Patterns of failure with ^{18}F-DCFPyL PSMA-PET/CT in the post-prostatectomy setting

A regional cohort analysis

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ABSTRACT

INTRODUCTION: This study aimed to assess the detection rate of prostate cancer recurrence by prostate-specific member antigen-positron emission tomography/computed tomography (PSMA-PET/CT) with ^{18}F-DCFPyL in patients with residual disease or biochemical recurrence (BCR), and its association with surgical pathology and prostate-specific antigen (PSA) kinetics.

METHODS: Men from South Central Ontario enrolled in the PSMA Registry for Recurrent Prostate cancer (PREP) between April 2019 and December 2021 after radical prostatectomy (RP) and who had 1) pathologic stage N1 or persistent elevated PSA; or 2) BCR (PSA ≥0.10 ng/mL) where initial postoperative PSA was undetectable were included.

RESULTS: A total of 169 men (median age 68 years; interquartile range [IQR] 62–71) with complete data met the above criteria. The median PSA was 0.27 ng/mL (IQR 0.16–0.85) prior to PSMA-PET. Overall positivity rate 59%; when PSA was <0.40 ng/mL, overall positivity rate 42% vs. 85% with PSA ≥0.40 ng/mL (p<0.001). Higher pathologic tumor stage increased detection of regional lymph nodes (LNs) (pT2-3a: 32% vs. pT3b: 69%, p<0.001) but not distant metastases (pT2-3a: 12% vs. pT3b: 24%, p=0.15). PSMA-PET detected 18% with prostate bed, 42% with regional LN disease, and 44% with pelvic-only disease. The three most involved LN chains were the internal (21%) and external (20%) iliac, and obturator chains (16%).

CONCLUSIONS: This prospective study of patients with residual disease or BCR after RP illustrates patterns of failure that could impact diagnosis and postoperative management. Such patients have significant risk of regional LN positivity on PSMA-PET, highlighting a need to include pelvic LNs within salvage radiotherapy volumes.

INTRODUCTION

Accurate localization of biochemical recurrence (BCR) post-radical prostatectomy (RP) is necessary to inform salvage therapies. Conventional imaging, consisting of computed tomography (CT) and bone scintigraphy, can be expected to help detect recurrent disease in under 10% of men at the time of BCR.[1] Positron emission tomography/computed tomography using a radiopharmaceutical that targets the prostate-specific member antigen (PSMA-PET/CT) is highly accurate in this setting, with a positive predictive value of 0.84 by histopathologic validation, with substantial inter-reader reproducibility, as PSMA-PET localizes recurrent prostate cancer in about 75% of patients in this setting.[2] The detection rate increases as serum prostate-specific antigen (PSA) increases.[2]

Up to 30% of patients were found to have at least one PSMA-PET-positive lesion not covered by the Radiation Therapy Oncology Group (RTOG) consensus salvage radiotherapy (RT) fields.[3] Prospective studies have suggested clinicians change their intended management after PSMA-PET in two-thirds of patients, a significantly increased rate compared to conventional CT restaging.[4,5] The LOCATE trial, which enrolled men with a median PSA of 0.42 after RP, found 48% of patients had a management change, 16% of which was RT target modification.[6]

The participants in this study were enrolled in the prospective,

multicenter registry (Ontario PSMA-PET Registry for Recurrent Prostate, or PREP, NCT03718260) and were referred for PSMA-PET using the radiopharmaceutical ^{18}F-DCFPyL in Hamilton, Canada. The registry is the only provincially funded access to PSMA-PET for patients in Ontario.[7]

We present our regional positivity rate of PSMA-PET for patients who experienced BCR after RP for localized prostate cancer, who were either pathologic stage node-positive or had a persistent PSA post-RP, labelled cohort 1 by the PREP study; or had initial undetectable PSA within three months of surgery and then experienced BCR (PREP cohort 2). The primary objective was to determine the proportion of men with positive findings at PSMA-PET; secondary objectives included determining the likelihood of disease detection at PSMA-PET according to serum PSA level, pathologic tumor stage, International Society of Urological Pathology (ISUP) grade group, and margin status; and the frequency of local-regional recurrence (defined as recurrence in the prostate bed and/or recurrence in regional nodes) and distant metastases.

METHODS

Study design and participants

The PREP registry is a prospective, single-arm, research ethics board-approved registry for individuals at five academic institutions across the province of Ontario (NCT03718260). Written informed consent was obtained from all participants. The present study analyzed PREP registry patients recruited in our region who underwent ^{18}F-DCFPyL PET in Hamilton, ON, under the predefined cohorts 1 and 2. Consecutive men fulfilling the following inclusion criteria were recruited between April 2019 and December 2021. Cohort 1 patients had either 1) persistent PSA post-RP or 2) pathologic lymph node (LN) involvement at time of RP; and cohort 2 had prior RP with rising serum PSA levels on at least two occasions measured at least one month apart and with the most recent PSA measurement >0.1 ng/mL.

Initially, all participants were required to have conventional imaging consisting of abdominopelvic CT and technetium 99m methylene-diphosphonate bone scintigraphy within three months of enrollment that was either negative, equivocal, or positive for oligometastatic disease, with four or fewer unequivocal lesions. The criteria were changed in September 2020 to require only conventional imaging for participants with a serum PSA value of ≥10.

Exclusion criteria included prostate cancer with substantial sarcomatoid, spindle cell, or neuroendocrine small cell components, extensive metastatic disease at conventional restaging (>4 sites), and prior PSMA-PET within six months of enrollment, or Eastern Cooperative Oncology Group (ECOG) performance status >1.

Retrospectively, two of the authors (SS and KaS) completed a chart review to verify the pathology details, including the biopsy ISUP grade group with the initial risk stratification group (low, intermediate, or high), serum PSA prior to time of biopsy, the date of the RP, and overall ISUP grade group, margin status, and pathologic tumor and node stage.

Study procedures

After participant registration, the demographic data, including age and serum PSA level at time of registration, were completed by the referring physician.

The integrated PET protocol included an unenhanced low-dose CT examination preceding PET acquisition, with coverage from the top of the skull to the upper thighs using standard local imaging protocol.[1]

All PSMA-PET scans were interpreted by a nuclear medicine physician according to previously described evaluation criteria.[8]

Descriptive statistics were used to summarize patient characteristics and outcomes. Statistical tests used were Wilcoxon rank sum tests (for continuous variables), Fisher's exact tests (for dichotomous variables), $\mathbf{X}^2$ tests (for categorical variables with >2 categories), and Cochran-Armitage test for trends (for ordinal variables). All tests were two-sided and a $p \leq 0.05$ was considered statistically significant. No adjustments were made for multiple testing and exact p-values are presented throughout.

RESULTS

Participant characteristics

In our region, 180 men were enrolled in the PREP met the above criteria. Eleven men were excluded because complete pathologic information was not available. Overall, 169 men were included in our analysis — 53 in cohort 1 and 116 in cohort 2 — with a median age of 68 years (interquartile range [IQR] 62–71) and a median serum PSA of 0.27 ng/mL (IQR 0.16–0.85) at registration (Table 1). The median time from RP to PSMA-PET was significantly longer for cohort 2 participants (Table 1).

Likelihood of positive PSMA-PET and site of recurrence by cohort

For this study, regional LN positivity is based on PSMA avid disease in the obturator, internal, external or common iliac, para-aortic, peri-rectal, or pre-sacral regions. Loco-regional recurrence is defined as prostate bed recurrence and/or regional LN involvement only with no distant disease detected on PSMA-PET. Oligometastatic disease is defined as four or fewer lesions, and distant metastatic disease is defined as at least one lesion detected on PSMA-PET outside the prostate bed or regional LNs. Cohort 1 patients had higher-risk disease, and accordingly there were higher overall detection rates (p=0.004) and regional lymphadenopathy (either recurrent disease or not detected prior to RP; p=0.001) compared to cohort 2. Prostate bed, oligometastatic, and distant metastatic disease detection rates were not statistically significantly different between the two groups (Table 2).

Patterns of disease recurrence at PSMA-PET

Overall, 100 of 169 men (59.2%) had disease recurrence detected with PSMA-PET; the distribution of positive findings at PSMA-PET is presented in Figure 1 and Table 2. Local recurrence in the prostate bed was identified on PSMA-PET in 31 of 169 men (18.3%) (Figure 1A). Any PSMA-PET recurrence detection in pelvic LNs is reported in Table 2 as regional LNs, which occurred in 71 men (42.0%); 74 men (43.8%) had loco-regional recurrence only.

There was a higher positivity rate of PSMA-PET in men with elevated serum PSA levels (p<0.001) (Table 3). Detection of prostate bed (p=0.031) and regional LNs (p<0.001) recurrence increased with increasing PSA, however, loco-regional-only recurrence (p=0.090) did not demonstrate this pattern (Figure 1A, Table 3).

Table 1. Participant characteristics

Variable	Cohort 1 data (n=53) n (%)	Cohort 2 data (n=116) n (%)	Overall data (N=169) n (%)	p (cohort 1 vs. 2)
Age (years)*	64 (59, 69)	69 (63, 72)	68 (62, 71)	<0.001
Serum PSA level at registration (ng/mL)*	1.20 (0.34, 2.44)	0.22 (0.14, 0.43)	0.27 (0.16, 0.85)	<0.001
Time from RP to PSMA-PET (months)	6.0 (3.0, 11.0)	43.5 (21.0, 81.0)	24.0 (9.0, 67.0)	<0.001
ISUP grade group				
1-2	19 (35.8)	70 (60.3)	89 (52.6)	0.007
3	22 (41.6)	34 (29.3)	56 (33.1)	
4-5	12 (22.6)	12 (10.3)	24 (14.2)	
Risk group				
Low or intermediate	7 (13.2)	58 (50.0)	65 (38.5)	<0.001
High	46 (86.8)	58 (50.0)	104 (61.5)	<0.001
Pathologic tumor stage				
pT2	10 (18.9)	65 (56.0)	75 (44.4)	<0.001
pT3a	12 (22.6)	37 (31.9)	49 (29.0)	
pT3b	31 (58.5)	14 (12.1)	45 (26.6)	
Margin status				
Positive	34 (64.2)	32 (27.6)	66 (39.1)	<0.001
Negative	19 (35.8)	84 (72.4)	103 (60.9)	
Pathologic nodal stage				
pN0	27 (50.9)	116 (100)	142 (84.0)	<0.001
pN1	26 (49.1)	0	27 (16.0)	

Note: Unless otherwise specified data are number of participants, with percentages in parentheses. *Data are medians with interquartile ranges in parentheses. ISUP: International Society of Urological Pathology; PSA: prostate-specific antigen; PSMA-PET: prostate-specific membrane antigen-positron emission tomography; RP: radical prostatectomy.

Table 2. PSMA-PET positivity and site of recurrence by cohort

Cohort	N	Overall positive findings n (%)	Prostate bed n (%)	Regional lymph nodes n (%)	Loco-regional recurrence n (%)	Oligo-metastatic disease n (%)	Distant metastases n (%)
1	53	40 (75.5)	8 (15.1)	32 (60.4)	29 (54.7)	7 (13.2)	11 (20.8)
2	116	60 (51.7)	23 (19.8)	39 (33.6)	45 (38.8)	11 (9.5)	15 (12.9)
All	169	100 (59.2)	31 (18.3)	71 (42.0)	74 (43.8)	18 (10.7)	26 (15.4)
p		0.004	0.53	0.001	0.066	0.59	0.25

Note: Data are number of participants, with percentages in parentheses. PSMA-PET: prostate-specific membrane antigen-positron emission tomography.

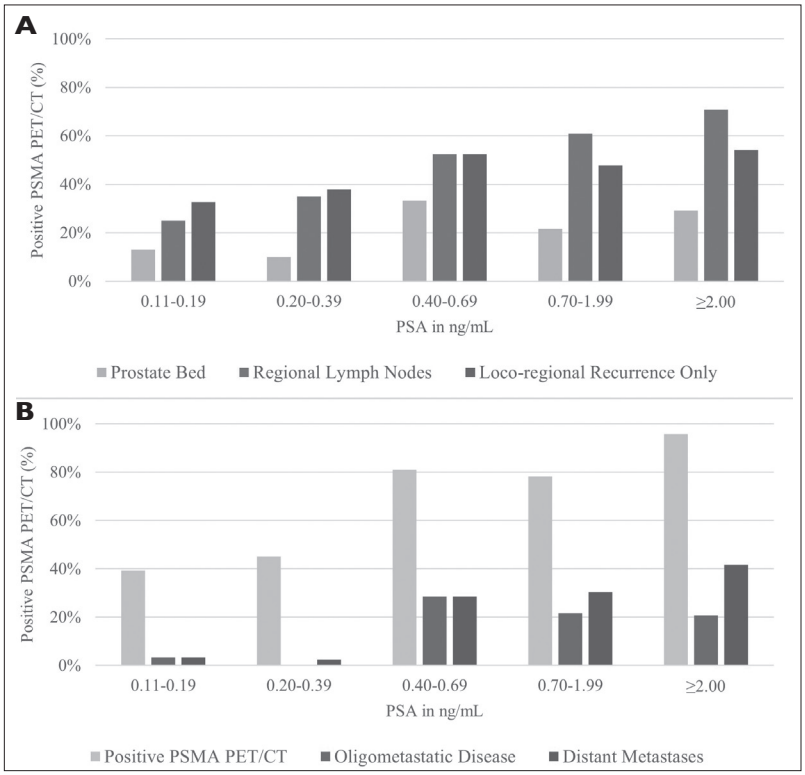

Figure 1. Sites of recurrence on prostate-specific membrane antigen-positron emission tomography (PSMA-PET) by prostate-specific antigen level at registration: (A) prostate bed, regional lymph nodes, and loco-regional recurrence only; and (B) likelihood of positive finding, oligometastatic disease, and distant metastases.

Incidence of oligometastatic and any distant metastatic disease demonstrated the largest increase at PSA levels of ≥0.40 ng/mL (Figure 1B, Table 3). There were three of 169 men (1.8%) with non-regional nodal metastases without skeletal or visceral metastases, and these were counted as metastatic disease not local-regional recurrence. Eighteen of the 26 men (69.2%) with metastatic disease, 10.7% of the entire cohort, had non-regional and/or oligometastatic disease recurrence that was potentially manageable with lesion-directed therapy (≤5 sites of non-regional recurrence or distant metastases).

Pathology features and PSMA-PET-detected recurrence

The distribution of positive findings at PSMA-PET by risk group classification and four pathologic features are presented in Table 4 and Supplementary Figure 1 (available at *cuaj.ca*). The positivity rate was not significantly different with increasing ISUP grade group (p=0.16) (Supplementary Figures 2, 3; available at *cuaj.ca*). The risk of distant metastases increased for the highest grade groups, as the rate of distant metastases is 17/145 men (11.7%) and 9/24 men (37.5%) for grade groups 1–3 and 4–5, respectively (p=0.003) (Supplementary Figure 3; available at *cuaj.ca*). The risk group was determined by the preoperative PSA (most up-to-date value prior to RP), overall ISUP grade group, and tumor stage. Only 5/169 men (3.0%) were classified as low risk. The rate of detecting prostate bed recurrence is similar for positive or negative surgical margin status (p=0.26).

There was a higher positivity rate of PSMA-PET in men with more advanced pathologic tumor (p<0.001) and nodal (p=0.004) stage (Supplementary Figure 1; available at *cuaj.ca*). The median PSA prior to PSMA-PET for earlier-stage disease was lower in both cases — pT1-3a 0.25 ng/mL (IQR 0.15–0.59) compared to 0.53 ng/mL (IQR 0.23–2.44) for pT3b disease — and for patients with pN0 disease, median PSA was 0.25 mg/mL (IQR 0.16–0.66) compared to 0.86 ng/mL (IQR 0.21–4.08) for pN1. Regional LN positivity rate on PSMA-PET appears to increase with higher risk group (p=0.010) and pathologic tumor (p<0.001), as well as nodal stage (p=0.010), but not with ISUP grade group (p=0.62) (Supplementary Figures 2, 4, 6, 10; available at *cuaj.ca*).

Frequency of lymph node recurrence by site

Seventy-one of 169 men (42.0%) had at least one site of regional LN recurrence. In total, there were 208 PSMA-PET-detected recurrent LNs in the pelvis. Figure 2 displays the frequency of at least one LN recurrence detected on PSMA-PET per region. In the entire cohort, 20.1% had ≥2 detected pelvic LN recurrences. The maximum number of LNs detected in a single participant was 34: 18 para-aortic, five pre-sacral, four common iliac, four internal iliac, and three external iliac LNs detected by PSMA-PET; this participant was in cohort 1. Seventeen of 71 men (23.9%) had LN involvement outside of NRG contouring atlas for pelvic radiotherapy fields for prostate cancer, and of those with loco-regional recurrence 7/74 men (9.5%) had disease outside the contouring atlas.[9]

DISCUSSION

The single imaging center results for this cohort included 169 patients who experienced biochemical failure after treatment with RP for localized prostate cancer. As expected and documented in the literature,[2] increasing PSA increased the detection rate of PSMA-avid disease (Figure 1). Our results are very similar to a much larger systematic review of 20 prospective studies that included 2110 men with BCR and found a PSMA-PET positivity rate of 63.2%, with the only factor consistently found to be associated with a positive result being PSA

Table 3. Number of positive findings at PSMA-PET and patterns of disease recurrence by PSA at registration

PSA (ng/mL)	N	Overall positive findings	Prostate bed	Regional lymph nodes	Loco-regional recurrence only	Oligometastatic disease	Distant metastases
0.11–0.19	61	24 (39.3)	8 (13.1)	15 (25.0)	22 (36.1)	2 (3.3)	2 (3.3)
0.20–0.39	40	18 (45.0)	4 (10.0)	14 (35.0)	17 (42.5)	0	1 (2.5)
0.40–0.69	21	17 (81.0)	7 (33.3)	11 (52.4)	11 (52.4)	6 (28.6)	6 (28.6)
0.70–1.99	23	18 (78.3)	5 (21.7)	14 (60.9)	11 (47.8)	5 (21.7)	7 (30.4)
≥2.00	24	23 (95.8)	7 (29.2)	17 (70.8)	13 (54.2)	5 (20.8)	10 (41.7)
p		<0.001	0.031	<0.001	0.090	<0.001	<0.001

Note: Data are number of participants, with percentages in parentheses. PSA: prostate-specific antigen; PSMA-PET: prostate-specific membrane antigen-positron emission tomography.

Table 4. Proportion of positive findings at PSMA-PET and patterns of disease recurrence by pathologic features

Pathologic variable	N	Overall positive findings	Prostate bed	Regional lymph nodes	Loco-regional recurrence only	Oligometastatic disease	Distant metastases
Overall ISUP grade group							
1–2	89	46 (51.7)	13 (14.6)	33 (37.1)	37 (41.6)	6 (6.7)	9 (10.1)
3	56	40 (71.4)	12 (21.4)	30 (53.6)	32 (57.1)	7 (12.5)	8 (14.3)
4–5	24	14 (58.3)	6 (25.0)	8 (33.3)	5 (20.8)	5 (20.8)	9 (37.5)
p		0.16	0.18	0.62	0.45	0.041	0.003
Tumor stage							
pT2	75	35 (46.7)	15 (20.0)	21 (28.0)	25 (33.3)	7 (9.3)	10 (13.3)
pT3a	49	30 (61.2)	11 (22.4)	19 (38.8)	25 (51.0)	4 (8.2)	5 (10.2)
pT3b	45	35 (77.8)	5 (11.1)	31 (68.9)	24 (53.3)	7 (15.6)	11 (24.4)
p		<0.001	0.28	<0.001	0.022	0.33	0.15
Nodal stage							
pN0	143	78 (54.5)	26 (18.2)	54 (37.8)	61 (42.7)	13 (9.1)	17 (11.9)
pN1	26	22 (84.6)	5 (19.2)	17 (65.4)	13 (50.0)	5 (19.2)	9 (34.6)
p		0.004	1.00	0.010	0.52	0.16	0.007
Margin status							
Negative	103	57 (55.3)	17 (16.5)	43 (41.7)	42 (40.8)	11 (10.7)	15 (14.6)
Positive	66	43 (65.2)	14 (21.2)	28 (42.4)	32 (48.5)	7 (10.6)	11 (16.7)
p		0.26	0.54	1.00	0.34	1.00	0.83
Risk group							
Low or intermediate	65	31 (47.7)	11 (16.9)	19 (29.2)	22 (33.9)	6 (9.2)	9 (13.9)
High	104	69 (66.3)	20 (19.2)	52 (50.0)	52 (50.0)	12 (11.5)	17 (16.3)
p		0.024	0.84	0.010	0.056	0.80	0.83

Note: Data are number of participants, with percentages in parentheses. ISUP: International Society of Urological Pathology; PSMA-PET: prostate-specific membrane antigen-positron emission tomography.

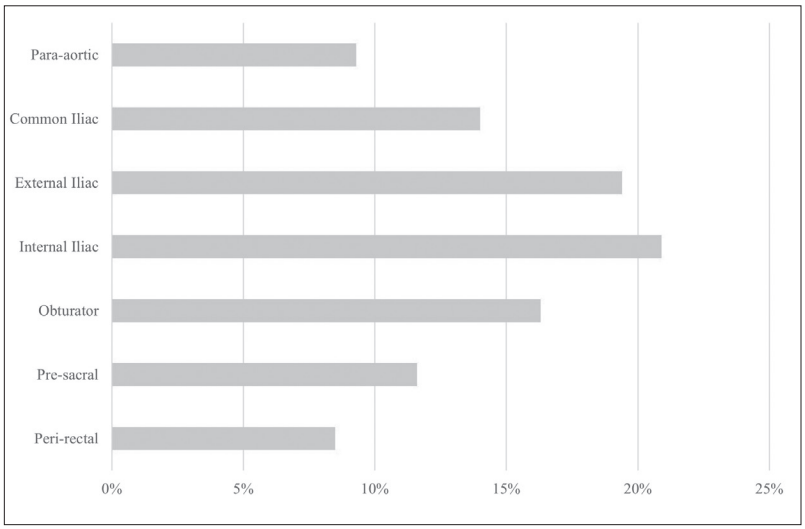

Figure 2. Frequency of pelvic lymph node recurrence by region.

level.[10] Interestingly, there is a stark contrast between likelihood of PSMA-PET-detected recurrence for men with PSA <0.4 ng/mL (41.6%) compared to ≥0.4 ng/mL (85.3%). This may be due to the small sample size (101 men with PSA <0.4 ng/mL compared to 68 with PSA ≥0.4 ng/mL).

Metser et al reported the overall multicenter results of the PREP registry analysis and the change in management intent after PSMA-PET, although they did not report on outcomes. Out of a total of 415 patients, which includes the 169 men reported in this study, only 5% switched from curative to palliative (systemic therapy only) intent, and 13% switched from palliative to curative intent.[1] This is demonstrated in our results, as 15.4% were found to have metastatic disease and 10.7% had oligometastatic disease and were treated with metastasis-directed therapy not labelled as palliative-intent therapy. The EMPIRE-1 trial, using fluciclovine PET, showed a statistically significant difference in three-year event-free survival (EFS) for patients randomized to RT volumes directed by a combination of PSMA-PET and conventional imaging compared to conventional imaging alone (75.5% vs. 63.0%, respectively).[11] There was similar toxicity between the two arms.[11]

In this study, 45 men (26.6%) had pT3b disease. In our cohort, pT3b disease is associated with a 77.8% likelihood of PSMA-PET-detected recurrence, largely due to the difference in detection of regional LN involvement. Seminal vesicle invasion is a known poor prognostic feature, with a rate of BCR found to be associated with increasing extent of seminal vesicle invasion.[12] In our series, this is similarly shown; however, strong conclusions are limited by our small sample size and the higher median PSA in patients with pT3b disease prior to PSMA-PET.

In our patient cohort, we demonstrate a significant increased likelihood of recurrence in the regional pelvic lymphatic chains for men with pT3b disease, although detection of distant metastatic disease was not significantly impacted by T stage (Table 4, Supplementary Figures 4 and 5; available at *cuaj.ca*). This is consistent with patterns seen in the literature. RADICALS-RT, RAVES, and GETUG-AFU 17 are phase 3 clinical trials that randomized patient's post-prostatectomy to adjuvant or salvage radiotherapy. RADICALS-RT and RAVES allowed men with pT3 disease or positive surgical margins,[13,14] and GETUG-AFU 17 included men with pT3-4a disease and positive surgical margins.[15] ARTISTIC is a meta-analysis of these three trials, and the subgroup analysis did not demonstrate a benefit of adjuvant radiotherapy to the prostate bed for men with seminal vesicle invasion or positive margins,[16] which is consistent with our results, thereby suggesting a lack of substantial difference in recurrence patterns for positive vs. negative margins (Table 4, Supplementary Figures 8, 9; available at *cuaj.ca*).

In the literature, the vesicourethral anastomosis is the most common site of recurrence post-RP, accounting for up to 62% of relapses.[17] In our sample, margin status is not significantly associated with increased risk of prostate bed recurrence, with 16.5% detected for negative margins and 21.2% for positive margin status (p=0.54) (Supplementary Figure 8; available at *cuaj.ca*); however, this may be due to the poor detection rate for local recurrence, with an average of 35% by PSMA-PET.[18] This may, in part, be due to the difficulty in differentiating uptake in recurrences vs. tracer excretion in the bladder. Our results are in keeping with this, as we observed an overall likelihood of prostate bed recurrence of 18.3%, thus our findings likely underestimate the actual prostate bed recurrence rate. One solution is combined imaging with PET and magnetic resolution imaging (MRI), which increases the detection rate of recurrent lesions, or using PSMA-targeting tracers with primarily GI excretion like PSMA 1007.[19]

High final Gleason score after RP is associated with worse survival rates.[20] Our data confirms these findings, as the rate of distant metastases was 37.5% for men with ISUP grade group 4–5 disease, while ISUP grade groups 1–2 and 3 had rates of distant metastases of 10.1% and 14.3%, respectively (p=0.003) (Supplementary Figure 3; available at *cuaj.ca*); however, we only have a small number of participants with ISUP grade group 4–5 disease (24 men, 14.2% of the sample).

Pathologic nodal disease upstages prostate cancer and is a risk factor for distant metastases. A retrospective study of 100 men with pN1 disease post-RP demonstrated a PSMA positivity rate of 68%.[21] The anatomical location was pelvic in 65%, while 40% had either distant-only or pelvic and distant sites of recurrence. Our cohort had similar increased risk of LN recurrence (p=0.010) and distant metastases (p=0.007) with pathologic nodal involvement, as the pN0 men had a rate of 37.8% and 11.9%, compared to the pN1 men with 65.4% and 34.6%, respectively (Supplementary Figures 6, 7; available at *cuaj.ca*); however, in our study all patients serum PSA was >0.1 with a median PSA of 0.86 ng/mL (IQR 0.21–4.08 ng/mL) for patients with pN1 disease.

The highest impact of PSMA-PET in the BCR post-RP setting is to avoid futile salvage therapy and to refine RT treatment volumes.[22] For men with a PSA <1.0 ng/mL, Calais et al found 19% of patients had at least one PSMA-avid lesion outside consensus RT volumes.[23] In this setting, our findings demonstrate the possible futility of prostate bed-only salvage RT due to the high likelihood of regional LN involvement, as even in the group with PSA <0.20 ng/mL the rate of regional LV recurrence was 25.0% (Table 3). Tailoring therapies to target nodal recurrences could potentially avoid long-term androgen deprivation therapy use.[22] The majority of regional recurrences were within accepted salvage RT volumes, since the most common sites were the internal iliac, external iliac, obturator, common iliac, and pre-sacral chains (Figure 2). Future work will involve reviewing the regional LV recurrences and assessing areas in the pelvis that had a recurrence and are not within the NRG Oncology International Consensus contouring atlas.[9]

Strengths and limitations

A strength of our study is minimal bias due to missing data, since complete pathologic information and PSMA-PET results were available for all participants, and 11 men at the outset were excluded from this analysis due to missing data.

The limitations of our work include biases inherent to prospective cohort methodologies. Confounders were not adjusted for, for example, the possibility that higher PSA at registration could be associated with pathologic node positive disease. Caution in applying our findings to all men with BCR post-RP is warranted due to the small sample size and even smaller numbers within the PSA and pathologic subclassifications. Additionally, selection bias is a possibility, since these men were willing to enroll on a registry and take part in a research study, although the impact this has on our results is lessened by the prospective nature of our study.

> “ There is significant risk of regional LN positivity on PSMA-PET, emphasizing the importance of including the pelvis within salvage radiation volumes. ”

CONCLUSIONS

Our prospective study elucidates patterns of failure for prostate cancer patients with either pathologic stage N1 disease or BCR after RP and could impact management at diagnosis and postoperatively. There is a significant risk of regional LN positivity on PSMA-PET, as 43.8% of this cohort had loco-regional recurrence only, and in 42.0% of men, there was regional LN positivity. This emphasizes the importance of including the pelvis within salvage radiation volumes. Unfortunately, 15.4% were found to have distant metastases, although the majority — 69.2% of the metastatic disease identified and 10.7% of the entire sample — had oligometastatic disease and could be considered for metastasis-directed therapy.

COMPETING INTERESTS. The authors do not report any competing personal or financial interests related to this work.

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This paper has been peer reviewed.

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