
Evaluation of Hybrid ^{68}Ga -PSMA Ligand PET/CT in 248 Patients with Biochemical Recurrence After Radical Prostatectomy

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The expression of prostate-specific membrane antigen (PSMA) is increased in prostate cancer. Recently, ^{68}Ga -PSMA (Glu-NH-CO-NH-Lys-(Ahx)-[^{68}Ga (HBED-CC)]) was developed as a PSMA ligand. The aim of this study was to investigate the detection rate of ^{68}Ga -PSMA PET/CT in patients with biochemical recurrence after radical prostatectomy. **Methods:** Two hundred forty-eight of 393 patients were evaluable for a retrospective analysis. Median prostate-specific antigen (PSA) level was 1.99 ng/mL (range, 0.2–59.4 ng/mL). All patients underwent contrast-enhanced PET/CT after injection of 155 ± 27 MBq of ^{68}Ga -PSMA ligand. The detection rates were correlated with PSA level and PSA kinetics. The influence of anti-hormonal treatment, primary Gleason score, and contribution of PET and morphologic imaging to the final diagnosis were assessed. **Results:** Two hundred twenty-two (89.5%) patients showed pathologic findings in ^{68}Ga -PSMA ligand PET/CT. The detection rates were 96.8%, 93.0%, 72.7%, and 57.9% for PSA levels of ≥ 2 , 1 to <2 , 0.5 to <1 , and 0.2 to <0.5 ng/mL, respectively. Whereas detection rates increased with a higher PSA velocity (81.8%, 82.4%, 92.1%, and 100% in <1 , 1 to <2 , 2 to <5 , and ≥ 5 ng/mL/y, respectively), no significant association could be found for PSA doubling time (82.7%, 96.2%, and 90.7% in >6 , 4–6, and <4 mo, respectively). ^{68}Ga -PSMA ligand PET (as compared with CT) exclusively provided pathologic findings in 81 (32.7%) patients. In 61 (24.6%) patients, it exclusively identified additional involved regions. In higher Gleason score (≤ 7 vs. ≥ 8), detection efficacy was significantly increased ($P = 0.0190$). No significant difference in detection efficacy was present regarding antiandrogen therapy ($P = 0.0783$). **Conclusion:** Hybrid ^{68}Ga -PSMA ligand PET/CT shows substantially higher detection rates than reported for other imaging modalities. Most importantly, it reveals a high number of positive findings in the clinically important range of low PSA values (<0.5 ng/mL), which in many cases can substantially influence the further clinical management.

Key Words: PSMA ligand; PET/CT; hybrid imaging; prostate cancer; biochemical recurrence

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In biochemical recurrence after radical prostatectomy (RP), an increase of the prostate-specific antigen (PSA) level precedes a clinically detectable recurrence by months to years (1). However, it cannot differentiate between local, regional, or systemic disease with the necessary precision that is essential for further disease management (2). Furthermore, PSA kinetics such as PSA velocity (PSAvel) and PSA doubling time (PSAdt) play an important role, with high PSA kinetics facilitating disease detection (3).

Morphologic imaging methods exhibit considerable limitations: sensitivity ranges between 25% and 54% for the detection of local recurrence by transrectal ultrasound or CT and is moderately improved using functional MR imaging techniques (2,4). The sensitivity for detection of lymph node metastases of CT or MR imaging is reported to be 30%–80% (5). Ultra-small particles of iron oxides proved to be effective; however, they have not been approved by regulatory authorities so far (6).

Various targets have been addressed by molecular imaging to improve the detection of recurrent prostate cancer (PC). For PET imaging, mainly ^{11}C - and ^{18}F -labeled choline derivatives have been used in the past (7–9). However, especially in patients with PSA values below 3 ng/mL, the detection rate is only 40%–60% (3,4,7). Recently, a new molecular probe targeting, for example, the gastrin-releasing peptide receptor or the prostate-specific membrane antigen (PSMA), has been developed (10–12). PSMA is a membrane-bound enzyme with significantly elevated expression in PC cells in comparison to benign prostatic tissue (13). The localization of the catalytic site of PSMA in the extracellular domain allows the development of small specific inhibitors that are internalized after ligand binding (14). Older agents targeting the intracellular domain of PSMA showed disappointing results due to low image contrast, low sensitivity, or high background signal (15). The recent development

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of ^{68}Ga -PSMA (Glu-NH-CO-NH-Lys-(Ahx)-[^{68}Ga (HBED-CC)]) as an extracellular PSMA inhibitor for PET imaging demonstrated a high specificity for PSMA tumor-expressing cells as well a high and specific uptake in a mouse model (16). A first preliminary study in PC patients revealed a higher image contrast and detection rate for ^{68}Ga -PSMA than ^{18}F -choline (17). In addition, further preliminary data in primary PC back the high specificity of ^{68}Ga -PSMA ligand PET imaging, ranging more than 95% at both patient- and field-based analysis for lymph node staging validated by extended pelvic lymph node dissection (18). Most recently, a large study including patients with different primary treatment was published encompassing patients with recurrent PC, supporting high detection rates (19). Consequently, PSMA targeting holds promise in being a superb biomarker for the early detection of recurrent disease allowing adequate stratification of patients for optimal treatment planning.

Thus, the purpose of our study was to assess the value of ^{68}Ga -PSMA ligand PET/CT for the detection and localization of recurrent disease in a large homogeneous series of patients after RP. Specifically, we aimed to describe the detection rate as a function of the absolute PSA level and PSA kinetics and the evaluation of the diagnostic performance, compared with primary histologic differentiation and antihormonal treatment.

MATERIALS AND METHODS

Patients

Three hundred ninety-three consecutive patients who underwent ^{68}Ga -PSMA ligand PET/CT imaging for recurrent PC were extracted from the institutions' database (November 2012 to April 2014). Only patients who had undergone RP, whose PSA level was ≥ 0.2 ng/mL and had not received chemotherapy, were included (Fig. 1). In total, 248 patients were included in this retrospective study. Patient characteristics are summarized in Table 1. Seventy patients had received androgen-deprivation therapy within the last 6 mo before the examination.

All patients gave written informed consent for the purpose of anonymized evaluation and publication of their data. All reported investigations were conducted in accordance with the Helsinki Declaration and with national regulations. The study was approved by the Ethics Committee of the Technical University Munich (permit 5665/13).

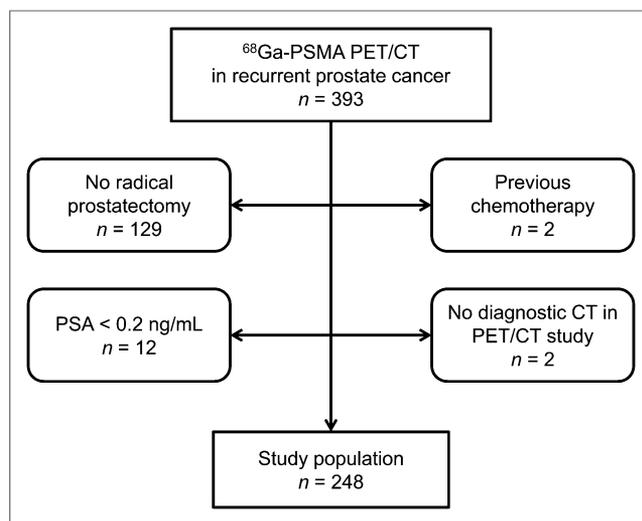


FIGURE 1. Flow chart of patient selection.

TABLE 1
Patient Characteristics

Characteristic	n
No. of patients	248
Primary RP	241 (97.2%)
Salvage prostatectomy after primary radiation therapy	7 (2.8%)
Age (y)	
Median	70
Range	46–85
Primary Gleason score*	
Median	7
Range	6–10
PSA (ng/mL)	
Median	1.99
Range	0.2–59.4
Further treatment	
No. of patients with external radiation after RP	20
No. of patients with antihormonal treatment during/within 6 mo prior imaging	70

*In 27 of 248 patients, no information concerning initial Gleason score could be obtained because primary treatment of several patients dated back between 10 and 20 y.

The serum PSA level at the time of the PET/CT scan was available in all patients. In addition, in 144 patients PSA kinetics (PSAvel and PSA_{dt}) were calculated as described previously (20). Only patients who were able to provide at least 2 PSA measurements after PSA progression (i.e., at least 3 PSA values) and in whom therapy had not been changed within the last 6 mo before imaging were included in this subgroup analysis.

Synthesis and Application of ^{68}Ga -PSMA Ligand

Images were obtained with the ^{68}Ga -labeled HBED-CC (16) that was synthesized as described previously (21). The ligand was labeled with $^{68}\text{Ga}^{3+}$ (half-life, 67.6 min) from a $^{68}\text{Ge}/^{68}\text{Ga}$ radionuclide generator (iThemba Labs) by means of a fully automated module (Scintomics) and good manufacturing practice-grade disposable cassettes and reagent kit (ABX) (16,22). The final product was dissolved in isotonic phosphate-buffered saline with subsequent sterile filtration.

The ^{68}Ga -PSMA ligand complex solution was applied to patients via an intravenous bolus (mean \pm SD, 155.5 ± 27.4 MBq; range, 88–240 MBq). Variation of injected radiotracer activity was caused by the short half-life of ^{68}Ga and variable elution efficiencies obtained during the lifetime of the $^{68}\text{Ge}/^{68}\text{Ga}$ radionuclide generator.

Imaging Protocol

PET acquisition was started at a mean time of 54.2 ± 7.1 min after tracer injection (range, 41–74 min). All patients underwent ^{68}Ga -PSMA ligand PET/CT on a Biograph mCT scanner (Siemens Medical Solutions). First, a diagnostic CT scan was obtained in the portal venous phase 80 s after intravenous injection of contrast agent (Imeron 300), followed by the PET scan. All patients received diluted oral contrast (300 mg of Telebrix) and a rectal filling with a negative contrast agent (100–150 mL). All PET scans were acquired in 3-dimensional mode

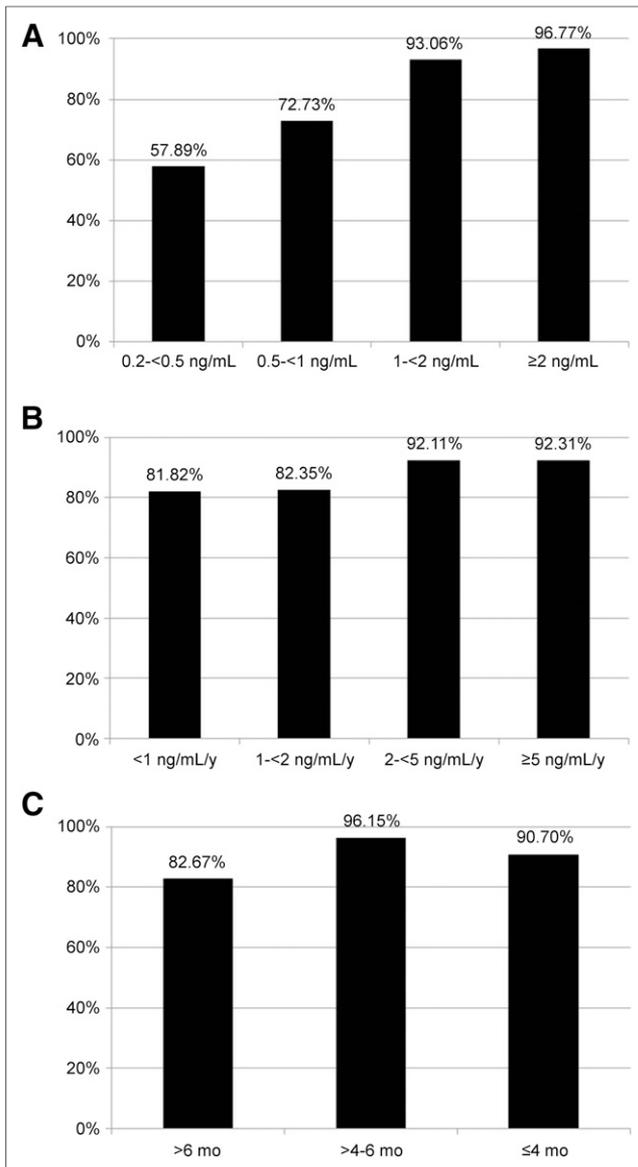


FIGURE 2. Detection rate of ^{68}Ga -PSMA ligand PET/CT in relation PSA level (A), PSAvel (B), and PSAdt (C).

with an acquisition time of 3–4 min per bed position. Emission data were corrected for randoms, dead time, scatter, and attenuation and were reconstructed iteratively by an ordered-subsets expectation maximization algorithm (4 iterations, 8 subsets) followed by a postreconstruction smoothing gaussian filter (5 mm in full width at one-half maximum).

Image Analysis

All images were interpreted by 1 board-certified nuclear medicine physician and 1 board-certified radiologist. Primarily, ^{68}Ga -PSMA ligand PET images and CT images were interpreted separately followed by a final consensus interpretation. All lesions suggestive for recurrent PC were noted and grouped into local recurrence, lymph node metastases (discrimination into pelvic, retroperitoneal, and supradiaphragmatic location), bone metastases, and other metastases (e.g., lung, liver).

To demonstrate the individual contribution of PET and CT for the final diagnosis, for every lesion the contribution of both PET and CT for defining malignancy was noted. In PET, any focal uptake of ^{68}Ga -PSMA ligand higher than the surrounding background and not associated

with physiologic uptake was considered suggestive for malignancy. For CT, for example, any pelvic/retroperitoneal lymph node station containing lymph nodes measuring at least 8 mm or any distinct sclerotic lesion not being associated with degenerative changes were judged as positive (4).

Statistical Analysis

The detection rate (number of patients with at least 1 positive finding) was plotted against the absolute PSA value and PSA kinetics. Two-sample *t* tests to evaluate differences between single groups (Gleason score, antihormonal treatment) and Mann-Whitney *U* tests to evaluate differences concerning PSA values between groups with and without pathologic uptakes were used. All tests were performed 2-sided, and a level of significance of $\alpha = 5\%$ was used. Statistical analyses were conducted with software (MedCalc, version 13.2.0, 2014; MedCalc).

RESULTS

Detection Efficacy

PSA Level. Of the 248 patients, 222 (89.5%) showed 1 or more localized areas suggestive for recurrent PC. The detection efficacy of ^{68}Ga -PSMA ligand PET/CT was 96.8% (120/124) for a PSA value of ≥ 2 ng/mL, 93.0% (67/72) for a PSA value of 1 to < 2 ng/mL, 72.7% (24/33) for a PSA value of 0.5 to < 1 ng/mL, and 57.9% (11/19) for a PSA value of 0.2 to < 0.5 ng/mL (Fig. 2A). The different regions involved by recurrent disease are listed in Table 2. Mean PSA was significantly lower in patients with negative ^{68}Ga -PSMA ligand PET/CT results than in patients with positive results ($P = 0.0080$; Table 3).

PSA Kinetics. PSAvel ranged from 0.1 to 42.5 ng/mL per year. The detection rates of ^{68}Ga -PSMA ligand PET/CT were 81.8% (54/66), 82.4% (14/17), 92.1% (35/38), and 100% (23/23) in patients with PSAvel values of, respectively, < 1 ng/mL/y, 1–2 ng/mL/y, 2–5 ng/mL/y, and > 5 ng/mL/y (Fig. 2B). Despite a strong tendency to a higher PSAvel in patients with positive ^{68}Ga -PSMA ligand PET/CT results than in those with negative results, no statistical significance was reached ($P = 0.0532$; Table 3).

PSAdt values ranged between 0.37 and 158 mo. The detection rates of ^{68}Ga -PSMA ligand PET/CT were 82.7% (62/75), 96.2% (25/26), and 90.7% (39/43) in patients with PSAdt values of > 6 mo, 4–6 mo, and ≤ 4 mo, respectively (Fig. 1C). Mean PSAdt was not significantly different in patients with ^{68}Ga -PSMA ligand PET/CT negative findings, compared with positive patients ($P = 0.2971$; Table 3).

TABLE 2

Different Regions Involved by Recurrent PC in ^{68}Ga -PSMA Ligand PET/CT

Region	No. of patients
Local recurrence	87 (35.1)
Lymph node metastases	
Abdominopelvic	130 (52.4)
Supradiaphragmatic	13 (5.2)
Bone metastases	89 (35.9)
Other (e.g., lung, liver) metastases	13 (5.2)

Data in parentheses are percentages.

TABLE 3

PSA Level and PSA Kinetics in Patients with Positive and Negative Findings in ⁶⁸Ga-PSMA Ligand PET/CT

Parameter	Positive findings	No findings	P
PSA level (ng/mL)	4.78 ± 7.00 (n = 222)	1.10 ± 1.00 (n = 26)	0.0080
PSAvel (ng/mL/y)	3.88 ± 6.52 (n = 126)	0.87 ± 0.96 (n = 18)	0.0532
PSAdt (mo)	10.02 ± 15.65 (n = 126)	14.01 ± 10.55 (n = 18)	0.2971

Data are mean ± SD.

Contribution of PET and Morphologic Imaging for Lesion Detection

The number and percentage of patients in whom PET and CT were concordantly detecting lesions or in whom PET or CT exclusively defined recurrent disease or showed additional involved regions (outside of primarily detected regions) are given in Figure 3. Notably, whereas ⁶⁸Ga-PSMA ligand PET (as compared with CT) exclusively provided relevant diagnostic information in 81 (32.7%) patients, CT (as compared with PET) was only able to exclusively provide the diagnostic information in 3 (1.2%) of the cases. Moreover, in 61 (24.6%) patients PET was able to identify additional involved regions, compared with 17 (6.9%) patients in whom CT showed additional regions (Table 4). In most of the cases in which PET provided additional information, lymph node metastases, local recurrence, or bone metastases could not be identified by CT (representative examples are given in Figs. 4 and 5 and Supplemental Fig. 1 [supplemental materials are available at <http://jnm.snmjournals.org>]). Most of the lesions in which CT provided exclusive information were (sclerotic) bone or lung metastases.

Influence of Anti-Androgen Therapy and Primary Histologic Differentiation

In our patient collective, no significant difference in detection efficacy could be observed with regard to antiandrogen therapy (P = 0.0783). Lesions were detected in 95.7% (67/70) of patients with antiandrogen therapy and 87.1% (155/178) of patients without antiandrogen therapy. Notably, PSA values were significantly higher in patients with than without antihormonal treatment (8.11 ± 10.83 vs. 2.93 ± 3.11 ng/mL).

With respect to histologic differentiation of the primary PC, ⁶⁸Ga-PSMA ligand PET/CT was positive in 86.7% (111/128) of patients with a Gleason score ≤ 7 and in 96.8% (90/93) of patients with a Gleason score ≥ 8 (P = 0.0190). No difference in PSA values was present between these 2 groups (PSA mean and median, 4.23 and 1.90 vs. 4.89 and 2.2 ng/mL, respectively).

DISCUSSION

PSA relapse after RP is a common clinical scenario. In this context, biochemical failure defined by a confirmed PSA value of >0.2 ng/mL after RP occurs long before recurrent disease can be localized clinically or by imaging. The goal in these patients is to distinguish whether disease relapse is localized to the prostate bed or whether metastatic disease is present because this affects further treatment. To date, the detection of lesions in biochemical recurrence (especially at PSA values < 1 ng/mL) of PC is a major challenge for all imaging modalities including PET with a variety of tracers (4,5,9).

In this study, we describe the detection rate of hybrid PET/CT imaging using a novel ⁶⁸Ga-PSMA ligand as a PET tracer in a large number of patients with biochemical recurrence after RP. Despite being retrospective in nature, the strength of our study consists in a homogeneous patient selection. Our results show a considerably higher detection of hybrid PET/CT imaging using the ⁶⁸Ga-PSMA ligand than reported for other PET tracers. Even in 67% of the patients with PSA levels < 1.0 ng/mL, the potential site of recurrence has been detected. Our data are in line with data by Afshar-Oromieh et al. published online only most recently (19). However, in our study only patients with biochemical recurrence after RP were included, creating the homogeneous patient collective in our study. In addition to the previously mentioned most recent work, we could show that compared with morphologic imaging the information provided by ⁶⁸Ga-PSMA ligand PET was essential in 58% of the patients: in 33% the site of recurrence could only be detected by PET whereas in an additional 25% of the patients PET showed additional lesions not detectable by CT imaging.

Our results suggest that ⁶⁸Ga-PSMA ligand PET/CT is highly effective in PC restaging because in our study 89.5% of patients showed at least 1 lesion regarded as characteristic for PC. Our data, based on a large and highly selected patient cohort, are in line with preliminary reports by Afshar-Oromieh (17,23). Compared with reports in the literature stating detection rates between 34% and 88% for ¹¹C-choline, 43%–79% for ¹⁸F-choline, and 59%–80% for ¹¹C-acetate (7,24–31), ⁶⁸Ga-PSMA ligand PET/CT offers a substantially higher detection efficacy. As known from other PET tracers, the detection rate of ⁶⁸Ga-PSMA ligand PET/CT also increases in parallel with rising PSA value (4). As an important finding, our study shows positive ⁶⁸Ga-PSMA ligand

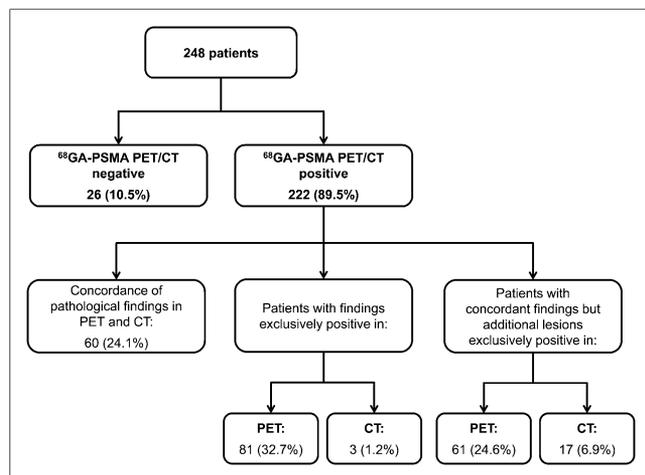


FIGURE 3. Contribution of PET and morphologic imaging for lesion detection.

TABLE 4
Malignant Lesions Exclusively Identified in ⁶⁸Ga-PSMA PET or CT

Region/combination of regions	No. of patients with positive findings exclusively demonstrated in ⁶⁸ Ga-PSMA		No. of patients with additional involved regions exclusively demonstrated in ⁶⁸ Ga-PSMA	
	PET	CT	PET	CT
LR only	18		11	
LN metastases only	31	1	17	2
Bone metastases only	9	1	24	7
LR + LN metastases	7		2	
LR + bone metastases	6		1	
LN + bone metastases	4		5	
LR + LN + bone metastases	1			
Other (e.g., lung, liver metastases)	5	1	1	17
Total	81 (32.7%)	3 (1.2%)	61 (24.6%)	17 (6.9%)

LR = local recurrence; LN = lymph node.

PET/CT findings for PSA values < 1 ng/mL in 67% of the patients, which is substantially higher than reported for choline-based PET tracers showing detection rates between 19% and 36%

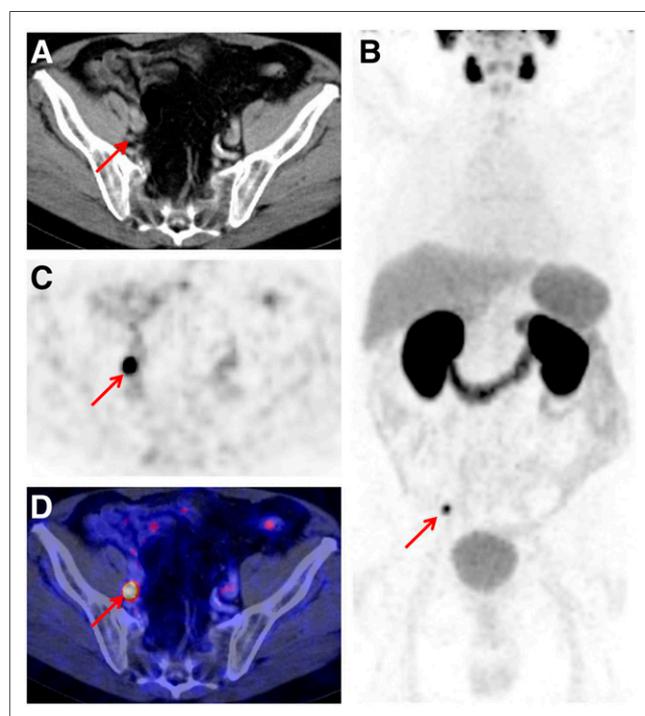


FIGURE 4. Set of images of a 75-y-old patient with status after RP (2000; Gleason score, 5; pT3b, pN1), radiation therapy (September 2011), and rising PSA value of 1.09 ng/mL (October 2013). CT images (A) reveal no suggestive finding, with 5-mm lymph node behind right external iliac vein. Corresponding PET (C) and fused PET/CT images (D) show intense uptake, with high lesion-to-background ratio in this small lymph node indicating lymph node metastasis. Whole-body maximum-intensity projection (B) displays this lymph node and demonstrates no other suggestive lesion. Selective lymph node picking was performed in December 2013, confirming single lymph node metastasis. Subsequently, PSA value dropped below detection limit (<0.07 ng/mL) without antihormonal treatment (last measurement April 2014).

at PSA levels below 1–1.5 ng/mL (3,7,32,33). Thus, ⁶⁸Ga-PSMA ligand PET/CT improves lesion detectability in the group of patients at an early state, potentially allowing more tailored salvage therapies. The detection rate of 58% in patients with a PSA level < 0.5 ng/mL has, in particular, a clinical impact because urological guidelines (e.g., European Association of Urology (34)) define a PSA value of 0.5 ng/mL as the upper limit for salvage radiation therapy. However, it has to be admitted that the overall detection rate of 89.5% implies a false-negative rate of 10.5% for ⁶⁸Ga-PSMA ligand PET/CT imaging because in the case of biochemical recurrence, by definition a viable recurring tumor must be present. In addition, it has to be mentioned that in this study the use of ⁶⁸Ga-PSMA ligand PET/CT was not limited to patients with prior negative conventional scans (e.g., bone scanning, CT, MR imaging). Thus, if ⁶⁸Ga-PSMA ligand PET/CT were used in that preselected setting, the detection rate would potentially be different.

Similarly to choline derivatives, our results state a higher detection rate in patients with a higher PSAvel, albeit the *P* value of 0.0532 could be designed as borderline from a purist statistical point of view (3,32,35). Nevertheless, ⁶⁸Ga-PSMA ligand PET/CT offers a high rate of positive findings also in patients with low changes in PSA kinetics, with a detection rate of 81.8% compared with 12% for ¹¹C-choline at a PSAvel of 1 ng/mL/Y (35). Notably, our data show no clear trend toward higher detection rates with a decreasing PSAvel, compared with reports for ¹¹C- and ¹⁸F-choline (32,35). However, especially at a low PSA value PSAvel is more susceptible to slight changes and thus not optimally suited in this patient collective. In addition, it has to be considered that data for PSAvel and PSAvel were only present in about 60% of the patients (as stated in the “Patients” section). Consequently, our data indicate that for ⁶⁸Ga-PSMA ligand PET/CT PSA kinetics are not as crucial as for choline derivatives because the detection rate is more than 75%, which is also true for patients with a low PSAvel or high PSAvel.

The substantial contribution of ⁶⁸Ga-PSMA ligand PET in the setting of hybrid PET/CT is reflected by the fact that in 33% of cases the sites of recurrent disease were identified only by PET (Fig. 3; Table 4). In an additional 25% of cases, PET was able to identify further clinically relevant lesions that were not detected by CT. However, the high number of patients in whom the diagnosis

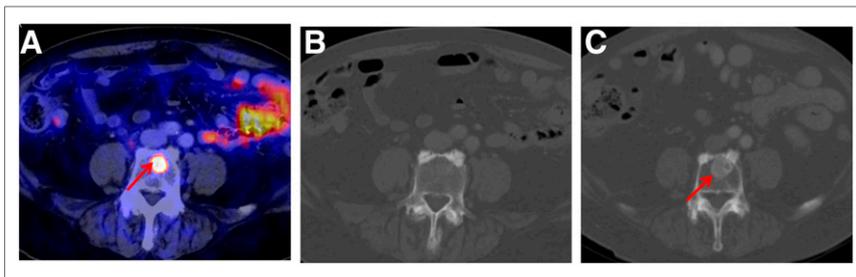


FIGURE 5. Set of images of a 73-y-old patient with status after RP (September 2013; Gleason score, 9; pT3b, pN0, PSA nadir below detection limit). Increase of PSA value to 2.0 ng/mL (December 2013) and start of antihormonal treatment. Fused PET/CT image (A) demonstrates high intense uptake in lumbar spine, with no suggestive osteoblastic lesion in corresponding CT image (B). Four months after radiation diffuse sclerosis can be found in CT image (C), indicating posttherapeutic changes/progression.

of recurrent disease was solely based on PET is not surprising because the limited role of CT imaging, especially for local recurrence and lymph node metastases, is well documented (2,36). Besides the potential results derived from a bone scan in this patient cohort, which with respect to the PSA value would be low, the finding of additional clinically relevant lesions documents the high value of ^{68}Ga -PSMA ligand PET in a setting in which prior conventional imaging would have been negative. Indeed, in our patient collective negative prior conventional imaging was not an inclusion criterion; however, this comparison indicates the potential high number of findings in a negatively preselected group.

Our data show a statistically significant higher detection rate in patients with a Gleason score ≥ 8 versus ≤ 7 , which could be potentially attributed to the fact that immunohistochemically PSMA expression is usually higher in lesions with a higher Gleason score than in lesions with a lower Gleason score (37). Our data show a trend toward a higher detection rate in patients with antiandrogen therapy within 6 mo before ^{68}Ga -PSMA ligand PET/CT imaging. However, these data do not reach statistical significance, and it has to be noted that mean PSA values were significantly higher in patients with antihormonal treatment, which could constitute a confounding factor. Nevertheless, there are reports stating a higher PSMA expression of PC tumor cells in the setting of antihormonal treatment (38,39), which could potentially be reflected in higher detection rates. This hypothesis has to be proven in further studies.

A major limitation of our study is the fact that histopathology as a gold standard was only available in a few cases. In 12 patients, ^{68}Ga -PSMA ligand PET/CT–positive lymph node metastases were histologically confirmed. However, a histopathologic confirmation in all patients is not feasible because practical and ethical issues in the setting of recurrent PC. Nevertheless, in 35 patients ^{68}Ga -PSMA ligand PET/CT–guided selective radiation therapy followed by a substantial decrease of PSA proved the nature of PSMA-positive lesions. In another 45 patients, follow-up/other imaging modalities unanimously proved that the positive lesions were metastases of PC. So in total, in 37.1% (92/248) of patients a comprehensive standard of reference (histopathology, decrease of PSA level after targeted radiation therapy, or undisputable follow-up/other imaging methods) was available. In all of these cases, concordant results in correlation with the findings derived from ^{68}Ga -PSMA ligand PET/CT were present.

CONCLUSION

In this study, ^{68}Ga -PSMA ligand PET/CT proved in a large number of patients with biochemical recurrence after RP a substantially

higher detection efficacy than reported for other tracers. With a detection rate of $>90\%$ at PSA levels more than 1 ng/mL, this method currently surpasses all other imaging modalities for the restaging of PC. In patients in whom salvage therapy decisions are pending, ^{68}Ga -PSMA ligand PET/CT imaging can also be performed at a lower PSA level, with the expectation of a detection rate of approximately 50% and offering the potential of guiding those treatments. In more than 50% of the cases, the information yielded by ^{68}Ga -PSMA PET was crucial for the final diagnosis showing findings that have not been visualized by CT. In addition, the high tumor uptake of PSMA inhibitors makes

these compounds in a subset of metastasized patients particularly attractive for endoradiotherapy. Hereby, imaging and therapeutic small-molecule inhibitors of PSMA could potentially be used as a theranostic strategy for patients with metastasized PC.

DISCLOSURE

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