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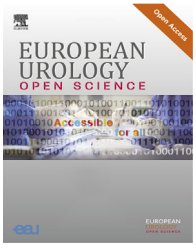

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Kidney Cancer

Impact of Prostate-specific Membrane Antigen Positron Emission Tomography/Computed Tomography in the Management of Oligometastatic Renal Cell Carcinoma

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Abstract

Background: Prostate-specific membrane antigen (PSMA) is overexpressed in the neovasculature of renal cell carcinoma (RCC). However, there remains limited evidence regarding the use of PSMA positron emission tomography/computed tomography (PET/CT) in RCC.

Objective: To assess the impact of PSMA PET/CT in the management of metastatic RCC.

Design, setting, and participants: This was a retrospective review of patients who underwent PSMA PET/CT from 2014 to 2020 for restaging or suspected metastatic RCC in a tertiary academic setting.

Outcome measurements and statistical analysis: Management plans before and after PSMA PET/CT were recorded. Impact was classified as high (change of treatment intent, modality, or site), medium (change in treatment method), or low. Secondary outcomes included the patient-level detection rate, PSMA PET/CT parameters, sensitivity, and comparison to CT and, if available, fluorodeoxyglucose (FDG) PET/CT.

Results and limitations: Sixty-one patients met the inclusion criteria, of whom 54 (89%) had clear cell RCC. PSMA-positive disease was detected in 51 patients (84%).

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Clear cell histology
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For 30 patients (49%) there was a change in management due to PSMA PET/CT (high impact, 29 patients, 48%). In 15 patients (25%), more metastases were detected on PSMA PET/CT than on CT. The sensitivity of combined PSMA PET/CT and diagnostic CT was 91% (95% confidence interval 77–98%). In a subcohort of 40 patients, the detection rate was 88% for PSMA and 75% for FDG PET/CT ($p = 0.17$). The maximum standardised uptake value (SUV_{max}) was higher for PSMA than for FDG PET/CT (15.2 vs 8.0; $p = 0.02$). Limitations include selection bias due to the retrospective design, and a lack of corresponding histopathology for all patients.

Conclusions: PSMA PET/CT is a promising imaging modality in metastatic RCC and led to a change in management in 49% of patients. PSMA PET/CT detected additional metastases compared to CT in 25% of patients and registered a significantly higher SUV_{max} than FDG PET/CT. Prospective studies are required to further define its role.

Patient summary: We report on a group of patients undergoing a new type of imaging for suspected advanced kidney cancer, called PSMA PET/CT. This imaging changed the management plan in 49% of the patients. PSMA PET/CT detected metastases in 84% of our patients and detected more metastases than computed tomography imaging in 25%.

1. Introduction

Approximately 10–15% of patients with renal cell carcinoma (RCC) present with de novo metastatic disease and a further 20% eventually develop metastases [1,2]. Common sites of RCC metastases include lymph nodes, lung, bone, and liver [3]. Computed tomography (CT), magnetic resonance imaging, and ultrasound are currently recommended as imaging modalities in guidelines [4,5]. Bone scintigraphy has a limited role in staging owing to the osteolytic nature of RCC bone metastases [6]. The role of molecular imaging with positron emission tomography (PET) is not established in RCC because of its limited specificity and sensitivity [4,7,8]. However, for patients with suspected recurrent RCC, PET may provide additional prognostic value over conventional imaging alone [9].

Prostate-specific membrane antigen (PSMA) is a transmembrane protein with high expression in prostate cancer, for which it has been demonstrated that PSMA PET/CT is superior to conventional imaging [10–12]. PSMA PET/CT in prostate cancer currently has a role in de novo staging [12] and in detection of recurrent advanced disease [11], and is being investigated in the response assessment setting [13]. In addition to prostate cancer, PSMA is also expressed in the neovasculature of other solid-organ malignancies, including RCC [14]. The use of PSMA PET/CT in RCC has been evaluated, but most evidence is from case reports or small series [13,15–17].

The primary objective of this study was to assess the incremental benefit of PSMA PET/CT over CT for patients with suspected metastatic RCC regarding diagnostic findings and impact on patient management.

2. Patients and methods

2.1. Inclusion criteria

A retrospective search was conducted of all patients undergoing PSMA PET/CT at a tertiary institution between June 2014 and April 2020. Patients whose clinical details included "renal cancer", "renal cell carcinoma", "RCC", or "clear cell" with the indication for the imaging for RCC were identified. Inclusion criteria included patients undergoing PSMA PET/CT for restaging or suspected metastatic RCC. All patients included had a corresponding contrast-enhanced CT scan. While PSMA PET/CT is not currently approved for RCC, we have previously reported its clinical utility [16]. Patients underwent PSMA PET/CT if it was thought that there was a potential to change management. This investigator-initiated retrospective study was approved by the local human research ethics committee with a waiver for patient consent.

2.2. Imaging

Patients were administered either [^{68}Ga]Ga-PSMA-11 or [^{18}F]DCFPyL, depending on tracer availability. For those receiving [^{68}Ga]Ga-PSMA-11, a weight-based dose of 2.6 MBq/kg was injected and scanning commenced approximately 60 min after injection. For those receiving [^{18}F]DCFPyL, a weight-based dose of 3.6 MBq/kg was injected and scanning commenced 120 min after injection. All patients were scanned using one of three General Electric Discovery PET/CT scanners (one model 690 and two model 710) and images were reconstructed using the ordered subset expectation maximisation algorithm incorporating time-of-flight.

2.3. Imaging interpretation and analysis

The number and location of metastases on CT and PSMA PET/CT were recorded. The detection rate was defined at a patient level as the presence of a finding considered to represent metastatic disease according to a review of reports by expert readers. The per-patient detection rate was used to reflect the clinical impact on a patient's management. For PSMA PET, this was defined as intensity of uptake above background that was not considered to be physiological or due to a nonmalignant cause. A concordant finding was defined as detection of the same number of PSMA-positive CT-positive metastases in a patient. PSMA+/CT− discordance was defined as more PSMA-positive lesions, and PSMA−/CT+ discordance as more CT-positive metastases. All PSMA-positive lesions were contoured using MIMencore version 7.1 with the PETedge gradient-based lesion contouring tool (MIM Software, Beachwood, OH, USA). The standardised uptake value (SUV) for metabolically avid disease on PSMA PET/CT was recorded and all lesions were summed

together for measurement of total disease burden, including PSMA molecular tumour volume (MTV-PSMA) and total lesion PSMA (TLP-PSMA; MTV-PSMA × SUV_{mean}).

2.4. Outcomes

All patients were discussed and had their imaging reviewed at an institutional genitourinary oncology multidisciplinary meeting. Management plans before and after PSMA PET/CT were recorded. A change in management was classified as a high, medium, or low impact as previously defined and published by our centre for various malignancies [18–20]. A high-impact change was defined as a change in treatment intent (eg, curative to palliative), modality (eg, systemic therapy to radiotherapy), or site. Medium impact was defined as a change in treatment method (eg, change in radiotherapy technique or dose) with no change in treatment intent, modality, or site. Low impact was defined as no change in treatment method, intent, modality, or site. Two authors (C.U. and W. L.O.) independently assessed the changes in management, and a third author (S.S.) reviewed the data if there was any disagreement. Patients with clear-cell RCC (ccRCC) and non-ccRCC were compared. Owing to the wide availability of PET at our institution, clinicians frequently requested both PSMA and fluorodeoxyglucose (FDG) PET/CT imaging, primarily to identify patients with PSMA-negative FDG-positive sites of disease. Therefore, for the subgroup of patients who also had corresponding FDG PET/CT images available, the imaging characteristics between PSMA and FDG PET/CT were compared.

2.5. Statistical analysis

Descriptive statistics to summarise clinical data are reported in the form of the mean, median, standard deviation, and range for quantitative variables. Categorical variables are reported as the count and percentage. The proportion of the impact of PSMA PET/CT is described using a 95% confidence interval (CI). PSMA PET/CT was not considered beneficial if the lower limit of the 95% CI for the high impact rate was <10%. The sensitivity of imaging modalities was calculated on the basis of histopathological confirmation at a per-lesion level. The McNemar test, Wilcoxon signed-rank test, and paired t test were used to compare FDG and PSMA findings. Fisher's exact test, an independent t test, and the Wilcoxon rank-sum test were used to compare non-ccRCC and ccRCC (Supplementary Table 3). All statistical analyses were performed in R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) [21].

3. Results

3.1. Patient and tumour characteristics

There were 3095 PSMA PET/CT examinations performed at our institution over the relevant time period, of which 83 were for RCC. There were 61 patients eligible for the study as they underwent PSMA PET/CT for restaging or suspected metastatic disease. The mean age was 65 yr (range 45–91 yr), with a male preponderance (56%, 34/61; Table 1). Primary management and tumour characteristics are detailed in Supplementary Table 1. The histology was ccRCC in 89% of patients. Rhabdoid and/or sarcomatoid differentiation was present in 18% of patients. There were ten patients (16%) with de novo metastatic disease and 28 patients (46%) with previous metastatic disease. Seven patients (11%) had been on systemic therapy, and three patients (5%) were currently on systemic treatment. The median time from primary RCC management to CT was 31 mo (interquartile range [IQR] 9–78). The indication for undergoing PSMA PET/CT was CT-positive metastatic disease in 57 patients (94%) and suspected metastatic disease in the remaining cases.

3.2. Impact of PSMA PET/CT

Overall, 30 patients (49%) had a change in management due to PSMA PET/CT (Table 2). Of these, 29 patients (48%, 95% CI 36–60%) had a high-impact change and one (1.6%) had a medium-impact change. For these patients, the most common change was in treatment modality, which occurred for 23 patients (77%). The most common change in management was from an initial plan for metastasis-directed therapy (MDT; stereotactic ablative radiotherapy [SABR] or metastasectomy) to systemic therapy or surveillance (15 patients; Fig. 1). Nine patients for whom systemic therapy or surveillance was planned before PSMA PET/CT subsequently underwent MDT. A further four patients received SABR to additional sites and two patients received SABR to fewer sites.

3.3. Detection rate

3.3.1. Detection rate and PET characteristics

The PSMA PET/CT patient-level detection rate was 84% (n = 51). The median SUV_{max} was 15 (IQR 6–28), the median SUV_{mean} was 7 (IQR 3–11), the median MTV-PSMA was 11 ml (IQR 5–29), and the median TLP-PSMA was 66 (IQR 2–242; Table 2).

3.3.2. PSMA PET/CT versus CT

There were PSMA-avid lesions on PET/CT in 84% of patients, whereas CT demonstrated lesions in 94% (p = 0.08). Of the ten patients with no PSMA-positive disease, seven had CT-positive metastases. Only one of the four CT-negative patients had PSMA-positive lesions. PSMA PET/CT and CT identified the same number of lesions in 30 patients (49%). PSMA PET/CT identified more lesions than CT in 15 patients (25%) and fewer lesions in 16 patients (26%).

Table 1 – Patient and tumour characteristics (n = 61)

Parameter	Result
Sex, *n* (%)	
Female	27 (44)
Male	34 (56)
Mean age, yr (range)	65 (57–72)
Histology, *n* (%)	
Clear cell	54 (89)
Chromophobe	2 (3)
Papillary	2 (3)
Clear cell/papillary	2 (3)
Unclassified variant	1 (2)
Differentiation, *n* (%)	
None	41 (79)
Rhabdoid	5 (10)
Sarcomatoid	3 (6)
Sarcomatoid/rhabdoid	3 (6)
Missing	9
Previous metastases, *n* (%)	
Current de novo	10 (16)
No	23 (38)
Yes	28 (46)
Systemic therapy, *n* (%)	
Current	3 (5)
Prior	7 (11)
No systemic therapy	51 (84)

Table 2 – Impact and characteristics of PSMA PET/CT for the 61 patients

Parameter	Result
Impact of PSMA, *n* (%)	
High	29 (48)
Medium	1 (2)
None	31 (51)
Management before PSMA PET/CT, *n* (%)	
Stereotactic ablative radiotherapy	43 (70)
Metastatectomy	1 (2)
Surveillance	11 (18)
Systemic ± palliative external beam radiotherapy	6 (10)
Management after PSMA PET/CT, *n* (%)	
Stereotactic ablative radiotherapy	36 (59%)
Metastectomy	2 (3%)
Surveillance	13 (21%)
Systemic ± palliative radiotherapy	10 (16%)
Reason for change of impact, *n* (%)	
Treatment method	1 (3)
Treatment modality	23 (77)
Treatment site (addition)	2 (7)
Treatment site (addition) and treatment method	1 (3)
Treatment site (addition) and treatment modality	1 (3)
Treatment site (omission)	2 (7)
PSMA-positive, *n* (%)	
No	10 (16)
Yes	51 (84)
Number of PSMA-positive metastases, *n* (%)	
0	10 (16)
1	20 (33)
2	13 (21)
3	5 (8)
4	5 (8)
5	2 (3%)
>5	6 (10%)
Median PSMA SUV_{max} (interquartile range)	15 (6–28
Median PSMA SUV_{mean} (interquartile range)	7 (3–11)
Median MTV-PSMA, ml (interquartile range)	11 (5–29)
Median total lesion PSMA (interquartile range)	66 (20–242)
Local recurrence, *n* (%)[a]	
No	46 (90%)
Yes	5 (10%)
Nodal metastases, *n* (%)	
0	45 (74)
1	9 (15)
2	5 (8)
3	2 (3)
Visceral metastases, *n* (%)	
0	29 (48)
1	18 (30)
2	7 (11)
3	5 (8)
>5	2 (3)
Bone metastases, *n* (%)	
0	43 (70)
1	9 (15)
2	3 (5)
3	2 (3)
4	2 (3)
5	1 (2)
>5	1 (2)
PSMA/CT concordance on a per-patient basis, *n* (%)	
PSMA+/CT+	50 (82)
PSMA+/CT−	1 (16)
PSMA−/CT+	7 (11)
PSMA−/CT−	3 (5)

PSMA = prostate-specific membrane antigen; PET = positron emission tomography; CT = computed tomography; SUV = standardized uptake value; MTV = metabolic tumour volume; TLP = total lesion PSMA.
[a] Excluding patients with PSMA PET/CT performed for primary staging.

Imaging for a patient with PSMA/CT discordant disease is shown in Figure 2. Histopathology was available in 36 patients and all had metastatic RCC confirmed.

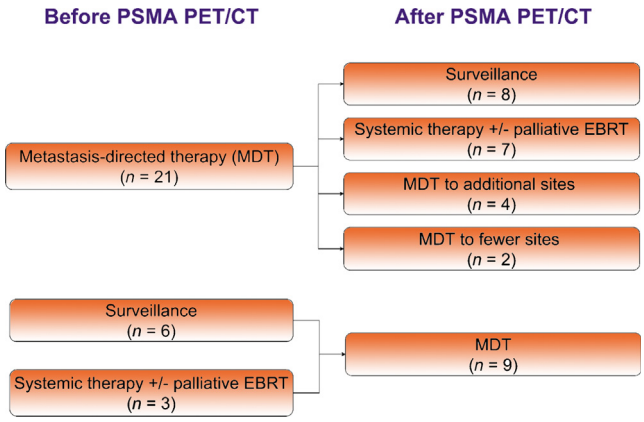

Fig. 1 – Patients with a change in management due to PSMA PET/CT (*n* = 30). PSMA = prostate-specific membrane antigen; PET = positron emission tomography; CT = computed tomography; EBRT = external beam radiation therapy.

Metastatectomy was performed before PSMA PET/CT but after CT in one patient and vice versa in another. PSMA PET/CT and CT were both positive in 32/35 patients (sensitivity 91%, 95% CI 77–98%).

3.3.3. *PSMA PET/CT versus FDG PET/CT*

A subgroup of 40 patients in our cohort had corresponding FDG PET/CT data (Supplementary Table 2). For these patients, the patient-level FDG PET/CT detection rate was 75% (30/40 patients) and the PSMA PET/CT detection rate was 88% (35/40 patients; $p = 0.18$). Twenty-eight patients had PSMA-positive FDG-positive disease and three patients had PSMA-negative FDG-negative disease. Seven patients had discordant PSMA-positive FDG-negative disease and two patients had discordant PSMA-negative FDG-positive disease. Images for two patients with discordant PSMA/FDG disease are shown in Figure 3. SUV characteristics were compared for the 28 patients with PSMA-positive FDG-positive disease. The SUV_{max} was higher for PSMA PET/CT than for FDG PET/CT (15.2 vs 8.0; $p = 0.02$).

3.3.4. *Subtypes and differentiation*

There was no significant difference in the PSMA PET/CT detection rate between ccRCC and non-ccRCC patients (46/54, 85% vs 5/7, 71%; $p = 0.32$; Supplementary Table 3). The median SUV_{max} was higher for ccRCC than for non-ccRCC metastases (16 vs 5; $p = 0.001$). There was no difference in median MTV-PSMA (ccRCC 12 ml vs non-ccRCC 8 ml; $p = 0.81$). PSMA-positive ccRCC metastases had significantly higher median TLP-PSMA (74 vs 40; $p = 0.007$). There was no difference in the detection rate between patients with either rhabdoid or sarcomatoid differentiation and those with no differentiation (90.9% vs 82.0%; $p = 0.46$).

4. Discussion

In the context of the literature previously published (Table 3), we report the largest series to date for PSMA PET/CT in RCC. In our cohort, approximately half of the patients had a change in management as a result of PSMA PET/CT findings, with 48% classified as high impact and

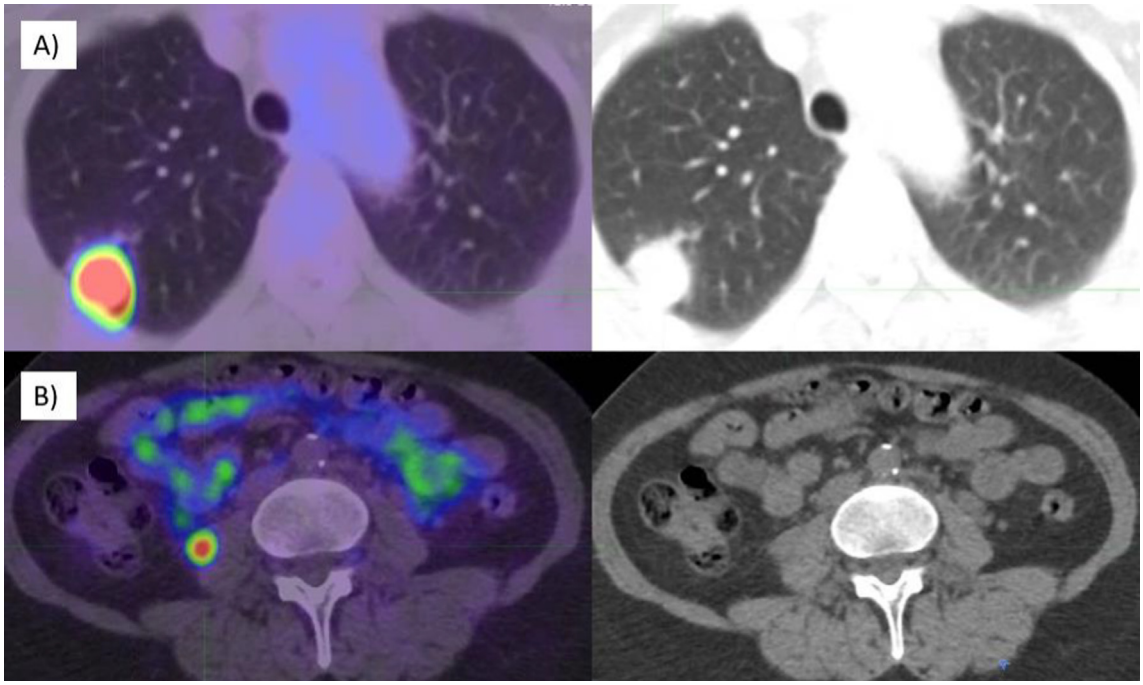

Fig. 2 – Discordant PSMA PET/CT and CT findings for a 57-yr-old female with clear-cell renal cell carcinoma, 9 mo after right nephrectomy. (a) PSMA-positive/CT-positive: lung metastasis in the right upper lobe. (b) PSMA-positive/CT-negative: recurrence in the right renal bed. PSMA = prostate-specific membrane antigen; PET = positron emission tomography; CT = computed tomography.

1.6% as medium impact. In some cases, either PSMA PET/CT was not concordant with CT-detected metastatic disease, or detected metastases that were not identified on CT. As this was a mostly CT-positive cohort, the change in management was primarily because of the number of metastases detected rather than upstaging from M0 to M1 or downstaging from M1 to M0. This led to patients undergoing systemic therapy or surveillance rather than MDT (23%), MDT rather than surveillance (10%), or MDT for additional sites (7%). Smaller studies have observed similar results, with the most common reason for a change in management being detection of more PSMA-positive disease [22–24]. A series of 38 patients had comparable findings to our study, with a change in management for 44% in the primary setting and 41% in the restaging setting [22]. Similar to our study, the most common reason was upstaging, for two patients (12.5%) in the primary setting and five patients (23%) in the restaging setting. In two further studies of ten and 14 patients, two (20%) and three (21%) patients, respectively, had additional disease detected via PSMA PET/CT. In some of these cases the patients did not undergo MDT as planned [23,24].

We found a patient-level PSMA PET/CT detection rate of 83.6% and a CT detection rate of 93.4%. In two smaller series of 14 and five patients, the lesion-level PSMA PET/CT detection rate was 87.9–96.6% and the CT detection rate was 62.1–63.6% [24,25]. A case report described one patient with 67 ccRCC metastases, of which 55 (82.1%) were detected on CT and 66 (98.5%) on PSMA PET/CT [26]. In our cohort, the sensitivity was 91.4% for both PSMA PET/CT and CT. This differs from other studies that demonstrated superior sensitivity of 92.1–94.7% for PSMA PET/CT, compared to 68.6–78.9% for CT [23,25]. Of note, our cohort differs somewhat in that the indication for PSMA PET/CT was at the time of established radiographic disease on CT for 94% of the patients. These findings suggest that PSMA PET/CT may be used in parallel with CT for restaging and influencing further management.

We report a median SUV_{max} of 15 (IQR 6–28) for PSMA-positive metastases, which is similar to other studies with a mean/median SUV_{max} of 11.7–19.5 for metastases and 13.4–23.9 for the primary tumour [23,27,28]. PSMA SUV_{max} may predict the grade of RCC in the primary setting, with higher median SUV_{max} observed for International Society of Urological Pathology grade 3–4 (23.9) than for grade 1–2 (13.4) tumours in a cohort of 36 patients [28] With a relatively high median SUV_{max}, the possibility that PSMA radioligand therapy may be useful for RCC is enticing. Trials evaluating the role of Lu-PSMA in prostate cancer have used SUV_{max} of 15 or intensity greater than that for liver as a threshold for inclusion [29,30]. This may not be as effective for RCC because the uptake is in the tumour vascular endothelium and not the tumour epithelial cells, resulting in washout rather than retention, although further research is needed given the absence of quality data [13,31].

We were able to compare PSMA and FDG PET/CT in 40 patients. The only other study comparing these two modalities involved a cohort of 15 patients [32]. Similar to our findings, SUV_{max} was significantly higher for PSMA PET/CT than for FDG PET/CT for both soft tissue and bone lesions. While the FDG detection rate was similar and the uptake intensity lower, FDG may still be valuable in identifying tumour heterogeneity via detection of FDG-positive PSMA-negative sites of disease. However, this only occurred in

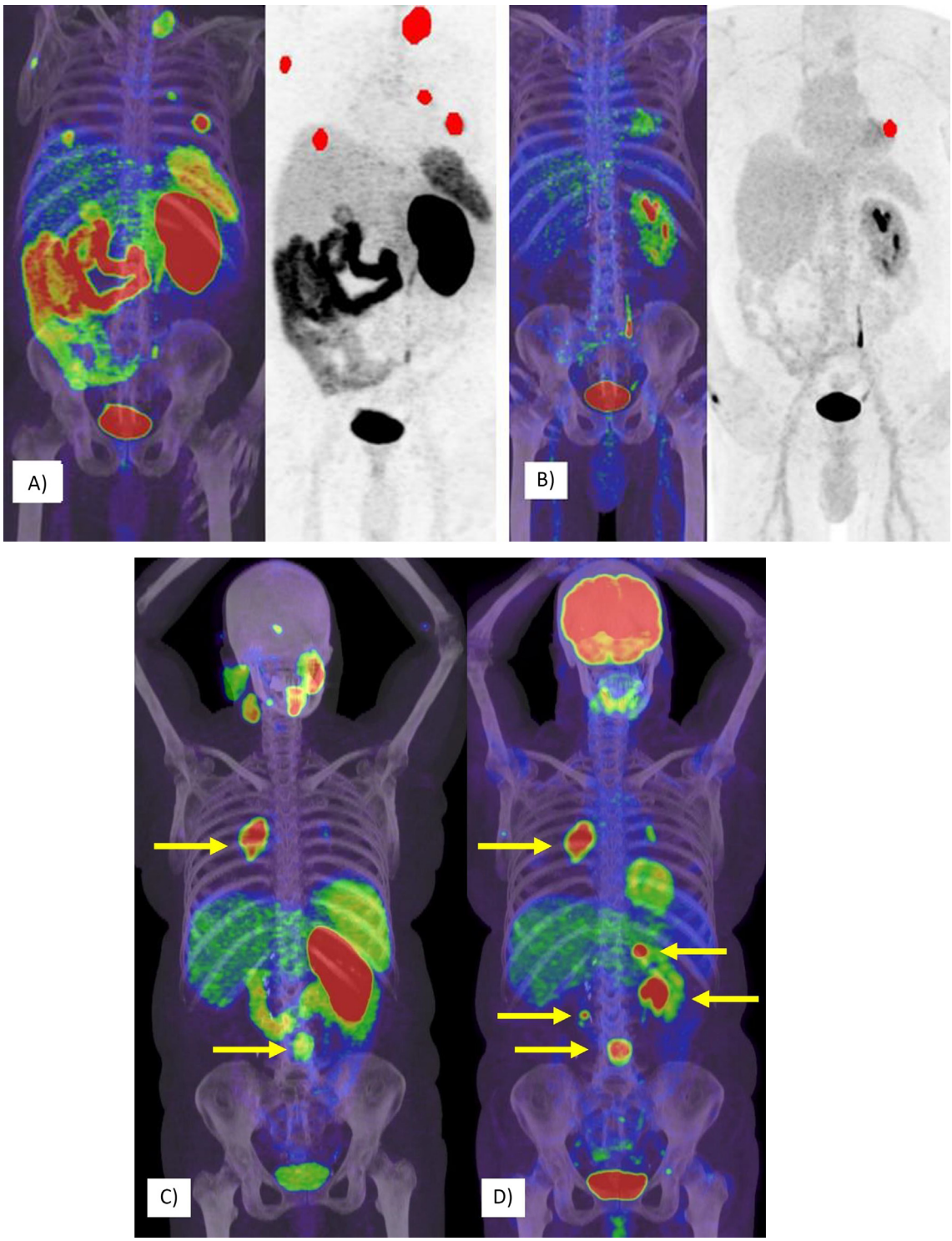

Fig. 3 – Discordant PSMA and FDG PET/CT findings. PSMA-positive/FDG-negative findings for a 64-yr-old male at 48 mo after a right nephrectomy for ccRCC: (A) PSMA PET/CT showing five metastases (left lung, left thoracic hilar lymph node, liver, right scapula, thyroid) and (B) FDG PET/CT showing one metastasis (left lung). PSMA-negative/FDG-positive findings for a 62-yr-old female at 5 mo after a right nephrectomy for de novo metastatic ccRCC: (C) PSMA PET/CT showing two metastases (central omental nodule, right thoracic hilar lymph node) and (D) FDG PET/CT showing five metastases (central omental, right thoracic hilar lymph node, left omental, left anterior diaphragmatic node, peripancreatic nodule). PSMA = prostate-specific membrane antigen; PET = positron emission tomography; CT = computed tomography; FDG = fluorodeoxyglucose; ccRCC = clear-cell renal cell carcinoma.

5% of patients. It has also been shown that FDG uptake intensity is an independent prognostic factor, while there are no data on PSMA [9].

RCC constitutes a heterogeneous classification, with multiple RCC subtypes. ccRCC has the highest PSMA expression (76.2–82.5%) and papillary RCC has the lowest

Table 3 – Series involving PSMA PET/CT in RCC and sample size for the overall cohort and subanalyses[a]

Series	Overall cohort	Histology available	Comparative FDG PET/CT	Non-ccRCC
Present study	61	36	40	7
Rowe 2015 [25]	5	0	0	0
Rhee 2016 [23]	10	10	0	2
Sawicki 2017 [27]	6	6	0	2
Siva 2017 [18][b]	8	2	7	0
Yin 2019 [36]	8	0	0	8
Meyer 2019 [24]	14	0	0	0
Raveenthiran 2019 [22]	38	3	0	4
Liu 2020 [32]	15	Not stated	15	0
Mittlmeier 2021 [37]	11	0	0	3
Gühne 2021 [38]	9	9	0	0
Golan 2021 [39]	27	27	0	11
Tariq 2022 [40]	11	11	11	1
Meng 2022 [41]	53	53	0	13
Tariq 2022 [42]	14	14	0	0

PSMA = prostate-specific membrane antigen; PET = positron emission tomography; CT = computed tomography; RCC = renal cell carcinoma; ccRCC = clear cell RCC; FDG = fluorodeoxyglucose.
[a] Publications with at least five patients.
[b] Previous publication by our institution.

[33–35]. In our cohort, we observed PSMA-positive metastases in 85% of patients with ccRCC (46 of 54) and 71% of patients with non-ccRCC (five of seven). Similar to the low expression in papillary RCC observed in laboratory-based studies, the only non-ccRCC cases with PSMA-negative metastases were patients with a papillary component (n = 2). However, there were another two patients with papillary RCC who did have PSMA-positive disease. There is limited evidence regarding PSMA PET/CT and non-ccRCC subtypes. A study of eight patients with non-ccRCC found that only 33% of suspicious metastases on conventional imaging had definitive or equivocal uptake [36]. We found that PSMA-positive ccRCC lesions had a significantly higher median SUV_{max} than PSMA-positive non-ccRCC lesions (16 vs five; p = 0.001). Lower PET characteristics for non-ccRCC have also been observed in eight non-ccRCC cases (median SUV_{max} 3.25) and in another study with two non-ccRCC (SUV_{max} 3.8–5.1) compared to three ccRCC cases (mean SUV_{max} 13.5, range 1.7–27.2) [27,36].

Limitations of our study include the retrospective nature and limited sample size. This is not an entirely homogeneous cohort, with differences in tumour, patient, and treatment characteristics. In addition, not all patients had histopathological correlation. As there are no guidelines on patients with RCC suitable for PSMA PET/CT, most patients in our cohort only had PSMA PET/CT if there was suspected metastatic disease on CT. Prospective studies are needed to ascertain the impact and detection rate of PSMA PET/CT in an unselected population. Furthermore, PET/CT may have limitations in detecting small metastases in the lungs, which are a common site of metastatic disease. In one study, all of the subcentimetre lung metastases were CT-positive but PSMA-negative [27]. However subcentimetre lung metastases were detected on PSMA PET-CT in another study [25]. In addition, we cannot draw any firm conclusions regarding patients with non-ccRCC or comparison of PSMA PET/CT with FDG PET/CT owing to the small sample size, and these outcomes should be considered exploratory.

5. Conclusions

PSMA PET/CT changed the management in a significant proportion (49%) of patients in this cohort. PSMA PET/CT in RCC can lead to either treatment intensification or de-escalation. The most frequent management changes were MDT to systemic therapy/surveillance, and systemic therapy/surveillance to MDT. Metastases had significantly higher avidity on PSMA PET/CT than on FDG PET/CT. As with any new imaging modality, caution is needed in upstaging or downstaging patients, particularly when applying treatment pathways proven on conventional imaging. PSMA PET/CT has the potential to complement CT in the diagnosis and management of suspected metastatic RCC. Similar to prostate cancer, prospective validation of PSMA PET/CT for RCC is warranted and a prospective registry at our institution is currently planned.

Author contributions: Shankar Siva and Cristian Udovocich had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Siva, Udovicich, Hofman, Callahan, Bressel.
Acquisition of data: Udovicich, Ong, Siva, Callahan.
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Appendix A. Supplementary data

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