Clinical Research

The Rates of Coexistence Metastases in Patients with Advanced Prostate Cancer in ^{68}Ga-PSMA PET/CT: A Retrospective Analysis

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ABSTRACT

Objective: To determine the rate of metastasis and coexistence metastases in patients with advanced prostate cancer in gallium 68 -prostate specific membrane antigen PET/CT (^{68}Ga-PSMA PET/CT).

Material and Method: A total of 234 consecutive patients with advanced prostate cancer who underwent ^{68}Ga-PSMA PET/CT were included in this retrospective study. Data on previous treatments, Gleason score, serum Prostate Specific Antigen (PSA) levels (ng/mL) and ^{68}Ga-PSMA PET/CT findings were recorded.

Results: The mean age of the patients was 67.6 ± 8.5 years. Median PSA level was 21.7 (0.2-880) ng/ml. Pelvic (41%) and abdominal (30.3%) lymph nodes were the most commonly involved lymph nodes, while bone metastases were multimetastatic and bone carcinomatosis in 22.2% and 30.6% of patients, respectively. Other common distant organ metastases were lung (7.6%) and liver (7.2%) metastases. Level 1-4 lymph node positivity was noted in 29.4%, 33.3% and 6.8% of patients with liver metastasis, lung metastasis and seminal vesicle invasion, respectively. Concomitant lung metastasis was evident in 41.1% of patients with liver metastasis, while lung or liver metastasis was evident in 13.6% of patients with seminal vesicle invasion. Bone metastasis was evident in all patients with liver and lung metastasis, and in 65.9% of patients with seminal vesicle invasion.

Conclusion: The findings of this study showed the value of ^{68}Ga-PSMA PET/CT in detecting coexistence rate of metastases in advanced prostate cancer.

Keywords: *Prostate Cancer; ^{68}Ga-PSMA; PET/CT; Coexistence Metastases.*

ÖZET

İleri Evre Prostat Kanserli Hastalarda ^{68}Ga-PSMA PET/BT'de Metastazların Birlikte Bulunma Oranları: Bir Retrospektif Analiz

Amaç: İleri evre prostat kanserli hastalarda galyum 68 prostat spesifik membran antijen PET/BT (^{68}Ga-PSMA PET/-BT) de saptanan metastaz ile birlikte bulunan metastazların oranlarını saptamak.

Gereç ve Yöntem: Bu retrospektif çalışmaya ilerlemiş prostat kanserli ^{68}Ga-PSMA PET-BT çekimi yapılmış 234 hasta dahil edildi. Hastaların önceki tedavileri, Gleason skorları, serum Prostat Spesifik Antijen (PSA) düzeyleri (ng/ml), ^{68}Ga-PSMA PET/BT bulguları kaydedildi.

Bulgular: Hastaların yaş ortalaması 67.6 ± 8.5 yıl bulundu. Ortanca PSA düzeyi 21.7 (0.2-880) ng/ml idi. Pelvik (%41) ve abdominal (%30.3) lenf nodları en sık görülen lenf nodları metastazları iken, kemik metastazları sırasıyla %22.2 ve %30.6 oranında multimetastatik ve kemik karsinomatozisi şeklindeydi. Diğer yaygın uzak organ metastazları akciğer (%7.6) ve karaciğer (%7.2) metastazları idi. Karaciğer metastazı, akciğer metastazı ve seminal vezikül invazyonu olan hastaların sırasıyla %29.4, %33.3 ve %6.8'inde seviye 1-4 lenf nodu pozitifliği saptandı. Karaciğer metastazı olan hastaların %41.1'inde eş zamanlı akciğer metastazı saptanırken, seminal vezikül invazyonu olan hastaların %13.6'sında akciğer veya karaciğer metastazı saptanmıştır. Karaciğer ve akciğer metastazı olan tüm hastalarda ve seminal vezikül invazyonu olan hastaların %65.9'unda kemik metastazı vardı.

Sonuç: Bu çalışmanın bulguları, ilerlemiş prostat kanserinde metastazların birlikte bulunma oranlarının saptanmasında ^{68}Ga-PSMA PET/BT'nin değerini göstermiştir.

Anahtar Sözcükler: *Prostat Kanseri; ^{68}Ga-PSMA; PET/BT; Birlikte Bulunan Metastazlar.*

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Prostate Cancer (PCa) is the most common cancer (except skin cancer) in men in Europe. Clinically, the most common diagnosis is recorded in Northern and Western Europe (> 1000 men/year>2), and the autopsy series has approximately the same incidence in different parts of the world (1).

Recurrent PCa is defined as an increase in two consecutive measurements of Prostate Specific Antigen (PSA) > 0.2 ng / ml (2). Because it changes the approach of local or systemic treatment, early detection of metastatic spread and biochemical recurrence in prostate cancer is important (3, 4). The main approaches to the progression of advanced prostate cancer, such as prostate-specific antigen (PSA), computed tomography (CT) and bone scan, have some diagnostic limitations (5-7).

The sensitivity of ^{11}C or ^{18}F Choline-labeled PET/CT tracers in patients with a PSA level of <1ng/mL has

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been reported as low as 19-36% (8-10). Therefore, an imaging method with higher sensitivity and specificity is required.

Prostate specific membrane antigen (PSMA) is a type II membrane protein consisting of 750 amino acids. PSMA is expressed in the normal prostate tissue and is highly expressed in the primary and metastatic prostate cancer (11).

The use of radiolabeled tracers acting as PSMA ligands for PET/CT is a novel diagnostic option in this context and gallium 68 (^{68}Ga) has emerged as a PSMA ligand and a promising new PET tracer in the diagnostic work-up of prostate cancer patients over the past few years (12-15).

The ^{68}Ga-PSMA ligand for imaging and therapy (I&T) PET/CT (^{68}Ga-PSMA-I&T PET/CT) has been associated with promising results including a substantially higher diagnostic accuracy for the detection of prostate cancer metastases compared to choline-based PET/CT, particularly in the case of lymph node metastases and at low PSA levels (12, 16-18).

This study was therefore designed to evaluate the concomitant metastases rate of advanced prostate cancer patients by means of ^{68}Ga-PSMA-I&T PET/CT in a retrospective cohort.

MATERIAL AND METHOD

A total of 234 consecutive patients with advanced prostate cancer who had metastatic disease at the initial diagnosis, resistance to primary therapy or PSA recurrence after radical-prostatectomy and/or hormonotherapy and/or radiotherapy and underwent ^{68}Ga-PSMA-I&T PET/CT were included in this retrospective study conducted in a tertiary care center between april 2017 and march 2018.

The study was conducted in full accordance with local Good Clinical Practice guidelines and current legislation, and permission was obtained from the Institutional Ethics Committee for the use of patient data for publication purposes (permit no: 057/2018).

Study Parameters

Data on previous treatments (radical prostatectomy, radiotherapy, androgen-deprivation therapy), Gleason score, serum PSA levels (ng/mL), ^{68}Ga-PSMA-I&T PET/CT findings on lymph node and distant organ metastases were recorded for each patient. Concomitant metastasis and level of lymph node positivity with respect to distant organ metastasis were also evaluated.

PSMA-PET/CT

The ^{68}Ga PSMA I&T was synthesized using the ^{68}Ge/^{68}Ga generator (iThemba. Labs, S.A) linked radiopharmacy application module (SCINTOMICS GmbH, Fürstenfeldbruck, Germany), disposable cassette kit (ABX, Radeberg, Germany), 22.5 µg (15 nmol), and unbound PSMA I&T peptide (SCINTOMICS GmbH, Fürstenfeldbruck, Germany) entirely automatically, following the Good Manufacturing Practice (GMP) procedures. Following high performance liquid chromatography-based quality control, 2 MBq/kg of ^{68}Ga-PSMA was injected. This was followed 60 minutes later by acquisition of contrast-CT (120 kV, 110 mA, 600 mm trans-axial FOV, no gap, 10Å~1.5 mm collimation, pitch 1.1, 0.5 s rotation time, 5 mm slice thickness, 512Å~512 matrix) and then PET emission data (3D FOV 15,5 cm, OSEM 2 iterations/8 subset, FWHM 5mm) for 3 minutes per supine position craniocaudally to the level of lower limbs via a dedicated PET/CT system (Siemens Biograph 6; Siemens, Knoxville, TX, USA).

Image Analysis

PET/CT images were visually analyzed for the presence and localization of suspicious lesions and interpreted by nuclear medicine physicians with 10 years of experience. The uptake characteristics in metastases were quantified using maximum standardized uptake values (SUVmax) of tumor lesions, which was calculated for lesions judged positive via volumes of interest (VOIs) drawn automatically. Local recurrences, lymph node metastasis (Level 1: pelvic, Level 2: abdominal, Level 3: mediastinal and Level 4: supraclavicular and/or neck), bone metastases (1 metastatic site: oligometastatic, 2-20 metastatic sites: multimetastatic and >20 metastatic sites: bone carcinomatosis) and other metastatic sites (lung, liver, adrenal gland, pleural/peritoneal metastases) were documented. Examples of patients undergoing ^{68}Ga-PSMA ligand PET/CT examination for metastases were presented in Figure 1A and Figure 1B.

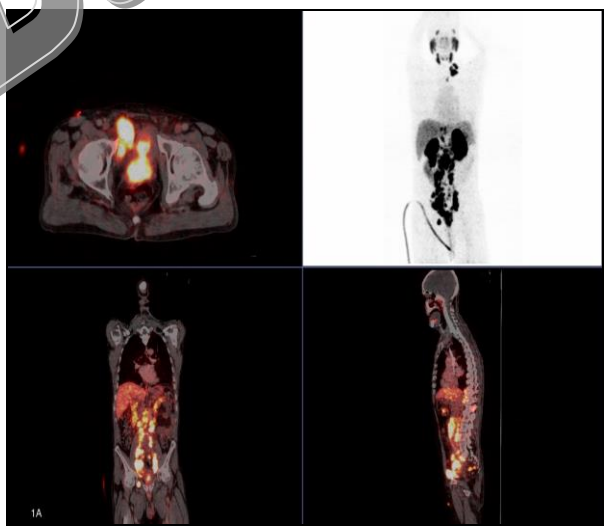

Figure 1A. *^{68}Ga-PSMA PET-CT findings related to ^{68}Ga-PSMA ligand uptake showing: malignant lesion in the prostate gland, seminal vesicle involvement, lymph node invasion and bone metastases in an 82-year old prostate cancer patient with prostate SUV max of 21.7, Gleason score of 9 and PSA level of 108 ng/ml.*

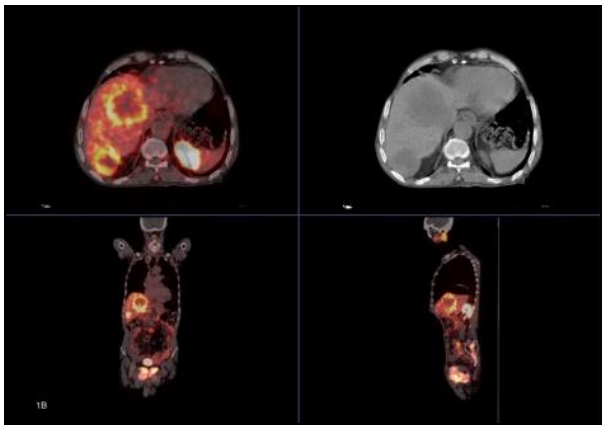

***Figure 1B**. ^{68}Ga-PSMA PET-CT findings related to ^{68}Ga-PSMA ligand uptake showing: mediastinal lymph node invasion, bone and liver metastases in a 62-year old prostate cancer patient with liver SUV max of 18.3, Gleason score of 10 and PSA level of 880 ng/ml.*

Statistical Analysis

Statistical analysis was made using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY). Descriptive statistics were reported and data were expressed as "mean ± (standard deviation; SD)", median (minimum-maximum) and percentage (%) where appropriate.

RESULTS

Patient Characteristics

Mean age of the patients was found 67.6 ± 8.5 years. Overall, 10.2% of patients had previously undergone surgery and 27.7% of patients had received radiotherapy. Bicalutamide (35.7%) and luteinizing hormone-releasing hormone (LHRH; 70.5%) were the most commonly used agents for androgen-deprivation therapy, while docetaxel (30.2%) was the most commonly administered chemotherapeutic agent (Table 1).

***Table 1.** The clinical characteristics of patients with advanced prostate carcinoma (n =234).*

		Mean (SD)		Median (min-max)
Age (years)		67.6 ± 8.5		68 (45-91)
Gleason score		8.1 ± 1.0		8 (6-10)
PSA level (ng/ml)		75.6 ± 117.5		21.7 (0.2-880)
		n (%)		
Invasion of seminal vesicle		44 (18.8)		
Treatment				
Radical prostatectomy		29 (10.2)		
Radiotherapy		59 (27.7)		
Bicalutamide		84 (35.7)		
LHRH analogue		165 (70.5)		
Docetaxel		71 (30.2)		
Abiraterone acetate		36 (15.3)		
Enzatulamide		8 (3.4)		
		n (%)	SUVmax Mean±SD (median)	Size Mean±SD (median) min-max Millimeter
Lymph node involvement		108 (46.1)		
Pelvic		96 (41)	13.6 ± 11.6 (10.5)	18.7 ± 8.8 (16.5) (7-50)
Abdominal		58 (30.3)	15.3 ± 13.0 (11.9)	19.3 ± 10.8 (15.5) (6-54)
Mediastinal		26 (11.1)	13.1 ± 8.0 (10.8)	17.3 ± 10.1 (16.0) (6-42)
Neck		21 (9.8)	11.3 ± 11.5 (8.7)	13.9 ± 6.8 (11.0) (5-29)
Distant organ metastasis				
Liver		17 (7.2)	10.8 ± 4.1 (10.1)	-
Lung		18 (7.6)	5.3 ± 4.2 (4.3)	-
Bone	Total	145 (61.9)	12.97 ±.6 (11.9)	-
	Oligometastatic	21 (8.9)		
	Multimetastatic	52 (22.2)		-
	Carcinomatosis	72 (30.6)		-
Pleura		7 (2.9)	3.3 ± 3.6 (1.8)	-
Adrenal		5 (2.5)	13.9 ± 4.2 (12.8)	-
Effusion/ascites		7 (2.9)	1.9 ± 1.0 (1.6)	-
Peritoneal		2 (0.8)	9.6 ± 1.8 (9.6)	-
Surrounding tissue invasion		28 (11.9)	-	-
Pelvic recurrence		5 (2.1)	8.2 ± 3.9 (9.1)	-

LHRH: Luteinizing hormone-releasing hormone.

Tumor-Metastasis Characteristics

Mean (SD) Gleason score was 8.1 ± 1.0 and median PSA level was 21.7 (0.2-880) ng/ml. The median SUVmax of pelvic lymph node was 10.5, compared to a median SUVmax of 11.9, 10.8 and 8.7 in abdominal, mediastinal and supraclavicular and/or neck lymph node tissue, respectively. Median SUVmax of 10.1, 4.3 and 11.9 was noted in liver, lung and bone tissue, respectively (Table 1).

The size of positive lymph nodes ranged from 13.9 ± 6.8 (5-29) mm for supraclavicular and/or neck lymph nodes to 19.3 ± 10.8 (6-54) mm for abdominal lymph nodes. The most commonly involved lymph nodes were pelvic (41%), abdominal (30.3%), mediastinal (11.1%) and supraclavicular and/or neck (9.8%) lymph nodes. Bone metastases were oligometastatic, multimetastatic and in 8.9% and 22.2% of patients, respectively, while bone carcinomatosis was noted in 30.6% of patients. Other common distant organ metastases were lung (7.6%) and liver (7.2%) metastases (Table 1).

Lymph Node Positivity in Patients with Respect to the Type of Metastasis

Level 1-4 lymph node positivity was noted in 29.4%, 33.3% and 6.8% of patients with liver metastasis, lung metastasis and seminal vesicle invasion, respectively. Level 1-2 lymph node positivity was more common for bone metastasis, comprising all lymph node metastasis for the oligometastatic stage (19% for each) with high rates in multimetastatic (21% and 15.3%, respectively) bone lesions or bone carcinomatosis (10.9% and 15%, respectively) (Table 2).

Table 2. *Lymph node positivity in patients with respect to type of metastasis.*

		Patients with metastases					
					Bone		
		Liver (n =17) (%)	**Lung (n =18)** (%)	**Seminal vesicle (n =44)** (%)	Oligometastatic (n =21) (%)	Multimetastatic (n =52) (%)	Carcinomatosis (n =73) (%)
Lymph node metastasis							
Level							
Level 1		1 (4.8)	4 (22.0)	12 (27.2)	4 (19)	11 (21.1)	8 (10.9)
Level 2		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (5.4)
Level 3		2 (11.7)	2 (11.1)	0 (0.0)	0 (0.0)	3 (5.7)	2 (2.7)
Level 1+2		0 (0.0)	1 (5.5)	6 (13.6)	4 (19)	8 (15.3)	11 (15)
Level 2+3		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Level 1+2+3		1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.6)	6 (8.2)
Level 1+2+4		1 (4.8)	0 (0.0)	11 (25.0)	0 (0.0)	6 (11.5)	6 (8.2)
Level 1+3+4		1 (4.8)	1 (5.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.7)
Level 1+2+3+4		5 (29.4)	6 (33.3)	3 (6.8)	0 (0.0)	6 (11.5)	4 (5.4)
Region							
Pelvic		10 (58.8)	11(61.1)	28 (63.6)	8 (38)	32 (61.5)	33 (45.2)
Abdominal		7 (41.1)	9(50)	16 (36.3)	3 (14.2)	23 (44.2)	30 (41.0)
Mediastinal		8 (47)	8(44.4)	3 (6.8)	0 (0.0)	11 (21.1)	13 (17.8)
Supraclavicular and/or neck		6 (35.2)	7(38.8)	11 (25)	0 (0.0)	12 (22.6)	13 (17.8)
Distant metastasis							
Lung		7 (41.1)	-	6 (13.6)			
Liver		-	5 (27.7)	6 (13.6)			
Bone	Oligometastatic	0 (0.0)	0 (0.0)	4 (9.0)			
	Multimetastatic	7 (41.1)	5 (27.7)	7 (15.9)			
	Carcinomatosis	9 (52.9)	11 (61.1)	18 (40.9)			

Concomitant lung metastasis was evident in 41.1% of patients with liver metastasis, while lung or liver metastasis was evident in 3.6% of patients with seminal vesicle invasion (Table 2).

Bone metastasis was evident in all patients with liver (multimetastatic in 41.1%, bone carcinomatosis in 52.9%) and lung (multimetastatic in 27.7%, bone carcinomatosis in 61.1%) metastases, and in 65.9% of patients with seminal vesicle invasion (oligometastatic in 9.0%, multimetastatic in 15.9%, bone carcinomatosis in 40.9%) (Table 2). In patients with oligometastatic stage bone metastasis, no concomitant lung or liver metastases or level 3-4 lymph node metastases were determined whereas there was positivity of seminal vesicle invasion.

DISCUSSION

This retrospective analysis of ^{68}Ga-PSMA PET/CT scans in 234 patients with advanced prostate cancer revealed a predominance of lymph node metastases in 46.1% (pelvic in 41% and abdominal in 30.3%) and bone metastases in 61.9% (bone carcinomatosis in 30.6% and oligometastatic in 8.9%). Level 1-4 lymph node positivity was evident in the presence of lung and liver metastasis or seminal vesicle invasion, whereas the presence of bone metastasis was associated with level 1-2 lymph node positivity. Bone metastasis was evident in all patients with liver and lung metastasis, while present at oligometastatic stage only in patients with seminal vesicle invasion.

In the current cohort: lymph node metastases in 46.1% of patients and bone metastases in 61.9%, as well as pulmonary (7.6%), hepatic (7.2%), adrenal (2.5%), peritoneal and (0.8%), pleural (2.9%) metastases in a previous retrospective analysis of 240 patients with prostate cancer, ^{68}Ga PSMA I&T PET/CT revealed lymph node metastases in 62.5% of patients and bone metastases in 33.7%, together with local recurrences (26.6%) as well as pulmonary (4%), hepatic (2%), adrenal (1%), peritoneal (0.5%), muscular (0.5%) and testicular (0.5%) metastases (19). In another retrospective analysis of 101 patients with increased PSA levels after radical prostatectomy, the ^{68}Ga-PSMA-I&T PET/CT revealed lymph node metastases in 73.3% of patients and bone metastases in 30.7%, together with local recurrences (16.8%) and other metastases (5.9%) (20). In a retrospective analysis of 83 consecutive patients (PSA: 0.81, range: 0.01 - 128 ng/mL) with biochemical relapse after prostatectomy, the ^{68}Ga PSMA I&T PET/CT revealed local recurrent cancer in 22% of the patients, lymph node metastases in 35% and distant metastases in 18% (17).

In a retrospective analysis of the diagnostic value of ^{68}Ga-PSMA PET/CT in 901 representative tumor lesions of 319 patients, 13 lesions were defined as local relapses after prostatectomy, while 328 were reported as lymph node metastases, 359 as bone metastases, 129 as soft tissue metastases and 72 as vital tumor lesions within the prostate gland (21).

In our patient group, median SUVmax in lymph nodes ranged from 8.7 in supraclavicular and/or neck lymph nodes to 11.9 in abdominal lymph nodes, while the size of lymph nodes detected via ^{68}Ga-PSMA PET/CT ranged from 13.9 (range: 5-29) mm (neck lymph nodes) to 19.3 (range: 6-29) mm (abdominal lymph nodes). Similarly, in a retrospective analysis of 90 patients with prostate cancer referred for ^{68}Ga-PSMA PET/CT, lymph node metastasis was reported in 26.7% of patients together with median nodal diameter of 10.9 mm (range: 3.9–32.9) and SUVmax of 10.6 (12).

In a previous study of 25 patients with biochemical recurrence after radical prostatectomy, ^{68}Ga-PSMA-I&T PET/CT revealed presence of lymph node metastases in 60.5% of patients and with SUVmax of 21.9 (ranged 4.2–89.0) (22).

The range (5-54 mm) for the size of lymph nodes detectable via ^{68}Ga-PSMA-I&T PET/CT in the current study seems notable given the significant difference reported in median size of lymph node metastases detected vs. undetected (13.6 versus 4.3 mm) via ^{68}Ga-PSMA PET/CT and the potential influence of lymph node metastasis size on the diagnostic accuracy of ^{68}Ga-PSMA PET/CT (23).

The sensitivity and specificity of ^{68}Ga-PSMA PET/CT in the detection of lymph node metastasis has been reported to range from 61.1-80.0% and 90.0-100.0%, respectively in past studies (6, 12, 21).

In accordance with consideration of bone as the most frequent site of metastatic spread in prostate cancer (24) bone metastases were detected in 61.9 % of patients and with median SUVmax of 11.9 in our cohort. Compared to the current study findings of the diagnostic accuracy of ^{68}Ga-PSMA PET/CT in detecting bone metastasis, lower detection rates (12.2%) with similar SUV (SUVmax: 11.6) (12) as well as lower detection rates (34.2-36%) (22, 25) with higher SUV (SUVmax: 27.1) (22) or lower PSA levels (median 1.99 ng/ml, ranged 0.2-53.4) (25) have been reported among recurrent prostate cancer patients in past studies.

In a retrospective study of 155 consecutive patients with recurrent disease, the overall rate of bone metastases was reported as 32%, which ranged from 15% in patients with PSA <1 ng/ml to 39% in those with PSA ≥2 ng/ml (26).

Accordingly, in a systematic review of 37 studies on the utility of ^{68}Ga-PSMA PET/CT for the detection of bone metastases, the prevalence of pathological bone lesions was reported ranging from 5% to 60% (24). The authors concluded that the diagnostic performance of ^{68}Ga-PSMA PET/CT was higher with increased PSA levels and it was superior to bone scintigraphy in the detection of bone lesions in terms of sensitivity (99% vs 73%) and specificity (100% vs. 98%), whereas its diagnostic performance in progressive metastatic disease was considered as questionable (24).

The lung was the second most common distant organ metastasis (7.6%) in our study and lung metastasis was associated with the lowest SUVmax scores (median 4.3) amongst other metastases. The lung has been considered as the second organ involved after bone in patients with prostate cancer, while the lack of any significant difference in SUVmax values between lung cancer and histologically proven prostate cancer has also been emphasized due to PSMA expression in tumor associated neo-vasculature in patients with primary lung cancer (27, 28). In fact, ^{68}Ga-PSMA PET/CT is considered less valuable in the lungs, since it fails to discriminate reliably between pulmonary metastases and primary lung cancer in prostate cancer patients (7, 28).

Gleason scores of > 7 or PSA levels ≥ 10 ng/ml have been associated with significantly higher uptake of ^{68}Ga-PSMA in patients with prostate cancers (29), while the increasing rate of bone metastases has been reported with higher PSA levels or the PSA doubling

time (24, 26). This seems notable given the median Gleason score of 8 (6-10) and median PSA level of 21.7 ng/mL (0.2-880) in the current study. Nonetheless, it has been emphasized that a continuous increase in PSA level does not automatically correlate with an increase in tumor detection (21) and a high PSA-value may also predict lower diagnostic performance of ^{68}Ga-PSMA PET/CT for detection of affected regions due to a higher likelihood of microscopic spread (30).

Given the earlier occurrence of increased PSMA expression than the expected morphological alterations in bone metastases (31) and the superiority of ^{68}Ga-PSMA-ligand imaging to morphological imaging in the detection of lymph node metastases (7, 32) the current study findings emphasize the role of ^{68}Ga-PSMA PET/CT in timely and accurate diagnosis of lymph node and bone involvement in patients with PSA persistence or progressive metastatic disease (19, 24). This seems critical in the management of prostate cancer in terms of potential for allowing planning of a more tailored therapeutic strategy and use of salvage procedures (e.g. secondary lymphadenectomy, targeted radiation therapy) with a potentially curative intent (7, 31, 33, 34). However, in unclear ^{68}Ga-PSMA PET positive lesions, further diagnostic work-up with morphological correlation and confirmation via other imaging techniques such as MRI, ultrasound or biopsy are considered necessary (7).

The current study findings also revealed data on the concomitant presence of lymph node and distant organ metastases. Level 1-4 lymph node positivity was evident in the presence of lung and liver metastasis or seminal vesicle invasion, whereas the presence of bone metastasis was associated with level 1-2 lymph node positivity. Although only 8.9% of bone metastases were at the oligometastatic stage compared with the detection of multi-metastatic bone metastases in 22.2% of patients in this cohort, it should be noted that bone metastasis was evident in all patients with liver and lung metastasis, while it was at the oligometastatic stage only in patients with seminal vesicle invasion. This finding revealed an absence of concomitant lung or liver metastases and level 3-4 lymph node metastases, but positivity of seminal vesicle invasion in patients with oligometastatic stage bone metastasis. This seems notable given that prompt detection of prostate cancer recurrence is considered of critical importance since metastases are more likely to be locally confined or oligometastatic at this point enabling the use of metastasis-directed therapies, both lymphadenectomy and radiotherapy (6).

This study has some limitations: The first is retrospective, single centered, study in a certain date range. A second limitation is the lack of histological validation for positive findings on ^{68}Ga-PSMA PET/CT. Despite these limitations, this study will provide valuable literary contributions to metastases in prostate cancer patients.

In conclusion, the findings of this retrospective cohort of patients with advanced prostate cancer showed the value of ^{68}Ga-PSMA PET/CT in detecting coexistence rates of metastases in advanced prostate cancer.

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