^{18}F-DCFPyL PSMA-PET affects management of salvage radiotherapy for post-prostatectomy patients with biochemical failure: A matched cohort study

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ABSTRACT

Introduction: Our objective was to assess the effect of ^{18}F-DCFPyL prostate-specific membrane antigen (PSMA) positron emission tomography (PET) on the management and outcomes of patients receiving salvage radiotherapy following biochemical failure (BF) post-radical prostatectomy (RP) using a matched cohort analysis.

Methods: A PSMA-PET cohort of patients with BF post-RP was identified through a prospective registry. Patients from this registry were included if they did not have disease outside of the pelvis and underwent salvage radiotherapy to the prostate and/or pelvis. Case-control matching was performed with a contemporary cohort of patients with BF post-RP without PSMA-PET information.

Results: Forty-four patients were included in the PSMA-PET cohort and 80 were analyzed in the non-PSMA-PET cohort. The PSMA-PET cohort had a significantly higher pre-radiotherapy median prostate-specific antigen (PSA) of 0.48 ng/mL compared to 0.20 ng/mL in the non-PSMA-PET cohort ($p<0.001$) but these levels were similar after matching. The PSMA-PET cohort had a higher proportion of patients receiving radiotherapy to pelvic lymph nodes (n=27

KEY MESSAGES

- PSMA-PET is more sensitive than conventional imaging in detecting recurrent prostate cancer.
- PSMA-PET is associated with more patients receiving pelvic radiation in addition to the prostate bed.
- Late salvage with PSMA-PET has similar outcomes to early salvage without PSMA-PET.

[61.4%] vs. n=16 [20.0%], p<0.001). Median followup was 26 months (interquartile range 18.8–33) for both cohorts. BF-free survival and event-free survival were not significantly different between the two cohorts for all (p=0.662 and >0.99) and matched patients (p=0.808 and 0.808), respectively. Metastasis-free survival was significantly higher in the matched PSMA-PET cohort compared to the matched non-PSMA-PET cohort (p=0.046), although a higher proportion of patients in the non-PSMA-PET cohort underwent PSMA-PET restaging after BF (52 vs. 20%, p=0.08726).
Conclusions: Our study showed that patients undergoing PSMA-PET scans after BF post-RP had a higher likelihood of pelvic nodal treatment at the time of salvage RT. Despite higher PSA levels at salvage, we identified no recurrence or survival differences.

INTRODUCTION

For curative intent treatment of localized prostate cancer, the two primary modalities are surgery or radiotherapy. Salvage radiotherapy is a common choice for patients progressing with biochemical failure (BF) post-radical prostatectomy (RP). A recent meta-analysis showed that adjuvant radiotherapy was not superior to early salvage radiotherapy with respect to event-free survival (EFS) (1). Early salvage radiotherapy is usually triggered by prostate-specific antigen (PSA) kinetics. However, there is increasing interest in using novel imaging techniques to improve decision making and target definition in this setting.

Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) uses a radiotracer that targets the PSMA receptor and has been shown to have higher sensitivity (75%) and specificity (99%) for detecting prostate cancer compared to conventional imaging and other radiopharmaceuticals (2). The improved ability to detect prostate cancer is posited to improve outcomes in recurrent prostate cancer or avoid futile treatment.
The goal of this study was to assess the effect of ^{18}F-DCFPyL PSMA-PET on the management and outcomes of patients receiving salvage radiotherapy for BF post-RP using a matched cohort analysis.

METHODS

Study design and data collection

This was a retrospective cohort study of patients who received salvage radiotherapy following BF post-RP with or without access to ^{18}F-DCFPyL PSMA-PET prior to radiotherapy. This study was reviewed and approved by our institutional review ethics board.

The cohort who received PSMA-PET after BF were prospectively identified on a registry study. Details of the registry and the PSMA-PET procedure can be found in a previous publication (3). Essentially, men were eligible for this prospective, provincial registry if they

were previously treated for prostate cancer with curative intent, were found to have suspected persistent or recurrent disease, had conventional imaging (bone scan and CT) showing negative or oligometastatic disease in or outside the pelvis and had an Eastern Cooperative Oncology Group performance status less than or equal to 1. Patients did not have access to PSMA-PET in the province outside of this registry. Patients were stratified into predefined cohorts depending clinical scenarios; the cohort included in this study were men with biochemical failure after initial RP (cohort 2 in the registry). Part way through this registry, the requirement for conventional imaging prior to PSMA-PET was dropped for patients with a PSA ≤ 10 ng/ml. All patients received radiotherapy between January 2018 and December 2020 in a single institution. From this cohort, patients were excluded based on the following criteria:

- Not receiving salvage radiation despite biochemical failure and no evidence of disease on PSMA-PET;
- Receiving non-standard treatment, including non-standard practices at the time of RP (e.g., patients receiving androgen deprivation therapy [ADT] prior to surgery) or during salvage radiotherapy (e.g., patients receiving stereotactic radiotherapy to pelvic lymph nodes without prostate bed radiotherapy);
- Missing baseline data (e.g., surgical details) or missing radiation details because patients received radiation in a different institution;
- Previous overlapping radiation volumes (e.g., previous pelvic radiation) precluding salvage radiotherapy doses; or
- Having distant metastatic disease identified on conventional imaging or PSMA-PET.

The non-PSMA-PET cohort included patients treated with salvage radiotherapy to the prostate bed ± lymph nodes identified retrospectively using our institution's radiotherapy electronic record by searching for patients who received 33 fractions of radiotherapy to the pelvis. These patients received radiotherapy between January 2016 and February 2021 and did not undergo PSMA-PET prior to salvage radiotherapy.

Data collected from both cohorts included demographic information, surgical details, salvage radiotherapy and ADT details, and outcomes. Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at Lawson Health Research Institute (4, 5).

Salvage therapy

All patients received salvage with external beam radiotherapy in 33 fractions via volumetric modulated arc therapy using standard photon linear accelerators. 66 Gy was delivered to the prostate bed and 50.4 Gy was delivered to the pelvic lymph nodes (if applicable) in 33 fractions. Boost to nodes or prostatic bed nodules (if applicable) ranged from 60 to 70 Gy via simultaneous

in-field boost. ADT use was left to the discretion of the treating oncologist and ranged from 4 months to 2 years.

Patients were followed with serial PSAs every 3 to 6 months at the discretion of the treating oncologist. Follow-up imaging was optional in the case of biochemical failure and was performed at the discretion of the most responsible physician.

Case-control matching

Case-control matching was performed matching patients with PSMA-PET (n = 44) ("cases") vs. no PSMA-PET (n = 80) ("controls") based on:

- Pre-radiotherapy PSA (± 0.5; ± 1.0; ± 1.5 ng/mL)
- Undetectable PSA defined as post-RP PSA < 0.1 ng/mL (same value: "No" or "Yes")
- Cancer of the Prostate Risk Assessment Post-Surgical (CAPRA-S) score (± 1; ± 2; ± 3; same risk group: "Low (0–2)", "Intermediate (3–5)" or "High (6–12)")
- ADT (same value: "No" or "Yes")

A total of 24 scenarios were examined based on initial sample sizes using ratios of 1:1 and 1:2 and varying callipers for pre-radiotherapy PSA (± 0.5; ± 1.0; ± 1.5 ng/mL) and CAPRA-S score (± 1; ± 2; ± 3; same risk group). To evaluate quality of matches and select an optimal final matched cohort for analysis, the final matched cohort had to satisfy the following the criteria:

- Minimizing imbalance between cohorts using the standard difference (S.D. < 0.10),
- Minimizing imbalance between cohorts using p-value from Chi-square test, Fisher's exact test or two sample t-test as appropriate, and
- Maximizing total sample size (maximizing power).

Selection of final matched cohorts are summarized in Supplemental Table 1.

Outcomes

The primary outcomes were salvage treatment details and biochemical failure-free survival (BFFS), which was calculated as time from date of salvage radiotherapy to date of biochemical failure, date of death (any cause) or date of last PSA follow-up, whichever occurs first. Secondary endpoints included metastasis-free survival (MFS), which was calculated as time from date of salvage EBRT to date of metastasis, date of death (any cause) or date of last follow-up, whichever occurs first; and event-free survival (EFS), which was calculated as time from date of salvage EBRT to date of biochemical failure, date of death (any cause), date of progression, date of metastasis or date of last follow-up, whichever occurs first. Metastatic events were defined as M1 disease detected on conventional or PSMA-PET imaging. Overall survival and cancer-specific survival were not examined due to no death events.

Statistical analyses

Descriptive statistics were generated for baseline characteristics stratified by cohort (PSMA-PET vs. no PSMA-PET) for all patients (n=124) and matched patients (n=68), compared using the Chi-square test, Fisher's exact test, two sample t-test or Wilcoxon rank sum test as appropriate. Variables included in case-control matching compared using the paired t-test, Wilcoxon signed rank test or McNemar's test as appropriate. Standardized difference computed for variables included in case-control matching.

Kaplan-Meier estimates were generated for all survival outcomes stratified by (1) cohort (PSMA-PET vs. no PSMA-PET) and (2) PSMA-PET and PSA level at the time of salvage (no PSMA-PET + PSA < 0.5 ng/mL vs. PSMA-PET + PSA 0.5-1.5 ng/mL) for all patients and matched patients. The latter analysis was done to compare patients without access to PSMA-PET receiving early salvage with those with access to PSMA-PET receiving late salvage. Comparisons were made using the log-rank test (unmatched patients) or stratified log-rank test (matched patients).

Univariable and multivariable Cox proportional hazards regression were performed for BFFS, MFS and EFS for all patients (n=124). For matched comparisons, models were additionally stratified by matched pair groups (to adjust for matched design). Multivariable models were generated by adjusting for cohort (PSMA-PET vs. no PSMA-PET), variables included in case-control matching (pre-radiotherapy PSA, undetectable PSA, CAPRA-S score, and androgen deprivation therapy), and imaging received.

All statistical analysis was performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA), using two-sided statistical testing at the 0.05 significance level.

RESULTS

A total of 151 patients were enrolled in the PSMA-PET registry for BF post-RP at our institution. Of these, 44 met inclusion criteria for our analysis. Figure 1 describes the screening process and reasons for exclusion for this cohort. Notably, 65 patients had a negative PSMA-PET and did not receive salvage radiotherapy. One patient had polymetastatic disease outside the pelvis identified on PSMA-PET, which was also identified on conventional imaging. There were no patients who had polymetastatic disease outside the pelvis identified on PSMA-PET alone. Three patients had oligometastatic disease in pelvic nodes detected on PSMA-PET but were treated with metastasis-directed therapy without treatment of the prostate bed and were excluded. A total of 80 patients were analysed In the non-PSMA-PET cohort.

Baseline characteristics of the PSMA-PET and non-PSMA-PET pre-matched and matched cohorts are summarized in Table 1. The median pre-surgery PSA was 7.81 ng/mL (interquartile range [IQR]: 5.85–11.34) and 7.45 ng/mL (IQR: 5.40–11.88) for the PSMA-PET and non-PSMA-PET cohorts, respectively with no significant differences (p=0.900). Most patients (n = 27 [61.4%] and n = 40 [50.0%], respectively) had a Gleason grade group 2 cancer at

the time of surgery. The median CAPRA-S score was 5 (IQR: 2.5–6) and 5 (IQR: 3–6.5) for both cohorts, respectively. Median follow-up was 1.93 years (95% confidence interval [CI]: 1.51–2.30) for the PSMA-PET cohort and 2.39 years (95% CI: 2.03–2.58) for the non-PSMA-PET cohort.

Among patients that received PSMA-PET, disease was detected in the prostate bed in two patients (4.6%) and pelvic nodes in 16 patients (36.4%). Most patients in this cohort underwent abdominopelvic CT (n = 42, 95.5%) and bone scan (n = 41, 93.2%). CT detected disease in the prostate bed in 1 patient (2.4%) and pelvic nodes in 3 patients (7.1%) in this cohort. Most patients in the non-PSMA-PET cohort did not have conventional staging investigations (n = 53 [66.3%]). In this cohort, 22 patients (27.5%) underwent abdominopelvic CT and 21 patients (26.3%) underwent bone scan. CT did not detect any prostate bed or nodal disease in this cohort.

Table 2 summarizes the salvage therapy details. The PSMA-PET cohort had a significantly higher median pre-salvage PSA of 0.48 ng/mL (IQR: 0.26-0.73) compared to 0.20 ng/mL (IQR: 0.14-0.28) in the non-PSMA-PET cohort ($p < 0.001$). This difference was not significant after matching. Other factors, including CAPRA-S score, ADT use, and proportion of patients with undetectable PSA post-surgery were not significantly different between cohorts. The PSMA-PET cohort had a statistically higher proportion of patients receiving extended radiotherapy to pelvic lymph nodes with or without an integrated boost to a node or prostatic bed nodule (n = 27 [61.4%] vs. n = 16 [20.0%], $p < 0.001$).

BFFS was not significantly different between the two cohorts for all patients ($p=0.662$) and matched patients ($p > 0.99$; Figure 2). The 2-year rates of BFFS were 76.0% and 73.0% for PSMA-PET and non-PSMA-PET matched cohorts, respectively. Similarly, EFS was not significantly different for all patients ($p = 0.675$) and matched patients ($p > 0.99$) with identical 2-year rates as reported for BFFS. This was largely attributed to any patients with local failure and/or metastatic events also having biochemical failure, and in most cases the biochemical failure event occurred first; therefore, only the first event was included in the estimates. MFS was significantly different in the matched cohorts ($p = 0.046$) and favoured the PSMA-PET cohort for all patients ($p = 0.083$; Figure 3) although not reaching significance. The 2-year rates of MFS were 97.0% and 84.9% for PSMA-PET and non-PSMA-PET matched patients, respectively.

Of the 10 patients that developed biochemical failure in the PSMA-PET arm, 2 patients (20%) underwent a repeat PSMA-PET, which did not detect any PSMA-avid disease. One patient (10%) was found to have extensive bone metastases on bone scan. Of the 21 patients that developed biochemical failure in the non-PSMA-PET arm, 11 patients (52%) underwent a PSMA-PET. Of these, 4 patients had disease in the retroperitoneal lymph nodes and 1 had bony metastases detected. Another 6 patients had metastatic disease outside the pelvis detected on conventional imaging, 5 on bone scan and 1 on CT.

Univariable and multivariable Cox proportional hazards regression models are summarized in Table 3. No analysed factors were found to be significantly associated with either BFFS or MFS based on multivariable or univariable analysis. As a sensitivity analysis, multivariable models were additionally adjusted for imaging modalities there were used (CT chest, CT abdomen and pelvis, bone scan and MRI prostate), which did not identify any significant predictive factors.

In our comparison of PSMA-PET patients with late salvage (pre-radiotherapy PSA 0.5–1.5 ng/mL) and non-PSMA-PET patients with early salvage (pre-radiotherapy PSA < 0.5 ng/mL), we found no significant differences in BFFS (p=0.764) and MFS (p=0.310) between groups (Supplemental Figure 1).

DISCUSSION

Our study found that PSMA-PET based treatment led to similar oncological outcomes for all patients, despite a significantly higher pre-salvage PSA in the PSMA-PET cohort. This held true when specifically comparing late salvage PSMA-PET patients (pre-salvage PSA between 0.5–1.5 ng/mL) and early salvage (PSA < 0.5 ng/mL) non-PSMA-PET patients, suggesting that a delay in treatment initiation for access to a PSMA-PET scan does not seem to compromise oncologic outcomes. Albeit small in numbers, this preliminary study's findings could provide some guidance for clinicians functioning in resource constrained or socialized health care systems, where patient access to this type of scan could take several weeks.

Thirty-six percent of patients had positive pelvic lymph nodes on PSMA-PET scanning, similar to the increase in the use of node-basin treatment in the PSMA-PET cohort vs the non-PET cohort (n = 27 [61.4%] vs. n = 16 [20.0%], p < 0.001). This is likely due to more frequent identification of nodal disease as approximately one third of patients in the PSMA-PET cohort were identified as having nodal metastases. Our findings corroborate the results from another prospective registry of patients with biochemical failure after primary therapy (3). This study reported that PSMA-PET helped detect additional sites of disease in 62% of men resulting in change of management in 58% of patients. Similar results were found by a recent systematic review and meta-analysis, which showed that PSMA-PET changed management in 54% (95% CI: 47–60%) of patients with primary and recurrent prostate cancer (6). A PSMA-PET scan may be able to help select patients who may benefit from the addition of nodal irradiation.

Our results are also in keeping with findings from the recently published EMPIRE-1 randomized clinical trial (7). This was a single-centre, phase 2/3 trial randomizing patients with detectable PSA after RP and negative conventional imaging in a 1:1 ratio to PSMA-PET-directed radiotherapy vs. radiotherapy without PSMA-PET. The authors found that 3-year EFS was significantly higher in the PSMA-PET arm compared to the conventional imaging arm (75.5% vs. 63.0%, 95% CI: 62.5–84.6%, p = 0.0028). A further analysis showed that although the

PSMA-PET arm had significantly larger clinical target volumes, toxicity was not different between the two arms (8).

On post-radiation follow-up, the matched PSMA-PET cohort was found to be correlated improved MFS when compared to the matched non-PSMA-PET cohort, although BFFS was not significantly different. This is likely because the non-PSMA-PET cohort had a larger proportion undergoing PSMA-PET staging post-biochemical failure (52 vs 20%, p = 0.08726), increasing sensitivity for detecting metastatic events in this cohort.

Strengths of this study include the identification of the PSMA-PET cohort from a prospective registry, limiting potential biases inherent with retrospective cohorts and the use of a contemporary comparator cohort. Further, we used practical inclusion criteria, allowing the use of ADT and variable treatment volumes according to the information available to the oncologist at time of treatment, which is more in keeping with current treatment paradigms and real-world practice. Limitations include potential selection bias from excluding three patients with PSMA-PET-detected oligometastatic disease in the pelvis who underwent metastasis-directed therapy. The small cohort from a single institution limits the statistical power of our analyses and generalizability to other institutions. Although there were baseline differences between cohorts with respect to access to conventional staging scans, we believe this difference does not impact the validity of these results as the sensitivity of conventional imaging in patients with low PSA levels post-radical prostatectomy is very low (9, 10). Future studies could compare early and late salvage of patients with PSMA-PET information (such as the cohort of patients who had a negative PSMA-PET and did not receive treatment) and assessing the trade-offs between more healing from surgery and potentially increasing radiation treatment volumes for those with nodal disease.

CONCLUSIONS

Our study showed that patients undergoing PSMA-PET scans after BF post-RP had a higher likelihood of pelvic node basin treatment at the time of salvage RT. Despite higher PSA levels at salvage, we identified no recurrence or survival differences. Further prospective studies are needed to validate outcomes associated with PSMA-PET use in this setting.

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FIGURES AND TABLES

Figure 1. PSMA-PET cohort screening process. PSMA-PET: prostate-specific membrane antigen positron emission tomography; RT: radiotherapy.

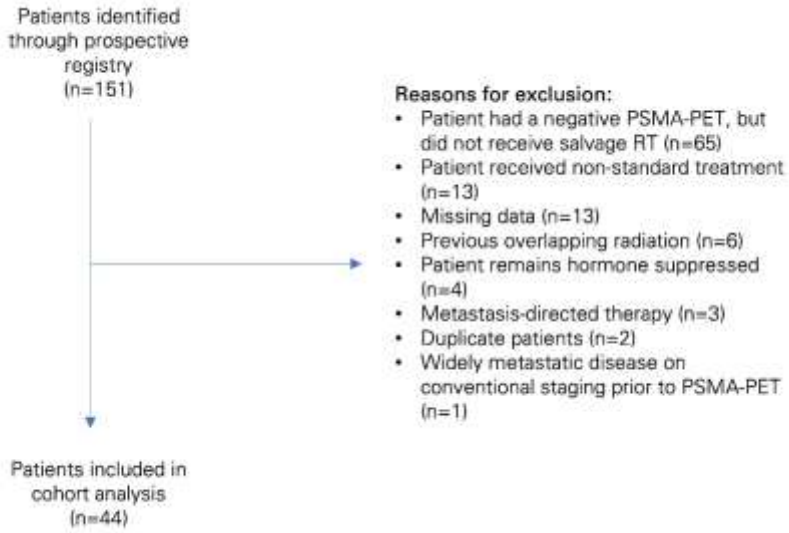

Figure 2. Biochemical failure-free survival of patients stratified by cohort for (A) all patients and (B) matched patients. BFF: biochemical failure-free; PSMA-PET: prostate-specific membrane antigen positron emission tomography.

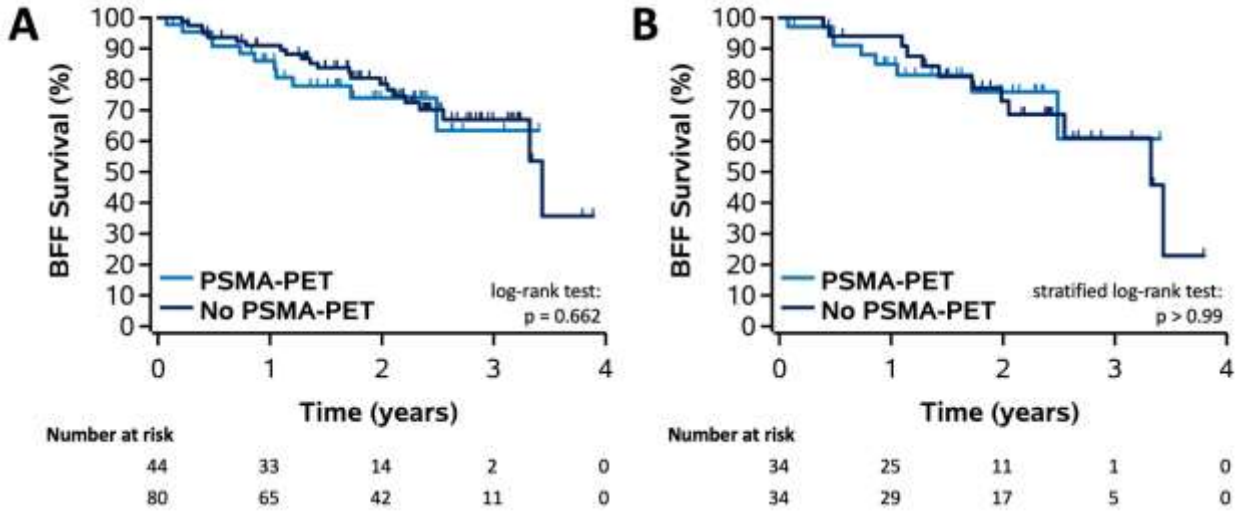

Figure 3. Metastasis-free survival of patients stratified by cohort for (A) all patients and (B) matched patients. PSMA-PET: prostate-specific membrane antigen positron emission tomography.

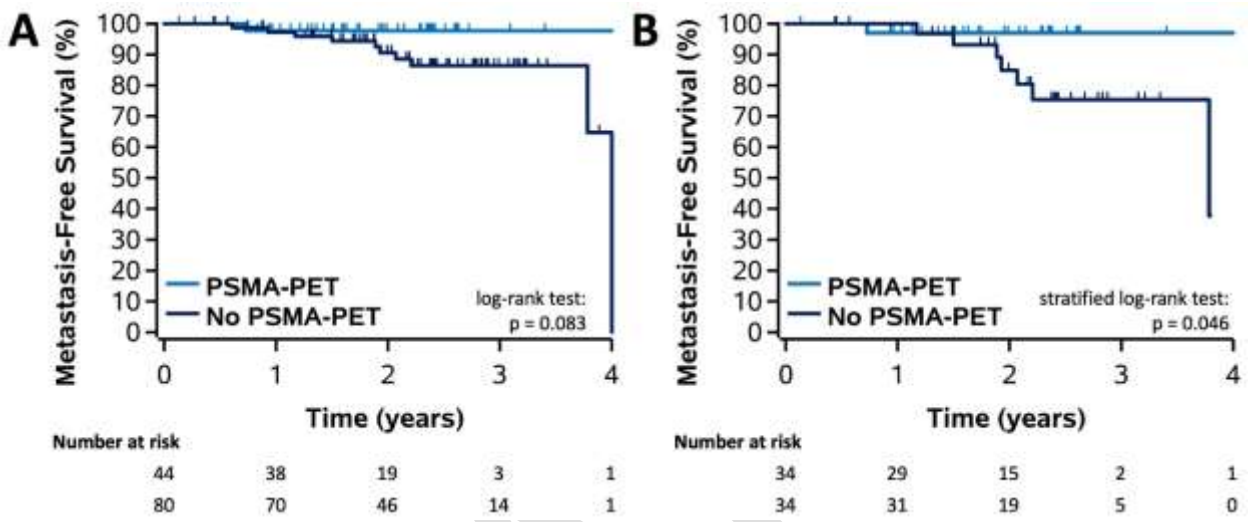

Table 1. Baseline patient characteristics stratified by cohort						
	All patients (n=124)			**Matched patients (n=68)**		
Characteristic	**PSMA-PET (n=44)**	**No PSMA-PET (n=80)**	**p-**	**PSMA-PET (n=34)**	**No PSMA-PET (n=34)**	**p**
Age at surgery, mean ± SD	63.7±6.2	63.9±5.9	0.881	63.3±6.1	64.7±5.6	0.314
Pre-surgery PSA (ng/mL), median (IQR)	7.81 (5.85–11.34)	7.45 (5.40–11.88)	0.900	7.40 (5.80–11.00)	7.05 (5.31–11.80)	0.802
Gleason grade group, n (%) 1 2 3 4 –5	 1 (2.3) 27 (61.4) 15 (34.1) 1 (2.3)	 1 (1.3) 40 (50.0) 33 (41.3) 6 (7.5)	0.417	 1 (2.9) 20 (58.8) 12 (35.3) 1 (2.9)	 0 (0) 18 (52.9) 14 (41.2) 2 (5.9)	0.777
Positive margins, n (%)	20 (45.5)	44 (55.0)	0.309	18 (52.9)	18 (52.9)	>0.99
Extracapsular extension, n (%)	26 (59.1)	54 (67.5)	0.349	21 (61.8)	25 (73.5)	0.300
Seminal vesicle involvement, n (%)	10 (22.7)	21 (26.3)	0.665	8 (23.5)	10 (29.4)	0.583

Lymph node involvement, n (%)	6 (13.6)	4 (5.0)	0.164	4 (11.8)	1 (2.9)	0.356
CAPRA-S, median (IQR)	5 (2.5–6)	5 (3–6.5)	0.354	5 (3–6)	5 (3–6)	0.052
CAPRA-S risk group, n (%)			0.221			>0.99
Low (0–2)	11 (25.0)	11 (13.8)	0.117	6 (17.7)	6 (17.7)	>0.99
Intermediate (3–5)	16 (36.4)	39 (48.8)	0.184	15 (44.1)	15 (44.1)	>0.99
High (6–12)	17 (38.6)	30 (37.5)	0.901	13 (38.2)	13 (38.2)	>0.99
Undetectable PSA* post-RP, n (%)	29 (65.9)	60 (75.0)	0.282	24 (70.6)	24 (70.6)	>0.99

*Undetectable PSA was defined as being <0.1 ng/mL. CAPRA-S: Cancer of the Prostate Risk Assessment Post-Surgical; IQR: interquartile range; PSA: prostate-specific antigen; RP: radical prostatectomy; SD: standard deviation.

Table 2. Salvage therapy details stratified by cohort

	All patients (n=124)			**Matched patients (n=68)**		
Characteristic	**PSMA-PET (n=44)**	**No PSMA-PET (n=80)**	**p**	**PSMA-PET (n=34)**	**No PSMA-PET (n=34)**	**p**
Age at RT, mean ± SD	66.8±7.2	66.3±6.1	0.674	65.9±6.4	67.8±5.8	0.223
Pre-RT PSA (ng/mL), median (IQR)	0.48 (0.26–0.73)	0.20 (0.14–0.28)	<0.001	0.34 (0.22–0.60)	0.21 (0.15–0.38)	0.095
Time from surgery to RT (months), median (IQR)	25.9 (11.0–53.9)	18.7 (7.0–38.4)	0.037	25.6 (11.0–45.5)	23.0 (7.0–45.5)	0.624
RT volumes treated, n (%)						
Prostate bed	17 (38.6)	64 (80.0)	<0.001	14 (41.2)	27 (79.4)	<0.001
Prostate bed + LN	15 (34.1)	16 (20.0)		10 (29.4)	7 (20.6)	
Prostate bed + LN + boost	12 (27.3)	0 (0)		10 (29.4)	0 (0)	
ADT use, n (%)	16 (36.4)	18 (22.5)	0.098	10 (29.4)	10 (29.4)	>0.99
ADT duration (months), median (IQR)	6.00 (4.67–6.05)	6.03 (5.95–11.99)	0.243	6.01 (5.95–6.05)	6.00 (5.95–11.99)	0.646

ADT: androgen deprivation therapy; IQR: interquartile range; LN: lymph nodes; PSA: prostate-specific antigen; RT: radiotherapy; SD: standard deviation.

Table 3. Univariable and multivariable Cox proportional hazards regression models				
Dependent variable	**Biochemical failure-free survival**		**Metastasis-free survival**	
Variable	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**
Univariable				
PSMA-PET vs. no PSMA-PET (all)	1.18 (0.57, 2.46)	0.662	0.19 (0.03, 1.53)	0.119
PSMA-PET vs. no PSMA-PET (matched)	1.00 (0.32, 3.10)	>0.99	NR	NR
Pre-RT PSA (per 1 ng/mL)	1.01 (0.75, 1.36)	0.943	0.70 (0.18, 2.71)	0.600
Undetectable PSA (vs. no)	0.56 (0.28, 1.13)	0.106	0.49 (0.13, 1.83)	0.289
CAPRA-S score (per 1 unit)	1.02 (0.88, 1.18)	0.790	1.12 (0.87, 1.44)	0.388
ADT (vs. no)	0.56 (0.23, 1.37)	0.204	NR	NR
Multivariable				
PSMA-PET vs. no PSMA-PET (all)	1.43 (0.65, 3.15)	0.380	0.24 (0.03, 2.05)	0.192
Pre-RT PSA (per 1 ng/mL)	0.97 (0.68, 1.39)	0.870	0.73 (0.22, 2.40)	0.602
Undetectable PSA (vs. no)	0.49 (0.23, 1.03)	0.061	0.41 (0.10, 1.62)	0.202
CAPRA-S score (per 1 unit)	1.03 (0.88, 1.20)	0.724	1.19 (0.89, 1.58)	0.250
ADT (vs. no)	0.44 (0.17, 1.14)	0.092	NR	NR

ADT: androgen deprivation therapy; CAPRA-S: Cancer of the Prostate Risk Assessment Post-Surgical; CI: confidence interval; HR: hazard ratio; NR: not reported; PSMA-PET: prostate-specific membrane antigen positron emission tomography; RT: radiotherapy.