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ORIGINAL ARTICLE

^{68}Ga-PSMA PET/CT in patients with recurrent prostate cancer after radical treatment: prospective results in 314 patients

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Abstract

Purpose We studied the usefulness of ^{68}Ga-prostate-specific membrane antigen (PSMA) PET/CT for detecting relapse in a prospective series of patients with biochemical recurrence (BCR) of prostate cancer (PCa) after radical treatment.

Methods Patients with BCR of PCa after radical surgery and/or radiotherapy with or without androgen-deprivation therapy were included in the study. ^{68}Ga-PSMA PET/CT scans performed from the top of the head to the mid-thigh 60 min after intravenous injection of 150 ± 50 MBq of ^{68}Ga-PSMA were interpreted by two nuclear medicine physicians. The results were correlated with prostate-specific antigen (PSA) levels at the time of the scan (PSApet), PSA doubling time, Gleason score, tumour stage, postsurgery tumour residue, time from primary therapy to BCR, and patient age. When available, ^{68}Ga-PSMA PET/CT scans were compared with negative ^{18}F-choline PET/CT scans routinely performed up to 1 month previously.

Results From November 2015 to October 2017, 314 PCa patients with BCR were evaluated. Their median age was 70 years (range 44–92 years) and their median PSApet was 0.83 ng/ml (range 0.003–80.0 ng/ml). ^{68}Ga-PSMA PET/CT was positive (one or more suspected PCa lesions detected) in 197 patients (62.7%). Lesions limited to the pelvis, i.e. the prostate/prostate bed and/or pelvic lymph nodes (LNs), were detected in 117 patients (59.4%). At least one distant lesion (LNs, bone, other organs, separately or combined with local lesions) was detected in 80 patients (40.6%). PSApet was higher in PET-positive than in PET-negative patients ($P < 0.0001$). Of 88 patients negative on choline PET/CT scans, 59 (67%) were positive on ^{68}Ga-PSMA PET/CT.

Conclusion We confirmed the value of ^{68}Ga-PSMA PET/CT in restaging PCa patients with BCR, highlighting its superior performance and safety compared with choline PET/CT. Higher PSApet was associated with a higher relapse detection rate.

Keywords PSMA · PET/CT · Prostate cancer · Biochemical recurrence · PSA

Introduction

Prostate cancer (PCa) is the second most frequent cancer and the fifth leading cause of cancer death in men worldwide [1]. PCa biochemical recurrence after primary treatment (BCR), defined as a prostate-specific antigen (PSA) level of >0.2 ng/ml after radical prostatectomy (RP) and a PSA level of >2 ng/ml above the PSA nadir after radiotherapy (RT), occurs in 20–30% of patients after surgery and in up to 60% of patients after primary external

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beam therapy [2, 3]. Conventional imaging modalities including transrectal ultrasonography (TRUS), computed tomography (CT), magnetic resonance imaging (MRI) and bone scintigraphy, are not always effective for the early and reliable detection of PCa relapse. The sensitivity of morphological imaging (TRUS and CT) in detecting local PCa relapse is relatively low (25–54%) and is only moderately improved by functional MRI techniques [4]. Thus, new molecular imaging modalities with improved specificity and sensitivity for recurrent PCa, especially at low PSA levels, are of particular clinical interest. In the last decade ^{11}C-choline and/or ^{18}F-choline positron emission tomography (PET)/CT has been widely studied and used for PCa restaging, but its value for the detection of recurrent PCa is limited in patients with a PSA level <2.5 ng/ml [5–9]. In patients with a PSA level <1.0 ng/ml, the probability of a positive choline PET/CT scan is only 19% and may be as low as 12.5% when the PSA level is <0.5 ng/ml [5].

In this context, prostate-specific membrane antigen (PSMA) has received increasing attention in recent years. PSMA is a transmembrane enzyme that is significantly overexpressed in the majority of prostatic adenocarcinomas. PSMA expression levels rise as tumour dedifferentiation increases in metastatic and hormone-refractory cancers [10–12]. Despite its name, PSMA is not specific to prostate tissue. Its physiological expression is also seen in other tissues such as the brain, kidney, salivary glands, liver, ganglia and small intestine [10, 13]. In the late 1990s it was found that the neovasculature of many solid tumours also expresses PSMA [13]. Recently, there have been many reports of the uptake of PSMA ligands in various nonprostate tissues [14–26].

Radiotracers targeting markers of PCa cells show enormous potential and PSMA is currently a 'hot topic' in this field. In 2011, ^{68}Ga-PSMA-11 (also known as HBED-CC, Glu-urea-Lys(Ahx)-HBED-CC, or PSMA-HBED-CC) was introduced for the clinical imaging of PCa. Since then, PET using ^{68}Ga-PSMA-11 has been regarded as an important step forward in the diagnosis of recurrent PCa. However, the majority of published studies are retrospective. The first reports indicated that this novel method is significantly superior to alternative methods used for the detection of recurrent PCa [27, 28], and subsequent studies have also confirmed the high sensitivity and specificity of ^{68}Ga-PSMA-11 PET/CT [29–32]. Possible interacting factors including PSA doubling time (PSAdt), PSA velocity (PSAvel), Gleason score (GS), ongoing androgen-deprivation therapy (ADT), patient age and amount of injected activity were prospectively analysed in cohorts of 319 and 248 patients [29, 30]. Similar studies with smaller patient cohorts have also been reported [3, 33].

In this prospective study we evaluated the usefulness of ^{68}Ga-PSMA PET/CT for detecting relapse in a large, prospective series of patients with BCR of PCa after primary radical treatment, and compared our findings with retrospective data on choline PET/CT and PSMA results.

Materials and methods

Study design and population characteristics

This was a prospective single-centre diagnostic study carried out in the Nuclear Medicine Unit of Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy, and was approved by the local ethics committee (protocol code IRST 185.02; EudraCT 2015-003397-33). The study was designed to evaluate PCa patients with BCR after RP or primary external beam RT. All patients gave written informed consent before entering the study. Enrolled patients were evaluated with ^{68}Ga-PSMA PET/CT, and local lesion recurrence limited to the pelvis (prostate bed and/or pelvic lymph nodes, LNs) was compared with systemic lesion recurrence (extrapelvic LNs and/or skeletal and/or visceral metastases). The results were compared with those obtained by ^{18}F-choline PET/CT, when available, performed as part of routine practice up to 1 month previously.

Inclusion criteria were as follows: histological or cytological confirmation of PCa, male gender, age ≥18 years, primary and radical treatment with curative intent (RP or RT) for localized PCa, negative or dubious ^{18}F-choline PET/CT, and PSA progression, defined as serum PSA level ≥0.2 ng/ml and/or an increase in serum PSA level defined as two confirmed consecutive values showing an increase at least 1 week apart. Exclusion criteria were age

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Histological or cytological confirmation of prostate cancer
	Male, aged >18 years
	Radical treatment for prostate cancer (radiotherapy or surgery)
	Negative or dubious 18F-choline PET/CT
	Patients with PSA progression defined as PSA ≥ 0.2 ng/mL and/or increased PSA defined as 2 subsequent values showing PSA increase at least 1 week apart
Exclusion criteria	Male, aged <18 years.
	Treatment with androgen deprivation therapy (ADT) ≤ 6 months before ^{68}Ga-PSMA PET/CT scan

<18 years and treatment with ADT ≤6 months before ^{68}Ga-PSMA PET/CT scan (Table 1).

Radiopharmaceutical protocol

^{68}Ga-PSMA-HBED-CC(Glu-NH-CO-NH-Lys(Ahx)-[^{68}Ga]Ga(*N*,*N*′-bis-[2-hydroxy-5-(carboxyethyl)-benzyl]ethylenediamine-*N*,*N*′-diacetic acid)) (^{68}Ga-PSMA) was prepared as described by Eder et al. [34] in accordance with national regulations and good radiopharmaceutical practice (GRP), as outlined in specific European Association of Nuclear Medicine (EANM) guidelines and *Norme di buona preparazione in medicina nucleare* (NBP MN). ^{68}Ga-PSMA was synthesized in the Radiopharmacy Unit of the Nuclear Medicine Unit at IRST IRCCS, Meldola. A mean dose of 150 ± 50 MBq of ^{68}Ga-PSMA was administered intravenously. All adverse events (AEs) reported by the patients or recorded by healthcare personnel were recorded for safety evaluation.

Imaging procedure and image analysis

^{68}Ga-PSMA PET/CT was performed using a standard technique on a dedicated 3D PET/CT system (Biograph mCT Flow; Siemens Medical Solutions, Malvern, PA, USA) at IRST IRCCS, Meldola. Patient preparation was not necessary before the procedure. PET/CT scanning was performed 50 min after intravenous injection of 100–200 MBq of ^{68}Ga-PSMA using an indwelling catheter to avoid extravasation. A low-dose CT scan (120 kV and 80 mA/s) was performed for attenuation correction of the PET emission data acquired from the mid-thigh to the top of the head. PET images were interpreted by two nuclear medicine physicians and visual interpretation was the main criterion for the final diagnosis. ^{68}Ga-PSMA uptake was considered as physiological in the following tissues: lachrymal and salivary glands, liver, spleen, small intestine, colon and kidneys. Only focal tracer uptake that was higher than that of adjacent background and not correlated with physiological tracer uptake was categorized as suggestive of PCa, and hence positive. PET-positive lesions were classified as suspected local relapse (prostate/prostate bed relapse and/or iliac LNs and/or pararectal LNs) or suspected distant relapse (retroperitoneal LNs and/or LNs above the iliac bifurcation and/or bone lesions and/or other visceral lesions).

In patients with a PSA level of >1 ng/ml, choline PET/CT was performed 45 min after intravenous injection of ^{18}F-methylcholine (3.7 MBq/kg body weight; Advanced Accelerator Applications, Venafro, Italy). Each scan was performed from the skull vertex to the mid-thigh. A low-dose unenhanced CT scan (120 kV, 80 mA) was performed for attenuation correction.

Statistical analysis

The detection rate of ^{68}Ga-PSMA PET/CT was defined as the ratio between the number of patients with a positive scan and the total number of patients who underwent the scan. Categorical variables are presented as numbers and percentages. Continuous variables are presented as means, medians and ranges. ^{68}Ga-PSMA PET/CT-positive and ^{68}Ga-PSMA PET/CT-negative patients were compared using the Wilcoxon rank-sum test for continuous variables and the chi-squared test or Fisher's exact test, as appropriate, for categorical variables. A multivariate logistic model was used to assess the association between PET/CT results (positive or negative) and demographic and clinical features. Variables that were significant in the univariate analysis, as well as nonsignificant well-established prognostic factors, were included in a multivariate model. Receiver operating characteristic (ROC) curve analysis was carried out and the area under the curve (AUC) was determined to evaluate continuous PSA levels at the time of the PET/CT scan (PSApet) as predictors of PET positivity. The Youden index was calculated to determine the cut-off values that gave the best combination of sensitivity and specificity. Age was coded as a continuous variable. PSApet values (grouped as <0.2 and ≥0.2, <0.5 and ≥0.5, <1 and ≥1, and <2 and ≥2 ng/ml), GS (<7, 7, 8 and ≥9), tumour stage (<T3 vs. ≥T3 and N0 vs. N1), residual disease after RP (R0 vs. R1), time from primary therapy to BCR (≤12 months vs. >12 months) and PSAdt were analysed as categorical variables. Box plots were used to show the distribution of continuous PSA values among ^{68}Ga-PSMA PET/CT-positive and ^{68}Ga-PSMA PET/CT-negative patients. A P value <0.05 was considered statistically significant. All analyses were carried out using STATA/MP 14.0 for Windows (StataCorp LLP, College Station, TX, USA).

Results

Patient enrolment and population characteristics

From November 2015 to October 2017, 314 PCa patients with BCR after radical primary treatment were enrolled for ^{68}Ga-PSMA PET/CT. All fulfilled the inclusion criteria for the present study. The median age of the whole patient group was 70 years (range 44–92 years). Of the 264 patients (84.1%) undergoing RP, 143 had RP alone,

Table 2 Patient characteristics

Characteristic	All patients	PSMA-positive on PET/CT	PSMA-negative on PET/CT	*P* value
Age (years)	*n* = 314	*n* = 197	*n* = 117	
Median ± SD	69.4 ± 7.36	69 ± 7.6	69 ± 7.0)	0.4208
Range	70 (44–92)	70 (45–92)	70 (44–82)	
Initial PSA (ng/ml)	*n* = 85	*n* = 56	*n* = 29	
Mean ± SD	12.3 ± 14.0)	13.5 ± 12.8)	9.9 ± 15.9)	0.0078
Range	7 (1.6–90.0)	8.5 (2.5–64.0)	6.1 (1.6–90.0)	
Trigger PSA (ng/ml)	*n* = 85	*n* = 56	*n* = 29	
Median ± SD	0.83	1.35	0.4	**<0.0001**
Range	0.003–80.0	0.06–80.0	0.003–5.6	
PSA value (ng/ml), *n* (%)	*n* = 314	*n* = 197	*n* = 117	
<0.2	33 (10.5)	9 (27.3)	24 (72.7)	**<0.0001**
≥0.2 to <0.5	78 (24.8)	33 (42.3)	45 (57.7)	
≥0.5 to <1	58 (18.5)	31 (53.5)	27 (46.5)	
≥1 to <2	68 (21.7)	51 (75.0)	17 (25.0)	
≥2	77 (24.5)	73 (94.8)	4 (5.2)	
PSA doubling time (months), *n* (%)	*n* = 89	*n* = 51	*n* = 38	
0–3	29 (32.6)	20 (68.9)	9 (31.1)	0.277
4–6	24 (27.0)	13 (54.2)	11 (45.8)	
7–12	9 (10.1)	6 (66.7)	3 (33.3)	
>12	27 (30.3)	12 (44.4)	16 (55.6)	
Tumour (T) stage, *n* (%)	*n* = 147	*n* = 97	*n* = 50	
<T3	70 (47.6)	41 (58.6)	29 (41.4)	0.070
≥T3	77 (52.4)	56 (72.7)	21 (27.3)	
Nodal (N) involvement, *n* (%)	*n* = 147	*n* = 97	*n* = 50	
N0	128 (87.1)	82 (64.1)	46 (35.9)	0.201
N1	19 (12.9)	15 (78.9)	4 (21.1)	
Radical prostatectomy, *n* (%)	*n* = 147	*n* = 97	*n* = 50	
R0	111 (75.5)	76 (68.5)	35 (32.4)	0.265
R1	36 (24.5)	21 (58.3)	15 (41.7)	
Gleason score, *n* (%)	*n* = 272	*n* = 178	*n* = 94	
<7	33 (12.1)	20 (60.6)	13 (39.4)	0.533
7	136 (50.0)	91 (66.9)	45 (33.1)	
8	62 (22.8)	40 (64.5)	22 (35.5)	
≥9	41 (15.1)	27 (65.9)	14 (34.1)	
Time to biochemical relapse (months), *n* (%)	*n* = 314	*n* = 197	*n* = 117	
≤12	42 (13.4)	30 (71.4)	12 (28.6)	0.211
>12	272 (86.6)	167 (61.4)	105 (38.6)	

P values in bold indicate that the values were statistically significant

100 had RP + salvage RT, 13 had RP + adjuvant ADT, and 8 had RP + salvage RT + ADT. Of the 314 patients, 50 (15.9%) were initially treated with RT, and 10 of these also received adjuvant ADT. Patient characteristics are shown in Table 2. The overall median PSApet level was 0.83 ng/ml (range 0.003–80 ng/ml). The PSApet level in 237 patients was <2 ng/ml. None of the patients experienced AEs or clinically detectable pharmacological effects after ^{68}Ga-PSMA injection.

PET/CT performance

^{68}Ga-PSMA PET/CT was positive (at least one suspected PCa lesion detected) in 197 of the 314 patients, representing an overall detection rate of 62.7%. A significant difference between ^{68}Ga-PSMA PET/CT-positive and ^{68}Ga-PSMA PET/CT-negative patients was observed with regard to PSApet values (higher values in positive patients; $P < 0.0001$). The distributions of PSApet between negative and positive scans

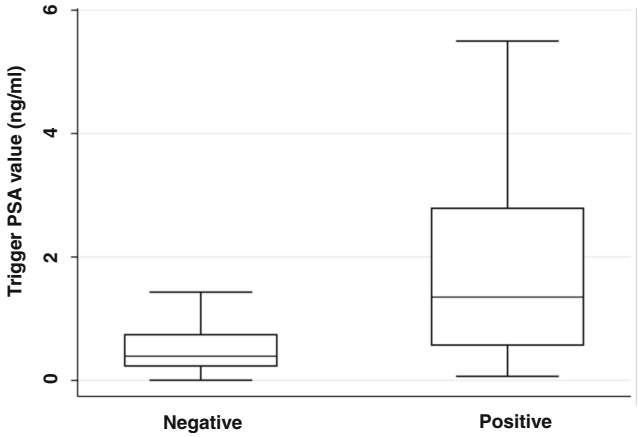

Fig. 1 PSA values at the time of the scanning in patients with positive and negative ^{68}Ga-PSMA PET/CT scans

are shown in Fig. 1. Although T stage was not significantly associated with a positive scan, more patients with higher T stages (T3 and T4) were positive on PSMA PET/CT ($P = 0.07$). Higher GS and shorter PSAdt, neither significant, were observed in patients with a positive scan ($P = 0.53$ and $P = 0.27$, respectively; Fig. 2).

In the multivariable logistic regression analysis, higher PSA, considered as a continuous value, was associated with a higher odds ratio for scan positivity (odds ratio 2.59, 95% confidence interval 1.45–4.65; Table 3). ROC curve analysis for PSApet showed an AUC of 0.78 (95% confidence interval 0.734–0.833; Fig. 3). The Youden index identified a PSA value of 1.062 ng/ml as the optimal cut-off value.

Considering the PSA categories 0–0.2, 0.2–1, 1–2 and >2 ng/ml, the detection rates of the scans were 27.3%, 47.1%, 75%, and 94.8%, respectively. In patients with a PSA level <0.5 ng/ml, the detection rate was 29.4%. Local lesions limited to the pelvis (prostate/prostate bed and/or pelvic LNs) were detected in 117 patients (59.4%). Specifically, 40 patients (20.3%) showed pathological local uptake (prostate/prostate bed), 61 (31.0%) had positive locoregional LNs, and 16 (8.1%) had both positive local and locoregional LNs. At least one distant lesion (distant LNs, bone or other organs, separately or combined with local lesions) was detected in 80 patients (40.6%). More than one lesion in a specific district (pelvic LNs and/or distant LNs and/or bone) was detected in 43 patients (21.8%). The lesion detection results are presented in Table 4.

Correlative choline PET/CT

Of the 88 patients with negative ^{18}F-choline PET/CT, 59 (67.0%) were positive on ^{68}Ga-PSMA PET/CT, and of these 57% had a PSA value <2 ng/ml and 81% had a GS of ≥7. A comparison between the two imagining modalities is shown in Fig. 4. Lesions were limited to the pelvis (prostate/prostate bed and/or pelvic LNs) in 40 patients (67.8%). Specifically, 16 patients (27.1%) had pathological local uptake (prostate/prostate bed), 7 (11.9%) had pathological uptake in local LNs (prostate bed/prostate) and locoregional LNs, and 17 (28.8%) had pathological uptake in locoregional LNs. At least one distant lesion (distant LNs, bone or other organs, separately or combined with local lesions) was detected in 19 (32.2%) of the 59 patients. Focal pathological bone uptake was detected in 11 (18%) of the 59 patients (Table 5).

Discussion

In this prospective study, we evaluated ^{68}Ga-PSMA PET/CT in 314 patients with BCR of PCa after primary curative treatment consisting of RP or RT. Of these patients, 131 also underwent salvage RT and/or adjuvant ADT. The overall

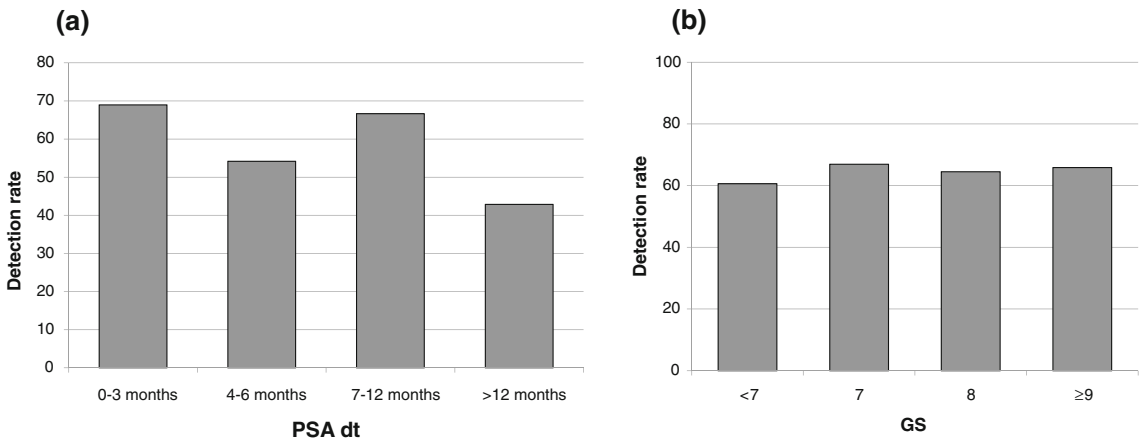

Fig. 2 ^{68}Ga-PSMA PET/CT detection rates in relation to (**a**) PSA doubling-time (PSAdt) and (**b**) Gleason score (GS)

Table 3 Multivariable logistic regression analysis

Variable	Odds ratio (95% confidence interval)	*P* value
Age (years), continuous	1.17 (0.52–2.63)	0.690
PSA, continuous	2.59 (1.45–4.65)	0.001
Tumour (T) stage		
<T3	1.00	0.130
≥T3	1.85 (0.83–4.11)	
Nodal (N) involvement		
N0	1.00	0.675
N1	1.34 (0.34–5.28)	
Gleason score		
<7	1.00	0.235
≥7	0.60 (0.26–1.39)	

median PSApet was 0.83 ng/ml, and 237 patients had a value of >2 ng/ml. The accuracy of this novel technique was assessed in a cohort of patients with a relatively low disease burden (only local recurrence or LN metastases). ^{68}Ga-PSMA PET/CT showed promising performance in detecting the suspected site of relapse with an overall detection rate of 62.7%.

A recent meta-analysis by an Australian group [35], which included 14 studies [29–33, 36–44] involving 1,052 patients (only two were prospective trials investigating 70 patients), showed an overall positive ^{68}Ga-PSMA PET/CT detection rate of 76% in PCa patients with BCR, with the percentage increasing with increasing PSApet values: 42% for 0–0.2 ng/ml, 58% for 0.2–1 ng/ml, 76% for 1–2 ng/ml, and 95% for >2 ng/ml. These results are similar to those of the present study, especially in those with a PSA value >1 ng/ml (76% vs. 75% 1–2 ng/ml, and 95% vs. 94.8% for >2 ng/ml). In patients with lower PSA values (0–0.2 ng/ml and 0.2–1 ng/ml), the detection rates were lower than those found in the meta-analysis (27.3% vs. 42% and 47.1% vs. 58%, respectively). There is increasing evidence that uptake of the PSMA ligand is not exclusively specific to PCa, and this may explain these findings. Sheikhbahaei et al. [45] recently reviewed a large number of reports of increased PSMA uptake in benign and inflammatory lesions (including neurogenic tissue, Paget's disease, thyroid adenoma, granulomatous disease, adrenal adenoma) and malignant diseases (including renal cell carcinoma, lung cancer, glioblastoma, hepatocellular carcinoma, thyroid cancer). Moreover, it is known that physiological uptake of the PSMA ligand is often increased in the autonomic nervous system, in particular the sacral, coeliac and stellate ganglia. Given that these nerve cells may be located near areas of frequent LN involvement, an accurate reading of CT images is crucial for reliable differentiation, especially in patients with a low disease burden. Thus, PSMA uptake foci are not automatically reported as PCa.

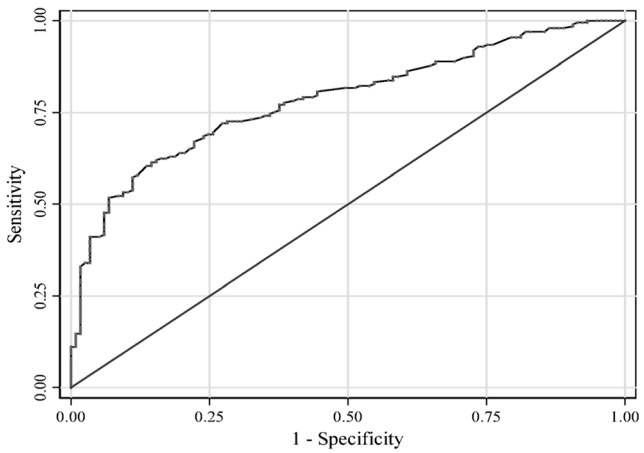

Fig. 3 ROC curve for PSApet (AUC 0.784)

Our results show that the performance of a promising a new imaging procedure in patients with very low PSA levels is still suboptimal (positive PET/CT in 29.4% of patients with PSA levels <0.5 ng/ml). Conversely, it is well known that small increases in PSA level after radical treatment, especially in low-risk patients, are not necessarily predictive of the development of metastases or death [46]. Long-term follow-up of patients negative on PSMA PET/CT is therefore needed to confirm its negative predictive value. Finally, in this context, low but measurable PSA levels are similar to low thyroglobulin levels after thyroidectomy. Blind salvage therapy may lead to a reduction in PSA levels, while a watch-and-wait approach only monitors PSA levels, but neither influences long-term outcome.

The availability of a new radiotracer able to detect the exact site and number of lesions in a high percentage of patients would have an important impact on treatment planning because the management in PCa is strongly associated with the site and extent of disease (local/nodal vs. systemic disease). In this study ^{68}Ga-PSMA PET/CT was positive in 56.4% of patients with a PSA value between 0.2 and 2 ng/ml. In contrast, Castellucci et al. [47] found that choline PET/CT was positive overall in 28.4% of patients with a PSA value <2 ng/ml (mean 1.07 ng/ml). We evaluated 88 patients negative on choline PET/CT, of whom 59 (67%) were positive on ^{68}Ga-PSMA PET/CT, and of these, 57% had a PSA value <2 ng/ml and 81% had a GS of ≥7. These results clearly confirm that ^{68}Ga-PSMA PET/CT is more accurate for PCa restaging than other currently used PET radiotracers.

Although a higher GS and shorter PSAdt were found in patients with positive scans, the differences were not

Table 4 Detection of suspicious sites of relapse by ^{68}Ga-PSMA PET/CT in patients with biochemical relapse of prostate cancer

Site	Number (%) of patients with suspicious site	Oligometastatic
Pelvic LNs	61 (30.9)	18
Local	40 (20.3)	
Pelvic LNs + distant LNs	17 (8.6)	3
Local + pelvic LNs	16 (8.1)	**3**
Pelvic LNs + bone	14 (7.1)	6
Distant LNs	11 (5.5)	5
Bone	10 (5.0)	2
Local + bone	7 (3.5)	2
Distant LNs + bone	5 (2.5)	1
Local + pelvic LNs + distant LNs	4 (2.0)	
Pelvic LNs + distant LNs + bone	4 (2.0)	
Lung ± liver	3 (1.5)	1
Local + distant LNs	2 (1.0)	
Local + pelvic LNs + distant LNs + bone	2 (1.0)	1
Local + pelvic LNs + bone	1 (0.5)	1
Patients with more than one lesion in a district		43

significant ($P = 0.53$ and $P = 0.27$, respectively). Shorter PSAdt is associated with high-risk disease in patients with BCR of PCa, but it is plausible that even the doubling of very low PSA levels may not be sufficient for PSMA expression to be detected by PET/CT because of its limited spatial resolution.

A major limitation of this study was the lack of histological proof of relapse in the majority of patients. However, given the

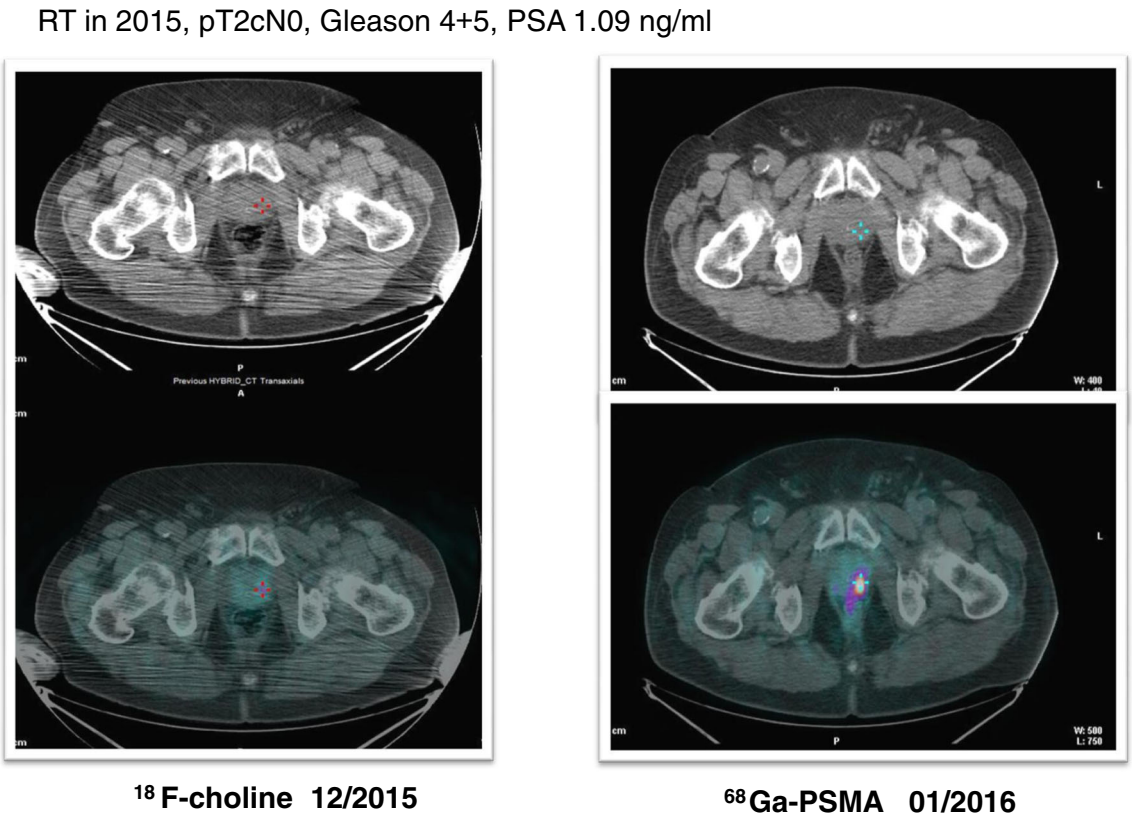

Fig. 4 Comparison between choline and PSMA imaging

Table 5 Per-patient analysis of the ^{68}Ga-PSMA PET/CT findings in 59 patients (67%) positive on PSMA PET/CT from among 88 patients negative on ^{18}F-choline PET/CT

Positive PSMA PET/CT	Number (%) of patients	Oligometastatic
Pelvic LNs	17 (28.81)	4
Local	16 (27.12)	
Local + pelvic LNs	7 (11.86)	
Pelvic LNs + distant LNs	4 (6.78)	
Pelvic LNs + bone	3 (5.08)	2
Bone	3 (5.08)	
Distant LNs	3 (5.08)	
Pelvic LNs + distant LNs + bone	3 (5.08)	
Local + bone	2 (3.39)	
Local + distant LNs	1 (1.69)	1
Patients with more than one lesion in a district		7
PSA <2 ng/ml	34 (57.6%)	
Gleason score ≥7	48 (81.4%)	

large, prospective case series included, the suspected lesions observed with ^{68}Ga-PSMA PET/CT can be considered to have been PCa recurrence.

Conclusion

^{68}Ga-PSMA PET/CT has become a clinically accepted technique for PCa imaging worldwide. The present prospective trial confirmed the value of ^{68}Ga-PSMA PET/CT in restaging PCa patients with BCR, its superiority over ^{18}F-choline PET/CT, and its good safety profile. Higher PSA levels were associated with a higher relapse detection rate. Overall, our results suggest that ^{68}Ga-PSMA PET/CT can substantially facilitate the clinical management of PCa patients after BCR.

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Collection and assembly of data: P.C., F.M. and I.S.
Data analysis and interpretation: F.F., I.S. and P.C.
Manuscript writing: All authors.
Final approval of manuscipt: All authors.
Accountable for all aspects of the work: All authors.

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Compliance with ethical standards

Conflicts of interest None.

Ethical approval The protocol was approved by the Ethics Committee of Area Vasta Romagna and by the competent Italian regulatory authorities. The study was performed in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice.

Informed consent All patients gave their written informed consent.

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