THE IMPACT OF 68GA-PSMA PET/CT ON THERAPY MANAGEMENT OF HIGH RISK PROSTATE CANCER

YÜKSEK RİSKLİ PROSTAT KANSERİNDE 68GA-PSMA PET/BT'NİN TEDAVİ YÖNETİMİNE ETKİSİ

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ABSTRACT

Objective: We evaluated the impact of 68Ga-PSMA PET/CT (PSMA PET) on therapy management of newly diagnosed high-risk prostate cancer (PCa).

Material and Method: Patients who underwent a PSMA PET for primary staging of high-risk PCa were evaluated retrospectively. Patients had abdominopelvic CT (n=126), pelvic MRI (n=42) and bone scintigraphy (BS) (n=40) prior to PSMA PET. All clinical, biochemical, and imaging data were documented. Increased PSMA uptakes related to PCa were documented according to previously described PSMA-RADS version 1.0 based on a five-point scale. The impact of PSMA PET on patient management was evaluated through pre and post PET/CT questionnaires, retrospectively. Management changes were categorized as inter or intramodality change, based on PSMA PET results. Paired samples t-test was used to compare subgroups in SPSS version 24.0 software. A p-value <0.05 was considered significant.

Results: A total of 126 patients were included in the study. The median PSA level was 30.8 ng/ml (95%CI: 2.1-268.6 ng/ml) and median GS was 8 (range: 6-10). Based on the PSMA PET findings, 41 patients (32.5%) had more extensive disease and 2 patients (1.6%) had less extensive disease. Overall, therapy management was changed in 38 patients (30.1%). Intermodality changes occurred in 29 patients (23%), and intramodality changes occurred in 9 patients (7.1%). The change in management was similar in patients with BS and without BS, 30% vs. 30.2%.

Conclusion: PSMA PET impacted the therapy management in almost one-third of patients in high-risk PCa even though they

ÖZET

Amaç: Yüksek riskli prostat kanserinde (PK) 68Ga-PSMA PET/BT'nin (PSMA PET) tedavi yönetimine etkisi değerlendirildi.

Gereç ve Yöntem: Yüksek riskli PK nedeniyle evreleme amaçlı PSMA PET yapılan hastalar retrospektif olarak değerlendirildi. Hastaların PSMA PET öncesi abdominopelvik BT (n=126), pelvik MR (n=42) ve kemik sintigrafisi (KS) (n=40) bulunmaktaydı. Tüm klinik, biyokimya ve görüntüleme datası belgelendi. Hastalara uygulanan tedavilerin incelenmesi amacıyla hastalar takibe alındı. PK ile ilişkili artmış PSMA tutulumları önceden PSMA-RADS versiyon 1,0'da tanımlanan 5 puanlı skalaya göre belgelendi. PSMA PET'in hasta yönetimine etkisi pre-post PET/BT anketler ile retrospektif olarak değerlendirildi. PSMA PET sonuçlarına göre yönetim değişikliği inter ve intramodalite değişiklik olarak kategorize edildi. Altgruplar eşleştirilmiş t-testi ile SPSS version 24,0 programında karşılaştırıldı. p değeri <0,05 anlamlı kabul edildi.

Bulgular: Toplam 126 hasta çalışmaya dahil edildi. Medyan PSA değeri 30,8 ng/ml (%95CI: 2,1-268,6 ng/ml) ve medyan GS 8 (range: 6-10) idi. PSMA PET sonuçlarına göre 41 hastada (%32,5) hastalık daha çok yaygın iken, 2 hastada (%1,6) daha az yaygın idi. Toplamda tedavi yönetimi 38 hastada (%30,1) değişti. Intermodalite değişiklik 29 hastada (%23) görülürken, intramodalite değişiklik 9 hastada (%7,1) görüldü. Yönetimdeki değişiklik KS olan ve olmayan grupta, %30 ve %30,2 ile benzerdi.

Sonuç: PSMA PET yüksek riskli PK'de hastalar standart görüntülemeler ile evrelense bile neredeyse üçte birinde tedavi yönetimini etkilemektedir.

had already been staged with standard imaging modalities.

Keywords: 68Ga-PSMA PET/CT, prostate cancer, staging, therapy management

INTRODUCTION

Prostate cancer (PCa) is one of the leading cancers in men worldwide (1). The incidence of PCa varies widely between different geographical areas, and increases largely due to the use of prostate-specific antigen (PSA) testing and the aging population (2). Different scenarios can be observed ranging from indolent to lethal tumors, based on tumor biology and stage at diagnosis. Therefore, accurate staging is crucial on deciding appropriate therapy for initial PCa, beyond the clinical and histopathological profile of the patient. In clinical practice, cross-sectional abdominopelvic imaging and bone scan were used for staging of PCa patients (3). However, these imaging modalities were limited for detection of all metastatic lesions (4, 5). Ultimately, 68Ga-PSMA PET/CT (PSMA PET) has entered the clinical practice, using prostate-specific membrane antigen (PSMA) as a target protein, which is significantly overexpressed in most of PCa cases (6). Up to now, PSMA PET has been shown to be superior to cross-sectional abdominopelvic imaging and bone scan for detection of PCa metastasis (7-9). Since the excellent results of PSMA PET were published, recent EAU Guideline have recommended PSMA PET for biochemical recurrence (BCR), however, they still recommend cross-sectional abdominopelvic imaging and bone scan for staging intermediate and high-risk PCa, due to the unclear results (3). In literature, most of the published studies investigated the impact of PSMA PET on the management of BCR of PCa (10-13), while limited studies investigated this issue in newly diagnosed PCa (14-16). We recently published a study where nearly half of the high-risk patients had isolated pelvic lymph node or distant metastases on staging PSMA PET (17). In this study, we evaluated the clinical impact of PSMA PET on newly diagnosed high-risk PCa, and investigated if a change occurred in therapy management after PSMA PET.

MATERIAL AND METHOD

Patients

Two hundred and eighty-nine patients who underwent a PSMA PET scan for primary staging of high-risk PCa between 2015 and 2019 were evaluated retrospectively from a prospectively collected database. However, 163 patients who had undergone prior therapy for PCa or without abdominopelvic CT/MRI and clinical-follow up data were excluded. All clinical, biochemical, and imaging data was documented. Patients were followed-up for analysis of applied therapies.

From the clinical point of view, EAU (2020) risk classification was used for describing the risk group of patients as low (PSA<10 ng/mL and GS<7 cT1-2a), intermediate (PSA: 10-20 ng/mL, GS 6-7a [GS3+4], or cT2b) or high-risk (PSA>20 ng/mL, GS 7b [GS4+3]-10, or cT3-T4) (3). Patients were also evaluated in different subgroups such as PSA≤20ng/ml vs. >20 ng/ml, GS6-7 vs. GS>7 and T1-2 stage vs. T3-4 stage subgroups. This study was approved by our institutional review board, and written informed consent was obtained from all patients.

68Ga-PSMA synthesis and PET/CT acquisition

We applied 68Ga-PSMA labelling according to the protocol as described in the literature (18). 68Ga-PSMA PET-CT was performed at 45–60 min after an intravenous injection of approximately 185 MBq of 68Ga-PSMA on a dedicated PET-CT scanner (Biograph TruePoint PET/CT; Siemens Healthcare. Erlangen, Germany), as we described previously (19). An iodine-based oral contrast agent was administered to all patients. All patients were scanned from the top of the head through the upper thigh. Additionally, a late pelvic scan was acquired for all patients. CT acquisition was performed on a spiral CT scanner, with a slice thickness of 4 mm and a pitch of 1. After the CT scan, 3D-PET images were acquired for 3 min per bed for limited whole body imaging and late pelvic imaging. CT-based attenuation correction of the emission images was used. PET images were reconstructed by the iterative method using ordered-subset expectation maximization (OSEM; 2 iterations and 8 subsets). After completion of the PET acquisition, the reconstructed attenuation corrected PET images, CT images, and fused images of PET and CT images were reviewed.

Image analysis

All images were evaluated retrospectively by two experienced nuclear medicine physicians. Increased PSMA uptake related to PCa were documented according to previously described PSMA-RADS version 1.0 system based on a five-point scale (from 1= no evidence of disease and definitively benign to 5= high certainty that PCa is present) (20). PSMA PET findings were interpreted similar to our previous study (17), based on a previously described flowchart in a review (21).

Evaluation of the impact of PSMA PET on patient management

The impact of PSMA PET on patient management was evaluated through pre and post PET/CT questionnaires, retrospectively. Pre-PET/CT questionnaires were filled out

by referring physicians including urologist and radiation oncologist, blinded to PET/CT findings. In the pre-PET/CT questionnaire, physicians reported the intended treatment strategy with available clinical and imaging results including abdominopelvic CT/MRI±bone scintigraphy (BS), before the PSMA PET imaging. In the post-PET/CT questionnaire, physicians were asked if PSMA PET findings caused any changes in patient management. Decisions were made based on recent guidelines (3). Management changes were categorized as inter or intramodality change, based on the PSMA PET results. Intermodality change was defined as a change in therapy modality (eg. surgery, radiotherapy, systemic therapy) or adding more therapy modalities. Intramodality change was defined as a difference in the same therapy modality (eg. change in lymph node dissection area, RT dose or field, chemotherapy in order to androgen deprivation therapy).

Statistics
SPSS version 24.0 software was used for calculation of continuous and qualitative variables including median, range and frequency of their modalities and normality analysis. Additionally, the paired samples t-test was used to compare the impact of PSMA PET on the management of subgroups. A p-value <0.05 was considered significant.

RESULTS

A total of 126 patients were included in the study. The median PSA level was 30.8 ng/ml (95%CI: 2.1-268.6 ng/ml) and median GS was 8 (range: 6-10). Demographic, clinic and pathologic details of patients are given in Table 1.

Abdominopelvic CT/MRI results
All patients had abdominopelvic CT and 42 patients had pelvic MRI. In addition to primary tumor, MRI determined the tumoral invasion to seminal vesicle and bladder in 7 and 2 of the patients, respectively. At least one metastatic lymph node was detected in 37 patients (29.3%) on abdominopelvic CT or MRI. Pelvic lymph node metastasis was defined in 36 patients, and abdominal lymph node metastasis was defined in 10 patients. Bone metastasis was detected in 9 patients and liver metastasis was present in 1 patient.

Bone scintigraphy results
BS was present in 40 patients, and 7 of them had at least one bone metastasis on BS. In three patients, 1-3 bone metastases were detected in the skeleton and categorized as low tumor volume M1 disease, while in 4 of them, widespread bone metastases were present and categorized as high tumor volume M1 disease based on CHAARTED criteria (22). In three patients, equivocal osteoblastic uptakes located in costa, sacrum, and vertebra were interpreted as suspicious for metastasis.

Table 1: Demographic and clinical characteristics of patients.

Characteristics of patients (n=126)	n (%)
Age	
Mean (range)	68 (51-90)
Baseline PSA levels (ng/ml)	
Median (range)	30.8 (95%CI: 2.1-268.6)
PSA levels	
PSA ≤ 20 ng/ml	37 (29.4%)
PSA > 20 ng/ml	89 (70.6%)
Gleason score at initial diagnosis	
Median (range)	8 (6-10)
6-7	35 (27.8%)
8-9-10	91 (72.2%)
Clinical T stage prior to PSMA PET	
T1-2	71 (56.3%)
T3-4	55 (43.7%)
Clinical N stage prior to PSMA PET	
N0	90 (71.4%)
N1	36 (28.6%)
Clinical M stage prior to PSMA PET	
M0	30 (23.8%)
M1a	10 (7.9%)
M1b	16 (12.7%)
M1c	1 (0.8%)
Mx	69 (54.8%)

PSMA PET results

Localised disease
A total of 123 (97.6%) patients had increased PSMA uptake in the primary tumor, while there was no significant PSMA uptake in 3 (2.4%) patients. On the other hand, invasion to the seminal vesicle (n=27), bladder (n=8) and/or rectum (n=1) were reported in a total of 31 patients (24.6%), with intense PSMA uptake on PSMA PET and anatomic correlation of gross invasion in CT or MRI.

Nodal metastasis
PSMA PET determined at least one metastatic lymph node (LN) in 66 of 126 patients (52.3%). Pelvic LNs were detected in 65 patients, and in 16 of them, pelvic lymph nodes were outside the PLND area, located in the common iliac (n=9), presacral (n=5) and/or pararectal/

perivesical (n=5) area. Abdominal LNs were detected in 25 patients and supradiaphragmatic LNs were detected in 15 patients.

Bone metastases

PSMA PET determined bone/bone marrow metastasis in 39 of 126 patients (30.9%). In 10 patients, 1-3 bone metastases were detected in the skeleton and categorized as low tumor volume M1 disease, while in 29 of them, multiple (4 or more) or widespread bone metastases were present in the skeleton and categorized as high tumor volume M1 disease based on CHAARTED criteria.

Visceral metastases

Visceral metastases were detected in 7 (5.5%) patients, which were located in lung (n=3) and/or liver (n:5).

Others

Additionally, a suspicious PSMA RADS-3C uptake in lung had diagnosed lung adenocarcinoma by biopsy. The other PSMA RADS-3C uptake in kidney was revealed as renal cell carcinoma, histopathologically.

Pre- PSMA PET therapy management

Before the PSMA PET scan, initial evaluations were assessed with clinical examination, present abdominopelvic CT/MRI and availiable BS findings. Local therapies were planned in 98 patients (77.8%). In 29 patients (23%), radical prostatectomy (RP) and extended pelvic lymph node dissection (ePLND)±external radiotherapy (RT) was the first therapy of choice, and in 47 patients (37.3%) surgery or RT was intended before the PET/CT. In the remaining 22 patients (17.5%), RT + androgen deprivation therapy (ADT) was planned due to the limited pelvic disease. On the other hand, systemic therapies were planned in 28 patients (22.2%). In the presence of high tumor volume, chemotherapy (CTx)+ADT or ADT was intended in 20 (15.9%) and 3 (2.3%) patients regarding clinic performance and age, while in 5 (4%) patients, ADT±RT was intended due to the low tumor volume.

Post-PSMA PET therapy management

Based on PSMA PET findings, 41 patients (32.5%) had more extensive disease and two patients (1.6%) had less extensive disease, based on stage. Overall, therapy management was changed in 38 patients (30.1%). Intermodality changes occurred in 29 patients (23%). Systemic CTx+ADT (n=13, 10.3%) or ADT±RT (n=5, 4%) was administered to 18 patients (14.2%) instead of surgery/RT based on metastatic tumor volume which was defined in the CHAARTED study (22) (Figure 1). In 6 patients (4.7%), whose treatment were intended as RT+ADT was changed as CTx+ADT (n=5) or ADT (n=1) due to the metastatic disease. In 3 patients (2.4%) who were planned ADT±RT were replaced as CTx+ADT after PSMA PET, due to the high volume metastatic disease. PSMA PET changed the tumor volume status in a total of 27 patients (21.4%),
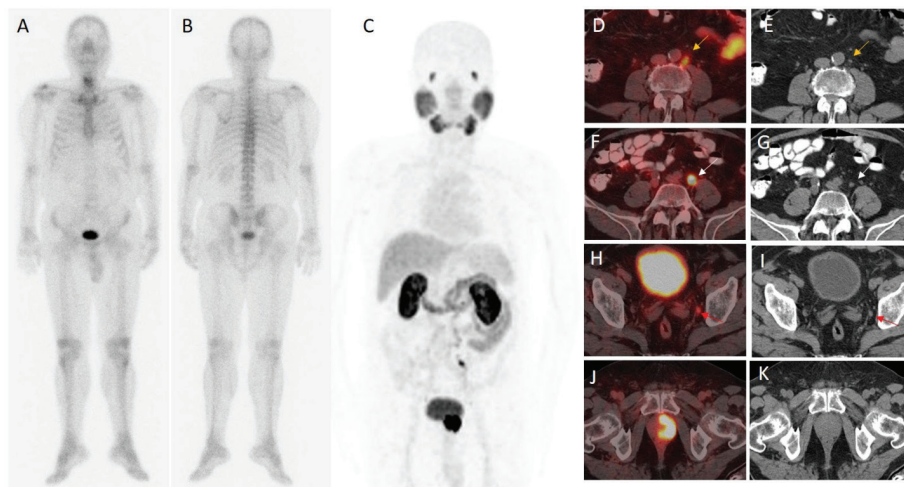
Figure 1: 73 years old man with newly diagnosed high risk prostate cancer (GS:4+4=8, cT3 and PSA:11 ng/ml). Bone scintigraphy (A-B) was negative and patients had no metastasis in abdominopelvic CT. Patient had intended to surgery +/- radiotherapy before the 68Ga-PSMA PET/CT. 68Ga-PSMA PET/CT (C) was performed for staging. Milimetric metastatic lymph nodes were detected in left paraortic (D-E: yellow arrows), left common iliac (F-G: White arrows) left internal iliac (H-I:red arrows) with increased PSMA uptake demonstrated in axial fusion and CT images. Intense PSMA uptake also detected in primary prostate cancer (J-K). Intermodality changes occurred. Androgen deprivation therapy +/- RT was planned after 68Ga-PSMA PET/CT.

and distant metastases were detected in 24 of patients (18.9%) who were intended local therapies at initial diagnosis. Besides that, local therapy was planned instead of RT+ADT after downstaging of 2 patients (1.5%)

Intramodality changes occurred in 9 patients (7.1%). In 6 patients (4.7%) who were planned local therapies, the radiation field size or surgery area was expanded after PSMA PET due to the newly diagnosed lymph node metastasis outside the template of the extended PLND area (Figure 2). The radiation field size also increased in the remaining 3 patients (2.4%) who were planned RT+ADT for low volume metastatic disease.

We also investigated the impact of PSMA PET on therapy management if BS was present or not prior to PSMA PET. In the BS group, the therapy management was changed in 12 of 40 patients (30%), by upstaging (n:10) or downstaging (n=2) of disease. Intermodality changes occurred in 9 of 40 patients (22.5%). In detail, a local therapy plan was shifted to CTx+ADT (n:3) or ADT±RT (n=2) in 5 patients based on tumor volume status, and RT+ADT plan was shifted to CTx+ADT in 2 patients due to the multimetastatic disease. In the remaining 2 patients, PSMA PET revealed the benign bone pathologies which were interpreted as metastasis on BS, and the therapy plan was changed to local therapy after PSMA PET. Intramodality changes occurred in 3 of 40 patients (7.5%). The radiation field size increased in 2 patients, and surgery area was expanded in one patient. Also, we evaluated 26 pa-

tients who had only localized disease based on MRI and BS findings separately. PSMA PET revealed pelvic lymph nodes (n=2) and distant metastases (n=4) in 6 of 26 (23%) and 5 of them (19.2%) the management was changed.

In 86 patients without BS, therapy management was changed in 26 patients (30.2%). Of them, 20 patient had intermodality changes by upgrading to CTx+ADT (n=10) or ADT±RT (n=3) instead of local therapies in 13 patients, and shifting to CTx+ADT from RT+ADT in seven patients after PSMA PET. The remaining 6 patients (6.9%) had intramodality changes which effected surgery or RT area. A summary of changes in therapy management are shown in Figure 3.

Subgroup analyses
The impact of PSMA PET on therapy management was not significantly different in PSA≤20ng/ml vs. >20 ng/ml (p=0.322) subgroups and in GS6-7 vs. GS>7 subgroups (p=0.951), while it was signifcantly different in patients with T1-2 stage vs. T3-4 stage (p=0.014).

DISCUSSION

Most of the published studies have investigated the impact of PSMA PET on the management of BCR of PCa (10-13), while limited studies have investigated this issue in newly diagnosed PCa (14-16). In our previous study, we evaluated 356 newly diagnosed PCa who performed PSMA PET for staging (17). We found that half of the
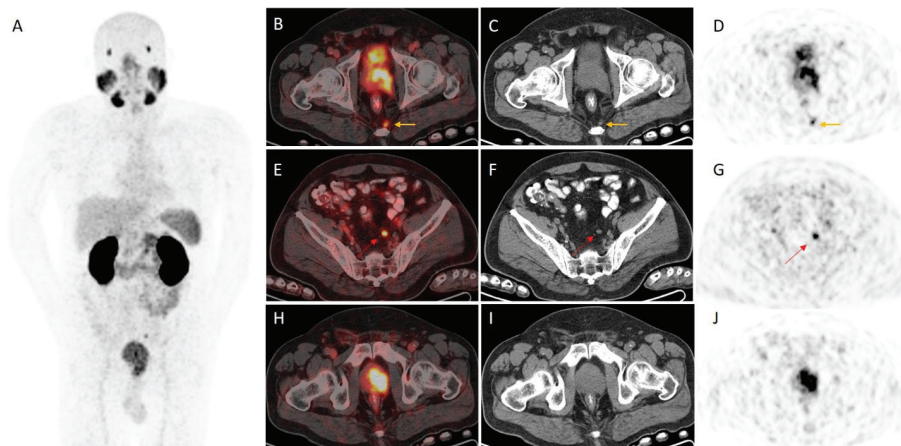
Figure 2: 67 years old man, who was diagnosed with prostate cancer (PSA: 36 ng/ml, cT3 and Gleason Score: 4+3=7). Patient had no metastasis on abdominopelvic CT, and intended to have surgery +/- radiotherapy before the 68Ga-PSMA PET/CT. 68Ga-PSMA PET/CT (A) was performed for staging. Milimetric metastatic lymph nodes were detected in left precoccygeal (B-C-D: yellow arrows) and left presacral (E-F-G: red arrows) with increased PSMA uptake demonstrated in axial images. Intense PSMA uptake was also detected in primary prostate cancer with extraprostatic extension (B-C-D-H-I-J). Intramodality changes occurred. Lymph nodes were located outside the surgery area which caused an expension of the surgery field.
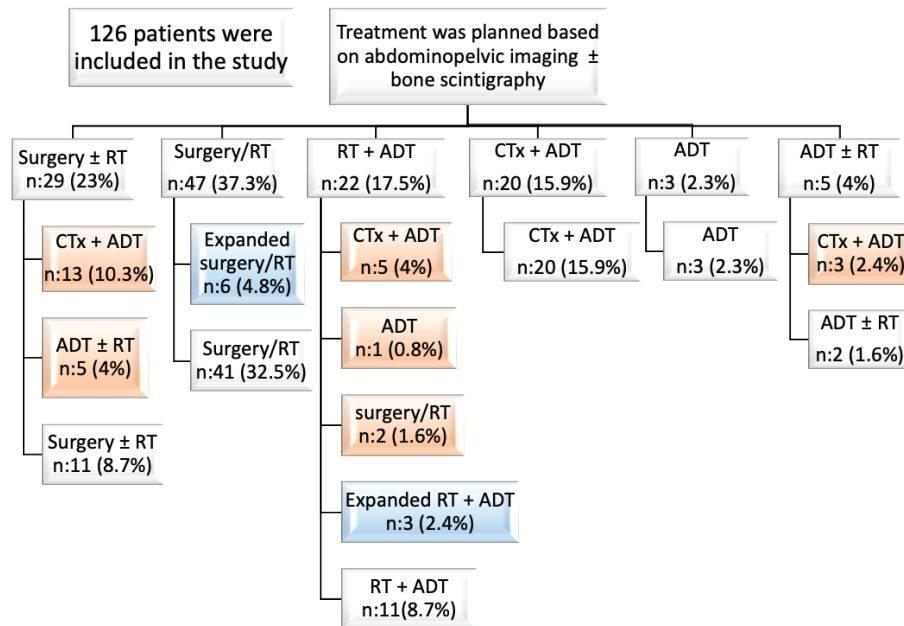
Figure 3: The flow chart of therapy management based on pre-post PSMA PET questionnaires. Intermodality changes are illustrated in the pink colored boxes. Intramodality changes are shown in the blue colored boxes.

high-risk patients had isolated pelvic lymph node or distant metastases on PSMA PET, while only pelvic lymph node metastases were defined in 3.7% intermediate-risk group and no metastasis was found in the low-risk group. Therefore, we evaluated the clinical impact of PSMA PET on newly diagnosed high-risk PCa and investigated if a change occurred in therapy management after PSMA PET in this follow-up study. Based on our PSMA PET findings, 32.5% of 126 patients had more extensive disease and 1.6% of patients had less extensive disease. Overall, therapy management was changed in 30.1% patients, the changes were intermodality in 23%, and intramodality in 7.1%. A prospective multicenter study involving 108 newly diagnosed PCa patients was published by Roach et al. where PSMA PET affected therapy management in 21% of patients by detection of more extensive disease (14). Moreover, Donjwisk et al. concluded that N and M status was upstaged in 23% and 13% of patients and was downstaged in 9% and 23% of patients, which resulted in a 36% treatment change (23). Our results were in concordance with the previous studies. However, both studies investigated intermediate and high risk patients with different proportions. The changes in management plan was not significantly different in the intermediate (36.6%) and high risk (63.4%) group in the Roach et al.' study, while Donjwisk et al. included only 13% of patients in their intermediate group and no subgroup data was available. One larger retrospective study investigated the impact of PSMA PET in 1253 newly diagnsoed PCa patients (24). They found that metastasis rate was higher in the high

risk group, compared to intermediate risk patients, 19.9% vs. 5.2%, in line with our previous study (17). Recently, Ferraro et al. published that PSMA PET significantly improved post-RP outcome comparison to conventional imaging, especially in high-risk PCa patients (25). These results suggest that the impact of PSMA PET is limited in therapy management of intermediate patients, compared to high risk patients.

In the present study, the impact of PSMA PET was mostly seen in patients who were intended to apply local therapies before PSMA PET. Of 18.9% patients, systemic therapies were administered instead of local therapies due to the metastatic disease, and of 4.7% patients, the radiation field size or surgery area was expanded. The ultimate principle of successful surgery is the accurate staging of cancer. In the clinical practice, the clinicopathologic TNM system is used for staging PCa (26). Patients were categorized based on local, nodal and distant metastasis by using clinical examination, surgery/biopsy data, ultrasonography, CT/MRI and BS as recommended in recent guidelines (3). However, local staging is limited to surgery field, and distant metastases are frequently missed with standard imaging modalities which have limited sensitivity for PCa metastasis (4, 5, 27). The diagnostic superiority of PSMA PET has been shown in comparison studies previously (9, 28, 29). In agreement with those studies, PSMA PET showed at least one local/metastatic lesion in 64.5% of patients with persisting detectable PSA after RP in a prospective study (30). Our results are in line with the

literature stating that patients can be understaged with standard modalities, and PSMA PET should be used to select the best candidate for local treatments to avoid early recurrence or persistance of disease.

The clinical outcomes of metastatic patients are heterogeneous due to the different tumor biology and metastatic spread of disease (22, 31, 32). The CHAARTED trial evaluated the outcomes of docetaxel in patients with low and high volume metastatic disease, based on the number and location of bone metastases (22). Patients with high tumor benefited from docetaxel therapy more than the patients with low volume metastatic disease. The STAMPEDE trial also showed that radical radiation therapy to the prostate could improve the overall survival in PCa patients with low tumor volume (33). In light of the available knowledge, castration combined with prostate radiotherapy is recommended for low volume metastatic disease, while no local therapies combined with ADT are recommended for high volume metastatic disease (3). In the present study, PSMA PET detected unknown bone lesions or visceral metastasis which affected the status of tumor volume in 21.4% of patients. PSMA PET determined the patients who had advanced stage and may need more aggressive treatment at initial diagnosis, which could contribute the improvement of outcomes in high risk PCa.

We evaluated the patients based on the presence of BS at initial diagnosis. The total ratio of therapy shift was similar in patients with BS and without BS, 30% vs. 30.2%. In the BS group, 5% of patients had downstaged, while all patients without BS had upstaged after PSMA PET. Besides that, of 19.2% patients who had only localized disease based on present MRI and BS findings, therapy management was changed due to the more extensive disease. Hruby et al. investigated the utility of PSMA PET in addition to CT, multiparametric MRI and BS in 109 intermediate and high risk PCa patients prior to the external RT (34). They revealed that PSMA PET upstaged 14.7% and 6.4% of patients to N1 and M1 disease, respectively, while 2.8% of them were downstaged from M1 to M0 disease. Overall, PSMA PET had an impact on therapy management in 23.9% of patients, even where abdominopelvic imaging and BS were present. Recently, we published a comparative study revealing that PSMA PET has significantly higher sensitivity and specificity for detection of BS, compared with BS and BS+SPECT/ CT (9). The sensitivity and specificity were 100-97.7% for PSMA PET in the staging group, 38.8-51.1% for BS and 428-81.8% for BS+SPECT/CT based on lesion analysis, respectively. These findings indicate that PSMA PET should be performed on all high risk PCa patients, unless high tumor volume metastatic disease was determined in BS.

We also performed subgroup analysis, including PSA, GS and T stage of patients at initial diagnosis. The impact of PSMA PET on therapy management was not significantly different in PSA≤ 20ng/ml vs. >20 ng/ml subgroups and in GS6-7 vs. GS>7 subgroups, while it was significantly different in patients with T1-2 stage vs. T3-4 stage (p=0.014). In line with that, Ferraro et al. found no significant differences in GS groups, while they found significant association in both initial PSA level and TNM stages of patients (15). They investigated intermediate PCa patients in addition to the high risk group, which could explain the contrary results.

The retrospective design, heterogeneous patient profile with different GS, PSA and T stage were some of the limitations. Besides that, pelvic MRI or BS was not present in most of the patients.

CONCLUSION

PSMA PET impacted the therapy management in almost one-third of patients in high risk PCa even though they had already been staged with standard imaging modalities. Our findings indicate that PSMA PET should be performed on all high risk PCa patients regardless of standard imaging modalities, unless high tumor volume metastatic disease was determined before the PSMA PET.

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