Salvage lymph node dissection at radiotracer-avid sites in recurrent prostate cancer: An early assessment of efficacy in a hormone naïve population

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BACKGROUND

- Prostate-specific radiotracers have enabled PET studies to accurately identify lymph nodes harboring metastasis [1].
- Standard treatment algorithms generally suggest systemic therapy in the context of nodal metastasis [2].
- Several reports have been made concerning the outcome of PET-directed pelvic lymph node dissections with feasibility and overall procedure safety deemed to be excellent [3]. However, overall benefit in mitigating disease progression has remained in question.
- We sought to add our PET-directed, salvage lymph node dissection outcomes to the small body of existing evidence.
- Additionally, our goal was to increase post-dissection PSA trend resolution in order to assess how PSA trends in hormone naïve lymph node dissection patients compare to patients receiving systemic therapy.

ABSTRACT

INTRODUCTION & OBJECTIVE: Prostate-specific radiotracers have enabled PET studies to accurately identify lymph nodes (LN) harboring metastasis. We seek to provide early assessment regarding the efficacy of targeted LN dissections in recurrence. Our objective was to quantify PSA response and characterize the durability of initial trends.
METHODS: A population of 230 receiving a PET/CT was queried for post-scan targeted LN dissections. Cases with false positive scans by histology or where PSA trend-confounding hormonal therapy was applied were excluded. 21 patient courses were identified where targeted LN dissection was performed, prostatic adenocarcinoma was confirmed by histology, and sufficient follow up data was present. PSA trends were characterized and durability assessed by three primary metrics: initial change as a percent of pre-dissection PSA, time to recurrence of 100% pre-dissection PSA, 12-month PSA recurrent rates with recurrence defined as > 0.2 ng / mL.
RESULTS: 17/21 achieved immediate down-trending PSA values confirmed by two results. 4/21 demonstrated a continued up-trend. 6/21 achieved immediately undetectable PSA (< 0.04 ng / mL) confirmed by two results. For the 17 with a down-trend, the average reduction, as a percent of pre-dissection PSA, was 89% with a range of 61 – 100%. In 16 patients with a minimum 12 month follow up, 8/16 patients remained below their PSA value at dissection. 4/16 remained below 0.2 ng/mL at 12 months. 3/16 remained below 0.2 ng/mL at 18 months with 2 remaining below 0.2 ng/mL at 32 and 45 months. Univariable and multivariable linear regression were used to assess for correlations in outcomes: PSA % change, months to 0.2 ng/mL, and months to >= 100% dissection PSA, and PSA response (<0.2 ng / mL). These outcomes were considered against independent variables PSA at dissection, number of avid nodes on PET, unilateral vs bilateral node dissection, and initial Gleason grade. No significant correlations were demonstrated. It is suspected that this is due to heterogeneity of the dissection population, limited follow up data, small population size, and non-uniform methods implemented in dissection procedures.
CONCLUSION: Targeted LN dissection offers some potential for durable, recurrence-free survival. However, >=100% pre-dissection PSA recurrence is common. Achieving and maintaining a stable PSA long term is possible but unlikely.

METHODS

- 230 PET scans were completed in the setting of biochemical recurrence after primary therapy. 21 patients with PET scans demonstrating disease isolated to lymph nodes and a strong preference to avoid hormonal therapy underwent robot assisted lymph node dissections.
- All 21 dissection cases retrieved malignancy positive nodes confirmed by histology.
- PSA at the time of robot assisted lymph node dissection and type of dissection performed were recorded for each patient.
- Post-dissection PSA trends were followed along with any surgical complications.
- STATA15 was used for regression calculations and the generation of survival curves.

METHODS

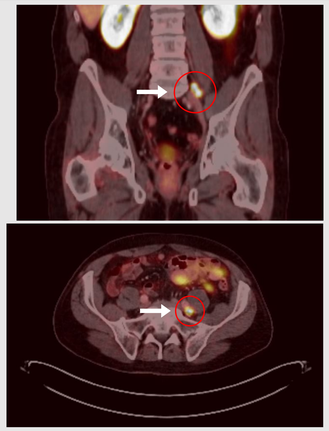

Figure 1
Coronal and axial Ga PSMA PET/CT demonstrating two avid nodes near the bifurcation of the left common iliac. The nodes were resected with a robot-assisted unilateral extended template dissection. Post dissection PSA trend correlates with **patient number 19** in the results section below.

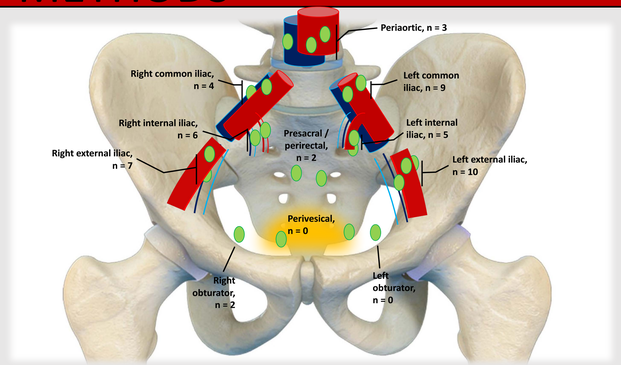

Figure 2
Schematic representation of where all 48 radiotracer avid lymph nodes were identified in our 21 patient cohort.

RESULTS

Patient #	Time since primary therapy (yrs)	Age	PSA at dissection (ng/mL)	% PSA change	Downtrend	Pre DT (Months)	Post DT (Months)
21	1.07	67	0.41	100%	YES	6.4	PSA undetectable
20	2.33	65	3.17	94%	YES	10.1	11.1
19	3.85	63	0.72	100%	YES	6	PSA undetectable
18	3.10	64	14	100%	YES	9.8	4
17	1.40	58	2.97	98%	YES	22	5.1
16	0.32	60	0.24	100%	YES	4	PSA undetectable
15	5.57	77	2.7	86%	YES	20.2	2.7
14	10.38	78	1.2	83%	YES	5	3.3
13	8.87	63	0.67	91%	YES	1.8	2.7
12	8.14	61	0.37	100%	YES	18.6	1 detectable value
11	2.32	67	5.6	61%	YES	4.1	1.5
10	7.73	70	0.26	100%	YES	6.7	PSA undetectable
9	7.49	59	0.82	90%	YES	2.2	9.8
8	0.31	67	19.5	99%	YES	3.9	9.6
7	2.55	66	2.4	80%	YES	1.3	1.3
6	1.68	66	6.8	69%	YES	2.3	3.4
5	1.24	67	0.37	68%	YES	9.3	3.6
4	0.31	57	7.51	0%	NO	2.6	Hormone therapy
3	5.65	61	22.12	0%	NO	4.3	6.6
2	6.27	63	2.05	0%	NO	3.6	1.2
1	8.33	76	0.63	0%	NO	3.3	1.6
MEAN	4.23	65.48	4.50	72.3%	17 / 21		
MEDIAN	3.10	65	2.05	90.0%	downtrend		

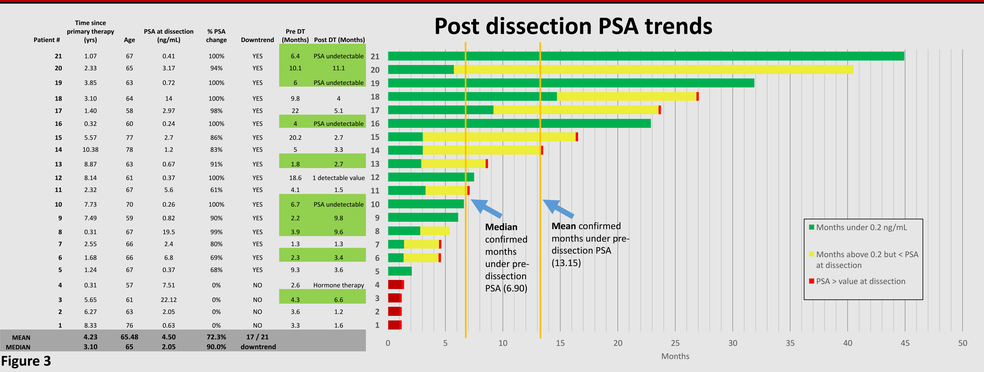

Figure 3

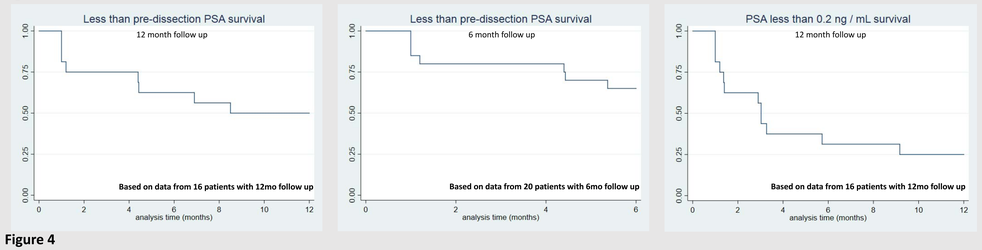

Figure 4

REFERENCES

1. Jaden D. Evans, MD, Krishan R. Jethway, MD, Brian J. Davis, MD, PhD, et al: Prostate cancer-specific PET radiotracers: A review on the clinical utility in recurrent disease. Practical Radiation Oncology 2017 Jul; 28 – 29.

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3. Amila Siriwardana, James Thompson, Pim J. Van Leeuwen, et al: Initial multicenter experience of 68gallium-PSMA PET/CT guided robot assisted salvage lymphadenectomy: Acceptable safety profile but oncological benefit appears limited. BJU Int 2017; 120: 673 – 681.

LIMITATIONS

- Some patients underwent targeted robot-assisted dissections within the year, thus 12 month follow up data is not available.
- Small cohort size limits generalizability of outcome data.
- Surgeon preference dictated type of lymph node dissection (unilateral, bilateral, extended).

CONCLUSIONS

- When targeted salvage lymph node dissection is applied in the context of biochemical relapse, durable stability of PSA is possible without adjuvant hormone therapy.
- A significant downtrend in PSA is likely following lymph node dissection with moderate potential for sustained decrease relative to pre-dissection levels, but the long term oncologic significance of this response remains difficult to determine.
- Careful selection of patients with early recurrence or a single lesion by PET is recommended. Additionally, some consideration for patient preference to avoid systemic therapy may be considered.
- Further study with increased cohort size, uniform follow up, and a randomized control group is necessary to define oncologic benefit and appropriate population.