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Serum PSA at the time of imaging predicts the detection rate but only weakly predicts lesion SUVmax on 68Ga-PSMA PET/CT after radical prostatectomy: a PSMA-RADS 2.0-based compartment-level analysis of 107 Vietnamese patients

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Research Article

Keywords: prostate cancer, biochemical recurrence, radical prostatectomy, 68Ga-PSMA PET/CT, PSMA-RADS, prostate-specific antigen, SUVmax, detection rate

Posted Date: November 23rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11585282/v1

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Abstract

Purpose

The detection rate of prostate-specific membrane antigen (PSMA) PET/CT after radical prostatectomy (RP) depends on serum prostate-specific antigen (PSA), but whether PSA also predicts the intensity of PSMA uptake in individual compartments is uncertain. We assessed how PSA at imaging relates to detection rates and lesion SUVmax on ^{68}Ga-PSMA PET/CT interpreted with PSMA-RADS 2.0.

Methods

We retrospectively analysed 107 consecutive men imaged for rising or persistent PSA after RP at a single centre (2023–2026). Lesions were classified in five compartments; a scan was positive when at least one lesion was PSMA-RADS 4–5, and PSMA-RADS 3 findings were reported separately. Trend tests, logistic regression, Spearman correlation and multivariable regression of log SUVmax were used.

Results

Median PSA was 2.24 ng/mL (IQR 0.38–6.46). The positivity rate was 52.3% (56/107), rising from 6.7% (1/15) at PSA < 0.2 ng/mL to 77.2% (44/57) at ≥ 2.0 ng/mL (p for trend < 0.001); rates for any PSMA-RADS 3–5 lesion were 33.3% and 93.0%. PSA discriminated positive from negative scans (AUC 0.84, 95% CI 0.76–0.91) and remained the dominant predictor after adjustment for age, interval from surgery, prior treatment and ISUP grade (OR 6.5 per 10-fold increase). Local and pelvic nodal recurrence increased with PSA, whereas bone metastases occurred across all strata, including 6.5% (2/31) of men with PSA < 0.5 ng/mL. Among 77 patients with PSMA-avid lesions, PSA correlated moderately with the highest SUVmax (ρ = 0.461), but the correlation weakened in PSMA-RADS 4–5 scans (ρ = 0.311) and was not significant within any compartment. After adjustment, a 10-fold increase in PSA corresponded to only a 43% (95% CI 11–85%) higher SUVmax.

Conclusion

PSA at imaging strongly predicts whether ^{68}Ga-PSMA PET/CT will localise disease but explains little of the variation in lesion SUVmax, which depends mainly on lesion category. PSA should guide the timing of imaging but cannot replace PET/CT for characterising lesions or excluding early metastasis.

1. INTRODUCTION

Prostate cancer is the second most frequently diagnosed cancer in men worldwide, and its incidence is rising rapidly in Asia as life expectancy and PSA testing increase [1]. After radical prostatectomy (RP),

20–40% of patients develop biochemical recurrence (BCR), conventionally defined as a confirmed PSA ≥ 0.2 ng/mL [2, 3]. The management of BCR depends on whether disease is confined to the prostate bed, limited to the pelvic nodes or already disseminated, and current guidelines recommend PSMA PET/CT as the imaging modality of choice whenever the result is likely to change treatment [4–6].

The single most important determinant of the detection rate of PSMA PET/CT in BCR is the serum PSA at the time of imaging. In the largest multicentre series of 2,533 post-prostatectomy patients, the detection rate of [^{68}Ga]Ga-PSMA-11 PET/CT increased from 43% at PSA ≤ 0.2 ng/mL to over 90% at PSA > 10 ng/mL [7], and similar PSA-dependent gradients have been documented in prospective trials [8, 9], in large retrospective cohorts [10, 11] and in meta-analyses [12]. However, most of these studies counted any suspicious uptake as positive. The PSMA-RADS version 2.0 framework now separates lesions of high certainty (PSMA-RADS 4–5) from equivocal findings (PSMA-RADS 3), and the proportion of equivocal findings is expected to be highest precisely where the detection rate is most uncertain, namely at low PSA levels [13, 14]. Few studies have reported detection rates stratified both by PSA and by PSMA-RADS category, and even fewer have done so separately for each anatomical compartment.

A second, less well-characterised question is whether PSA predicts the intensity of PSMA uptake. Moderate correlations between PSA and SUVmax have been reported in the primary tumour before treatment [15, 16] and in recurrent disease [17], and SUVmax itself has emerged as a prognostic variable after PSMA PET-guided salvage radiotherapy [18, 19]. Yet serum PSA reflects the total burden of PSA-secreting tumour cells, whereas SUVmax reflects PSMA receptor density, lesion size and partial-volume effects in a single lesion; whether the two are related within specific compartments such as the prostate bed or bone has rarely been examined.

Data on PSMA PET/CT from Southeast Asia remain limited [20]. Vietnamese surgical cohorts are characterised by a high proportion of high-risk disease and limited pelvic lymph node dissection [21], and PET/CT has until recently been requested relatively late in the course of BCR. The aims of this study were therefore (1) to describe patient-level and compartment-level detection rates of ^{68}Ga-PSMA PET/CT across PSA strata using PSMA-RADS 2.0, (2) to identify clinical predictors of a positive scan and of distant metastasis, and (3) to quantify the correlation between PSA and lesion SUVmax overall and within each compartment.

2. MATERIALS AND METHODS

2.1. Study design and population

This retrospective cross-sectional study was conducted at the PET/CT and Cyclotron Unit, Department of Nuclear Medicine, Cho Ray Hospital, Ho Chi Minh City, Vietnam, a tertiary referral centre. The protocol was approved by the Ethics Committee in Biomedical Research of Pham Ngoc Thach University of Medicine (approval No. 1495/TĐHYKPNT-HĐĐĐ, 28 November 2025) and the requirement for individual informed consent was waived because of the retrospective design; all data were pseudonymised before

analysis. We screened all ^{68}Ga-PSMA PET/CT examinations performed between November 2023 and June 2026 and included consecutive men who (i) had undergone RP for histologically confirmed prostate adenocarcinoma, (ii) were referred for a rising PSA after an undetectable nadir (BCR, confirmed PSA ≥ 0.2 ng/mL), for persistent PSA after surgery, or for restaging under treatment because of rising PSA or suspected progression, and (iii) had a serum PSA measured within 4 weeks before the scan. Patients with unavailable images or missing PSA were excluded. The final cohort comprised 107 patients.

2.2. Clinical data

Age, interval from RP to PET/CT, ISUP grade group of the RP specimen (available in 83 patients), prior post-operative treatment (androgen deprivation therapy [ADT], radiotherapy, orchiectomy, chemotherapy), PSA course (BCR versus PSA persistence) and PSA at imaging were extracted from the medical records onto a standardised data collection form. Serum PSA was measured by electrochemiluminescence immunoassay on an automated analyser in the hospital laboratory. PSA was analysed as a continuous (log10-transformed) variable and in five strata widely used in the literature (< 0.2; 0.2–< 0.5; 0.5–< 1.0; 1.0–< 2.0; ≥ 2.0 ng/mL) [7, 10]; three clinically relevant cut-offs (0.5, 1.0 and 2.0 ng/mL) were also examined.

2.3. PET/CT acquisition

^{68}Ga-PSMA-11 (^{68}Ga-Glu-NH-CO-NH-Lys-(Ahx)-HBED-CC) was labelled on site from a ^{68}Ge/^{68}Ga generator in accordance with the joint EANM/SNMMI procedure guideline [6]. Patients fasted for 4–6 h, were hydrated with 500–1,000 mL of water during the 2 h before injection and voided immediately before imaging; 10–20 mg of furosemide could be given intravenously at the time of injection to reduce urinary activity in the bladder and urethra. The target activity was 1.8–2.2 MBq/kg body weight; the median administered activity was 159 MBq (IQR 139.5–173.9) and the median uptake time 60 min (IQR 54.5–60; protocol range 50–70 min). Imaging was performed from the vertex to the mid-thigh on a Biograph mCT time-of-flight PET/CT system (Siemens Healthineers, Erlangen, Germany) with the patient supine and arms raised. A low-dose CT (120 kV, automatic tube current modulation 30–80 mAs, pitch 0.98–1.2, reconstructed slice thickness 3–5 mm) was acquired for attenuation correction and anatomical localisation; a diagnostic contrast-enhanced CT (1.3 mL/kg of iodinated contrast at 300 mgI/mL, 2 mL/s) was added when detailed assessment of the pelvis, lymph nodes or viscera was required, which was the case in 72.0% (77/107) of patients. PET data were acquired in three-dimensional mode at 2–3 min per bed position with 20–25% bed overlap and reconstructed with an ordered-subsets expectation-maximisation algorithm incorporating time-of-flight and point-spread-function modelling, with attenuation, scatter and random corrections. When the prostate bed was obscured by bladder activity, patients voided again and additional delayed pelvic images were obtained 90–120 min after injection. Images were analysed on a dedicated workstation (syngo.via, Siemens Healthineers).

2.4. Image interpretation and definitions

All examinations were re-reviewed for this study by the two authors (T.A.N., a radiologist, and C.X.N., a nuclear medicine physician), both trained in PSMA-RADS version 2.0 with more than 2 years of experience in PSMA PET/CT, with access to the clinical information as in routine practice; discrepancies were resolved by consensus. Findings were classified with PSMA-RADS version 2.0 [13] and recorded in five compartments following the PROMISE framework [22, 23]: prostate bed (local recurrence, miTr), pelvic lymph nodes (miN1), extrapelvic lymph nodes (miM1a; including common iliac nodes), bone (miM1b) and visceral or soft-tissue sites (miM1c). For each compartment the lesion with the highest uptake was characterised: its SUVmax (body-weight normalised) was measured with a volume of interest encompassing the lesion, the PSMA expression score was graded against blood pool, liver and parotid uptake, and lesion size was measured on the corresponding CT images (short-axis diameter for nodes, largest diameter for prostate bed and visceral lesions). The highest SUVmax of any lesion defined the patient-level SUVmax.

We used a two-tier definition of positivity. A compartment was considered involved only when it contained at least one lesion classified as PSMA-RADS 4 or 5; a scan was positive when at least one compartment was involved, so that the overall PSMA-RADS score of a positive scan was 4 or 5 by construction. PSMA-RADS 3A/3B/3D findings were considered equivocal: they were not counted as involvement but were tabulated separately, and the proportion of patients with any PSMA-RADS 3–5 lesion was reported to allow comparison with studies that used a more inclusive definition of detection rate. Distant metastasis (miM1) was defined as involvement of the extrapelvic nodal, bone or visceral compartment.

2.5. Statistical analysis

Continuous variables are presented as mean ± standard deviation or median with interquartile range (IQR), and categorical variables as counts and percentages with the denominator stated. Proportions are given with Wilson 95% confidence intervals (CI). Detection rates across PSA strata were compared with the chi-square or Fisher exact test and with the Cochran–Armitage test for trend. The ability of PSA to discriminate positive from negative scans was summarised by the area under the receiver operating characteristic curve (AUC) with a 2,000-sample bootstrap CI, and sensitivity and specificity were reported at the pre-specified cut-offs. Univariable and multivariable logistic regression was used to identify predictors of a positive scan and of distant metastasis; log10 PSA, age, log10 interval from surgery and prior treatment were included a priori in the full-cohort model, and ISUP grade group (4–5 versus 1–3) was added in a sensitivity model restricted to the 83 patients with pathology data. Because events were limited, no more than five covariates were entered. SUVmax was compared across PSA strata with the Kruskal–Wallis test and between two groups with the Mann–Whitney U test. The correlation between PSA and SUVmax was quantified with Spearman's ρ and a 5,000-sample bootstrap CI, overall, within PSMA-RADS categories, within PSA ranges and within each compartment. Finally, multivariable linear regression of log10 SUVmax on log10 PSA, adjusted for lesion category (PSMA-RADS 4–5 versus 3), ongoing ADT and presence of distant metastasis, was used to estimate the proportional change in SUVmax per 10-fold increase in PSA. Missing data were not imputed. All tests were two-sided and $p <$

0.05 was considered significant; compartment-level and subgroup analyses were regarded as exploratory and were not adjusted for multiplicity. Analyses were performed with SPSS (IBM Corp., Armonk, NY) and Python (SciPy and statsmodels libraries).

3. RESULTS

3.1. Patient characteristics

The characteristics of the 107 patients are summarised in Table 1. Mean age was 67.3 ± 7.2 years and the median interval from RP to PET/CT was 22.2 months (IQR 8.1–59.0). Among the 83 patients with pathology data, 43.4% (36/83) had ISUP grade group 4–5. Median PSA at imaging was 2.24 ng/mL (IQR 0.38–6.46); 29.0% (31/107) were imaged at PSA < 0.5 ng/mL and 53.3% (57/107) at PSA ≥ 2.0 ng/mL. One third of patients (35.5%, 38/107) had received post-operative treatment before PET/CT, most often ADT (30.8%, 33/107). The scan was positive (PSMA-RADS 4–5) in 52.3% (56/107; 95% CI 43.0–61.6), equivocal (PSMA-RADS 3) in 20.6% (22/107) and negative in 27.1% (29/107); 72.9% (78/107; 95% CI 63.8–80.4) had at least one PSMA-RADS 3–5 lesion. Local recurrence was identified in 31.8% (34/107), pelvic nodal metastasis in 18.7% (20/107) and distant metastasis in 29.0% (31/107; 95% CI 21.2–38.2).

Table 1
Characteristics of the study population (N = 107)

Characteristic	Value
Age (years), mean ± SD; range	67.3 ± 7.2; 50–84
Interval from radical prostatectomy to PET/CT (months), median (IQR)	22.2 (8.1–59.0)
≤ 12 / > 12–60 / > 60 months, n (%)	39 (36.4) / 43 (40.2) / 25 (23.4)
ISUP grade group of the prostatectomy specimen (n = 83), n (%)	
1 / 2 / 3 / 4 / 5	6 (7.2) / 14 (16.9) / 27 (32.5) / 8 (9.6) / 28 (33.7)
PSA course, n (%)	
Biochemical recurrence / PSA persistence / not classifiable[a]	73 (68.2) / 6 (5.6) / 28 (26.2)
PSA at PET/CT (ng/mL), median (IQR)	2.24 (0.38–6.46)
< 0.2 / 0.2–< 0.5 / 0.5–< 1.0 / 1.0–< 2.0 / ≥ 2.0, n (%)	15 (14.0) / 16 (15.0) / 7 (6.5) / 12 (11.2) / 57 (53.3)
Any post-operative treatment before PET/CT, n (%)	38 (35.5)
Androgen deprivation therapy / radiotherapy / orchiectomy / chemotherapy	33 (30.8) / 12 (11.2) / 4 (3.7) / 2 (1.9)
Injected activity (MBq), median (IQR)	159 (139.5–173.9)
Contrast-enhanced diagnostic CT, n (%)	77 (72.0)
Overall PSMA-RADS 2.0 category, n (%)	
1–2 / 3 (3A 18, 3B 3, 3D 1) / 4 / 5	29 (27.1) / 22 (20.6) / 33 (30.8) / 23 (21.5)
Compartment involvement (PSMA-RADS 4–5), n (%)	
Prostate bed / pelvic nodes / extrapelvic nodes / bone / viscera	34 (31.8) / 20 (18.7) / 14 (13.1) / 19 (17.8) / 5 (4.7)
Pelvis-confined disease / distant metastasis (miM1), n (%)	25 (23.4) / 31 (29.0)

SD, standard deviation; IQR, interquartile range; ISUP, International Society of Urological Pathology. [a] *PSA rising under treatment or not yet confirmed by a second measurement at the time of referral.*

3.2. Detection rate according to PSA level

Detection rates across PSA strata are shown in Table 2 and Fig. 1. The positivity rate increased from 6.7% (1/15) at PSA < 0.2 ng/mL to 25.0% (4/16) at 0.2–< 0.5, 14.3% (1/7) at 0.5–< 1.0, 50.0% (6/12) at

1.0–< 2.0 and 77.2% (44/57) at ≥ 2.0 ng/mL (chi-square $p < 0.001$; p for trend < 0.001). When equivocal PSMA-RADS 3 findings were included, the corresponding rates were 33.3% (5/15), 50.0% (8/16), 57.1% (4/7), 66.7% (8/12) and 93.0% (53/57). The gap between the two definitions was largest in the low PSA strata: among the 38 patients with PSA < 1.0 ng/mL, 11 had only PSMA-RADS 3 lesions compared with 6 who had PSMA-RADS 4–5 lesions. The rate of distant metastasis rose from 6.7% (1/15) to 43.9% (25/57) across the strata ($p = 0.009$; p for trend < 0.001). Using dichotomous cut-offs, the scan was positive in 16.1% (5/31) versus 67.1% (51/76) of patients below and above 0.5 ng/mL, in 15.8% (6/38) versus 72.5% (50/69) at 1.0 ng/mL, and in 24.0% (12/50) versus 77.2% (44/57) at 2.0 ng/mL (all $p < 0.001$). Median PSA increased stepwise from PSMA-RADS 1–2 (0.33 ng/mL, IQR 0.11–1.05) to PSMA-RADS 3 (1.28, IQR 0.36–3.67) and PSMA-RADS 4–5 scans (5.92, IQR 2.24–10.84; Kruskal–Wallis $p < 0.001$).

PSA alone discriminated positive from negative scans with an AUC of 0.84 (95% CI 0.76–0.91) and distant metastasis with an AUC of 0.78 (Fig. 3). The Youden-optimal threshold was 1.27 ng/mL (sensitivity 89.3%, specificity 66.7%); the pre-specified cut-offs of 0.5, 1.0 and 2.0 ng/mL yielded sensitivities of 91.1%, 89.3% and 78.6% with specificities of 51.0%, 62.7% and 74.5%, respectively.

Table 2

Patient-level detection rate of ^{68}Ga-PSMA PET/CT according to serum PSA at the time of imaging (N = 107)

PSA (ng/mL)	n	PSMA-RADS 4–5 (positive), n (%; 95% CI)	Any PSMA-RADS 3–5 lesion, n (%; 95% CI)	Distant metastasis (miM1), n (%; 95% CI)
< 0.2	15	1 (6.7; 1.2–29.8)	5 (33.3; 15.2–58.3)	1 (6.7; 1.2–29.8)
0.2–< 0.5	16	4 (25.0; 10.2–49.5)	8 (50.0; 28.0–72.0)	2 (12.5; 3.5–36.0)
0.5–< 1.0	7	1 (14.3; 2.6–51.3)	4 (57.1; 25.0–84.2)	1 (14.3; 2.6–51.3)
1.0–< 2.0	12	6 (50.0; 25.4–74.6)	8 (66.7; 39.1–86.2)	2 (16.7; 4.7–44.8)
≥ 2.0	57	44 (77.2; 64.8–86.2)	53 (93.0; 83.3–97.2)	25 (43.9; 31.8–56.7)
Total	**107**	**56 (52.3; 43.0–61.6)**	**78 (72.9; 63.8–80.4)**	**31 (29.0; 21.2–38.2)**
p (chi-square / Fisher)		< 0.001	< 0.001	0.009
p for trend (Cochran–Armitage)		< 0.001	< 0.001	< 0.001
Dichotomous cut-offs				
< 0.5 vs ≥ 0.5	31 / 76	5 (16.1) vs 51 (67.1); p < 0.001	13 (41.9) vs 65 (85.5); p < 0.001	3 (9.7) vs 28 (36.8); p = 0.005
< 1.0 vs ≥ 1.0	38 / 69	6 (15.8) vs 50 (72.5); p < 0.001	17 (44.7) vs 61 (88.4); p < 0.001	4 (10.5) vs 27 (39.1); p = 0.002
< 2.0 vs ≥ 2.0	50 / 57	12 (24.0) vs 44 (77.2); p < 0.001	25 (50.0) vs 53 (93.0); p < 0.001	6 (12.0) vs 25 (43.9); p < 0.001

CI, Wilson 95% confidence interval. Positive scan: at least one PSMA-RADS 4–5 lesion in any compartment. Distant metastasis: PSMA-RADS 4–5 lesion in extrapelvic nodes, bone or viscera.

3.3. Compartment-specific detection according to PSA level

The PSA dependence differed between compartments (Table 3). Local recurrence was essentially confined to patients with PSA ≥ 1.0 ng/mL (33/34 cases) and its frequency rose steeply to 49.1% (28/57) at PSA ≥ 2.0 ng/mL (p < 0.001; p for trend < 0.001). Pelvic nodal metastasis also increased with PSA (p = 0.032; p for trend = 0.010), with 85.0% (17/20) of cases occurring at PSA ≥ 2.0 ng/mL. By contrast, bone metastasis was distributed across all strata, including one patient with PSA < 0.2 ng/mL and 6.5% (2/31) of patients with PSA < 0.5 ng/mL; the chi-square test across strata was not significant (p = 0.332)

although a monotonic trend was present (p for trend = 0.036). Extrapelvic nodal metastasis clustered at PSA ≥ 2.0 ng/mL (85.7%, 12/14) but the difference across strata did not reach significance (p = 0.124). Overall, 9.7% (3/31) of patients with PSA < 0.5 ng/mL already had distant metastasis on PET/CT.

Table 3
Compartment-specific detection of PSMA-RADS 4–5 lesions according to serum PSA at the time of imaging (N = 107)

PSA (ng/mL)	n	Prostate bed, n (%)	Pelvic nodes (miN1), n (%)	Extrapelvic nodes (miM1a), n (%)	Bone (miM1b), n (%)	Viscera (miM1c), n (%)
< 0.2	15	0 (0.0)	1 (6.7)	1 (6.7)	1 (6.7)	1 (6.7)
0.2–< 0.5	16	1 (6.3)	1 (6.3)	1 (6.3)	1 (6.3)	0 (0.0)
0.5–< 1.0	7	0 (0.0)	1 (14.3)	0 (0.0)	1 (14.3)	0 (0.0)
1.0–< 2.0	12	5 (41.7)	0 (0.0)	0 (0.0)	2 (16.7)	0 (0.0)
≥ 2.0	57	28 (49.1)	17 (29.8)	12 (21.1)	14 (24.6)	4 (7.0)
Total	**107**	**34 (31.8)**	**20 (18.7)**	**14 (13.1)**	**19 (17.8)**	**5 (4.7)**
Share of cases at PSA ≥ 2.0 ng/mL		82.4% (28/34)	85.0% (17/20)	85.7% (12/14)	73.7% (14/19)	80.0% (4/5)
p (chi-square / Fisher)		< 0.001	0.032	0.124	0.332	0.635
p for trend		< 0.001	0.010	0.051	0.036	0.503

Percentages are column-wise within each PSA stratum. Equivocal PSMA-RADS 3 findings were not counted as involvement: 8 additional patients had PSMA-RADS 3A findings in the prostate bed, 26 in pelvic nodes, 11 in extrapelvic nodes, 7 in bone (PSMA-RADS 3B) and 2 in viscera.

3.4. Predictors of a positive scan and of distant metastasis

In univariable analysis (Table 4), a positive scan was associated with higher PSA (OR 6.99 per 10-fold increase, 95% CI 3.20–15.28), older age (OR 1.09 per year, 95% CI 1.03–1.15) and a longer interval from surgery (OR 2.07 per 10-fold increase in months, 95% CI 1.03–4.16), but not with prior treatment or ISUP grade group. In the full-cohort multivariable model, PSA (OR 6.93, 95% CI 3.05–15.75; equivalent to OR 1.79, 95% CI 1.40–2.29, per doubling of PSA) and age (OR 1.09, 95% CI 1.01–1.17) remained independent predictors, whereas the interval from surgery did not. Results were similar in the model including ISUP grade group (n = 83; PSA OR 6.48, 95% CI 2.66–15.81; McFadden pseudo-R^2 0.30). For distant metastasis, PSA (OR 4.34, 95% CI 1.88–10.01) and ISUP grade group 4–5 (OR 12.57, 95% CI 3.27–48.23) were independent predictors, while age, interval and prior treatment were not; notably, the

rate of distant metastasis in ISUP 4–5 was 50.0% (18/36) compared with 10.6% (5/47) in ISUP 1–3 despite similar PSA levels (median 1.60 vs 2.15 ng/mL, p = 0.974).

Table 4

Univariable and multivariable logistic regression for a positive ^{68}Ga-PSMA PET/CT (PSMA-RADS 4–5) and for distant metastasis

Variable	Positive scan (56/107 events)		Distant metastasis (31/107 events)	
	Univariable OR (95% CI); p	Multivariable[a] OR (95% CI); p	Univariable OR (95% CI); p	Multivariable[a] OR (95% CI); p
PSA at imaging, per 10-fold increase	6.99 (3.20–15.28); < 0.001	6.48 (2.66–15.81); < 0.001	4.47 (2.09–9.58); < 0.001	4.34 (1.88–10.01); 0.001
Age, per year	1.09 (1.03–1.15); 0.005	1.08 (1.00–1.17); 0.056	1.04 (0.98–1.10); 0.233	1.02 (0.93–1.12); 0.618
Interval from surgery, per 10-fold increase (months)	2.07 (1.03–4.16); 0.041	1.81 (0.58–5.66); 0.308	1.59 (0.74–3.44); 0.236	0.87 (0.26–2.87); 0.814
Prior post-operative treatment (yes vs no)	1.98 (0.88–4.46); 0.098	1.30 (0.35–4.93); 0.695	3.18 (1.34–7.57); 0.009	2.20 (0.52–9.32); 0.287
ISUP grade group 4–5 vs 1–3 (n = 83)	1.42 (0.59–3.40); 0.430	2.14 (0.67–6.87); 0.199	8.40 (2.70–26.11); < 0.001	12.57 (3.27–48.23); < 0.001

OR, odds ratio; CI, confidence interval. [a] Multivariable models restricted to the 83 patients with ISUP grade group available. In the full cohort (n = 107, without ISUP), the multivariable OR for PSA was 6.93 (3.05–15.75) for a positive scan and 4.00 (1.90–8.44) for distant metastasis; age remained significant for a positive scan (OR 1.09, 1.01–1.17; p = 0.021).

3.5. Relationship between PSA and lesion SUVmax

Seventy-seven patients had at least one PSMA-avid lesion suitable for SUVmax analysis (56 PSMA-RADS 4–5 and 21 PSMA-RADS 3A/3B; the single PSMA-RADS 3D case without uptake was excluded). The highest lesion SUVmax increased across PSA strata, with medians of 2.4, 4.8, 6.5, 11.0 and 17.9 in the five strata (Kruskal–Wallis p = 0.001), and was approximately three times higher in patients with PSA ≥ 0.5 ng/mL than in those with PSA < 0.5 ng/mL (11.9 [IQR 7.9–28.7] versus 4.0 [2.4–6.7]; p < 0.001). However, SUVmax was far more strongly determined by lesion category: the median was 4.0 (IQR 2.4–4.8) in PSMA-RADS 3 scans and 16.6 (8.9–33.3) in PSMA-RADS 4–5 scans (p < 0.001), and 9.5 and 28.5 in overall PSMA-RADS 4 and 5, respectively. Among PSMA-RADS 4–5 scans alone, the gradient across PSA strata was attenuated (medians 13.0, 6.1, 8.8, 11.5 and 22.7; p = 0.061).

PSA correlated moderately with the highest lesion SUVmax in all 77 patients (Spearman ρ = 0.461, 95% CI 0.25–0.63; p < 0.001; Fig. 2a). The correlation weakened to ρ = 0.311 (95% CI 0.04–0.55; p = 0.020) when restricted to the 56 PSMA-RADS 4–5 scans and was absent within the 21 PSMA-RADS 3 scans (ρ

= 0.253; p = 0.268), indicating that a substantial part of the overall association arose from the contrast between low-PSA patients with equivocal, low-uptake lesions and high-PSA patients with definite lesions. The correlation was considerably stronger below 2.0 ng/mL (ρ = 0.596, 95% CI 0.23–0.84; n = 24; p = 0.002) than at or above 2.0 ng/mL (ρ = 0.213, 95% CI − 0.07–0.47; n = 53; p = 0.127), and was similar in patients with (ρ = 0.397) and without (ρ = 0.395) ongoing ADT. Among positive scans, PSA also correlated with the number of involved compartments (ρ = 0.338; p = 0.011).

At the compartment level (Table 5, Fig. 2b), PSA was not significantly correlated with the SUVmax of PSMA-RADS 4–5 lesions in any compartment: pelvic nodes ρ = 0.427 (95% CI − 0.04–0.77; n = 20; p = 0.060), bone ρ = 0.256 (n = 19; p = 0.290), prostate bed ρ = 0.199 (n = 34; p = 0.260) and extrapelvic nodes ρ = 0.182 (n = 14; p = 0.533). When equivocal lesions were included in each compartment, the pelvic nodal correlation became nominally significant (ρ = 0.327; n = 46; p = 0.026) but the other compartments did not. In multivariable linear regression, log10 SUVmax increased by 0.156 (95% CI 0.044–0.267; p = 0.007) per unit increase in log10 PSA after adjustment for lesion category, ADT and distant metastasis, corresponding to a 43% (95% CI 11–85%) higher SUVmax per 10-fold increase in PSA; lesion category was the dominant term (β = 0.457, p < 0.001, i.e. 2.9-fold higher SUVmax for PSMA-RADS 4–5 versus 3), ADT showed a borderline positive association (β = 0.137, p = 0.084) and distant metastasis none (p = 0.187). The model explained 53% of the variance in log SUVmax, compared with 25% for PSA alone.

Table 5
Highest lesion SUVmax according to PSA level and Spearman correlation between PSA and SUVmax, overall and by compartment

Analysis set	n	SUVmax, median (IQR)	Spearman ρ (95% CI)	p
SUVmax by PSA stratum (all PSMA-avid patients)				
< 0.2 ng/mL	5	2.4 (2.0–4.0)		
0.2–< 0.5 ng/mL	8	4.8 (3.6–6.7)		
0.5–< 1.0 ng/mL	4	6.5 (3.7–10.8)		
1.0–< 2.0 ng/mL	7	11.0 (8.4–14.8)		
≥ 2.0 ng/mL	53	17.9 (7.7–33.6)		0.001[b]
Patient-level correlation (highest lesion SUVmax)				
All PSMA-avid patients (PSMA-RADS 3–5)	77	10.1 (5.1–25.3)	0.461 (0.25–0.63)	< 0.001
PSMA-RADS 4–5 scans	56	16.6 (8.9–33.3)	0.311 (0.04–0.55)	0.020
PSMA-RADS 3 scans	21	4.0 (2.4–4.8)	0.253 (− 0.26–0.68)	0.268
PSA < 2.0 ng/mL	24	6.8 (3.6–11.5)	0.596 (0.23–0.84)	0.002
PSA ≥ 2.0 ng/mL	53	17.9 (7.7–33.6)	0.213 (− 0.07–0.47)	0.127
No ongoing ADT	50	8.5 (4.2–19.8)	0.395 (0.10–0.63)	0.005
Ongoing ADT	27	13.0 (9.0–46.2)	0.397 (− 0.02–0.72)	0.041
Compartment-level correlation (PSMA-RADS 4–5 lesions)				
Prostate bed	34	11.0 (8.2–23.2)	0.199 (− 0.15–0.51)	0.260
Pelvic nodes (miN1)	20	19.1 (11.6–29.6)	0.427 (− 0.04–0.77)	0.060
Extrapelvic nodes (miM1a)	14	17.4 (11.6–43.0)	0.182 (− 0.43–0.71)	0.533
Bone (miM1b)	19	10.7 (8.5–28.1)	0.256 (− 0.25–0.68)	0.290
Compartment-level correlation including PSMA-RADS 3 lesions				
Prostate bed	42	—	0.268 (− 0.07–0.55)	0.086

Analysis set	n	SUVmax, median (IQR)	Spearman ρ (95% CI)	p
SUVmax by PSA stratum (all PSMA-avid patients)				
Pelvic nodes (miN1)	46	—	0.327 (0.04–0.57)	0.026
Extrapelvic nodes (miM1a)	24	—	0.316 (− 0.11–0.67)	0.133
Bone (miM1b)	26	—	0.371 (− 0.01–0.67)	0.062

IQR, interquartile range; CI, 5,000-sample bootstrap percentile confidence interval; ADT, androgen deprivation therapy. [b] *Kruskal–Wallis test across the five strata. The median SUVmax for the 77 PSMA-avid patients is given for descriptive purposes; the visceral compartment (n = 5) was not analysed.*

4. DISCUSSION

In this consecutive single-centre cohort of 107 Vietnamese men imaged after RP, serum PSA at the time of ^{68}Ga-PSMA PET/CT was a strong and independent predictor of whether the scan localised disease, with a positivity rate that rose from 7% below 0.2 ng/mL to 77% at or above 2.0 ng/mL and an AUC of 0.84. In contrast, PSA was only weakly related to how intensely the detected lesions accumulated the tracer: the correlation with the highest lesion SUVmax was moderate overall, was attenuated once equivocal lesions were set aside, was not significant within any single compartment, and translated into only a 43% increase in SUVmax per 10-fold rise in PSA after adjustment for lesion category. To our knowledge this is the first study to report PSA-stratified detection rates with PSMA-RADS 2.0 separately for each compartment together with compartment-level PSA–SUVmax correlations.

4.1. Detection rate across PSA strata

The PSA-dependent detection curve observed here closely parallels those of the large Western series despite differences in tracer, definition of positivity and case mix. When equivocal lesions were included, our rates of 33%, 50%, 57%, 67% and 93% across the five strata lie within the ranges reported by Afshar-Oromieh et al. (43%, 58%, 72% and up to 93%) [7], Eiber et al. (58%, 73%, 93% and 97% for 0.2–< 0.5, 0.5–< 1, 1–< 2 and ≥ 2 ng/mL) [10], the prospective trial of Fendler et al. (38% at < 0.5 and 97% at ≥ 5.0 ng/mL) [8], the CONDOR trial (36% at < 0.5 and 97% at ≥ 5.0 ng/mL) [9] and the PSMA-RADS 2.0-based series of Masselli et al. (38%, 57%, 77% and 95%) [14]. Our strict positivity rates were approximately 20 percentage points lower, and the difference was entirely attributable to PSMA-RADS 3 findings, which accounted for two thirds of all detected abnormalities in patients with PSA < 1.0 ng/mL. This observation has practical consequences: the headline "detection rate" of PSMA PET at very low PSA levels in the literature [24, 25] includes a sizeable fraction of lesions whose malignant nature is uncertain, and reporting the two tiers separately, as recommended by PSMA-RADS 2.0 [13], gives referring clinicians a more honest estimate of what a scan at a given PSA level is likely to deliver. The lower overall rate in our

cohort was also influenced by the choice of a conservative threshold rather than by a lower sensitivity of the technique, since median PSA (2.24 ng/mL) was comparable to or higher than in most of the comparator series [8, 10, 20].

The non-monotonic dip at 0.5–< 1.0 ng/mL (1/7 positive) reflects small numbers rather than a biological phenomenon, as shown by the significant trend tests and by the smooth increase in median PSA from negative to equivocal to positive scans. The pre-specified cut-offs behaved as expected: a threshold of 1.0 ng/mL retained 89% sensitivity for a positive scan while excluding 63% of negative scans, which is consistent with the ROC-derived thresholds of 0.8–1.3 ng/mL in earlier reports [11]. These figures should not, however, be used to withhold imaging below the threshold, because 16% of patients with PSA < 0.5 ng/mL had a definite lesion and 10% already had distant metastasis, in line with the 34% detection rate and frequent extrapelvic disease reported by others at this PSA level [24–26]. Current guidelines therefore recommend PSMA PET as soon as BCR is confirmed when the result could change management [4, 5], and our data support that position in a Southeast Asian setting.

4.2. Compartment-specific patterns

Stratifying by compartment revealed that the PSA dependence is not uniform. Local recurrence was almost exclusively detected at PSA ≥ 1.0 ng/mL, and 82% of cases occurred at ≥ 2.0 ng/mL, which is consistent with the relatively large size of prostate bed recurrences in our series (median 16.5 mm) and with the known limitation of PET in detecting small lesions adjacent to the bladder [27, 28]. Pelvic nodal metastasis also increased with PSA, as in the PREP cohort where PSA was the strongest predictor of nodal and distant disease [29]. Bone metastases, by contrast, were found across the whole PSA range and the chi-square test across strata was not significant; together with the finding that ISUP grade group 4–5 carried a 12-fold higher adjusted odds of distant metastasis at similar PSA levels, this suggests that in poorly differentiated tumours the PSA level underestimates the metastatic burden. Verburg et al. similarly showed that Gleason score and PSA independently determined the extent of disease on PSMA PET [30], and Afshar-Oromieh et al. identified Gleason score as an independent predictor of a positive scan [7]. The clinical message is that a low PSA does not exclude osseous metastasis in high-grade disease, and that PSMA PET/CT, which outperforms bone scintigraphy and CT for skeletal and nodal staging [31, 32], is justified before committing such patients to prostate bed salvage radiotherapy alone.

Older age and a longer interval from surgery were associated with a positive scan in univariable analysis, but only age remained marginally significant after adjustment for PSA. Later imaging after surgery probably captures patients with slower PSA kinetics who were referred late at higher PSA levels; we could not analyse PSA doubling time, which has been shown to add to PSA level in predicting positivity [11], because serial PSA values before referral were not systematically available. Patients imaged under ADT had higher rates of distant metastasis but not of a positive scan after adjustment, most plausibly because this group consisted largely of men progressing on therapy rather than because ADT itself enhanced PSMA expression.

4.3. PSA and lesion SUVmax

The moderate overall correlation between PSA and the highest lesion SUVmax (ρ = 0.46) is in line with previous reports in the primary tumour (r = 0.42 in Uprimny et al.) [15, 16] and in recurrent disease, where Fragkiadaki et al. found correlations of 0.33–0.45 between PSA and both SUVmax and total PSMA tumour volume [17]. Our analysis adds three nuances. First, much of the association was generated by the contrast between equivocal, low-uptake lesions in low-PSA patients and definite lesions in high-PSA patients; within PSMA-RADS 4–5 scans the correlation fell to 0.31, and within PSMA-RADS 3 scans it was absent. Second, the correlation was strong below 2.0 ng/mL (ρ = 0.60) but weak above it (ρ = 0.21), which is biologically plausible: at low PSA the burden is usually a single lesion whose uptake tracks the number of secreting cells, whereas at higher PSA the burden is distributed across several lesions and compartments, so that the SUVmax of the most avid lesion no longer reflects the total tumour load; indeed, PSA correlated with the number of involved compartments among positive scans. Third, no compartment showed a significant correlation in the strict PSMA-RADS 4–5 analysis, the strongest trend being in pelvic nodes (ρ = 0.43, p = 0.06). The weak local correlation may additionally reflect contamination of prostate bed SUVmax by urinary activity and partial-volume effects in small lesions [28, 33]. After adjustment, lesion category explained far more of the variance in SUVmax than PSA did, and SUVmax differed almost three-fold between PSMA-RADS 4–5 and PSMA-RADS 3 scans, confirming that uptake intensity is primarily a property of the lesion rather than of the serum marker.

These findings have two implications. PSA cannot be used to anticipate the SUVmax of a lesion, and SUVmax therefore carries information that PSA does not; this is consistent with the independent prognostic value of SUVmax for outcome after PSMA PET-guided salvage radiotherapy [18, 19] and for BCR after RP [34]. Conversely, a low SUVmax in a patient with a high PSA should prompt a search for additional disease rather than reassurance, because the index lesion may represent only a fraction of the burden. Whether total PSMA tumour volume, which integrates uptake across all lesions, correlates more closely with PSA than SUVmax in this population is a question for future work [17].

4.4. Strengths and limitations

Strengths of this study include the consecutive enrolment, the uniform re-reading of all scans with PSMA-RADS 2.0 and the PROMISE compartment structure, the explicit two-tier reporting of definite and equivocal findings, and the use of bootstrap intervals and adjusted models rather than unadjusted correlations alone. It is also one of the few PSMA PET/CT series from Southeast Asia [20], where surgical cohorts contain a high proportion of high-risk disease and limited lymph node dissection [21].

Several limitations must be acknowledged. First, the design was retrospective and single-centre, and no histological or follow-up reference standard was available; we therefore report positivity and detection rates rather than sensitivity or positive predictive value, and some PSMA-RADS 3 findings will have been true metastases while a few PSMA-RADS 4 findings may have been benign [13, 14]. Second, pathology data were missing in 22% of patients and PSA kinetics were unavailable, which limited the multivariable models; with 56 and 31 events the models were deliberately parsimonious and the ISUP-adjusted estimates have wide confidence intervals. Third, 26% of patients did not strictly meet the standard definitions of BCR or PSA persistence, and one third had received prior treatment, reflecting the real-

world referral pattern in our setting but reducing homogeneity [35]. Fourth, SUVmax is sensitive to scanner, reconstruction, uptake time and lesion size, and we analysed a single representative lesion per compartment rather than all lesions or volumetric parameters. Fifth, the compartment-level correlation analyses had small sample sizes and were exploratory; the confidence intervals in Table 5 are wide and the absence of significance should not be read as proof of absence. Finally, the readers were the study authors and had access to clinical information, as in routine reporting; although discrepancies were resolved by consensus, formal inter-reader agreement was not assessed, and knowledge of the PSA level may have influenced PSMA-RADS assignment, particularly for equivocal lesions.

5. CONCLUSION

Serum PSA at the time of imaging is the dominant determinant of whether ^{68}Ga-PSMA PET/CT localises disease after radical prostatectomy, with a positivity rate rising from 7% below 0.2 ng/mL to 77% at or above 2.0 ng/mL under a strict PSMA-RADS 4–5 definition, and it remains an independent predictor after adjustment for age, interval from surgery, prior treatment and tumour grade. The PSA dependence is strongest for local recurrence and pelvic nodal disease, whereas bone metastases occur across the PSA range and are driven mainly by tumour grade. PSA correlates only moderately with the highest lesion SUVmax and not significantly with SUVmax within any individual compartment; lesion category explains most of the variation in uptake. PSA should therefore guide the timing of PSMA PET/CT, but it cannot replace imaging for characterising lesions, quantifying uptake or excluding early metastatic disease, and PSMA PET/CT should be offered early in the course of biochemical recurrence, particularly in men with high-grade tumours.

Abbreviations

ADT, androgen deprivation therapy; AUC, area under the receiver operating characteristic curve; BCR, biochemical recurrence; CI, confidence interval; IQR, interquartile range; ISUP, International Society of Urological Pathology; miTNM, molecular imaging TNM (PROMISE); OR, odds ratio; PET/CT, positron emission tomography/computed tomography; PROMISE, Prostate Cancer Molecular Imaging Standardized Evaluation; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; PSMA-RADS, PSMA Reporting and Data System; RP, radical prostatectomy; SD, standard deviation; SUVmax, maximum standardised uptake value.

Declarations

Human Ethics and Consent to Participate: The study protocol ("The role of ^{68}Ga-PSMA PET/CT in the evaluation of prostate cancer after surgery"; principal investigator Tuan A. Nguyen) was reviewed and approved by the Ethics Committee in Biomedical Research of Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam (approval No. 1495/TĐHYKPNT-HĐĐĐ, dated 28 November 2025; expedited review). All procedures were performed in accordance with the Declaration of Helsinki and the ethical standards of the institutional research committee. Because the study was a retrospective analysis of

pseudonymised data from examinations performed as part of routine clinical care, the Ethics Committee in Biomedical Research of Pham Ngoc Thach University of Medicine waived the requirement for written informed consent to participate.

Consent for publication: Not applicable. The manuscript does not contain any individual person's data, images or details that could allow identification of an individual.

Competing interests: The authors declare that they have no competing interests.

Funding: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Authors' contributions: Tuan Anh Nguyen: conceptualisation, methodology, image interpretation, data curation, formal analysis, writing – original draft. Canh Xuan Nguyen: conceptualisation, image interpretation, validation, supervision, writing – review and editing. Both authors read and approved the final manuscript.

Availability of data and materials: The pseudonymised dataset analysed during the current study is available from the corresponding author on reasonable request, subject to approval by the institutional ethics committee.

Acknowledgements: The authors thank the physicians, technologists and radiochemists of the PET/CT and Cyclotron Unit, Department of Nuclear Medicine, Cho Ray Hospital, for their assistance with image acquisition and data collection.

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Figures

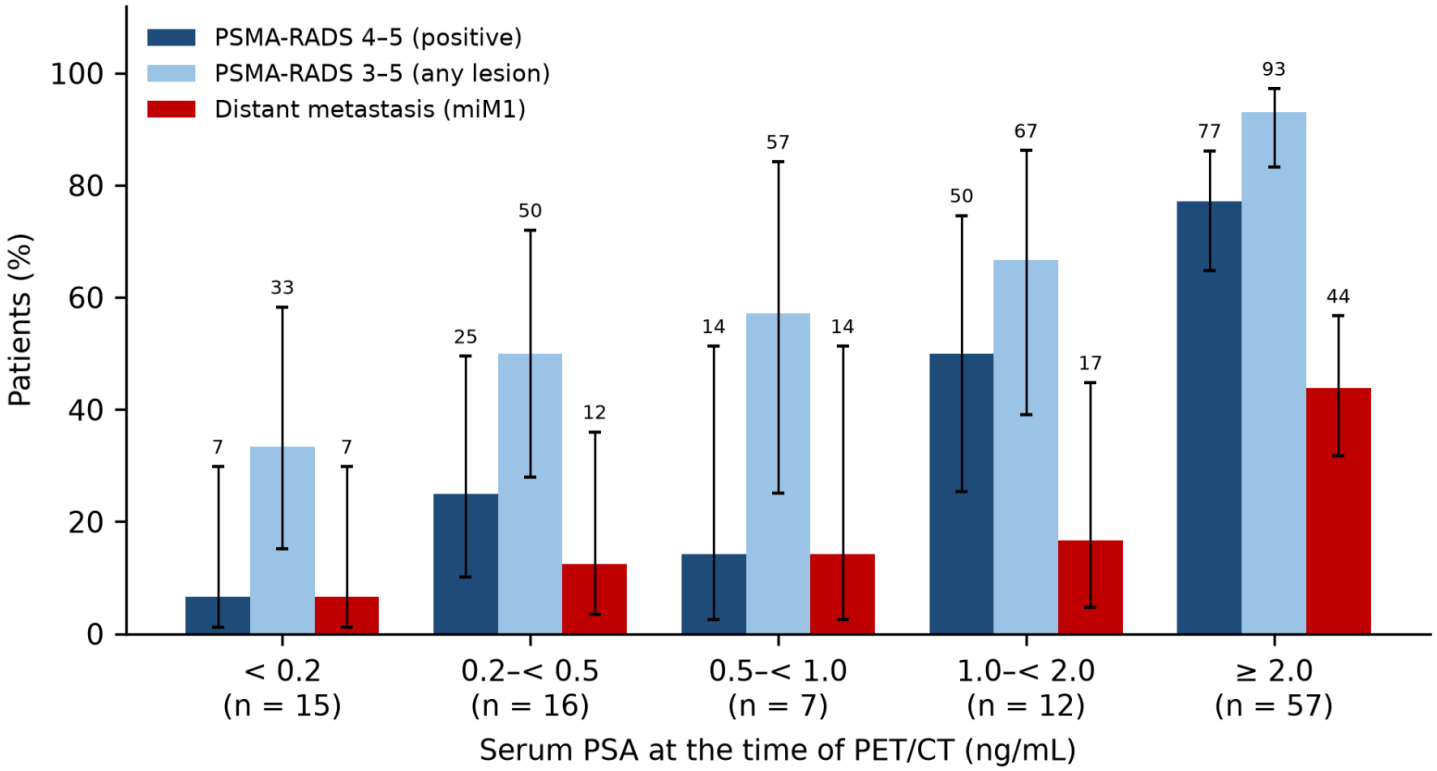

Figure 1

Detection rate of ^{68}Ga-PSMA PET/CT according to serum PSA at the time of imaging (N = 107). Bars show the percentage of patients with a positive scan (PSMA-RADS 4–5), with any PSMA-RADS 3–5 lesion and with distant metastasis in each PSA stratum; error bars are Wilson 95% confidence intervals. All three indices increased across strata (p for trend < 0.001).

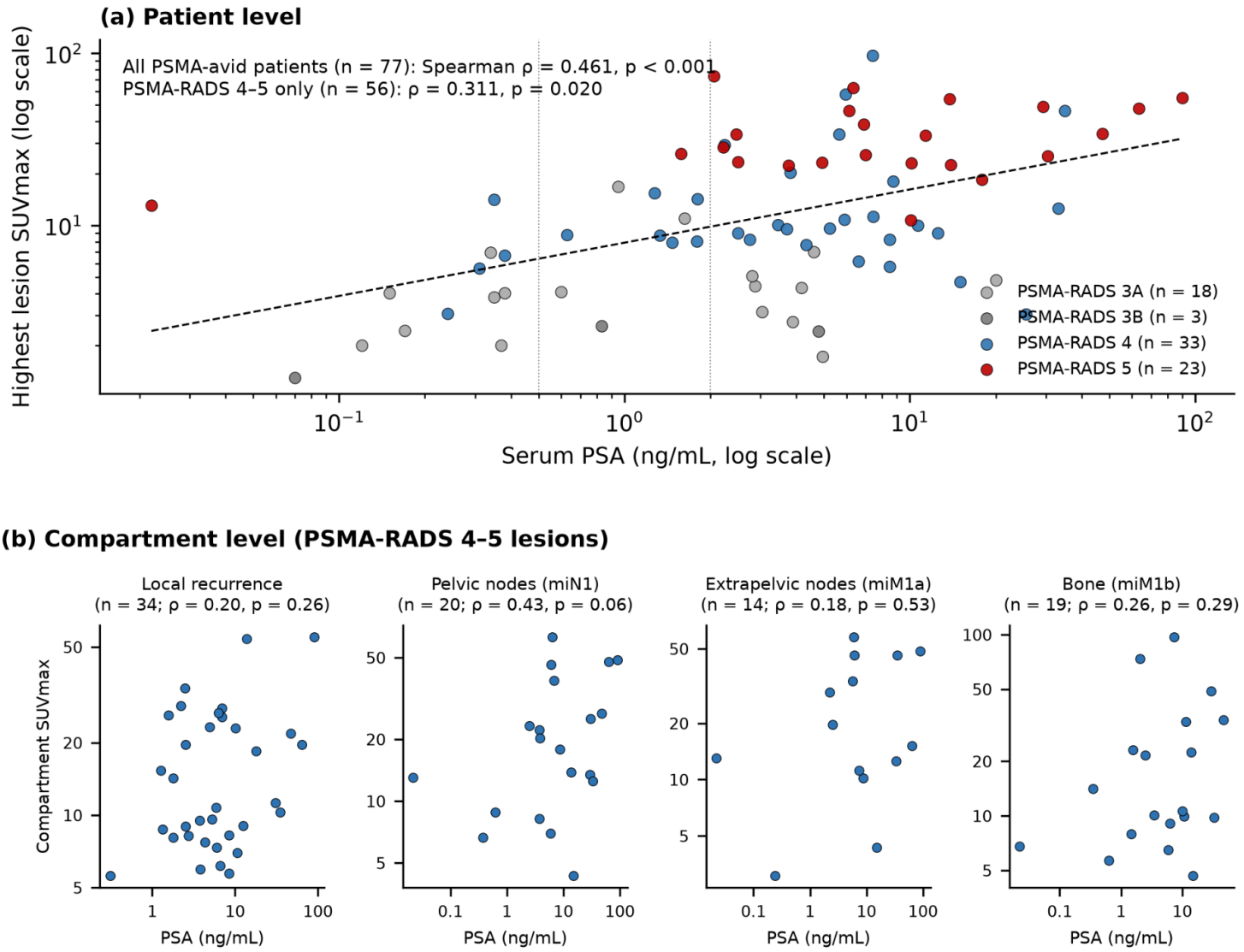

Figure 2

Relationship between serum PSA and lesion SUVmax on ^{68}Ga-PSMA PET/CT (log–log scales). (a) Highest lesion SUVmax per patient in the 77 patients with PSMA-avid lesions, coloured by overall PSMA-RADS category; the dashed line is the least-squares fit of log SUVmax on log PSA and the dotted vertical lines mark 0.5 and 2.0 ng/mL. Patients with PSMA-RADS 3 scans cluster at low PSA and low SUVmax, whereas PSMA-RADS 4–5 scans are widely dispersed at PSA ≥ 2.0 ng/mL. (b) Compartment-level SUVmax of PSMA-RADS 4–5 lesions versus PSA for the prostate bed, pelvic nodes, extrapelvic nodes and bone; no compartment showed a significant correlation.

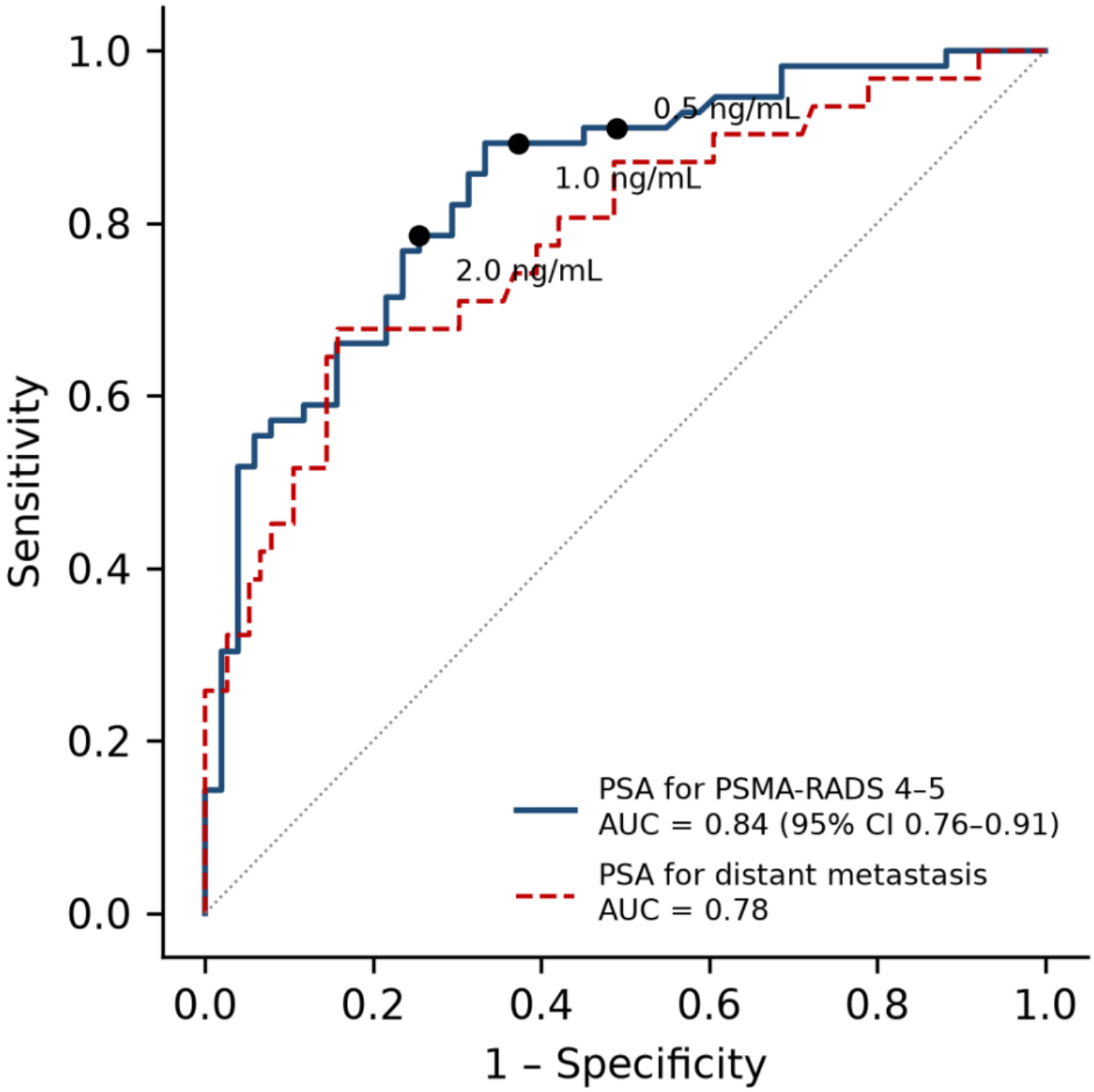

Figure 3

Receiver operating characteristic curves of serum PSA at the time of imaging for predicting a positive ^{68}Ga-PSMA PET/CT (PSMA-RADS 4–5; solid line, AUC 0.84, 95% CI 0.76–0.91) and distant metastasis (dashed line, AUC 0.78). Black dots mark the operating points of the 0.5, 1.0 and 2.0 ng/mL cut-offs for a positive scan.