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Original research article

Impact of ^{68}Ga-PSMA PET/CT in the treatment of prostate cancer: Initial experience in Spain

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ABSTRACT

Aim: To evaluate whether positron-emission tomography/computed tomography with ^{68}Ga-PSMA (^{68}Ga-PSMA PET/CT) influences the therapeutic management of patients with primary or recurrent prostate cancer (PCa).
Background: Although ^{68}Ga-PSMA PET/CT is one of the best options for staging or restaging patients with PCa, its availability is still very limited in Spain. The present study reports the results of the first group of patients in Spain who underwent ^{68}Ga-PSMA PET/CT imaging.
Materials and methods: All patients (n = 27) with a histological diagnosis of PCa who underwent ^{68}Ga-PSMA PET/CT prior to the definitive treatment decision at the only centre with this technology in Spain during 2017–2018 were included. Two nuclear medicine physicians and a radiologist reviewed the imaging studies. The clinical impact was assessed from a theoretical perspective, based on the treatment that would have been applied if no data from the ^{68}Ga-PSMA PET/CT were available.
Results: Most patients (n = 26; 96%) had persistent disease or biochemical recurrence after radical prostatectomy, radiotherapy, or combined treatment. One patient underwent ^{68}Ga-PSMA PET/CT imaging to stage high-risk PCa. Overall, ^{68}Ga-PSMA PET/CT was positive in 19 patients (70.4%). In 68.75% of these patients, none of the other imaging tests—MRI, CT, or bone scans—performed prior to the ^{68}Ga-PSMA PET/CT were able to detect the presence of cancerous lesions. Overall, the findings of the ^{68}Ga-PSMA PET/CT led to a modification of the therapeutic approach in 62.96% of the patients in the study.
Conclusions: ^{68}Ga-PSMA PET/CT alters the therapeutic approach in a substantial proportion of patients with PCa.

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1. Introduction

Prostate cancer (PCa) is the most common cancer in men, accounting for 15% of all diagnosed cancers, with a rising incidence, especially in Southern and Eastern Europe.[1–3] In recent years, important advances in imaging have improved diagnosis and staging in patients with PCa. Positron-emission tomography/computed tomography (PET/CT) with ^{68}Ga-PSMA is a molecular imaging technique based on the detection of the prostate specific membrane antigen (PSMA), which is overexpressed in PCa cells.[4] In the last decade, several radiopharmaceuticals, including 18 F/11C-Choline, 11C-acetate and 18 F-16B-fluoro-5α-dihydrotestosterone have been incorporated into routine practice, but none of these has demonstrated a potential of ^{68}Ga-PSMA in PCa. The PSMA protein is found in various locations in the human body, including the small intestine, the renal proximal tubule, and the salivary glands; however, its expression in tumours of the prostate gland is up to 1000 times greater than in those other locations.[5] Due to this high specificity, PSMA has generated immense interest as a potential ligand for enzymatic inhibitors, monoclonal antibodies, or as a radiological marker. The therapeutic use of PSMA has yielded promising initial results. Although more data are needed, the application of PSMA for diagnostic purposes has already been validated and is now recommended in main clinical guidelines.

^{68}Ga-PSMA PET/CT has proven to be a highly valuable morpho-functional test to evaluate recurrent disease after radical intent surgery or radiotherapy. The accuracy of ^{68}Ga-PSMA PET/CT has been proven, even in patients with low (< 1 ng/mL) PSA levels. Indeed, the diagnostic yield of this test is markedly better than other diagnostic tests such as CT, bone scans, or even 18 F/11C-Choline, which have long been the standard in this clinical setting. This imaging modality can detect both primary tumours and nodal disease, as well as soft tissue or bone lesions, with a high sensitivity and specificity (84% and 100%, respectively).[6] The published data—mainly from retrospective studies—indicate that detection rates for extraprostatic disease for ^{68}Ga-PSMA PET/CT vary according to PSA levels, as follows: 0.2–0.5 ng/mL (15%-58%); 0.5–1 ng/mL (25%-73%); 1–2 ng/mL (69%-100%); and> 2 ng/mL (71%-100%).[7–9]

Interest in ^{68}Ga-PSMA PET/CT continues to grow due to its potential impact on the therapeutic management of patients with PCa, especially its capacity to accurately identify the number and location of distant lesions, thus allowing clinicians to differentiate between metastatic patients with a high or low tumour burden. The utility of ^{68}Ga-PSMA PET/CT has been proven in at least three specific clinical scenarios: 1) staging prior to selection of radical treatment, in which the imaging findings can alter the initial radiotherapy treatment plan in more than 50% of cases[10,11]; 2) staging biochemically-recurrent PCa after radical prostatectomy (RP) or radiotherapy in which ^{68}Ga-PSMA can detect the presence of disease in up to 82% and 87% of cases, respectively[8,12–13]; and 3) in patients with an initial diagnosis of metastatic PCa, in whom the response to androgen deprivation therapy (ADT) and docetaxel are known, but the data on androgen receptor therapies require a longer follow-up.[14,15]

Patients with "oligometastatic" disease in particular could benefit from ^{68}Ga-PSMA PET/CT imaging due to the potential large impact that selective treatment of those lesions could have on treatment outcomes. In a prospective study in Australia, Roach et al. found that the results of ^{68}Ga-PSMA PET/CT altered the therapeutic approach in 62% of cases, thus providing a good example of the potential magnitude of the impact that this imaging modality could have on the therapeutic approach in patients with PCa given its capacity to detect unsuspected disease in patients considered M0.[16]

In this context, the aim of the present study was to describe our initial experience in Spain with ^{68}Ga-PSMA PET/CT in a series of patients diagnosed with PCa. Specifically, we evaluated the impact of ^{68}Ga-PSMA PET/CT imaging on the therapeutic management of these patients.

Table 1
Clinical characteristics of the patients (n = 27) included in the study.

Characteristic		
Age, years, median (IQR)	66	8
PSA at biochemical recurrence (*n = 25;* ng/mL), median (IQR)	0.90	1.76
PSA prior to ^{68}Ga-PSMA PET/CT (*n = 26;* ng/mL), median (IQR)	1.96	2.77
PSADT, months (*n = 15*), median (IQR)	6.00	12.20
Indication for ^{68}Ga-PSMA PET/CT (n, %)		
Biochemical recurrence	26	96.30%
Staging	1	3.70%
Gleason score at biopsy (*n = 23;* n, %)		
6 (3 + 3)	6	26.10%
7 (3 + 4)	7	30.40%
7 (4 + 3)	4	17.40%
8 (3 + 5)	1	4.30%
8 (4 + 4)	5	21.70%
Gleason score at prostatectomy (*n = 20;* n, %)		
6 (3 + 3)	1	5.00%
7 (3 + 4)	5	25.00%
7 (4 + 3)	7	35.00%
8 (4 + 4)	5	25.00%
9 (4 + 5)	1	5.00%
9 (5 + 4)	1	5.00%
T stage, clinical (*n = 11;* n, %)		
T1	4	36.40%
T2	5	45.50%
T3	1	9.10%
T4	1	9.10%
T stage, pathologic (*n = 21;* n, %)		
T2	9	42.90%
T3	12	57.10%
N stage, clinical (*n = 20;* n, %)		
N0	16	80.00%
N1	2	10.00%
Nx	2	10.00%
N stage, pathologic (*n = 22;* n, %)		
N0	12	54.40%
N1	2	9.10%
Nx	8	36.40%
Risk group (*n = 26;* n, %)		
Low	2	7.70%
Intermediate	10	38.50%
High	14	53.80%
Initial treatment (*n = 27;* n, %)		
Surgery alone	20	74.10%
RT alone	4	14.80%
RT + ADT	3	11.10%

PSA, prostate-specific antigen; PSADT, PSA doubling time; IQR, interquartile range; ADT, androgen deprivation therapy; RT, radiotherapy.

2. Material and methods

2.1. Study population

This multi-institutional, retrospective study included all patients (n = 27) with a histological diagnosis of PCa from three hospitals in Spain in the years 2017–2018 who had undergone ^{68}Ga-PSMA PET/CT imaging prior to the definitive treatment decision. Most of these patients (n = 26; 96.3%) were diagnosed with biochemical recurrence after surgery (n = 20) or radiotherapy (n = 6), while the other case involved a patient who underwent ^{68}Ga-PSMA PET/CT imaging for the initial staging of high-risk PCa. In all cases, the ^{68}Ga-PSMA PET/CT was performed at a single centre in Spain (CIMES, in Málaga Spain), which was the only centre with this technology during the study period.

Biochemical recurrence after RP was defined as two consecutive rises in PSA levels > 0.2 ng/mL. Biochemical recurrence after radical radiotherapy was defined according to Phoenix criteria (PSA nadir + 2 ng/mL).

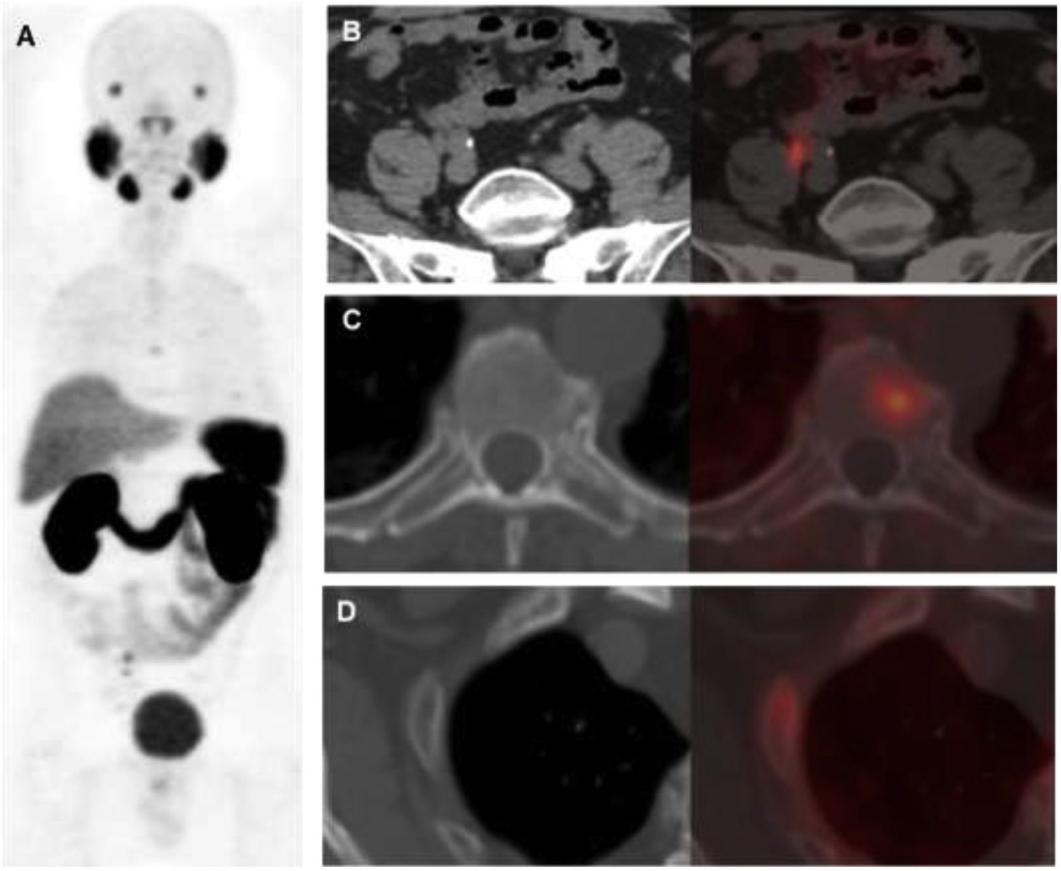

Fig. 1. A 69-year-old patient with a history of stage T3b N0 M0 prostate adenocarcinoma, Gleason 7 (4 + 3), treated with surgery and radiotherapy two years ago, and one-year of intermittent hormonotherapy. The patient presents elevated PSA levels(current: 1.64). No evidence of disease on CT, MRI, or 18 F-Fluorocholine PET-CT. ^{68}Ga-PSMA PET-CT is performed: (A) coronal MIP image; (B, C and D): axial CT and PET-CT images. Subcentimetric nodal lesions were observed in the right common iliac chain, with bone lesions in the spinal column and rib cage, and PSMA overexpression. The bone lesions are not visible on CT.

Table 1 shows the patients' characteristics. On the ^{68}Ga-PSMA PET/CT images, the presence of a markedly higher level of tracer uptake compared to physiological uptake (and above the adjacent background noise) was considered a positive result. The lesions were classified by localization, as follows: tumour bed/prostate gland; lymph node; bone; or viscera. The imaging studies were reviewed by two nuclear medicine physicians and a radiologist. All interventions performed to treat local or systemic recurrence were recorded, as was the influence of the findings of ^{68}Ga-PSMA PET/CT on the treatment decision. Clinical impact was assessed from a theoretical perspective, based on the treatment that would have been applied if data from the ^{68}Ga-PSMA PET/CT were not available. This study was approved by the ethics committees of the participating hospitals.

2.2. ^{68}Ga-PSMA PET/CT protocol

To obtain the ^{68}Ga-PSMA-11, GalliaPharm germanium-68/gallium-68 generator (Eckert & Ziegler Radiopharma GmbH) and PSMA-11 (GMP) were used as a precursor (ABX, advanced biochemical compounds). Radiosynthesis of ^{68}Ga-PSMA-11 was carried out using a fully automated method, with a final radiochemical purity > 97% in all cases.

Patients were allowed to continue taking all of their usual medications. All patients received a mean dose of 212 MBq ^{68}Ga-PSMA-11 (2.2 MBq/kg), injected as an intravenous bolus flushing with at least the same volume of saline (NaCl, 0.9%). To avoid artefacts due to excessive urinary activity (halo effect) or false positives due to the persistence of activity in the ureters, patients were asked to arrive for the exam well-hydrated. Furosemide (20 mg, i.v) was injected immediately after intravenous administration of the tracer; in patients with medical contraindications to furosemide (including allergies such as sulfa allergies), this drug was not administered.

The images were obtained a mean of 62.6 min after tracer administration using the GE Discovery STE4 PET/CT hybrid tomography (GE Healthcare, Waukesha, WI, USA). If the first image showed excessive urinary activity, or if this interfered with the correct assessment of the prostate or adjacent structures, a late acquisition was performed approximately 3 h after the initial tracer administration (mean: 164 min). The images were corrected for attenuation and scatter using the CT data. Image acquisition was performed using low-dose CT (autoMA, 120KVp) with the patient in a supine position with both arms raised. This was followed by 3D mode PET imaging (matrix size: 128 × 128pixels), with an acquisition time of 3–4 min per bed position in the initial study ranging from the mid-thighs to the top of the skull. In the late scans, the acquisition time was 6 min. The images were reconstructed using the built-in GE VUEpoint iterative reconstruction algorithm.

2.3. Image analysis

Pathological uptake associated with PCa was interpreted as all focal tracer deposits observed that could not be justified as a physiological uptake, or by pathologies unrelated to the primary tumour and congruent with the natural history of the disease. Maximum SUV (SUVmax) and lesion size (mm) were measured in all lesions.

Table 2
Localization of the metastatic lesion in the 19 patients with a positive result on the ^{68}Ga-PSMA PET/CT.

Localization	n	%
Single localization		
Nodal	8	42.10%
Prostate/Prostate bed	5	26.30%
Bone	2	10.50%
Viscera	1	5.30%
Multiple localizations		
Nodal + Prostate/Prostate bed	2	42.10%
Nodal + Prostate/Prostate bed + bone	1	26.30%

2.4. Statistical analysis

Statistical review of the study was performed by a biomedical statistician. Quantitative variables are given as medians with interquartile range (IQR) or as a mean ± standard deviation (SD). For qualitative variables, absolute and relative frequencies are given in percentages. The chi-square test was used to analyze qualitative variables. The student's T test or the Mann-Whitney U Test were used, as appropriate, to analyze significant differences among the quantitative variables. A logistic regression analysis was performed to identify independent variables associated with the imaging findings. The statistical analysis was performed using SPSS, v. 21.0 (IBM Corp; Armonk, NY; USA), with $p < 0.05$ considered significant for all analyses.

3. Results

3.1. Clinical characteristics of patients

Between 2017 and 2018, 27 patients with a histological diagnosis of PCa underwent ^{68}Ga-PSMA PET/CT. In 26 patients, the imaging test performed after biochemical recurrence (first recurrence in 5 patients and second or subsequent recurrences in 21 patients). In one patient with high-risk disease, the imaging study was performed as part of the initial staging. Table 1 summarizes the clinical characteristics of the patients.

RP was the exclusive initial treatment in 20 patients (74.1%). The remaining 7 patients received radiotherapy as initial treatment, and three of these also received ADT.

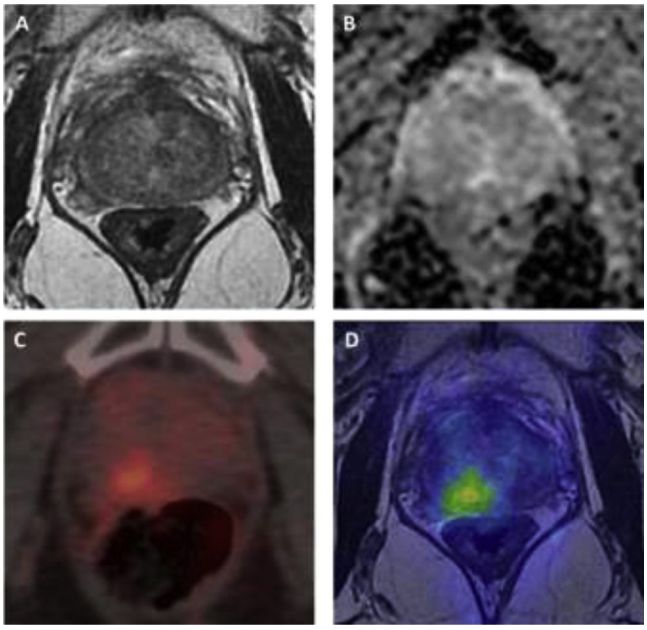

Fig. 2. A 64-year-old patient with prostate adenocarcinoma, Gleason 7 (3 + 4), treated with radiotherapy and 6 months of hormonotherapy. The PSA nadir was 0.1 ng/mL. Seven years after treatment, the patient developed a progressive increase in PSA, with a current PSA of 3 ng/mL. Prostate MRI was negative for tumour recurrence and ^{68}Ga-PSMA PET/CT was performed. (A) Axial T2-weighted FSE prostate MRI. The prostate shows a marked hyposignal secondary to treatment without evidence of nodular lesions. (B) Prostate MRI with ADC mapping with a b-value of 1400s /mm^2 with no diffusion restriction. (C) Axial ^{68}Ga-PSMA PET/CT image and (D) ^{68}Ga-PSMA PET/MRI co-registered image. A nodule located in the posterior peripheral area of the right lobe of the prostate with PSMA overexpression.

The median (IQR) PSA at the time of biochemical recurrence was 0.90 (1.76) ng/mL and 1.96 (2.77) ng/mL immediately prior to the ^{68}Ga-PSMA PET/CT.

3.2. Findings of ^{68}Ga-PSMA PET/CT and factors associated with positivity

Findings from the ^{68}Ga-PSMA PET/CT were positive in 19 patients (70.40%), Fig. 1 and Fig. 2. In 68.75% of these patients, none of the other imaging tests—MRI, CT, or bone scans—performed prior

Table 3
Clinical factors associated with positivity on the ^{68}Ga-PSMA PET/CT in all patients (n = 27) and in patients whose initial treatment was radical prostatectomy (n = 20).

	All patients (n = 27)				**Patients with prostatectomy (n = 20)**			
Variable	**n positive / n category**	**OR**	**(95% CI)**	**p-value**	**n positive / n category**	**OR**	**(95% CI)**	**p-value**
Age	NA	1.142	(0.965 – 1.355)	0.122	NA	1.140	(0.931 – 1.396)	0.225
Gleason at biopsy								
≤ 7 (3 + 4)	9 / 13	ref.			5 / 9	ref.		
≥ 7 (4 + 3)	8 / 10	2.000	(0.282 – 14.198)	0.488	7 / 9	2.800	(0.361 – 21.727)	0.325
Gleason at prostatectomy								
≤ 7 (3 + 4)	3 / 6	ref.			3 / 6	ref.		
≥ 7 (4 + 3)	9 / 14	1.800	(0.259 – 12.502)	0.552	9 / 14	1.800	(0.259 – 12.502)	0.552
Risk group								
Low o Intermediate	7 / 12	ref.			5 / 9	ref.		
High	12 / 15	2.619	(0.471 – 14.577)	0.272	8 / 11	3.333	(0.515 – 21.584)	0.206
PSA at biochemical recurrence								
≤ 1 ng/mL	7 / 14	ref.			7 / 14	ref.		
> 1 ng/mL	10 / 11	10.000	(0.995 – 100.462)	0.500	4 / 5	4.000	(0.393 – 45.384)	0.263
PSA prior to ^{68}Ga-PSMA PET/CT								
≤ 0.5 ng/mL	1 / 4	ref.			1 / 4	ref.		
> 0.5 ng/mL	18 / 22	13.500	(1.098 – 165.972)	**0.042**	11 / 15	8.250	(0.023 – 11.088)	0.103
PSADT								
≤ 6 months	7 / 8	ref.			6 / 7	ref.		
> 6 months	6 / 7	0.857	(0.044 – 16.851)	0.919	3 / 4	0.500	(0.023 – 11.088)	0.661

NA, Not applicable; OR, Odds Ratio; 95% CI, 95% confidence interval; PSADT, PSA doubling time.

Table 4
Treatments administered in the 19 patients with a positive ^{68}Ga-PSMA PET/CT.

Patient	Initial treatment	Treatment after biochemical recurrence (prior to ^{68}Ga-PSMA PET/CT)	Tumour localization on ^{68}Ga-PSMA PET/CT	Change in treatment after positive result on ^{68}Ga-PSMA PET/CT
1	Surgery	NA	Nodal	HT
2	Surgery	NA	Nodal	HT
3	Surgery	NA	Prostate/Prostate bed	RT + HT
4	Surgery	NA	Nodal	RT + HT
5	Surgery	RT	Visceral	Surgery
6	Surgery	RT + HT	Bone	SBRT
7	Surgery	RT + HT	Nodal	RT + HT
8	Surgery	RT + HT	Nodal	QT + HT
9	Surgery	RT + HT	Nodal	SBRT + HT
10	Surgery	RT + HT	Bone	HT + Abiraterone
11	RT	NA	Nodal + Prostate/Prostate bed	RT + HT
12	RT	NA	Prostate/Prostate bed	SBRT
13	RT	NA	Nodal + Prostate/Prostate bed	HT
14	RT + HT	NA	Nodal + Prostate/Prostate bed + Bone	Surgery
15	RT + HT	NA	Prostate/Prostate bed	Surgery
16	RT + HT	NA	Nodal	Surgery
17	Surgery	NA	Prostate/Prostate bed	Unchanged
18	Surgery	HT	Nodal	Unchanged
19	RT	HT	Prostate/Prostate bed	Unchanged

NA, not applicable; RT, radiotherapy; SBRT, stereotactic body radiotherapy; HT, hormonal therapy.

to the ^{68}Ga-PSMA PET/CT were able to detect the presence of cancerous lesions. The most common location detected by ^{68}Ga-PSMA was the lymph nodes, followed by the tumour bed/prostate gland (Table 2).

In the patients with a positive ^{68}Ga-PSMA PET/CT, the median PSA (IQR) prior to imaging was 2.40 (3.90) ng/mL; in patients with a negative finding, the median PSA was 0.57 (0.48) ($p = 0.001$). On the univariate logistic regression analysis, the odds of a positive result were 13.50 (95% CI: 1.10–165.97; $p = 0.042$) times higher in patients with a pre-imaging PSA > 0.5 ng/mL than in those with PSA ≤ 0.5 ng/mL (Table 3). However, this risk factor was not significant in the regression analysis that included only patients with initial prostatectomy, although PSA levels prior to ^{68}Ga-PSMA PET/CT imaging were significantly higher ($p = 0.003$) in patients with a positive imaging result versus those with negative findings. The clinical data for the patients with negative results are provided in the supplementary Table.

3.3. Impact on therapeutic management

The imaging findings altered the therapeutic approach in 16 of the 19 patients (84.2%) who had a positive finding (Table 4). In one patient, the negative ^{68}Ga-PSMA PET/CT result led to a change in treatment to active surveillance. Overall, the findings of the ^{68}Ga-PSMA PET/CT led to a modification of the therapeutic approach in 62.96% of the patients in the study.

4. Discussion

The present study reports the results of the first group of patients in Spain who underwent ^{68}Ga-PSMA PET/CT imaging. Our aim was to determine the impact of the findings of ^{68}Ga-PSMA PET/CT on the therapeutic management of these patients. We found that ^{68}Ga-PSMA was useful—that is, it led to a therapeutic change—in 62% of patients, a rate that is consistent with previous reports (50%-75%)[17] and with the results of the largest (n = 431) prospective study conducted to date,[16] which found that ^{68}Ga-PSMA changed the therapeutic approach in 62% of patients with biochemically-recurrent disease.

^{68}Ga-PSMA PET/CT has a strong capacity to detect involved lymph nodes prior to radical treatment, with a sensitivity of 84% and a specificity of 97%.[18] In patients with biochemical recurrence, detection rates range from 50%-95% and generally correspond with the PSA level (the higher the PSA, the higher the detection rate).[15] In our series, the focus of recurrence was detected in 70% of the patient cohort (median PSA: 1.9 ng/mL). However, in patients with lower PSA levels (<1 ng/mL), the detection rate was only 50%, a finding that is in line with the results of a meta-analysis involving 1309 patients.[19] Importantly, we found that the PSA level prior to ^{68}Ga-PSMA PET/CT was independently associated with positivity.

Approximately one-third of patients who undergo RP or primary radiotherapy for prostate cancer will develop biochemical recurrence, and most of these patients will develop metastasis within 5–8 years after primary treatment.[3] Conventional diagnostic imaging techniques are unable to detect the foci of recurrent disease underlying the progressive rise in PSA levels, especially in the initial stages of recurrence when PSA levels are quite low.[3] In cases in which the foci of the recurrence cannot be located, the usual treatment is antiandrogen therapy, which carries the risk of important adverse effects (i.e., reduced quality of life and, potentially, a higher risk of cardiovascular disease).[3] In patients with low to very low PSA levels (≤0.5 ng/mL), the use of a diagnostic test—such as ^{68}Ga-PSMA PET/CT—capable of detecting small-volume metastatic disease (oligometastasis) is essential since the findings can be used to guide localized, curative-intent treatment.[3] Although the scientific evidence accumulated to date remains insufficient to demonstrate an overall survival benefit for the treatment of oligometastatic patients, prospective studies have shown that treatment can delay the initiation of antiandrogen therapy by at least 2 years.[20] Currently, several randomized, multicenter prospective studies are underway to further evaluate the benefit of treating oligometastatic patients.[21] However, for initial staging of PCa, PSMA-PET/CT has proven to be at least as efficient as conventional imaging techniques. Moreover, this imaging modality has a greater sensitivity and specificity to detect nodal disease and bone metastases, thus allowing radiation oncologists and urologists to individualize treatment plans.[15] Although the results published to date regarding PSMA-PET/CT for initial staging are promising, more prospective data are needed to demonstrate the positive impact of this technique and to confirm its superiority over other currently-accepted techniques.

The benefits of ^{68}Ga-PSMA PET/CT have been evaluated in several European countries, with results from both retrospective and

prospective studies demonstrating that this imaging modality is the best option for restaging patients with biochemically-recurrent PCa after radical treatment (RP or primary radiotherapy). Indeed, based on the findings from those studies, ^{68}Ga-PSMA PET/CT is now recommended in the most recent guidelines published by the European Urology Association (EAU, 2019).[3] Nevertheless, the availability of this imaging technique is still very limited in Spain.[15]

In some cases, the findings of ^{68}Ga-PSMA PET/CT may be negative, even in patients with a known recurrence. Several hypotheses have been proposed to explain this phenomenon, including the presence of undetectable millimetric-sized lesions, lesions located adjacent to the urinary activity of the bladder (which could mask small local recurrences), and the presence of a non-PSA secreting undifferentiated prostate tumour or tumours of neuroendocrine origin.[22] In this regard, non-neuroendocrine undifferentiated prostate tumours usually present with intense PSMA expression even though they are non-PSA secretors. Moreover, despite the high specificity of ^{68}Ga-PSMA, other diseases may also overexpress PSMA, including benign pathologies such as Paget's disease of bone, hemangioma, and fibrous dysplasia, probably due to the presence of PSMA in the membranes of neovessels.[23–25] Some other malignant cancers may also overexpress PSMA, including clear cell kidney cancer, breast cancer, and some sarcomas, usually with associated neovascularization.[26]

The main aim of this study was to assess the clinical impact of ^{68}Ga-PSMA PET/CT. The utility of an imaging test is directly related to its impact on the therapeutic decision and on whether it contributes to clinical improvement and better öutcomes. In the present cohort of Spanish patients, ^{68}Ga-PSMA altered the therapeutic approach in 62% of the patients. Although the long-term benefit of this altered therapeutic approach in these patients remains to be confirmed, the published data indicate that up to 20% of patients with biochemical recurrence after RP who are re-evaluated by ^{68}Ga-PSMA PET/CT present a lesion located outside of the theoretical salvage radiotherapy volume[27]; consequently, the data from this imaging scan are highly valuable as it allows us to deliver more precise treatments, likely improving the patients' quality of life.

The present study is not without limitations, primarily the limited number of patients, the retrospective study design, and the lack of a comparison arm. In addition, the theoretical treatment that would have been administered is a purely theoretical exercise based on routine clinical practice and international guidelines. Given these limitations, the results presented here should be interpreted cautiously.

Molecular imaging studies, such as ^{68}Ga-PSMA, are more sensitive and specific than other currently-available diagnostic imaging techniques. For this reason, it is reasonable to consider changing the treatment approach based on the findings of this highly accurate imaging study, thus allowing clinicians to offer more individualized treatment to patients with biochemically-recurrent PCa. However, it is still not clear whether this strategy will improve PFS and/or OS in these patients, which is why prospective studies are needed.

5. Conclusion

The present retrospective study reports findings from the first cohort of patients in Spain who underwent ^{68}Ga-PSMA PET/CT either to detect biochemically-recurrent prostate cancer or initial staging prior to radical treatment. The findings of this imaging test resulted in the modification of the therapeutic approach in 62% of patients. Prospective studies should be conducted to confirm these results and to evaluate the long-term impact on survival outcomes.

Conflicts of interest

All authors declare no conflicts of interest related to this article.

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