Clinical Oncology 45 (2025) 103900

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Real-World Experience of 18F-PSMA-1007 Positron Emission Tomography-Computed Tomography Scanning for Initial Staging of High-Risk Nonmetastatic Prostate Cancer: Scan Results and Treatment Decisions

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Abstract

Aims: Recent literature has shown the higher accuracy of staging prostate-specific membrane antigen positron emission tomography (PSMA-PET) scans over conventional imaging for high-risk localised prostate cancer patients suitable for radical treatment. All-Wales guidelines recommended PSMA-PET scans prior to radical therapy in 2020.

Materials and Methods: We have studied the outcome of high-risk prostate cancer patients referred for a staging PSMA-PET CT scan in Cardiff to identify the proportion for nodal or distant metastases, the association between risk factors and PET positivity, how treatment varied by PET result, and the outcome of men undergoing surgery.

Results: Two hundred men underwent staging PSMA PET scans, of whom 143 had no evidence or suspicion of nodal or distant metastases on conventional imaging. Of these 143 patients, 102 (71%), 25 (17.5%), and 16 (11.2%) had post-PET staging of TxN0M0 ($_{PET}$N0M0), TxN1M0 ($_{PET}$N1M0) and TxNxM1 ($_{PET}$M1), respectively. The risk of harbouring microscopic nodal or distant metastases was 12%, 38%, and 72% for men with 1, 2, or 3 high-risk factors, respectively. The risk also increased as the extent of each risk factor increased. The nodal false negative rate for the 22 men with $_{PET}$N0M0 disease undergoing prostatectomy was 9.1%, despite the median number of nodes identified being only 8. Considering the entire 200-patient cohort, treatment was strongly influenced by PET results: 56% of $_{PET}$N0M0 men had radical treatment to the prostate and 37% to prostate + nodes, 87% of $_{PET}$N1M0 men had prostate and pelvic nodal radiotherapy with long-course androgen deprivation therapy (ADT) ± androgen receptor pathway inhibitor (ARPI), whereas 95% of men with $_{PET}$M1 disease had permanent ADT therapy ± radiotherapy ± ARPI.

Conclusions: Our results reflect international literature and strongly support the role of staging PSMA-PET scans prior to radical therapy in all high-risk prostate cancer patients. Extension to unfavourable intermediate-risk should be considered.

Key words: 18F-PSMA-1007 PET-CT; high-risk localised prostate cancer

Abbreviations: 18F-PSMA-1007 PET-CT, 18-fluorine prostate specific membrane antigen-positron emission tomography-computerised tomography scan; ; PSA, prostate specific antigen; ISUP, International Society of Urological Pathology; MRI, magnetic resonance imaging; MDT, multi-disciplinary team; ADT, androgen deprivation therapy; PPNRT, prostate + pelvic nodal radiotherapy; ARPI, Androgen receptor pathway inhibitor; CPG, Cambridge Prognostic Groups; HIFU, high-intensity focused ultrasound; RALP, robot assisted laparascopic prostatectomy.

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https://doi.org/10.1016/j.clon.2025.103900

Introduction

Prostate-specific membrane antigen positron emission tomography-computed tomography (PSMA PET-CT) scanning has superior diagnostic accuracy over conventional imaging in staging patients with high-risk prostate cancer due to its ability to detect occult extra-prostatic disease [1]. National Health Service (NHS) Wales Commissioning Policy CP50 guidelines allowed ^{18}F-choline or ^{18}F-PSMA PET-CT scanning for the 'staging of high-risk patients (defined as clinical T3 or above, or prostate specific antigen (PSA) >20, or Gleason 8 or above) who are considered suitable for curative treatment following conventional imaging', ie fit for radical treatment and without unequivocal metastatic disease [2]. Patients with unequivocal prebiopsy magnetic resonance imaging (MRI) stage of ≥T3 (and no other risk factors) or extra-prostatic extension on biopsy could also be referred for PET scanning. All patients referred for a PSMA-PET scan must have been reviewed within a urological cancer multidisciplinary team (MDT) meeting.

We sought to explore the proportion of patients undergoing for PET scanning for high-risk prostate cancer at the Wales Research and Diagnostic Positron Emission Tomography Imaging Centre (PETIC) with pelvic nodal and/or distant metastatic disease in the 18 months after ^{18}F-PSMA 1007 was first commissioned by the Welsh Health Specialised Services Committee (WHSSC). We aimed to identify the relationship between the presence of different risk factors and PET positivity. We also aimed to assess the false negative rate using the final histopathology of patients undergoing robot-assisted laparoscopic prostatectomy (RALP) with or without lymph node sampling or dissection. We report the different treatment protocols recommended following PET scanning of the entire cohort.

Materials and Methods

The local Picture archiving and communication system (PACS) database was searched to identify all patients undergoing an ^{18}F-PSMA-1007 PET-CT scan on our GE Discovery 690 PET/CT Scanner with time-of-flight (TOF) capability in an 18-month period from 01/01/2020 to 30/06/2021.^{18}F-PSMA-1007 was produced on site using a radiochemistry facility according to Good Manufacturing Practices (GMP) with fluorine-18 produced from an in-house cyclotron. Patients were scanned prior to any androgen deprivation therapy (ADT) or oral antiandrogen having been started. Clinical records were reviewed to identify eligible men and exclude patients having repeat staging scans or scans after prior radical therapy. Relevant disease parameters that triggered referral (PSA, stage and pathology) were retrieved. Diagnostic imaging was reviewed to confirm T stage; all patients had a pre-biopsy bi- or multi-parametric MRI of the pelvis. Patients were classified as having 1) high-risk only disease after conventional imaging ($_{conv}$N0M0), 2) evidence of or suspicion of pelvic lymph node metastases without suspicion of distant metastases ($_{conv}$N1/xM0) or 3) imaging suspicious of distant metastatic disease, including nonregional nodes in the pelvis eg mesorectal nodes, ($_{conv}$Mx). The details of high-risk factors for each $_{conv}$N0M0 were analysed to explore whether there was a relationship with the final post-PET stage.

PSMA PET scan reports, subsequent MDT meeting records, and further investigations were reviewed to categorise patients as having $_{PET}$N0M0, $_{PET}$N1M0, $_{PET}$M1a (including nonregional nodes in the pelvis), $_{PET}$M1b (bone metastases), or $_{PET}$M1c (visceral metastases eg lung or liver) disease. Treatment recommendations were summarised as 'surveillance' (active surveillance or watchful waiting), 'surgical' (high-intensity focused ultrasound [HIFU] or RALP ± pelvic node sampling/dissection), 'prostate radiotherapy' (radiation therapy to the prostate ± seminal vesicles ± short course ADT), 'long-course ADT + prostate radiotherapy (radiation therapy to the prostate ± seminal vesicles +12−36 months of ADT), 'long-course ADT + prostate + pelvic nodal radiotherapy (PPNRT)' (PPNRT +12−36 months of ADT), 'long-course ADT, androgen receptor pathway inhibitor (ARPI) + loco-regional radiotherapy' (24−36m ADT and ARPI + prostate RT ± PPNRT ± radiotherapy to paraortic nodes or small-volume metastases within pelvic bones), 'permanent ADT with radiotherapy' (permanent ADT ± ARPI + prostate ± seminal vesicles ± pelvic nodal radiotherapy) or 'ADT ± ARPI' (permanent ADT ± ARPI ± investigational agents). Histopathological reports and subsequent clinical records from patients undergoing RALP were reviewed to identify the number of nodes retrieved, final pathological stage, and any interventions for recurrent disease.

All data were entered onto a password protected Excel spreadsheet and analysed. Chi-squared test for trend was used to explore the relationship between number and extent of high-risk factors and PET positivity (nodal or distant metastases). High-risk factors were categorised as: 1, 2, or 3; PSA as <20, 20−39 or ≥40; International Society of Urological Pathology (ISUP) grade group as 1, 2−3, 4 or 5 and T stage as 1−2 or 3−4.

Results

A total of 411 consecutive patients underwent an ^{18}F-PSMA-1007 PET-CT scan in the PETIC centre between 01/01/2020 to 30/06/2021, of whom 200 underwent an initial staging scan in the setting of potentially curable high-risk disease without unequivocal distant metastatic disease, following the NHS Wales PET Commissioning Policy; other patients were excluded as duplicates, repeat staging scans, or were being scanned following biochemical recurrence after prior radical therapy. Of these 200 patients, 143 (71.5%) were $_{conv}$N0M0, 33 (16.5%) were $_{conv}$N1/xM0, and 24 (12%) were $_{conv}$Mx.

The presenting features of all patients are shown in Table 1. 49% and 19% of $_{conv}$N0M0 patients had PSA ≥20 and ≥40ng/ml, respectively; 68% had ≥T3 disease and 32% were T3b-T4; 68% had ISUP ≥3 disease. 51%, 36% and 13% had 1, 2, or 3 high-risk factors, respectively, and 40% and

Table 1
Presenting features of patients.

		$_{conv}$N0M0 (%)	$_{conv}$Nx/1M0 (%)	$_{conv}$Mx (%)	All patients (%)
Number		143 (71.5%)	33 (16.5%)	24 (12%)	200 (100%)
Age years	Median (IQR)	72.2 (65.9–76.5)	74.3 (66.8–76.9)	67.3 (63.7–72.2)	71.7 (65.3–76.4)
PSA ng/ml	Mean (SD)	29.8 (38.5)	42.8 (47.3)	36.7 (40.2)	32.8 (40.3)
	Median (IQR)	17.7 (9.4–29.8)	20.2 (13.6–47.2)	18.0 (7.6–56.3)	19.8 (9.5–34.4)
	≥20	70 (49%)	18 (55%)	10 (42%)	98 (49%)
	≥40	27 (19%)	11 (33%)	7 (29%)	45 (23%)
T Stage	≥T3	97 (68%)	27 (82%)	17 (71%)	147 (74%)
	T3b or T4	45 (32%)	13 (39%)	12 (50%)	84 (42%)
ISUP	1–2	46 (32%)	9 (27%)	7 (30%)	62 (31%)
	3	32 (23%)	9 (27%)	5 (23%)	46 (23%)
	4	26 (19%)	4 (12%0	3 (14%)	33 (17%)
	5	37 (26%)	11 (33%)	7 (32%)	55 (28%)
CPG	1–3	0 (0%)	4 (12%)	3 (12%)	7 (4%)
	4	63 (44%)	7 (21%)	9 (38%)	79 (40%)
	5	80 (56%)	22 (67%)	12 (50%)	114 (57%)
High-risk factors	1	73 (51%)	8 (24%)	10 (42%)	91 (46%)
	2	51 (36%)	17 (52%)	7 (29%)	75 (38%)
	3	18 (13%)	8 (24%)	5 (21%)	31 (16%)

ConvMx, Conventional imaging stage Tany Nany Mx; ConvN0M0, Conventional imaging stage N0 M0; ConvN1xM0, Conventional imaging stage Tany N1/X M0; CPG, Cambridge Prognostic Groups – using clinical, pathological and imaging data for T stage only, i.e. T2N1 disease incorporated into CPG using T2 only; ISUP, International Society of Urological Pathology; PSA, prostate specific antigen.

57% were Cambridge Prognostic Groups (CPGs) 4 and 5, with the remaining 7 patients all having definitive/equivocal nodal or equivocal distant metastases on conventional imaging.

125 (62.5%), 37 (18.5%), and 38 (19.0%) of all patients had $_{PET}$N0M0, $_{PET}$N1M0, and $_{PET}$M1 as their final disease state. Figure 1 shows the proportion of final PET stages by their conventional imaging stage. 102 (71.3%), 25 (17.5%), and 16 (11.2%) of the $_{conv}$N0M0 patients had $_{PET}$N0M0, $_{PET}$N1M0 and $_{PET}$M1 as their final disease state; of the 16 $_{conv}$N0M0 $_{PET}$M1 patients 4, 11 and 1 had $_{PET}$M1a, $_{PET}$M1b and $_{PET}$M1c disease, respectively.

The proportion of men with high-risk only disease on conventional imaging with nodal or distant metastatic disease on PSMA PET scanning was strongly influenced by the number of risk factors: 65 (88%), 5 (7%) and 4 (5%) of $_{conv}$N0M0 patients with 1 high-risk factor had $_{PET}$N0M0, $_{PET}$N1M0, and $_{PET}$M1 disease compared to 31 (62%), 13 (26%) and 6 (12%), and 5 (28%), 7 (39%) and 6 (33%), for 2 and 3 risk factors ($P < 0.001$) (Figure 2). The proportion of patients with nodal or distant metastases was related to PSA value, pre-PET T stage and ISUP grade group (all $P < 0.01$). The proportion of $_{conv}$N0M0 patients with nodal or distant metastases on PET imaging was 8.7%, 15.8%, and 12.5% if the only high-risk factor was PSA ≥20ng/ml, ISUP grade group ≥4 and T stage ≥T3a, respectively. Figure 3 shows this data by the extent of the three risk factors; PET positivity ranged from 6.7% if the PSA was between 20-39 ng/ml to 22.2% if the ISUP grade group was 5, although patient numbers were only 8–20 per group.

In total 28 men (27 $_{PET}$N0M0, 1 $_{PET}$NxM0) had RALP, 26 within the NHS sector in Wales. Of the 23 men with known surgical nodal assessment, the median number of nodes identified was 8, 11 had ≥11 nodes identified pathologically, and 4 had no nodes removed. Final pathological T stage was pT2 in 5, 13 pT3a, 8 pT3b, and 1 pT4; 20 patients were pN0 and 3 pN1, including the man with $_{PET}$NxM0 disease whose nodal status was considered equivocal after PSMA PET at MDT review. 10 men have relapsed after RALP: 8 have been treated with locoregional salvage radiotherapy with or without ADT and ARPI, and 2 have been treated with permanent ADT with or without ARPI.

We were not able to comment on pre-PET treatment options as clinical/MDT records noted 'referral for staging PSMA PET scan'. However, Figure 4 shows the treatment approaches planned with the clinician and patients after MDT review following the PSMA PET scan of the entire 200 patient cohort. Several key patterns regarding treatment emerged. 58% of $_{PET}$N0M0 had radical treatment to the prostate (RALP or prostate radiotherapy) with variable durations of ADT ± ARPI, and 35% had PPNRT with variable durations of ADT ± ARPI, compared to 6% and 87% for $_{PET}$N1M0, respectively. 58%, 30%, and 60% with CPG 3, 4, and 5 disease with $_{PET}$N0M0 disease who had radical radiotherapy also received adjuvant whole pelvic radiotherapy.

40% of men with $_{PET}$M1a disease had a radical approach including radiotherapy to all sites of known disease and long-course (but not permanent) ADT ± ARPI. 95% (20) of men with $_{PET}$M1b/c disease had permanent ADT ± ARPI, of whom 90% (18) had local radiotherapy to the prostate ± pelvic lymph nodes and only. In total, 10 men (4.3%) received ADT only, without any local radiotherapy. To assess potential under-treatment based on PSMA PET imaging we reviewed the 10 patients identified as having been treated with ADT with or without ARPI. Seven of these had disease just in the pelvis ($_{PET}$N0M0 or $_{PET}$N1M0); 5

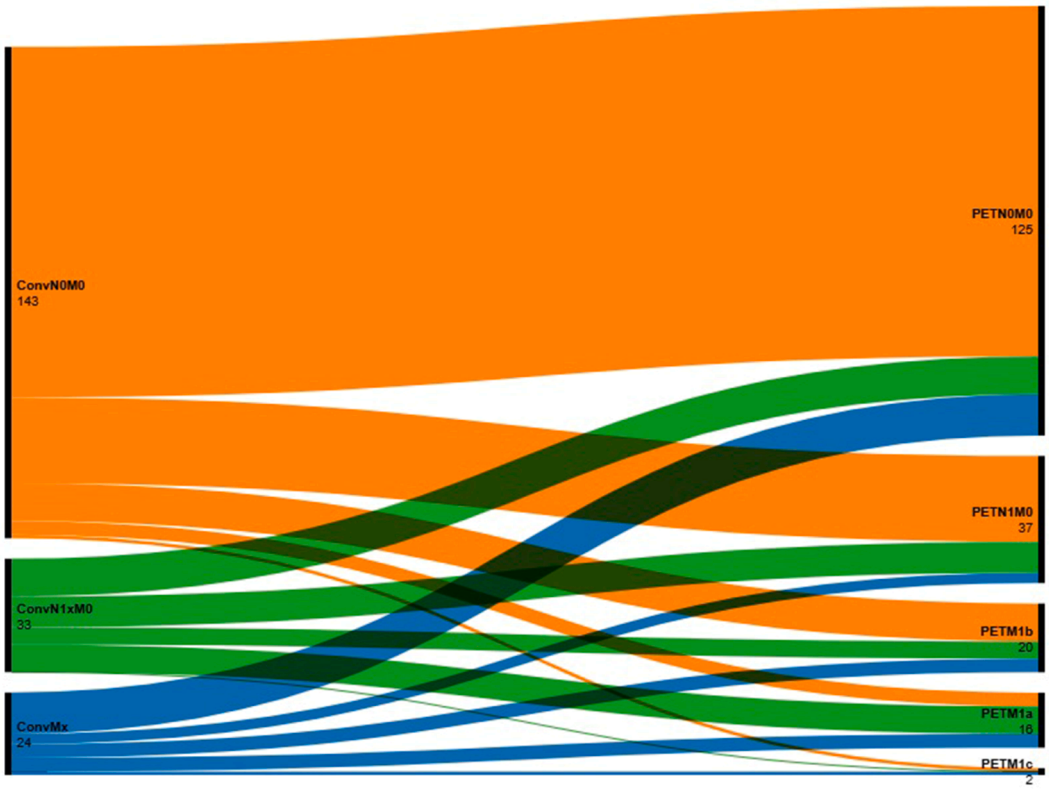

Fig 1. PET results by conventional imaging stage.
Sankey diagram to show the number of men with conventional imaging stage N0M0 (ConvN0M0), N1/XM0 (ConvN1xM0), or Mx (ConvMx) disease who had a final post-PET and MDT review stage of $_{PET}$N0M0, $_{PET}$N1M0, $_{PET}$M1a, $_{PET}$M1b, and $_{PET}$M1c (in frequency order). MDT, multidisciplinary team; PET, positron emission tomography.

opted for ADT alone due to coexisting medical conditions (colitis, irritable bowel syndrome, deteriorating dementia, and an incidental liposarcoma requiring surgery), and two died before the radiotherapy was started for nonprostate cancer conditions. A patient with $_{PET}$M1a disease was treated with ADT and enzalutamide, with no initial discussion of locoregional radiotherapy; he had prostate and pelvic radiotherapy added 2.5 years later when his PSA was still $<$0.1ng/ml. One patient had $>$20 bone metastases on PSMA PET and one had multiple bone metastases and 2 pulmonary metastases; both were treated with ADT and an ARPI.

Six patients (3%), all with PSA $\leq$20 and had ISUP grade group 2 or 3, had low PSMA avidity within the prostate primary lesion, of whom only 1 showed any evidence of metastatic disease on the PET-CT scan. PSMA uptake was also seen in patients with the following synchronous diagnoses: incidental lung cancer (x3), mild to moderate uptake in a known synchronously diagnosed rectal cancer, multinodular benign thyroid gland, diffuse bone marrow and nodal uptake in a patient with known HIV infection and nodal uptake in a patient with known follicular lymphoma.

Discussion

This study shows the real-world experience across South Wales of introducing ^{18}F-PSMA-1007 PET imaging for the staging of men with high-risk prostate cancer otherwise considered suitable for curative treatment after MDT review following a change in indications. In an 18-month period 200 men underwent a PSMA PET scan, of whom 143 had no suspicion of nodal or distant metastases on conventional imaging. 17.5% (25) of these 143 men had pelvic nodal metastases and 11.2% (16) had distant metastases, 5 (3%) of whom also had pelvic nodal disease. The risk of PET positivity was associated with the number and severity of high-risk factors. Our analysis of the men with only a single high-risk factor should be interpreted with caution as the numbers of men in each group was fairly low; the lowest PET positivity rate was 6.7% in the men with a PSA between 20 and 39, rising to 22.2% for men with just ISUP grade group 5 disease.

Our results show slightly lower PET positivity rates than seen in the ProPSMA trial, which underpinned the change in our commissioning guidelines [1]. In this trial of 302 patients with at least one high-risk feature, 20% had pelvic

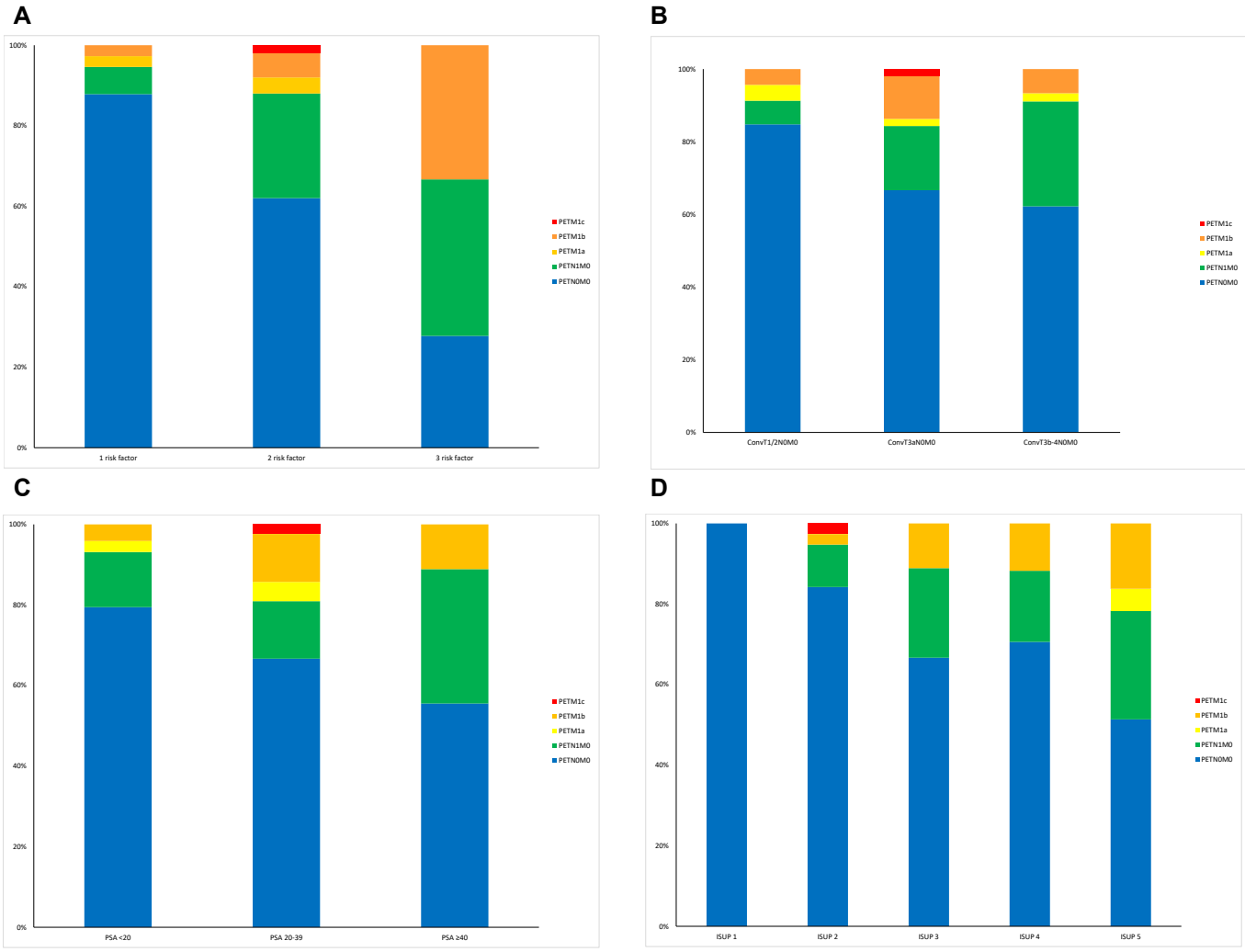

Fig 2. The association between risk factor and PET positivity in $_{Conv}$N0M0 patients.
The proportion of men with conventional imaging stage N0M0 (ConvN0M0) and different number and extent of high-risk factors who had a final post-PET and MDT review stage of $_{PET}$N0M0, $_{PET}$N1M0, $_{PET}$M1a, $_{PET}$M1b, and $_{PET}$M1c. A: number of high-risk factors, B: T stage based on clinical and MRI findings, C: PSA (ng/ml) and D: ISUP grade 1 to 5. MDT, multidisciplinary team; MRI, magnetic resonance imaging; PET, positron emission tomography; PSA, prostate specific antigen.

nodal disease, 9% abdominal nodal disease, and 11% distant metastases. It should be noted that 64% of their cohort had ISUP grade group $\geq$4 compared to 45% of our $_{conv}$N0M0 patient cohort, and 42% in the ProPSMA trial underwent RALP compared to just 15% in our entire cohort. We surmise that our use of PSMA PET scanning for men with unequivocal radiological T3 disease has resulted in our lower prevalence of metastases. Luining *et al.* reported on the prevalence of metastatic disease on PSMA PET scanning using multiple tracers in a series of 2630 men with newly diagnosed prostate cancer from 2017-2022 with men risk stratified using 4 different international systems [3]; of the men with high-risk disease 10–11% had regional nodal disease and 35–37% had distant metastases. Different PET tracers have different levels of accuracy [4,5].

Management plans were not formally recorded prior to PSMA PET in clinic letters, MDT meetings or PET referral forms, as the management decision was 'refer for PSMA PET scan', and so change in management for individual patients resulting from PET cannot be accurately presented. The ProPSMA study reported that 28% of men had management changed after first-line PSMA PET-CT, with changes including curative to palliative intent and changes in radiotherapy or surgical technique [1]. Our data supports the assumption that the treatment received was driven by the PET scan results, with the rates of potentially curative local and locoregional therapy being 93% for $_{PET}$N0-1M0 disease, whereas 95% of men with $_{PET}$M1b/c disease had a noncurative approach, although most received local radiotherapy in keeping with the results of the STAMPEDE trial [6]. Patients with M1a disease were low in number (15); 40% received permanent ADT and locoregional radiotherapy $\pm$ ARPI, and 40% received potential curative treatment with all sites of known disease irradiated and received ADT $\pm$ ARPI for 2–3 years only; very few patients in this cohort received metastases-directed therapy. On

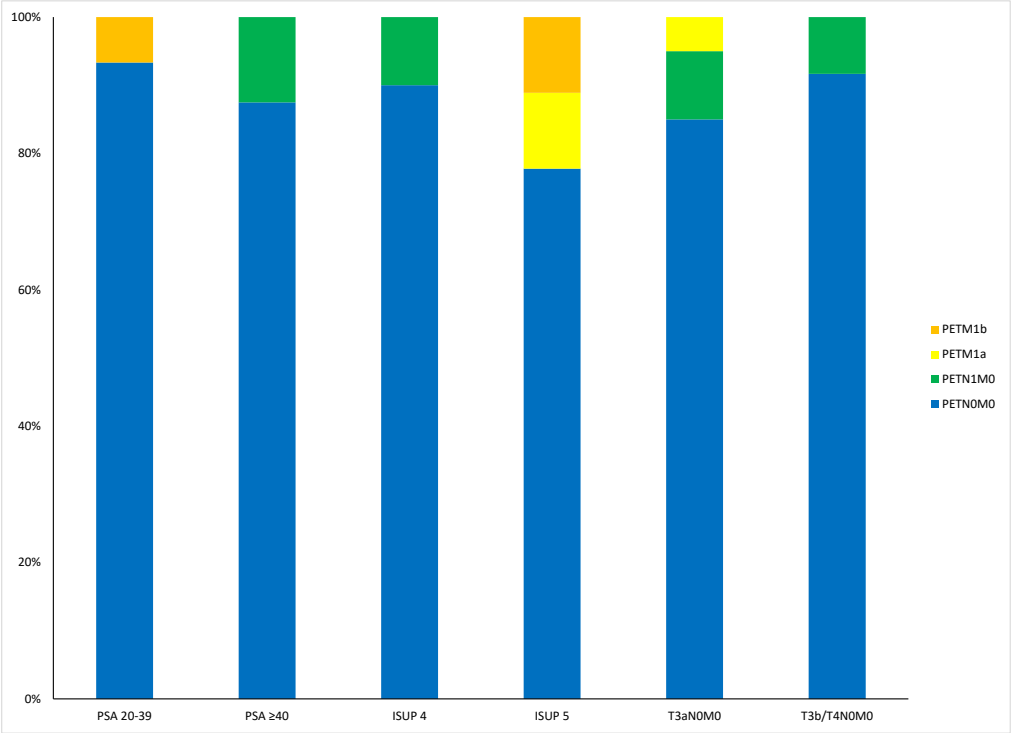

Fig 3. PET results of patients referred with a single high-risk factor.
The proportion of the 74 men with conventional imaging stage N0M0 (ConvN0M0) and a single high-risk factor who had a final post-PET and MDT review stage of $_{PET}$N0M0, $_{PET}$N1M0, $_{PET}$M1a, and $_{PET}$M1b. MDT, multidisciplinary team; PET, positron emission tomography.

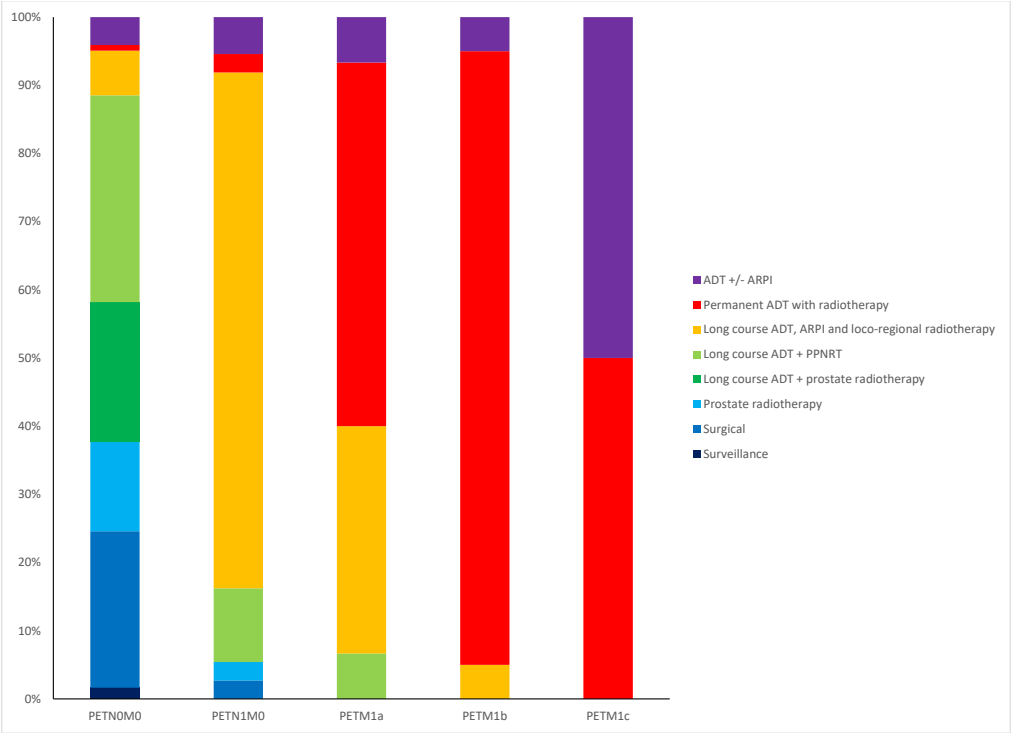

Fig 4. Treatment recommended by PET stage.
Final treatment recommended and accepted by patient after PET, MDT review, and clinical discussion with patient, by PET stage. ADT ± ARPI with or without novel hormonal agents, PPNRT, long-course ADT, at least 12 months of ADT, surgical = HIFU or RALP with or without pelvic nodal sampling or dissection. ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; HIFU, high-intensity focused ultrasound; MDT, multidisciplinary team; PET, positron emission tomography; PPNRT, prostate and pelvic nodal radiotherapy; RALP, robot-assisted laparoscopic prostatectomy.

review 3 patients with metastatic disease were only treated with ADT ± ARPI without treatment to the prostate, potentially representing under-treatment [7]. Of these, one received locoregional radiotherapy over 2 years after initiating ADT and two had multiple bone metastases, one with pulmonary metastases. We believe this reflects appropriate omission of radiotherapy, despite them being nonmetastatic on conventional imaging. We found that 3 of the 23 (13%) men who had RALP with nodal assessment had microscopic nodal disease at surgery, despite the relatively low number of extended pelvic lymphadenectomies carried out (median nodal yield 8). Of these one had equivocal pelvic nodal disease at PET scanning, giving a negative predictive value (NPV) of 91%. This is in keeping with the systemic review by Stabile *et al.* which showed an overall NPV of 79%, but with a range of 84%–99% depending on the underlying risk of nodal disease [8]. The difficulty in managing the nodal region in $_{PET}$N0M0 is partly driven by this NPV and is reflected in the variable use of pelvic nodal radiotherapy in our series. Other factors include the underlying risk of nodal disease, patient factors, and the lack of high-quality data showing a benefit from adjuvant nodal treatment in high-risk prostate cancer. Results of ongoing trials will hopefully help refine this decision-making: PivotalBoost ISRCTN80146950, PACE NODES NCT 05613023, and RTOG-0924 [9].

Our commissioning guidelines are based on whether PET imaging has been shown to alter long-term outcomes or treatment decisions, which we are unable to address in this study. However, we have not been able to identify a subgroup of high-risk patients with a risk of PET positivity under 5%, which we believe to be appropriate use of resource. Luining *et al.* have shown 6–7% and 13% of favourable and unfavourable intermediate-risk prostate cancer harbour nodal or distant metastases on PSMA PET imaging [3], raising the question of whether our guidelines should be extended to men with multiple intermediate-risk factors.

We are aware that the ProPSMA study showed that the radiation exposure from 1st-line conventional imaging was 10.9 mSv higher than the PSMA PET-first approach (19.2 mSv vs 8.4 mSv; $P < 0.001$) [1]. However, as access to PSMA PET is limited in Wales and across the UK, we continue to use a conventional imaging-first approach to exclude patients with metastatic disease. An audit of access to PSMA PET scan should be considered to ensure equitable access and identify barriers to future expansion eg for selected patients with unfavourable intermediate-risk disease.

Conclusions

We have reported the PSMA PET scanning results in a real-world setting of 143 men with high-risk prostate cancer without evidence of nodal or bone metastases on conventional imaging and shown that 17.5% had pelvic nodal metastases without distant metastases, and 11.2% had distant metastases with or without pelvic nodal metastases. Furthermore, we have shown that the risk of pelvic nodal or distant metastatic disease increased with number of high-risk factors: 12%, 38%, and 72% for men with 1, 2, and 3 risk factors, respectively. We strongly recommend that all men with high-risk localised prostate cancer should have a staging PSMA-PET scan prior to radical therapy to ensure an optimal treatment approach is agreed with the patient.

Author contribution

Professor John Staffurth: guarantor of integrity of the entire study, study concepts and design, literature research, clinical studies, experimental studies/data analysis, statistical analysis, manuscript preparation, manuscript editing.

Dr Saptarshi Mukherjee: study concepts and design, literature research, clinical studies, experimental studies/data analysis, manuscript editing.

Dr Patrick Fielding: clinical studies, manuscript editing.

Dr Emily Renninson: statistical analysis, manuscript editing.

Dr John I Rees: study concepts and design, literature research, clinical studies, experimental studies/data analysis, manuscript editing.

Ethics

This work was registered and approved by the Velindre NHS University Trust's audit department.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: John Staffurth reports a relationship with Novartis that includes: consulting or advisory. John Staffurth reports a relationship with Johnson and Johnson Ltd that includes: speaking and lecture fees and travel reimbursement. John Staffurth reports a relationship with Amgen Inc that includes: consulting or advisory. John Staffurth reports a relationship with AstraZeneca that includes: lecture fees and travel reimbursement. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Hofman MS, Lawrentschuk N, Francis RJ, Tang C, Vela I, Thomas P, *et al.* Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent

surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. *Lancet* 2020 Apr 11;395(10231):1208–1216. https://doi.org/10.1016/S0140-6736(20)30314-7.

[2] Welsh Health Specialised Services Committee. Positron Emission Tomography (PET) Commissioning Policy: CP50 https://whssc.nhs.wales/commissioning/whssc-policies/cancer/positron-emission-tomography-pet-cp50-commissioning-policy-april-2024/.

[3] Luining WI, Boevé LMS, Hagens MJ, Meijer D, de Weijer T, Ettema RH, *et al*. A Comparison of Globally Applied Prognostic Risk Groups and the Prevalence of Metastatic Disease on Prostate-specific Membrane Antigen Positron Emission Tomography in Patients with Newly Diagnosed Prostate Cancer. *Eur Urol Oncol* 2024 Apr;30(24):S2588–S9311. https://doi.org/10.1016/j.euo.2024.04.005. 00097-X.

[4] Farolfi A, Calderoni L, Mattana F, Mei R, Telo S, Fanti S, *et al*. Current and Emerging Clinical Applications of PSMA PET Diagnostic Imaging for Prostate Cancer. *J Nucl Med* 2021 May 10;62(5):596–604. https://doi.org/10.2967/jnumed.120.257238.

[5] Annunziata S, Pizzuto DA, Treglia G. Diagnostic Performance of PET Imaging Using Different Radiopharmaceuticals in Prostate Cancer According to Published Meta-Analyses. *Cancers (Basel)* 2020 Aug 4;12(8):2153. https://doi.org/10.3390/cancers12082153.

[6] Syndikus I, Cruickshank C, Staffurth J, Tree A, Henry A, Naismith O, *et al*. Abiraterone acetate plus prednisolone with or without enzalutamide for patients with metastatic prostate cancer starting androgen deprivation therapy: final results from two randomised phase 3 trials of the STAMPEDE platform protocol. *Lancet Oncol* 2023 May;24(5):443–456. https://doi.org/10.1016/S1470-2045(23)00148-1.

[7] Burdett S, Moeve L, Ingleby F, Fisher D, Rydzewska L, Vale C, *et al*. Prostate Radiotherapy for Metastatic Hormone-sensitive Prostate Cancer: A STOPCAP Systematic Review and Meta-analysis. *Eur Urol* 2019 Jul;76(1):115–124. https://doi.org/10.1016/j.eururo.2019.02.003.

[8] Stabile A, Pellegrino A, Mazzone E, Cannoletta D, de Angelis M, Barletta F, *et al*. Can negative prostate-specific membrane antigen positron emission tomography/computed tomography avoid the need for pelvic lymph node dissection in newly diagnosed prostate cancer patients? A systematic review and meta-analysis with backup histology as reference standard. *Eur Urol Oncol* 2022 Feb;5(1):1–17. https://doi.org/10.1016/j.euo.2021.08.001.

[9] Syndikus I, Cruickshank C, Staffurth J, Tree A, Henry A, *et al*. PIVOTALboost: A phase III randomised controlled trial of prostate and pelvis versus prostate alone radiotherapy with or without prostate boost (CRUK/16/018). *Clin Transl Radiat Oncol* 2020;1(25):22–28.