
The Impact of ^{68}Ga -PSMA PET/CT on Management Intent in Prostate Cancer: Results of an Australian Prospective Multicenter Study

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^{68}Ga -PSMA PET/CT scanning has been shown to be more sensitive than conventional imaging techniques in patients with prostate cancer. This prospective Australian multicenter study assessed whether ^{68}Ga -PSMA PET/CT imaging affects management intent in patients with primary or recurrent prostate cancer. **Methods:** Before undertaking ^{68}Ga -PSMA PET imaging, referring medical specialists completed a questionnaire detailing relevant demographic and clinical data as well as their proposed management plan. A separate follow-up questionnaire was completed after the ^{68}Ga -PSMA PET/CT scan results were available to determine whether the management plan would change. **Results:** A total of 431 patients with prostate cancer from 4 Australian centers had pre- and post- ^{68}Ga -PSMA management plans completed. Scans were obtained for primary staging of intermediate- and high-risk disease in 25% of patients and for restaging/biochemical recurrence in 75% of patients. Overall, ^{68}Ga -PSMA PET/CT scanning led to a change in planned management in 51% of patients. The impact was greater in the group of patients with biochemical failure after definitive surgery or radiation treatment (62% change in management intent) than in patients undergoing primary staging (21% change). Imaging with ^{68}Ga -PSMA PET/CT revealed unsuspected disease in the prostate bed in 27% of patients, locoregional lymph nodes in 39%, and distant metastatic disease in 16%. **Conclusion:** ^{68}Ga -PSMA PET/CT scans detect previously unsuspected disease and may influence planned clinical management in a high proportion of patients with prostate cancer. The impact was greater in patients with biochemical recurrence. These results demonstrate the potential clinical value of ^{68}Ga -PSMA PET/CT in management of prostate cancer.

Key Words: prostate cancer; PET/CT; PSMA; management impact
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Conventional imaging has limitations in the evaluation of prostate cancer. For men undergoing primary staging, the sensitivity of CT and bone scans is relatively low (1). In patients with biochemical failure (BF), the diagnostic yield is suboptimal, particularly in patients with low prostate-specific antigen (PSA) levels (<20 ng/mL), which represent most cases (2,3). Accurate delineation of sites of tumor recurrence is important because this will determine whether targeted therapies (e.g., stereotactic radiotherapy or salvage surgery) or systemic treatments such as androgen deprivation therapy (ADT) or chemotherapy are used (4).

Prostate-specific membrane antigen (PSMA), a transmembrane type II glycoprotein found both in local and in metastatic prostate cancer cells, can be radiolabeled with ^{68}Ga (5). Because it was first introduced clinically in 2011, ^{68}Ga -PSMA PET/CT has become increasingly used in clinical practice, with the literature consistently reporting a high detection rate of disease, particularly in the setting of BF, even at low PSA levels (5–9). This facilitates the use of salvage procedures (e.g., secondary lymphadenectomy or targeted radiation therapy) with potentially curative intent (10,11). Consequently, ^{68}Ga -PSMA PET/CT has been rapidly adopted into clinical practice in many countries, including Australia.

Although there are several reports in the literature describing the management impact of ^{68}Ga -PSMA PET/CT in patients with prostate cancer, these series have been single-center studies, with small numbers, and usually retrospective in design (8,12–14). The primary aim of this study was to evaluate the impact of ^{68}Ga -PSMA PET/CT on management intent in patients with prostate cancer in a large prospective multicenter study.

MATERIALS AND METHODS

This prospective study was conducted at 4 Australian PET/CT centers. Eligible patients had a histologic diagnosis of prostate cancer and were referred for ^{68}Ga -PSMA PET/CT imaging for 1 of 2 indications. One group (primary staging cohort) comprised men undergoing primary staging of either high-grade disease (PSA > 20 ng/mL, Gleason score \geq 8, and with clinical, or MRI, evidence of \geq T3 disease) or intermediate-grade disease (PSA 10–20 ng/mL, Gleason

TABLE 1
Clinical Indications, Patient Age, PSA Results, and Management Intent Change

Indication for ⁶⁸ Ga-PSMA PET/CT scan	<i>n</i>	%	Age (y)	Median PSA ± SD (ng/mL)	Management change (<i>n</i>)	%
Primary staging	108	26%	67.4 ± 8.7	8.6 ± 15.4 (range, 0.18–120)	23	21
BF	312	74%	68.9 ± 7.5	1.1 ± 8.4 (range, 0.01–75)	192	62
Total	420	100%	68.5 ± 8.0	2.9 ± 14.6 (range, 0.01–120)	215	51

score = 7, and with clinical, or MRI, evidence of T2 disease). The second group comprised patients undergoing imaging for BF with detectable PSA but negative, or equivocal, conventional imaging, or in a small number of cases, evaluation of known disease. Informed written consent was obtained from all patients, and Institutional Human Research Committee Ethics approval was obtained at each site.

⁶⁸Ga-PSMA PET/CT scans were acquired using a standard protocol at each institution. Patients were injected with ⁶⁸Ga-PSMA (H-BED CC) (1.8–2.2 MBq/kg), and 45–60 min later whole-body PET/CT imaging was performed on a time-of-flight PET/CT scanner. ⁶⁸Ga-PSMA PET/CT scans were interpreted locally by experienced, credentialed nuclear medicine specialists with full knowledge of clinical history, biochemical results, and results of conventional imaging.

Before obtaining the ⁶⁸Ga-PSMA PET/CT scan, referring clinicians recorded relevant clinical history (including surgical history and the details of prior radiotherapy, chemotherapy, or ADT) as well as PSA results and doubling times, Gleason score, and results of conventional imaging, such as CT scans, bone scintigraphy, and MRI scans. They also completed a patient management plan. The management questionnaire was devised by the Australasian Radiopharmaceutical Trials Network and comprised a series of questions in a tick box format (Supplemental Fig. 1; supplemental materials are available at <http://jnm.snmjournals.org>) requiring referring clinicians to document their overall treatment plan (targeted/localized, systemic treatment or observation) and to nominate which treatment modality (or modalities) they intended to use and to provide details of their planned management.

Between 4 and 5 wk later, clinicians completed a follow-up questionnaire, now being aware of the ⁶⁸Ga-PSMA PET/CT result (Supplemental Fig. 2). Questions related to whether their overall management would change, their treatment intent, and their suspected extent of disease. Additional information was collected, including whether the scan detected local, nodal, or metastatic disease that was not previously suspected and whether it would lead to (or obviate

the need for) additional imaging or biopsies, whether the disease was more (or less) extensive than previously thought based on conventional imaging, and any change to patient prognosis.

Statistical analysis was performed using McNemar χ^2 tests. *P* values were calculated using paired responses on the pre- and post-⁶⁸Ga-PSMA questionnaires.

RESULTS

Patient Demographics

Between January 2015 and June 2016, 431 patients had pre-⁶⁸Ga-PSMA PET/CT and post-⁶⁸Ga-PSMA PET/CT management forms completed. The number of patients recruited at each site was 228, St Vincent's Hospital Sydney; 105, Sir Charles Gairdner and Fiona Stanley Hospitals Perth; and 98, Royal North Shore Hospital Sydney.

A total of 108 patients were scanned for primary staging of intermediate- and high-risk disease. The remaining 323 patients were scanned for restaging purposes, predominantly for BF with negative or equivocal conventional imaging (*n* = 312). A small number were imaged for the evaluation of known metastatic disease (*n* = 6) or for other reasons (*n* = 5) (or for reasons that were not clearly stated). These 11 patients were excluded from subsequent analysis. The indications for the ⁶⁸Ga-PSMA PET/CT, patient age, and PSA levels are recorded in Table 1.

Overall Management Impact

Clinical management intent changed in 51% as a consequence of findings on the ⁶⁸Ga-PSMA PET/CT scans (Table 1). The change of management intent was significantly higher in men with BF (192/312, 62%) than in those in the primary staging cohort (23/108, 21%) (χ^2 statistic, 54.26; *P* < 0.0001). The change in management intent remained high, even at low PSA values, with no significant difference between PSA cohorts. In the primary staging cohort, there was no significant change in management intent comparing intermediate- versus high-grade disease (Table 2).

Extent of Disease

In the primary staging cohort, after ⁶⁸Ga-PSMA PET/CT there was a slight increase in the number of men considered to have oligometastatic disease (1–3 lesions), a significant increase in those considered to have polymetastatic disease (≥ 4 lesions), and a significant reduction in the number considered to have disease confined to the prostate (Table 3).

In the BF cohort, a more substantial impact was documented, with a significant reduction in the number of men in whom the site of disease recurrence was unknown and significant increases in the detection of presumed oligometastatic and polymetastatic disease.

Detection of Additional Sites of Unknown Disease

⁶⁸Ga-PSMA PET/CT detected additional local disease in 27% of patients, nodal disease in 39%, and metastatic disease in 16% of

TABLE 2
Management Intent Based on PSA (BF) and Tumor Grade (Primary Staging)

Cohort	Management change		
	<i>n</i>	%	<i>P</i>
BF			
PSA level (ng/mL)			
<0.2	28/42	67%	Not significant
0.2–0.5	44/73	60%	Not significant
>0.5	113/189	60%	Not significant
Primary staging			
Tumor grade			
Intermediate	6/37	16%	Not significant
High	14/64	22%	Not significant

TABLE 3
Extent of Disease Assessed by Referring Clinicians

Extent of disease	Primary staging			BF			Total		
	Before ⁶⁸ Ga-PSMA	After ⁶⁸ Ga-PSMA	<i>P</i>	Before ⁶⁸ Ga-PSMA	After ⁶⁸ Ga-PSMA	<i>P</i>	Before ⁶⁸ Ga-PSMA	After ⁶⁸ Ga-PSMA	<i>P</i>
No evidence of active disease	0 (0%)	0 (0%)	NS	22 (7%)	21 (7%)	NS	22 (5%)	21 (5%)	NS
Biochemical recurrence, site unknown	5 (5%)	0 (0%)	NS	240 (77%)	59 (19%)	<0.001	245 (59%)	59 (14%)	<0.001
Disease confined to prostate bed	92 (85%)	80 (74%)	0.012	12 (4%)	51 (16%)	<0.001	104 (24%)	131 (31%)	0.004
Oligometastatic (1–3 lesions) disease	9 (8%)	16 (15%)	NS	32 (10%)	119 (38%)	<0.001	41 (10%)	135 (32%)	<0.001
Polymetastatic disease (≥4 lesions)	2 (2%)	12 (11%)	<0.002	2 (1%)	60 (19%)	<0.001	4 (1%)	72 (17%)	<0.002
Not stated/incomplete	0	0		4 (1%)	2 (1%)		4(1%)	2 (1%)	
Total	108 (100%)	108 (100%)		312 (100%)	312 (100%)		420 (100%)	420 (100%)	

NS = not significant.

patients at sites that were previously unknown based on clinical findings and results of conventional imaging (Table 4). Higher rates of detection of additional sites of disease were noted in each category for the BF cohort compared with the primary staging cohort.

Change in Extent of Disease Assessed by Referring Clinicians

Overall, ⁶⁸Ga-PSMA PET/CT resulted in upstaging in a substantial number of patients (Table 5). Although disease was considered to be more extensive in 43% of patients, it was considered to be less extensive in only 7%. Compared with the primary staging cohort, a greater change was noted in the BF cohort, with disease considered to be more extensive in 51% of patients and less extensive in 10%. Only 29% of patients in the BF cohort had no change in disease extent after ⁶⁸Ga-PSMA PET/CT scanning.

Overall Treatment Plan

The intended overall treatment plan, when categorized into surveillance, targeted/localized, or systemic therapy, did not change significantly after ⁶⁸Ga-PSMA PET/CT scanning (Table 6). In particular, there was minimal change in the primary staging cohort; however, a slightly greater change was noted in the BF cohort

with fewer patients planned to undergo observation and targeted/localized treatment and more patients to undergo systemic treatment.

Prognosis

Clinicians indicated that the ⁶⁸Ga-PSMA PET/CT resulted in no change to prognosis in 40%, a worse prognosis in 36%, and an improved prognosis in 9% (Table 7). In the primary staging group, clinicians indicated no change in prognosis in 75%, a worsening in 10%, and improvement in 1%. By comparison, prognosis was worse in 42%, improved in 12%, and unchanged in 28% of the BF cohort.

Therapy Plans

Surgery. The intended surgical treatment plans are shown in Figure 1 and Supplemental Table 2. ⁶⁸Ga-PSMA PET/CT resulted in a significant increase in the number of patients being planned for surgery in the BF cohort, specifically related to regional node dissection. There was little overall increase in planned surgery in the primary staging cohort; however, more patients underwent combined prostatectomy and regional lymph node dissection, rather than prostatectomy only. Incidental

TABLE 4
Patients with Additional Sites of Disease Detected on ⁶⁸Ga-PSMA PET/CT

Staging	Local	Nodal	Metastatic	Not answered
Primary (<i>n</i> = 108)	15 (14)	27 (25)	7 (6)	0
BF (<i>n</i> = 312)	99 (32)	135 (43)	61 (20)	1
Overall (<i>n</i> = 420)	114 (27)	162 (39)	68 (16)	1

Data in parentheses are percentages.

TABLE 5
Clinicians Assessment of Overall Disease Extent After ⁶⁸Ga-PSMA PET/CT

Disease extent	Primary staging		BF		Overall	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
More extensive	22	20	158	51	180	43
Less extensive	1	1	30	10	31	7
Unchanged	81	75	89	29	170	40
Unsure/equivocal	4	4	32	10	36	9
Not answered	0	0	3	1	3	1
Total	108	100	312	100	420	100

TABLE 6
Overall Treatment Plan Before and After ⁶⁸Ga-PSMA PET/CT

Treatment plan	Primary staging					BF					Total				
	Before ⁶⁸ Ga-PSMA		After ⁶⁸ Ga-PSMA		P	Before ⁶⁸ Ga-PSMA		After ⁶⁸ Ga-PSMA		P	Before ⁶⁸ Ga-PSMA		After ⁶⁸ Ga-PSMA		P
	n	%	n	%		n	%	n	%		n	%	n	%	
Surveillance	4	4%	3	3%	NS	78	25%	75	24%	NS	82	20%	78	19%	NS
Targeted/localized	72	66%	73	68%	NS	126	40%	119	38%	NS	198	47%	192	46%	NS
Systemic therapy	32	30%	32	29%	NS	105	34%	116	37%	NS	137	32%	148	35%	NS
Not stated/incomplete	0	0%	0	0%		3	1%	2	1%		3	1%	2	0%	
Total	108	100%	108	100%		312	100%	312	100%		420	100%	420	100%	

NS = not significant.

TABLE 7
Change in Overall Prognosis After ⁶⁸Ga-PSMA PET/CT

Prognosis	Primary staging		BF		Overall	
	n	%	n	%	n	%
Better	1	1	36	12	37	9
Worse	21	10	131	42	152	36
Unchanged	81	75	86	28	167	40
Unsure/equivocal	5	5	57	18	62	15
Not answered	0	0	2	1	2	0
Total	108	100	312	100	420	100

findings resulted in surgery being performed on 4 patients, including the excision of lung lesions in 2 patients and a renal cell cancer in another.

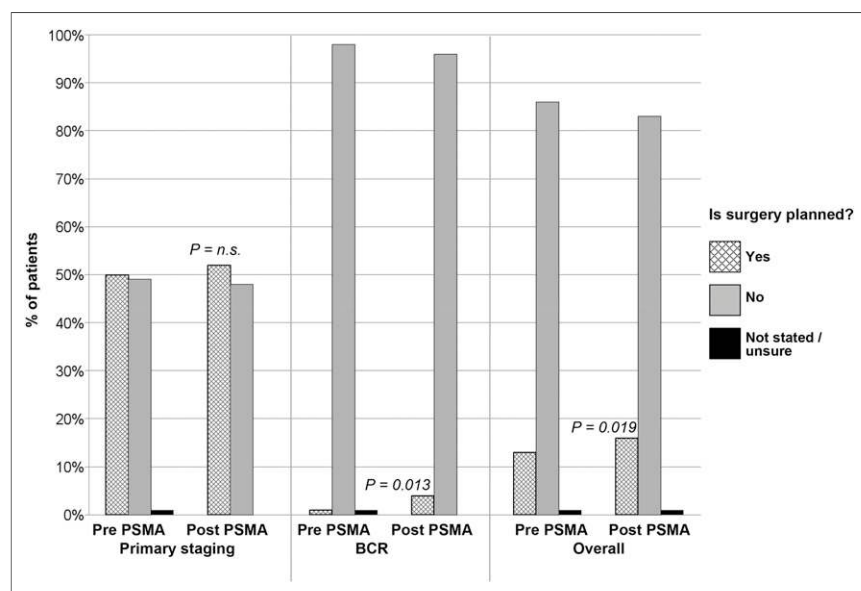


FIGURE 1. Radiation therapy management intent before and after ⁶⁸Ga-PSMA PET/CT. Although there was no change in planned radiotherapy in primary staging cohort, there was small (but not significant) increase in BF cohort. n.s. = not significant.

Radiation Treatment (RT). The intended RT plans of referring clinicians are shown in Figure 2. In the primary staging group, there was no change in the number of men in whom RT was planned. However, a larger dose or higher volume was planned for 15% of patients undergoing RT once the results of the ⁶⁸Ga-PSMA PET/CT scans were available.

In the BF group, there was a small increase in the number of men planned for RT overall; however, the type, or extent, of RT being planned changed in many patients. In this cohort, there was a significant reduction in planned prostate bed RT after ⁶⁸Ga-PSMA PET/CT and significant increases in the uses of stereotactic body RT and RT to pelvic nodes in addition to the fossa (Supplemental Table 1).

In men planned for RT, ⁶⁸Ga-PSMA PET/CT resulted in referring clinicians intending to increase the size of the radiation field (12% of patients), or introduce a radiation boost (15% of patients) in many patients in the BF cohort. A lower dose, or smaller volume, was planned in only 4% of patients as determined by ⁶⁸Ga-PSMA PET/CT scans, presumably due to exclusion of previously assumed sites of disease.

Systemic Therapy. Overall, there was little change in the intention to treat with ADT after ⁶⁸Ga-PSMA PET/CT (Fig. 3). Although few men overall had chemotherapy planned, there was an increase in the total number of patients in whom management intent included chemotherapy (Fig. 4). The increase was statistically significant in the BF cohort.

Additional Imaging. Referring clinicians were asked whether the ⁶⁸Ga-PSMA PET/CT findings would result in additional diagnostic imaging be performed, or alternatively, might obviate the need for planned biopsies to be undertaken. In the primary staging cohort, there was 1 additional bone scan and 2 pelvic MRI scans required. In the BF cohort, although there was some additional imaging considered necessary (26 scans, comprising 11 CT scans, 4 bone scans, 9 MRI, and

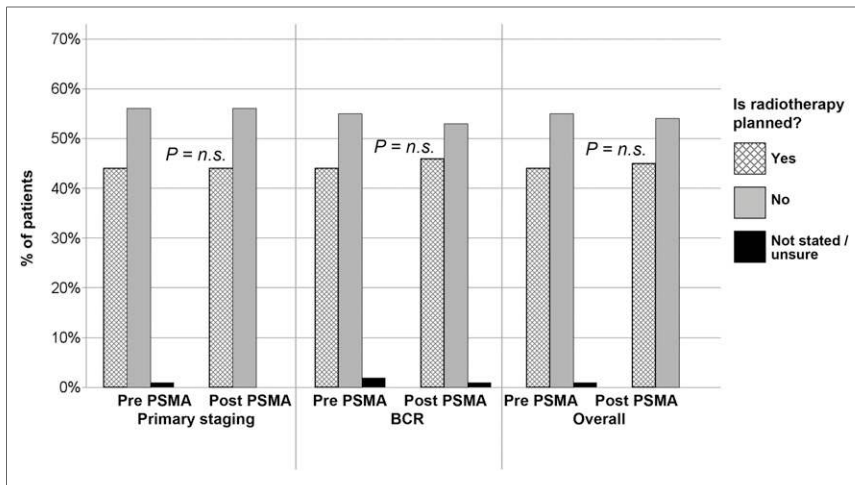


FIGURE 2. Surgery management intent before and after ^{68}Ga -PSMA PET/CT. Significantly more men had surgery (specifically regional lymph node dissection) planned in BF cohort. Increase was not significant in primary staging cohort after ^{68}Ga -PSMA PET/CT. n.s. = not significant.

2 ^{18}F -FDG PET/CT scans), the net impact was to obviate the need for further planned imaging with a total of 137 scans no longer required (44 CT scans, 30 bone scans, 40 MRI scans, and 23 ^{18}F -FDG PET/CT scans).

Additional Biopsies. The study assessed whether the ^{68}Ga -PSMA PET/CT findings would result in additional biopsies being performed, or alternatively, might obviate the need for planned biopsies. The change to planned biopsies was minimal, with no biopsies planned in most patients (94%). ^{68}Ga -PSMA PET/CT resulted in intended additional biopsies in 15 patients (3%), changed the planned biopsy site in 1 patient (0.5%), and eliminated the need for biopsies in 3 patients (1%). In the primary staging cohort, 2 additional biopsies were required, one of a femoral node and the other of a prostate gland. In the BF cohort, there were planned additional biopsies of axillary lymph nodes, a brain lesion, 2 lung lesions, 5 prostate biopsies, and 1 of the seminal vesicles. In the 1 patient in whom the biopsy site was changed, this was amended to involve the seminal vesicle.

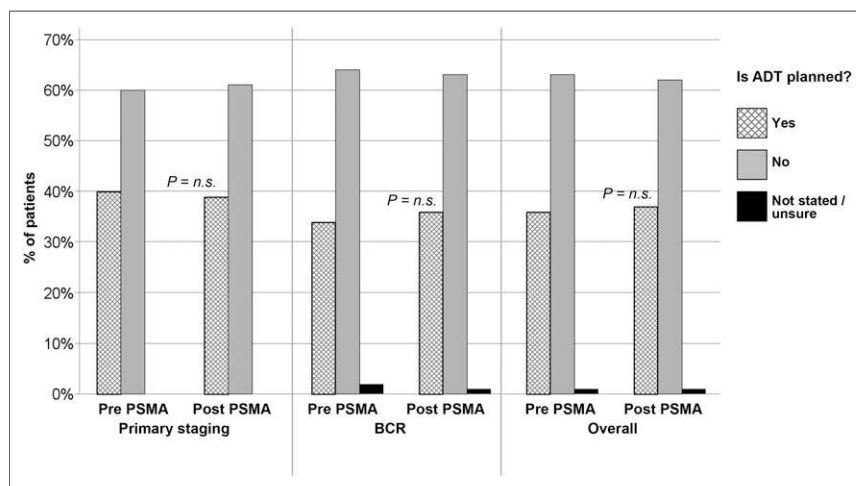


FIGURE 3. ADT management intent before and after ^{68}Ga -PSMA PET/CT. There was little change in intention to treat with ADT after ^{68}Ga -PSMA PET/CT. n.s. = not significant.

Confirmation of ^{68}Ga -PSMA-Detected Sites of Disease

As noted in Table 4, many additional abnormalities were detected on ^{68}Ga -PSMA PET/CT scans compared with conventional imaging. Figure 5 shows whether referring clinicians considered that sites of uptake were likely to be prostate cancer and how this would be confirmed. The results show that referring clinicians considered that sites of uptake on ^{68}Ga -PSMA PET/CT were unequivocally prostate cancer in most men. Biopsies were performed in only 2 patients to confirm the ^{68}Ga -PSMA PET/CT scan findings. There were 8 patients with uptake considered to be a likely false-positive finding. The scan findings were deemed by the referring clinician to be inconclusive in 24 cases.

DISCUSSION

This prospective, multicenter study is, to our knowledge, the largest series published to date evaluating the management intent of ^{68}Ga -PSMA PET/CT scanning in patients with prostate cancer. It confirms that ^{68}Ga -PSMA PET/CT scanning has a high management impact in many patients. Overall, our study showed that ^{68}Ga -PSMA PET/CT changed management intent in 51% of patients. The impact was significantly higher in the BF cohort, with a planned management change identified in 62% of patients, including those with low PSA levels.

Although there have been other reports of the management impact of ^{68}Ga -PSMA PET/CT in patients with prostate cancer, to date, these have been small series, single site, and largely retrospective. Overall management impact has been reported in the range from 51% to 76%, with radiation therapy changed in 29%–46% of patients and hormonal therapy in 33% (3,4,8,12–14). In a prospective study of 38 patients, Morigi et al. reported that the use of ^{18}F -fluoromethylcholine and ^{68}Ga -PSMA resulted in a change of management in 24 patients (63%), with 54% (13/24 patients) being due to ^{68}Ga -PSMA imaging alone (15).

There is increasing evidence supporting the role of ^{68}Ga -PSMA PET/CT in the evaluation of prostate cancer, particularly in the setting of BF after definitive therapy (16). Published literature describes detection rates in the order of 75%–90% (5–9). Overall, we found that ^{68}Ga -PSMA PET/CT detected new sites of uptake in many patients. The detection of additional sites of disease has important implications for patient management, because recurrence localized to the tumor bed can potentially be treated with curative and directed stereotactic radiation therapy, oligometastatic disease can be treated with targeted therapies such as stereotactic body radiation

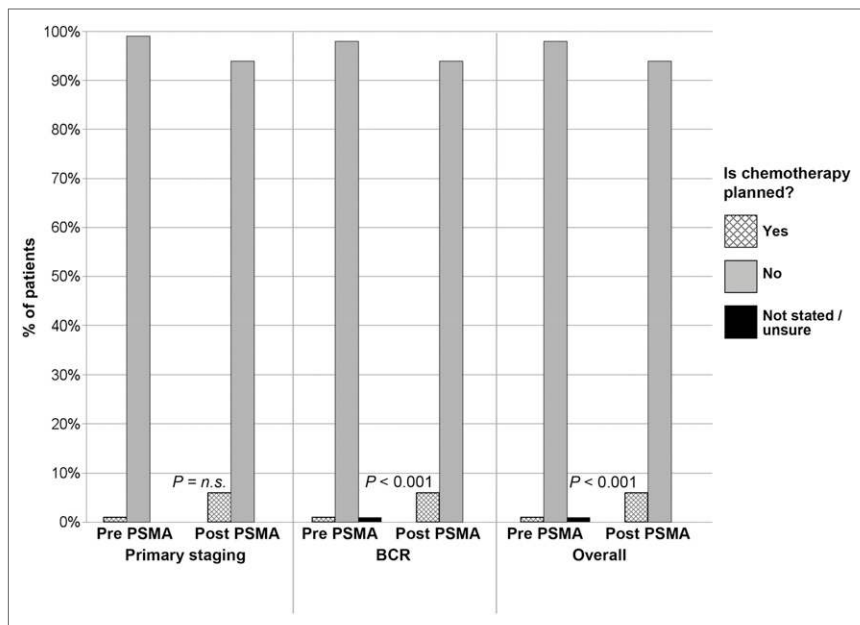


FIGURE 4. Chemotherapy management intent before and after ^{68}Ga -PSMA PET/CT. Significantly more men had chemotherapy planned in BF cohort. Increase was not significant in primary staging cohort after ^{68}Ga -PSMA PET/CT. n.s. = not significant.

therapy or surgical lymph node dissection, and patients with metastatic disease may start systemic treatment and be spared RT to the prostatic fossa (15).

Our study found that the biggest impact of management intent was in patients with BF, with a 62% intended management change noted. ^{68}Ga -PSMA scanning resulted in a 76% reduction in patients with BF with site unknown, because scans detected either oligometastatic disease or polymetastatic disease in most patients. The high lesion detection in this cohort changed planned management in several ways. For RT, only 2% more patients overall would have radiotherapy added to their treatment plan. However, changes to the planned radiotherapy fields were seen in many patients, and there were significant increases in plans to include regional nodes in radiotherapy fields, as well as the use of stereotactic body radiation therapy. The detection of additional nodes also resulted in a significant increase in the number of patients being considered for surgery, with regional lymph node dissection planned in additional

patients. Positive ^{68}Ga -PSMA PET/CT scan findings resulted in a reclassification of management intent from targeted/localized therapy or surveillance to systemic treatment in 10% of patients. As a result, there was an increase in the use of systemic therapies including ADT and a significant increase in the use of chemotherapy. Although the major impact of ^{68}Ga -PSMA PET/CT in the BF cohort was to demonstrate more extensive disease, the scan was able to confirm disease confined to the prostatic fossa in some patients. The ability of ^{68}Ga -PSMA PET/CT to exclude other sites of nodal or metastatic involvement resulted in disease being considered less extensive in 10% of patients, with the prognosis considered to be improved in 12% of patients.

In patients undergoing primary staging for intermediate- and high-risk prostate cancer, the change in management intent was smaller (21%), but not inconsequential. Although there was no change in disease extent in most patients (75%), ^{68}Ga -PSMA PET/CT detected oligometastases in some patients and significantly increased the detection of polymetastatic disease in others, with disease considered to be more extensive in 20% of patients. Although there was little impact on RT, the detection of regional lymph nodes resulted in a 27% increase in the inclusion of regional node dissection into planned primary surgery.

There has been rapid adoption of ^{68}Ga -PSMA PET/CT imaging into clinical practice, despite limited data documenting overall accuracy and limitations of the scans. Although sites of uptake are often revealed that are not identified on conventional imaging, ^{68}Ga -PSMA is not specific for prostate cancer and uptake can be seen with other conditions. Our study assessed whether additional imaging or biopsies would be required to confirm the scan findings. We found that although ^{68}Ga -PSMA PET/CT resulted in additional imaging being required in some patients ($n = 29$), the net impact was to obviate the need for further imaging in many more ($n = 137$). In particular, our study found that ^{68}Ga -PSMA PET/CT reduces the need for bone scintigraphy, CT scans, MRI, and ^{18}F -FDG PET/CT scans. We also found that despite additional sites of uptake being detected in many patients, no additional biopsies were required in most patients (95%) once the scan findings were made available. Overall, we noted only a small net increase in the number of biopsies being planned. These findings suggest that referring clinicians have a high degree of confidence that abnormalities detected on ^{68}Ga -PSMA PET/CT scans are true-positive. Although this may be reasonable in many patients in this cohort with proven prostate cancer, it is important for clinicians to be aware that uptake can be demonstrated with other malignancies (including glioblastoma,

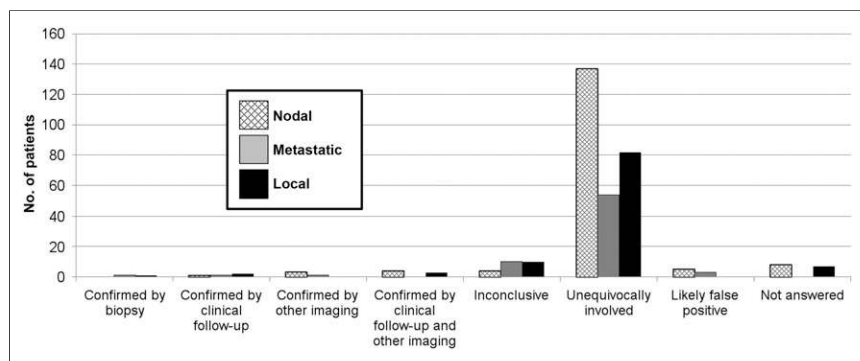


FIGURE 5. Sites of uptake on ^{68}Ga -PSMA PET/CT: clinicians' impression of likelihood of disease and method of confirmation. Clinicians considered that sites of uptake reflected sites of prostate cancer in most cases. Small number was considered to be inconclusive, and few confirmatory biopsies were performed.

hepatocellular carcinoma, lung cancer, renal cell cancer, thyroid cancer, and follicular lymphoma), benign conditions (e.g., schwannomas and thyroid adenomas), and physiologic structures, including celiac ganglia (11).

An important limitation of our study is that the completed questionnaires reflect management intent, not actual management. Treating physicians were asked to indicate their planned management after ^{68}Ga -PSMA PET/CT, which may not always have been the actual management that subsequently occurred in each individual patient.

CONCLUSION

These data represent the largest prospective study yet reported that examines the impact of ^{68}Ga -PSMA PET/CT on patient management intent in patients with prostate cancer. Our study found a high impact on management intent, with a planned management change in 51% of patients. The impact was even higher in the subset of patients with BF after definitive therapy, with a 62% management intent change noted, including those with low PSA values. Our study further supports that ^{68}Ga -PSMA PET/CT is a valuable diagnostic tool in the management of many patients with prostate cancer.

DISCLOSURE

We thank the Australian Commonwealth Department of Health for the financial support of the Australian Prostate Cancer Research Centre–NSW. No other potential conflict of interest relevant to this article was reported.

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REFERENCES

1. Hövels AM, Heesakkers RA, Adang EM, et al. The diagnostic accuracy of CT and MRI in the staging of pelvic lymph nodes in patients with prostate cancer: a meta-analysis. *Clin Radiol*. 2008;63:387–395.
2. Beresford MJ, Gillatt D, Benson RJ, Ajithkumar T. A systematic review of the role of imaging before salvage radiotherapy for post-prostatectomy biochemical recurrence. *Clin Oncol (R Coll Radiol)*. 2010;22:46–55.
3. van Leeuwen PJ, Stricker P, Hruby G, et al. ^{68}Ga -PSMA has a high detection rate of prostate cancer recurrence outside the prostatic fossa in patients being considered for salvage radiation treatment. *BJU Int*. 2016;117:732–739.
4. Albisinni S, Artigas C, Aoun F, et al. Clinical impact of ^{68}Ga -prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) in patients with prostate cancer with rising prostate-specific antigen after treatment with curative intent: preliminary analysis of a multidisciplinary approach. *BJU Int*. 2017;120:197–203.
5. Afshar-Oromieh A, Zechmann CM, Malcher A, et al. Comparison of PET imaging with a ^{68}Ga -labelled PSMA ligand and ^{18}F -choline-based PET/CT for the diagnosis of recurrent prostate cancer. *Eur J Nucl Med Mol Imaging*. 2014;41:11–20.
6. Afshar-Oromieh A, Avtzi E, Giesel FL, et al. The diagnostic value of PET/CT imaging with the ^{68}Ga -labelled PSMA ligand HBED-CC in the diagnosis of recurrent prostate cancer. *Eur J Nucl Med Mol Imaging*. 2015;42:197–209.
7. Bluemel C, Krebs M, Polat B, et al. ^{68}Ga -PSMA-PET/CT in patients with biochemical prostate cancer recurrence and negative ^{18}F -choline-PET/CT. *Clin Nucl Med*. 2016;41:515–521.
8. Bluemel C, Linke F, Herrmann K, et al. Impact of ^{68}Ga -PSMA PET/CT on salvage radiotherapy planning in patients with prostate cancer and persisting PSA values or biochemical relapse after prostatectomy. *EJNMMI Res*. 2016;6:78.
9. Eiber M, Maurer T, Souvatzoglou M, et al. Evaluation of hybrid ^{68}Ga -PSMA ligand PET/CT in 248 patients with biochemical recurrence after radical prostatectomy. *J Nucl Med*. 2015;56:668–674.
10. Maurer T, Weirich G, Schottelius M, et al. Prostate-specific membrane antigen-radioguided surgery for metastatic lymph nodes in prostate cancer. *Eur Urol*. 2015;68:530–534.
11. Rauscher I, Maurer T, Fendler WP, Sommer WH, Schwaiger M, Eiber M. ^{68}Ga -PSMA ligand PET/CT in patients with prostate cancer: how we review and report. *Cancer Imaging*. 2016;16:14.
12. Shakespeare TP. Effect of prostate-specific membrane antigen positron emission tomography on the decision-making of radiation oncologists. *Radiat Oncol*. 2015;10:233.
13. Sterzing F, Kratochwil C, Fiedler H, et al. ^{68}Ga -PSMA-11 PET/CT: a new technique with high potential for the radiotherapeutic management of prostate cancer patients. *Eur J Nucl Med Mol Imaging*. 2016;43:34–41.
14. Dewes S, Schiller K, Sauter K, et al. Integration of ^{68}Ga -PSMA-PET imaging in planning of primary definitive radiotherapy in prostate cancer: a retrospective study. *Radiat Oncol*. 2016;11:73.
15. Morigi JJ, Stricker PD, van Leeuwen PJ, et al. Prospective comparison of ^{18}F -fluoromethylcholine versus ^{68}Ga -PSMA PET/CT in prostate cancer patients who have rising PSA after curative treatment and are being considered for targeted therapy. *J Nucl Med*. 2015;56:1185–1190.
16. Sathianathan NJ, Lamb A, Nair R, et al. Updates of prostate cancer staging: prostate-specific membrane antigen. *Investig Clin Urol*. 2016;57(suppl 2):S147–S154.