT (e.g., SBRT) or adjust systemic therapy if polymetastatic; 17% would confirm findings with conventional imaging, and 10% preferred to wait for biochemical or clinical evidence (Fig. 8, bottom).

Among nuclear medicine physicians, adoption of PSMA PET/CT was even more consistent. Seventy-eight percent selected PSMA PET/CT as the reference technique for baseline staging, whereas only 11% and 9% selected conventional imaging and choline PET, respectively (Fig. 9, left). Results for CRPC restaging and response assessment closely mirrored those of clinicians (Fig. 9, right), yet nuclear medicine physicians displayed a more imaging-driven approach overall.

Their perspective on PSMA RLT (Fig. 10) provided additional insight. Forty-eight percent considered the low-dose CT included in PSMA PET/CT sufficient for detecting PSMA-negative lesions, while 37% supported adding CT plus bone scintigraphy—closely matching clinician preferences. However, differences emerged in the use of FDG PET: 77.6% of nuclear medicine physicians viewed it as useful in selected cases and 11.2% would apply it systematically, reflecting slightly greater enthusiasm than clinicians, among whom nearly a quarter would omit it altogether.

Triggers for FDG PET were also broader among nuclear medicine specialists, who emphasized short PSA doubling time, multiple prior treatment lines, short response to hormonal or taxane therapy, and high biochemical activity—beyond the primarily discordant or aggressive profiles cited by clinicians. For treatment monitoring during PSMA RLT, nuclear medicine physicians adopted an integrated approach combining biochemical monitoring (29%), clinical assessment (23%), and PSMA PET imaging (35%), with conventional imaging used in approximately 11% of cases. Compared with clinicians, this pattern indicates a stronger reliance on molecular imaging as the central component of follow-up.

Discussion

Overall, this survey highlights broad multidisciplinary agreement on the central role of PSMA PET/CT across all stages of advanced prostate cancer, while also revealing areas of variability and unmet need—particularly concerning the management of PSMA PET–negative patients after restaging, PSA thresholds for imaging, disease-volume assessment, interpretation of PSMA PET–only progression, imaging used to support MDT, integration of FDG PET in candidates to RLT, and imaging requirements before and after PSMA RLT.

The survey revealed near-universal consensus among clinicians and nuclear medicine physicians on the early use of PSMA PET to manage PSA persistence after RP and BCR after radical treatment. This likely reflects the substantial body of evidence supporting its diagnostic accuracy and clinical utility. Phase III studies [5, 6] have demonstrated detection rates above 80% even at low PSA levels, whereas false-positive findings with conventional imaging can approach 25% [6]. Early use of PSMA PET may therefore help identify limited, potentially curable recurrences suitable for targeted salvage radiotherapy (sRT). A notable observation from the survey concerns the management of negative PSMA PET findings: most clinicians (64%) and nuclear medicine physicians (73%) reported repeating PSMA PET after PSA rise. This pattern reflects strong confidence in PSMA PET as the reference imaging modality, even in initially negative cases, but also underscores the need for standardised guidance on the optimal timing and frequency of repeat imaging to avoid unnecessary delays in initiating effective sRT [7]. Multidisciplinary interpretation remains essential; while PSMA PET positivity can refine sRT planning, current guidelines emphasise that a negative scan should not delay early sRT in patients at high risk of disease progression [1–3], including those with low PSA levels. The prevailing preference among survey participants to integrate PSMA PET results within multidisciplinary discussions, rather than treating them as stand-alone determinants, supports this balanced approach. Collectively, these results indicate that PSMA PET/CT has already become the standard for restaging in PSA persistence and BCR in Italy, but also that national consensus recommendations are needed to ensure consistent and timely integration into clinical workflows, particularly regarding early salvage treatment.

The survey also confirmed the expanding role of PSMA PET/CT in oligometastatic prostate cancer, particularly in patients with BCR or limited metastatic burden after local therapy. Over 80% of respondents selected PSMA PET as the preferred imaging modality to guide MDT, reflecting a shift toward molecularly guided focal treatment strategies,

such as stereotactic body radiotherapy (SBRT) or salvage nodal dissection. These findings align with real-world evidence [8, 9], which showed that PSMA PET–guided MDT was associated with improved progression-free, metastasis-free, and overall survival compared with choline PET/CT. This likely reflects the higher sensitivity of PSMA PET, particularly for low-volume nodal and bone disease. The strong preference for PSMA PET–guided MDT among Italian specialists underscores the rapid translation of molecular imaging evidence into clinical practice but also highlights a persistent gap between practice and evidence, as prospective trials are still lacking to define optimal imaging protocols, radiopharmaceutical selection, and patient eligibility. These findings portray a pragmatic, forward-looking approach that anticipates forthcoming validation studies and supports the need for harmonized national recommendations for imaging-guided MDT.

In the mHSPC setting, the survey confirmed the broad adoption of PSMA PET/CT as the primary imaging modality for staging and monitoring. Over 80% of respondents reported using it to guide management decisions, reflecting the transition from conventional to next-generation imaging and its growing impact on disease reclassification and treatment planning. A key finding concerns disease-volume assessment: most clinicians (84%) reported applying the CHAARTED criteria directly to PSMA PET findings, even though these criteria were originally defined using conventional imaging [10]. This response represents a pragmatic, real-world adaptation to an existing evidence gap—clinicians are using established frameworks to maintain clinical continuity in the absence of validated molecular definitions. The small minority (13%) who continue to rely on conventional imaging or express uncertainty further highlight the need for harmonised, prospectively validated PET-based criteria for defining "high-volume" and "low-volume" disease. However, PSMA PET in this setting could be useful to reduce false positive findings otherwise reported by conventional imaging, such as bone scan [11]. Bridging this gap between evolving imaging practice and evidence derived from landmark trials will be crucial to ensure consistent interpretation and decision-making in the PSMA PET era.

Regarding treatment response assessment, the survey revealed a growing trend toward incorporating PSMA PET/CT into follow-up alongside PSA and clinical monitoring. Approximately 45% of clinicians already use PSMA PET for response evaluation, and 62% indicated they would act upon PSMA PET–only progression, either with MDT in oligometastatic cases or by adapting systemic therapy in polymetastatic disease. This pattern contrasts with current international guidelines [1–3], which recommend monitoring mHSPC patients on systemic treatment primarily through biochemical and clinical evaluation, and do not recommend routine imaging in the absence of symptoms or biochemical progression. At present, no validated criteria exist for PSMA PET–based response assessment in the hormone-sensitive setting. The recently proposed frameworks, PSMA PET Progression (PPP) [12] and RECIP 1.0 [13], were developed for mCRPC, particularly in the context of RLT and cannot yet be extrapolated to hormone-sensitive disease without proper validation. The widespread use of PSMA PET observed in this survey, therefore, reflects a real-world practice evolving ahead of the evidence, driven by clinicians' confidence in molecular imaging. While this underscores PSMA PET's perceived value as a tool for dynamic disease assessment, it also reveals a critical evidence gap, reinforcing the need for prospective studies and harmonised response criteria tailored explicitly to the mHSPC setting.

In the mCRPC setting, the survey confirms that PSMA PET/CT is widely adopted in clinical practice for staging, restaging, and therapy monitoring. However, this extensive use contrasts with current international guidelines [1, 2] and consensus recommendations [14], which restrict the recommended role of PSMA PET mainly to patient selection for PSMA-targeted RLT, while recognising its emerging—but still unvalidated—role in other contexts. The survey results, therefore, highlight a disconnect between clinical practice and guideline-based evidence, suggesting that PSMA PET/CT is already perceived as the de facto standard even before formal endorsement.

A key aspect of the survey was the imaging work-up before RLT. Most clinicians (58%) and a similar proportion of nuclear medicine specialists (48%) considered the low-dose CT component of PSMA PET/CT sufficient for detecting PSMA-negative lesions. In contrast, 37% in both groups recommended adding conventional imaging to obtain a more comprehensive assessment and exclude PSMA-negative disease, consistent with currently available phase 3 trials [15, 16]. This pattern again reflects a divergence between real-world practice and evidence-based recommendations [17], while also underscoring the persistent uncertainty regarding the optimal baseline imaging strategy for RLT eligibility, as well as variability in institutional logistics and regulatory requirements. An additional area of interest concerned the integration of FDG PET in the imaging pathway before RLT. About two-thirds of respondents considered FDG PET useful only in selected cases, while smaller proportions supported its systematic use or complete exclusion. This distribution aligns with current international recommendations [1–3], expert opinions [14, 18] and with the results of a previous international survey on the topic [19], which agree that FDG PET should not be performed routinely but may provide complementary information in specific scenarios. However, it remains unclear how to define these "selected

cases" in everyday practice. The survey findings help clarify this point, indicating that clinicians and nuclear medicine specialists tend to reserve FDG PET for cases characterised by discordant PSMA uptake on imaging, aggressive histopathologic features (e.g., high Gleason score or neuroendocrine differentiation), rapid PSA kinetics, or unusually short responses to prior systemic therapies. These insights offer a pragmatic, real-world contribution to refining the indications for FDG PET integration before RLT.

Regarding RLT response assessment, most nuclear medicine physicians reported combining biochemical and clinical monitoring with PSMA PET/CT findings, while conventional imaging was used in a minority of cases. This reflects increasing reliance on molecular imaging to evaluate treatment efficacy, despite the lack of standardised criteria for interpreting PSMA PET changes during or after RLT. Proposed frameworks such as PPP [11] and RECIP 1.0 [12] represent early attempts to standardise the assessment of responses using PSMA PET. More recently, the Prostate Cancer Working Group 4 (PCWG4) recommendations [20] have incorporated PSMA PET–based imaging characteristics as exploratory criteria for progression assessment in clinical trials, while PET-based response metrics remain investigational pending prospective validation [21]. This scenario exemplifies how clinical practice is once again advancing ahead of evidence collection and guideline endorsement. Importantly, this discrepancy is not unique to PSMA-targeted therapies: conventional response frameworks such as Response Evaluation Criteria in Solid Tumors 1.1 (RECIST 1.1) have long shown substantial limitations in PCa, largely because the predominantly osteoblastic nature of bone metastases renders most lesions non-measurable, while bone scintigraphy suffers from slow response kinetics, the flare phenomenon, and limited utility in patients with extensive skeletal disease [22]. These historical shortcomings prompted the development of the PCWG2 and PCWG3 criteria, which introduced a compartment-specific approach and strategies such as the "2 + 2 rule" to mitigate misinterpretation of bone progression. The emergence of PSMA PET has partially overcome these limitations by enabling detection of lesions invisible to RECIST and by offering quantitative parameters. However, the prognostic relevance of quantitative metric changes, the significance of new PSMA PET–detected lesions, and their correlation with clinical outcomes remain to be validated in prospective research. This lack of standardised, validated response metrics partly explains why most phase II and III trials investigating PSMA-targeted therapies continue to define radiographic progression-free survival, often the primary endpoint, using conventional imaging criteria rather than molecular parameters [23, 24]. Bridging this gap between trial methodology and real-world practice will require prospective trials that integrate PSMA PET with conventional imaging, enabling direct comparison across modalities and identifying which imaging-derived indicators correlate most closely with meaningful patient outcomes.

Conclusion

In summary, this national survey provides a comprehensive overview of how PSMA PET is being integrated into PCa management across Italy, revealing widespread clinical confidence in its diagnostic accuracy and utility across disease stages. The findings show that clinical adoption has progressed faster than supporting evidence, underscoring the need for prospective validation, harmonised interpretation criteria, and unified national recommendations. Bridging these gaps will be essential to ensure that PSMA PET is applied consistently and effectively, in alignment with evolving clinical evidence and international guidelines.

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Author contributions M.B., L.E., L.S., P.A.Z., and G.F. conceived and designed the study. M.B., L.E., L.S., M.M., A.F., M.L.D.R., O.C., C.M., M.M., G.P., M.K., A.M., R.S., S.B., R.M.D., A.L., P.A.Z., and G.F. contributed to survey development, data interpretation, and manuscript drafting. M.B. performed data analysis and coordinated manuscript preparation. All authors participated in data review, contributed to the critical revision of the manuscript for important intellectual content, and approved the final version for submission. M.B. supervised the overall project. The PSMA PET Italian Survey Collaborators contributed to data collection and validation across participating centers, and their names and affiliations are provided in the Supplementary Materials.

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Declarations

Competing interests The authors declare no competing interests.

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