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Communication

A single centre pilot experience with ^{18}F-JK-PSMA-7 PET-CT in the staging of prostate cancer

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Abstract

Background: The sensitivity and specificity of bone scintigraphy and thoraco-abdominopelvic CT scans traditionally used for the staging of prostate cancer don't meet clinical requirements. In 2020 ^{18}F-JK-PSMA-7 positron emission tomography-computed tomography (PET-CT) became available in our country for routine clinical diagnostics. **Methods**: As part of our self-assessment, we retrospectively analysed the results of 24 PSMA PET-CTs realised for our patients up to 31 December 2020. **Results**: The indication of the examination was biochemical recurrence after radical prostatectomy (prostate specific antigen (PSA) >0.2 ng/mL) for 16 patients and primary staging (PSA range: 5.2–70 ng/mL) for 8 patients. Biochemical recurrence was related to local relapse in 2 cases, regional lymph node involvement in 5 cases, oligo- and multi-metastatic spread in 1 and 3 cases respectively. 5 patients had no detectable lesion. Patients with PSA <1 ng/mL showed no extrapelvic enhancement. At primary staging 3 patients presented distant metastases. There was no correlation between PSA level and disease extent. In total PSMA PET-CT results changed the treatment strategy for 7 patients. **Conclusions**: ^{18}F-JK-PSMA-7 PET-CT is a useful diagnostic tool. The examination can lead to change the treatment decision at primary staging as well as at biochemical recurrence. The results of this pilot study may support the strategy that patients with biochemical recurrence following radical prostatectomy receive salvage radiotherapy to the prostate bed and the pelvic lymphatic regions without any imaging examination when PSA <1 ng/mL.

Keywords: Prostate cancer; PSMA PET-CT; Biochemical relapse; Therapy optimisation

1. Introduction

One of the most important challenges of the management of prostate cancer is the differentiation between localised and metastatic disease. A treatment with curative intent is only possible in localised and oligometastatic stage. On the other hand local treatment modalities (surgery and radiotherapy of the prostate) may have serious side effects therefore they should be reserved for patients who are potentially curable. The need for a highly sensitive imaging technic is urging.

99m Tc bone scintigraphy and thoraco-abdominopelvic computed tomography are standard staging examinations for prostate cancer, but their sensitivity and specificity don't meet the clinical requirements. The ^{18}F labelled FDG PET-CT, generally used in oncology for staging of various cancer types is not appropriate for the detection of prostate cancer.

Prostate specific membrane antigen (PSMA) is a protein overexpressed on the surface of prostate cancer cells, thus being a potential target for the diagnosis and the treatment of the disease. Numerous ligands binding to PSMA have been developed. These ligands may be labelled with various isotopes such as ^{11}C, ^{18}F, ^{64}Cu,^{68}Ga, ^{89}Zr, ^{131}I or ^{177}Lu rendering them convenient tracers for PET-CT examinations. PSMA PET-CT is recognised to improve the detection rate of prostate cancer [1,2]. The two most frequently used isotopes are ^{18}F and ^{68}Ga tested with at least 10 and 5 different ligands respectively [3]. Comparative studies for the accuracy of the different tracers are lacking. ^{18}F-JK-PSMA-7 was recently developed [4] and made available in Hungary the last year as the first and yet the only tracer for the diagnosis of prostate cancer. Although sensitive, PSMA PET-CTs also have some limitations. Their sensitivity depends on the PSA value. At PSA <0.5 ng/mL, their detection rate is no more than 60% [2,3,5].

The reliable evaluation of the disease extent is particularly important in two situations: at primary staging for patients with moderately elevated PSA and at biochemical failure following radical prostatectomy. Before PSMA PET-CT was made available in the first situation we used to opt for local treatment for patients with PSA <40 ng/mL and negative staging in the second situation we used to deliver salvage radiotherapy without any imaging examination for patients with PSA ranging between 0.2–2 ng/mL [6].

The aim of our study was to investigate whether the use of ^{18}F-JK-PSMA-7 PET-CT for the staging of prostate

Table 1. Patients at biochemical recurrence following radical prostatectomy.

Age	Gleason score	PSA (ng/mL)	Treatment decision before PSMA PET-CT	PSMA PET-CT results	Change of the stage	Treatment decision after PSMA PET-CT	Change of the therapy
76	4 + 4	4.00	radiotherapy	peritoneal metastases	yes	chemotherapy	yes
60	3 + 4	7.75	radiotherapy	multiple metastases	yes	chemotherapy	yes
67	4 + 3	1.00	radiotherapy	single lung metastasis	yes	SBRT	yes
68	5 + 5	2.90	radiotherapy	single bone metastasis	yes	radiotherapy	yes
65	4 + 5	0.43	radiotherapy	regional lymphnode	yes	radiotherapy	no
64	4 + 3	0.43	radiotherapy	regional lymphnode	yes	radiotherapy	no
73	4 + 4	0.44	radiotherapy	regional lymphnode	yes	radiotherapy	no
66	5 + 5	1.90	radiotherapy	regional lymphnode	yes	radiotherapy	no
71	3 + 4	0.64	radiotherapy	regional lymphnode	yes	radiotherapy	no
62	4 + 3	0.62	radiotherapy	local relapse	no	radiotherapy	no
53	3 + 3	1.24	radiotherapy	local relapse	no	radiotherapy	no
66	4 + 3	0.55	radiotherapy	no detectable lesion	no	radiotherapy	no
65	3 + 3	0.27	radiotherapy	no detectable lesion	no	radiotherapy	no
73	3 + 4	0.40	radiotherapy	no detectable lesion	no	radiotherapy	no
69	3 + 4	0.49	radiotherapy	no detectable lesion	no	radiotherapy	no
58	3 + 4	0.27	radiotherapy	no detectable lesion	no	radiotherapy	no

cancer would change our attitude.

2. Material and methods

As part of our self-assessment, 24 ^{18}F-JK-PSMA-7 PET-CT results were analysed. Median age of the patients was 68 years (range: 53–77 years). The indication of the examination was biochemical failure following radical prostatectomy (PSA >0.2 ng/mL) for 16 patients and primary staging (PSA range: 5.2–70 ng/mL) for 8 patients. Patients undergoing radical prostatectomy had three monthly PSA controls in the first year, six monthly controls in the second year and yearly controls thereafter for life.

The inclusion was stopped on the 31st of December 2020. The follow-up was closed on the 31th of July 2021 for statistical analysis. At that moment all patients were alive and none of them was lost of follow-up.

The realisation of a PSMA PET-CT was always decided on tumour boards. Once the examination was done the board re-evaluated the treatment plan. The use of LHRH agonist injection before PSMA PET-CT was allowed.

Investigation has been conducted in accordance with the national and international ethical standards and the Declaration of Helsinki.

3. Results

Biochemical recurrence was related to local recurrence in 2 cases, regional lymph node involvement in 5 cases, oligo- and multi-metastatic spread in 1 and 3 cases respectively. 5 patients had no detectable lesion. Patients with PSA <1 ng/mL showed no extrapelvic enhancement (Table 1).

^{18}F-JK-PSMA-7 PET-CT allowed the detection of distant metastases in 4 cases and regional lymph node involvement in 5 cases. None of these lesions were showed by the traditional imaging examinations. The treatment plan was modified for the 4 metastatic patients. We underline the case presenting a single pulmonary metastasis that was treated with external beam stereotactic radiation therapy [7].

At primary staging distant metastases were detected in 3 patients and no distant enhancing lesion was found in 5 patients. There was no correlation between PSA level and disease extent. The treatment plan was modified for 3 patients (Table 2).

In total ^{18}F-JK-PSMA PET-CT result changed the treatment strategy for 7 patients.

4. Discussion

In this paper, we report our first experiences with ^{18}F-JK-PSMA PET-CT imaging. The examination can lead to change the treatment decision at primary staging as well as at biochemical recurrence. The high detection rate of PSMA PET-CT allows clinicians to notice distant metastases early, even in oligometastatic stage when curative treatment may be an option [8]. Sensitivity of PSMA PET-CT decreases at PSA level less than 1 ng/mL [9]. Indeed, no extrapelvic lesion was identified in this range in our study, taking into account the limited value of a pilot study involving only a few cases.

Table 2. Patients at primary staging.

Age	Gleason score	PSA (ng/mL)	Treatment decision before PSMA PET-CT	PSMA PET-CT results	Change of the stage	Treatment decision after PSMA PET-CT	Change of the therapy
72	3 + 5	32	chemotherapy	distant spread	no	chemotherapy	no
66	4 + 5	5.2	chemotherapy	distant spread	no	chemotherapy	no
77	3 + 4	17.2	radiotherapy	distant spread	yes	chemotherapy	yes
67	3 + 3	10.6	radiotherapy	regional spread	yes	prostatectomy	yes
70	3 + 4	70	radiotherapy	localised	no	radiotherapy	no
74	3 + 4	14.7	radiotherapy	localised	no	radiotherapy	no
77	3 + 5	6.2	radiotherapy	localised	no	radiotherapy	no
73	3 + 4	26.6	radiotherapy	localised	no	close monitoring	yes

Approximately three quarters of the patients with prostate cancer can be cured either with radical prostatectomy or radiation therapy or the combination of these two modalities [10]. When postoperative PSA falls below 0.01 ng/mL, it shows that all prostatic and malignant tissue was successfully removed. Still, relapse may occur in one third of the operated patients. Disease recurrence can usually be detected earlier by PSA rise than by any imaging result [9]. In case of biochemical failure when the disease remains exclusively loco-regional or oligometastatic an adapted therapy may have the value of a "second line curative treatment". This possibility explains the importance of the exact determination of the disease extent. The early management of small lesions detected by PSMA PET-CT may allow a better curative rate and a longer survival benefit [11].

PSMA PET-CT also has some limitations. False positive findings may occur in about 10% of the patients. Benign bone disorders, granulomatous diseases and other malignancies may stay behind these perturbations. False negative results may occur at low PSA level as mentioned before and also in neuroendocrine prostate cancer [3]. These limitations contribute to explain why PSMA PET-CT has not become a standard of care in primary staging of prostate cancer. Nevertheless, its use is recommended by the guideline of the European Association of Urology at biochemical recurrence [6,12]. Our findings are in line with the international guideline. We believe that the target volume can be more precisely determined for radiation therapy even in case of pelvic recurrence, allowing a better tumour control and the minimisation of side effects in the same time.

Finally, we mention that PSMA ligands coupled with gamma and beta emitting ^{177}Lu or alfa emitting ^{225}Ac or ^{227}Th may allow targeted radioligand therapy of metastatic prostate cancer [3].

5. Conclusions

^{18}F-JK-PSMA-7 PET-CT is a useful diagnostic tool. The examination can lead to change the treatment decision at primary staging as well as at biochemical recurrence. The results of this pilot study may support the strategy that patients with biochemical recurrence following radical prostatectomy receive salvage radiotherapy to the prostate bed and the pelvic lymphatic regions without any imaging examination when PSA $<$1 ng/mL.

Abbreviations

CT, computed tomography; FDG, fluoro-desoxy-glucose; PET, positron emission tomography; PSA, prostate specific antigen; PSMA, prostate specific membrane antigen; SBRT, stereotactic body radiation therapy.

Author contributions

All authors had equal contribution to the management of the patients. SA and KT prepared the manuscript. KK, AA, KN, SZ contributed to data collection. All authors accepted the revised form.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

References

[1] Grubmüller B, Baum RP, Capasso E, Singh A, Ahmadi Y, Knoll P, *et al*. ^{64}Cu-PSMA-617 PET/CT Imaging of Prostate Adenocarcinoma: first in-Human Studies. Cancer Biotherapy and Radiopharmaceuticals. 2016; 31: 277–286.

[2] Eiber M, Maurer T, Souvatzoglou M, Beer AJ, Ruffani A, Haller B, *et al*. Evaluation of Hybrid 68Ga-PSMA Ligand PET/CT in 248 Patients with Biochemical Recurrence after Radical Prostatectomy. Journal of Nuclear Medicine. 2015; 56: 668–674.

[3] Tateishi U. Prostate-specific membrane antigen (PSMA)–ligand positron emission tomography and radioligand therapy (RLT) of

prostate cancer. Japanese Journal of Clinical Oncology. 2020; 50: 349–356.

[4] Dietlein F, Hohberg M, Kobe C, Zlatopolskiy BD, Krapf P, Endepols H, *et al*. An 18F-Labeled PSMA Ligand for PET/CT of Prostate Cancer: first-in-Humans Observational Study and Clinical Experience with 18F-JK-PSMA-7 during the first Year of Application. Journal of Nuclear Medicine. 2020; 61: 202–209.

[5] Morigi JJ, Stricker PD, van Leeuwen PJ, Tang R, Ho B, Nguyen Q, *et al*. Prospective Comparison of 18F-Fluoromethylcholine Versus 68Ga-PSMA PET/CT in Prostate Cancer Patients who have Rising PSA after Curative Treatment and are being Considered for Targeted Therapy. Journal of Nuclear Medicine. 2015; 56: 1185–1190.

[6] Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, *et al*. EAU guidelines on prostate cancer. part 1: screening, diagnosis, and local treatment with curative intent–update 2013. European Urology. 2014; 65: 124–137.

[7] Kneebone A, Hruby G, Ainsworth H, Byrne K, Brown C, Guo L, *et al*. Stereotactic Body Radiotherapy for Oligometastatic Prostate Cancer Detected via Prostate-specific Membrane Antigen Positron Emission Tomography. European Urology Oncology. 2019; 1: 531–537.

[8] Kimura S, Abufaraj M, Janisch F, Iwata T, Parizi MK, Foerster B, *et al*. Performance of [68Ga] Ga-PSMA 11 PET for detecting prostate cancer in the lymph nodes before salvage lymph node dissection: a systematic review and meta-analysis. Prostate Cancer and Prostatic Diseases. 2020; 23: 1-10.

[9] Perera M, Papa N, Christidis D, Wetherell D, Hofman MS, Murphy DG, *et al*. Sensitivity, Specificity, and Predictors of Positive 68Ga-Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer: a Systematic Review and Meta-analysis. European Urology. 2017; 70: 926–937.

[10] Calais J, Ceci F, Eiber M, Hope TA, Hofman MS, Rischpler C, *et al*. 18F-fluciclovine PET-CT and 68Ga-PSMA-11 PET-CT in patients with early biochemical recurrence after prostatectomy: a prospective, single-centre, single-arm, comparative imaging trial. The Lancet Oncology. 2019; 20: 1286–1294.

[11] Hofman MS, Lawrentschuk N, Francis RJ, Tang C, Vela I, Thomas P, *et al*. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. The Lancet. 2020; 395: 1208–1216.

[12] Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, *et al*. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. European Urology. 2018; 71: 618–629.