Patient reported outcomes among treatment modalities for prostate cancer

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Introduction: *To characterize patient reported outcomes for urinary and sexual function using International Prostate Symptom Score (IPSS) and Sexual Health Inventory for Men (SHIM) comparing intensity modulated radiation therapy (IMRT), low dose rate brachytherapy (LDR), post-prostatectomy IMRT (PPRT), and radical prostatectomy (RP).*

Materials and methods: *Patients treated for prostate cancer from 2001-2012 completed self-reported SHIM and IPSS surveys. Subgroups were created by baseline score. Mean change from baseline was determined at each time point for the cohort and subgroups. Statistical analysis was performed with generalized estimating equation method. Incontinence was not captured in the questionnaires.*

Results: *A total of 14,523 IPSS surveys from 3,515 men were evaluated. Patients treated with IMRT experienced a minimal decrease in IPSS score from baseline. PPRT scores did not differ from IMRT at any time point (range: +/- 3 points from baseline in IPSS score over 50 months). LDR had an initial IPSS rise (between 5-10 points on the IPSS over 1-9 months) versus IMRT but returned to comparable levels at 34 months. RP was associated with a lower IPSS versus IMRT. LDR had the largest rise from baseline, with return toward baseline. A total of 2,624 SHIM surveys from 857 men were evaluated. LDR and PPRT did not differ from IMRT at any time point (range: +/- 5 points from baseline in SHIM score for 36 months). RP experienced the largest decline from baseline (up to -7 points on SHIM score), at 3 to 7 months; RP had a larger early decrease in SHIM score versus IMRT between 3 and 22 months, after which there was no difference.*

Conclusions: *IPSS and SHIM score patterns differed among treatment modalities. These data can be used to predict changes in urinary and sexual function over time based on modality and baseline score.*

Key Words: sexual function, brachytherapy, prostate cancer, prostatectomy, radiation therapy, quality of life, comparative effectiveness research, personalized medicine, treatment selection, brachytherapy, toxicity, genitourinary, gastrointestinal, prostatectomy

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Introduction

Prostate cancer is the most common cancer to affect men in the United States, with an estimated 220,800 cases that will be diagnosed in 2016.[1] Treatment options for localized disease include intensity-modulated radiation therapy to the intact prostate (IMRT), low dose rate brachytherapy (LDR), radical prostatectomy (RP), post-prostatectomy IMRT (PPRT).[2] Each of the treatment modalities used to treat localized prostate cancer are associated with their own set of adverse effects and have varying degrees of impact on a patient's quality of life.[3-5] For many men with prostate cancer, the treatment decision is based on the

potential toxicity and anticipated impact on quality of life, as prostate cancer cure rates are roughly equivalent across modalities stage for stage.[6,7]

Despite increasing awareness of the importance of monitoring patient-reported outcomes following treatment for prostate cancer, the ability to select the optimal treatment modality based on the expected impact on urinary and sexual function remains poorly defined.[4,8,9] Results from the CaPSURE database[10] and Massachusetts General Hospital[11] have helped to characterize patient-reported outcomes and quality of life. These studies allow clinicians to stratify treatment-related outcomes by pretreatment functional status and to display the proportions of patients with improved, stable, or worsened function after treatment; the results provide expected impact of treatment to patients choosing among localized prostate cancer treatments.[11]

We sought to expand on these findings by investigating the impact of different prostate cancer treatment modalities on patient-reported urinary and sexual outcomes in a contemporary patient population at a National Cancer Institute (NCI)-designated comprehensive cancer center. Specifically, our aim was to compare patient reported outcomes after IMRT, LDR brachytherapy, RP, and PPRT.

Materials and methods

Treatment

We queried our prospectively-collected institutional prostate cancer database for men with prostate cancer treated from 2001 to 2012 at an NCI-designated comprehensive cancer center. Patients were included if they had undergone treatment with IMRT, LDR brachytherapy, RP, or PPRT. Patients were not allowed to receive more than one treatment (with the exception of PPRT, which includes RP and IMRT).

Prostate cancer risk groups are defined by National Comprehensive Cancer Network (NCCN) classification, the preferred prognostication system.[12] For NCCN low-risk patients treated with IMRT, the clinical target volume 1 (CTV1) includes the prostate and proximal third of the seminal vesicles (SVs); the volume is expanded 5 mm posteriorly and 8 mm elsewhere to make the planning target volume (PTV). The dose is prescribed so that 78 Gy (in 39 fraction) is delivered to >95% of the PTV. For intermediate risk patients, the distal SVs are contoured as CTV2. The prescription is 80 Gy to the CTV1 and 56 Gy to CTV2 (both in 40 fractions). The treatment of high-risk patients is per Radiation Therapy Oncology Group (RTOG) guidelines.[13] CTV2 may include some pelvic lymph nodes (e.g. distal common iliac, presacral, external iliac, internal iliac, and obturator), depending on anticipated risk of involvement.[14] Per the RTOG guidelines, the pelvic LN CTV may begin superiorly at the L5-S1 interspace and end inferiorly at the superior border of the pubic bone.[13]

For PPRT, we do not restrict the interval between surgery and IMRT. For the 414 PPRT patients, the median interval was 18.5 months, the mean was 28 months (min, 2 months; max, 131 months). One of the goals is to wait for urinary function to stabilize before delivering treatment, which typically takes 3-6 months.

Several sets of consensus guidelines have been developed to guide prostate bed target volume delineation for PPRT,[15-18] which rely on locations of clinical and radiographic sites of recurrence,[19,20] anatomy, and expert opinion. The vesicourethral anastomosis (VUA), bladder neck, retrovesical region, and SV stumps are at highest risk of clinical recurrence following prostatectomy,[18,21] and the consensus volumes encompass these regions. The RTOG-recommended prostate fossa CTV (PF-CTV) includes the caudal vas deferens remnant cranially down to a caudal border that is 8 mm-12 mm inferior to the VUA. The PF-CTV extends anteriorly to the posterior aspect of the pubis below the cranial border of the pubic symphysis and encompasses the posterior 1 cm-2 cm of the bladder wall above the pubic symphysis. The posterior border of the PF-CTV extends to the mesorectal fascia superiorly and the rectum inferiorly. The lateral border of the PF-CTV is at the sacrorectogenitopubic fascia superiorly and the levator ani muscles inferiorly.[18] The inclusion of pelvic LNs depends on the patient and treating physician; notably, this is an unresolved question and is currently being evaluated by RTOG 0534.[22] The dose is 68 Gy prescribed to 95% of the PTV. For LDR-brachytherapy, the planning and procedure technique have been previously described.[23] Briefly, the number and activity of I-125 seeds for each patient is calculated using an MRI-generated, physician-contoured volume with experience (i.e. > 50 cases performed) and reviewed with at least one other experienced attending physician. During the procedure, the patient is placed under general anesthesia in extended dorsal lithotomy position. Intraoperative planning and seed placement is performed under real-time ultrasound guidance using physician-generated contours of the prostate. A 3 mm-5 mm anterior and lateral expansion is applied to the prostate volume to create the treatment volume. A total of 145 Gy is prescribed to cover 100% of the prostate volume. Per American Brachytherapy Society guidelines,[24] an acceptable plan must achieve a D90 > 90%, V100 > 90%, urethral maximum dose < 150%, and V100 of the rectum to be less than 1 cm^3.

Midway through treatment and at the end of treatment, patients undergo fluoroscopic examination to document proper seed placement. Rigid cystoscopy by the urologic oncologist is performed to ensure the absence of seeds in the urethra or bladder at the end of the procedure. Approximately 4 hours after the implant, the Foley catheter is removed and patients undergo post-implant CT and MRI to establish baseline dosimetry. Patients return in approximately 3-4 weeks after implant to repeat the CT and MRI and generate the 3 week post-implant dosimetry for confirmation of dosimetric quality.[25]

Although different fractionation techniques (e.g. hypofractionated RT[26] and stereotactic body RT[27]) are emerging treatment options for prostate cancer, these were not evaluated in this study, as they were experimental during the 2000s. Additionally, high dose rate (HDR) brachytherapy (monotherapy[28] or boost[29,30]) is an acceptable treatment option for many patients; this had been available to certain patients at our institution, but there were not enough patients for statistical analysis. These patients had a baseline score and at least 1 post-treatment score. The baseline score was defined as a score < 6 months prior to the date of RP or LDR, or start date of IMRT of PPRT.

Quality of life reporting

The International Prostate Symptom Score (IPSS)[31] is an 8 question instrument to assess urinary symptoms, except incontinence. The IPSS is an instrument derived from the American Urologic Association Symptom Index (AUASI) intended to evaluate men with benign prostatic hyperplasia. A score of 0-7 indicates "mildly symptomatic," a score of 8-19 indicates "moderately symptomatic," and a score of 20-35 indicates "severely symptomatic." The 8th question, added later and distinguishing the IPSS from the original American Urological Association (AUA) tool, is an overall urinary quality of life (QOL) rating. Urinary QOL was analyzed as a separate outcome.

The Sexual Health Inventory for Men (SHIM) score is an assessment tool for the screening and diagnosis of erectile dysfunction (ED). This tool was designed as an abridged, easy to administer version of the International Index of Erectile Function (IIEF).[32,33] The total score is classified as: 0-7 "severe ED," 8-11 "moderate ED," 12-16 mild-to-moderate ED," 17-21 mild ED," and 22-25 "no ED."

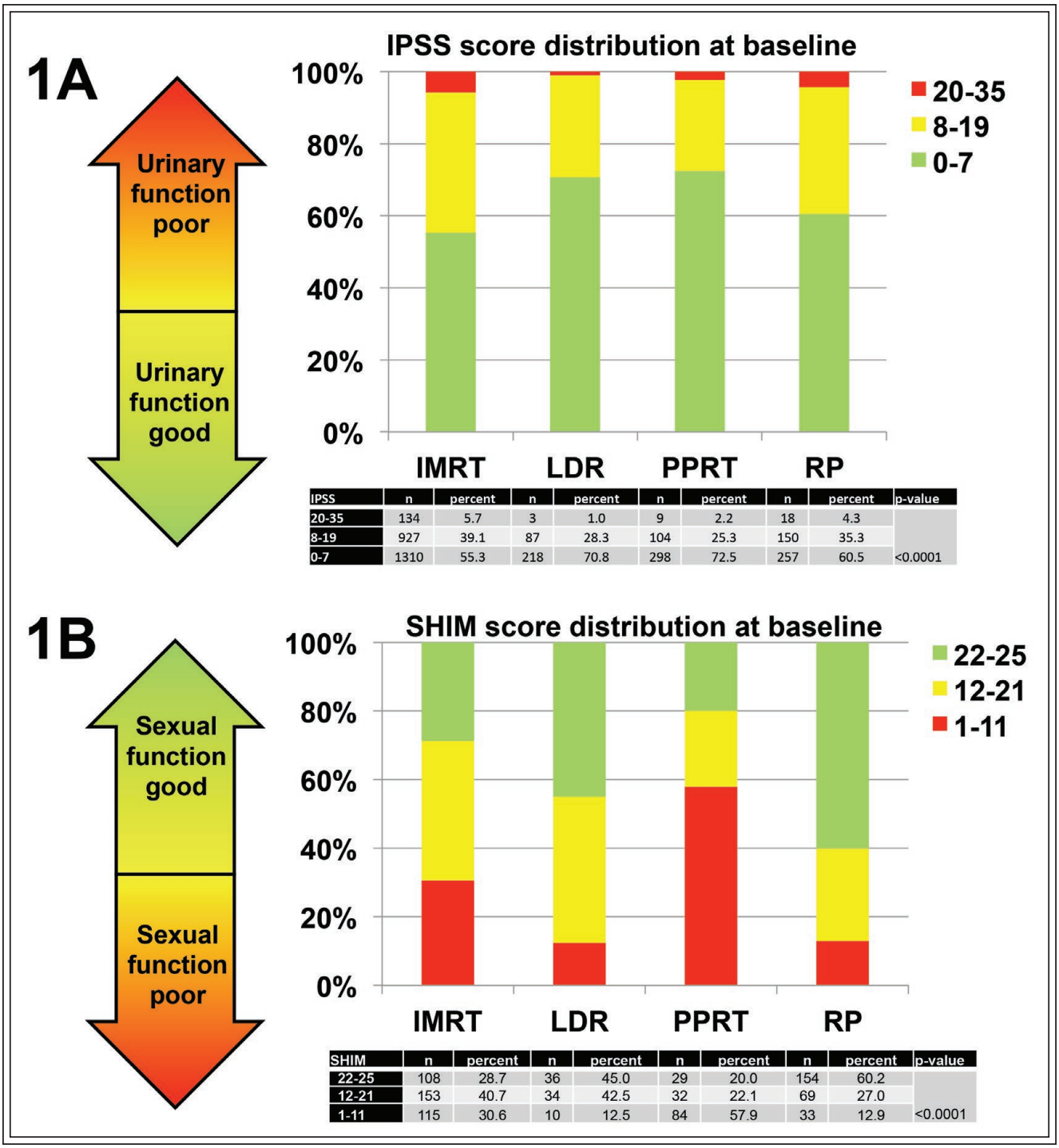
The baseline score was defined as the most recent response < 6 months prior to the date of RP or LDR, or IMRT start date. Patients usually completed this at the initial consult visit. If there were multiple scores within the 6 month window, the most recent score prior to initial androgen deprivation therapy (ADT) was used. At baseline, there were differences in AUA and SHIM scores by treatment, shown in Figure 1. Differences in the categories of IPSS at baseline by treatment were statistically significant, chi-square test p value < 0.0001. Similarly, SHIM scores at baseline differed significantly, p value < 0.0001.

We do not include the PSA responses for several reasons. First, the treatment for each individual patient was tailored for his disease. For example, a patient with obstructive symptoms (e.g. secondary to BPH or a T3 tumor) may have preferentially received RP; with T3 disease, he would be at higher risk to have a positive surgical margin, extracapsular spread, or seminal vesicle involvement, and would be recommended to receive PPRT. Patients like this would have worse biochemical failure rates than patients who were treated with a single modality (e.g. a man with a Gleason 6, cT1c cancer and no other genitourinary symptoms), and this difference in biochemical failure rates would not necessarily be due to treatment. Second, to compare patient outcomes fairly, propensity score matching would need to be performed to include many other factors (e.g. race, physical comorbidities, psychiatric comorbidities, medications, age, education status, BMI, marriage status, insurance status), which have all been shown to affect outcomes.[34] The current dataset does not include sufficient information for this type of analysis.

Statistical analysis

Follow up visit patterns were plotted in order to create time intervals that correlated to the most common follow-up schedule. Scores for each patient were then binned into these intervals. In the event that a patient had more than one score within an interval, those scores were averaged. The time intervals were defined as the following months: 1.5, 5, 10, 16, 22, 28, 34, 43, 55.

We examined patterns up to 60 months follow up for AUA and quality of life score, and up to 36 months of follow up for SHIM scores, as data collection started later for this questionnaire. We included patients immediately after treatment, certain treatments (e.g. LDR) may impact quality of life immediately after the procedure. The baseline characteristics of the treatment groups were compared, including age at the completion of treatment, race, Gleason score (Gleason score is from biopsy data for IMRT and LDR, and from pathology data for PPRT and RP), pre-treatment PSA, and stage (T stage is clinical for IMRT and LDR, and pathologic for PPRT and RP). Baseline differences between the groups were compared using Chi-square tests for categorical variables and Wilcoxon rank-sum test for age distribution. ADT is an important part of multimodal



IPSS	n	percent	n	percent	n	percent	n	percent	p-value
20-35	134	5.7	3	1.0	9	2.2	18	4.3	
8-19	927	39.1	87	28.3	104	25.3	150	35.3	
0-7	1310	55.3	218	70.8	298	72.5	257	60.5	<0.0001

SHIM	n	percent	n	percent	n	percent	n	percent	p-value
22-25	108	28.7	36	45.0	29	20.0	154	60.2	
12-21	153	40.7	34	42.5	32	22.1	69	27.0	
1-11	115	30.6	10	12.5	84	57.9	33	12.9	<0.0001

Figure 1. A) distribution of baseline IPSS score subgroups by treatment modality. **B)** distribution of baseline SHIM score subgroups by treatment modality.

therapy for high-risk prostate cancer patients and has been shown to negatively impact quality of life.[35] ADT use was disproportionately used among these patients. The initial ADT use was as follows: 28.5% (675/2372) for IMRT patients; 1.6% (5/308) for LDR patients; 11.6% (48/414) for PPRT patients, prior to RT; and 1.6% (7/435) for RP patients. ADT was not included in the models for the following reasons: (1) there was an imbalance in ADT use among the treatments (highest in IMRT); (2) there was physician bias in prescribing ADT to different

patients, which was in part based on initial urinary quality of life; (3) duration of ADT among high-risk patients varied.

The mean score change from baseline was determined at each time point for the IPSS, quality of life, and SHIM cohorts for each treatment modality. IPSS subgroups were defined as: "mild," "moderate," and "severe." SHIM subgroups were defined as "severe," "moderate," "mild to moderate," "no ED." Three subgroups were created for the IPSS urinary quality of life, with "mixed" being the middle group.

To visually evaluate trends of AUA, quality of life, and SHIM scores, we plotted the unadjusted differences from baseline at each time point by treatment modality both for the analysis cohort and stratified by baseline subgroup. We compared treatments by fitting a separate multiple linear regression model using generalized estimating equation (GEE) for each outcome. The GEE method adjusts for within-patient correlation in responses. The dependent variable was the AUA, quality of life, or SHIM score at each follow up time point. We included treatment modality, time point and their interaction as categorical variables. We ran two versions of each model, one with the full cohort and an additional variable to adjust for baseline subgroup, and a second version that stratified by baseline subgroup. IMRT was selected as the reference treatment group, as this was the largest subset of patients. At each time point, we estimated the difference in the patient reported outcome score relative to the IMRT group based on the treatment and interaction terms. Significance was assessed with Wald chi-square tests. A total of twelve separate GEE models were created: one for the entire IPSS cohort, three for the IPSS subgroups, one for the entire quality of life cohort, three for the quality of life subgroups, one for the entire SHIM cohort, and three for the SHIM subgroups.

This work was performed in accordance with approval from our institutional review board. All statistical analysis was performed using SAS version 9.3 (Cary, NC, USA).

Results

In the IPSS cohort, 14,523 surveys from 3,515 men were analyzed. Median follow up was 28 months (range 0.2-60). The treatment modality was IMRT in 2,371 patients, LDR in 308, PPRT in 411, and RP in 425. Notably, these four groups of patients, Table 1, are mutually exclusive. There were 435 patients who underwent radical prostatectomy without IMRT; of these, 425 had AUA scores and included in the IPSS cohort. Similarly, there were 414 patients who had radical prostatectomy followed later by RT (PPRT); of these, 411 had AUA scores.

In the SHIM cohort, 2,624 surveys from 857 men were analyzed. Median follow up was 18 months (range 0.2-36). The treatment modality was IMRT in 376 patients, LDR in 80, PPRT in 145, and RP in 256. Patient descriptives are detailed in Table 1. In general, IMRT patients were older than LDR, PPRT, and RP patients ($p < 0.01$). LDR patients had a lower Gleason score than the other groups ($p < 0.01$). Groups did not differ by race. The IMRT group contained more patients with PSA values of 10 ng/mL or higher than the RP group ($p < 0.01$).

The mean (standard deviation) baseline IPSS score for IMRT was 8.0 (6.2), for LDR was 5.8 (4.7), for PPRT was 5.8 (4.7), and RP was 7.3 (5.9). The distribution of patients into baseline IPSS subgroups is shown in Figure 1a. The median (standard deviation) baseline SHIM score for IMRT was 16.1 (6.9), for LDR was 19.1 (6.0), for PPRT was 12.1 (7.6), and for RP was 20.2 (5.7). The distribution of patients into SHIM subgroups is shown in Figure 1b.

IPSS score change from baseline over time for the entire cohort is shown in Figure 2a. IPSS score change from baseline for the subgroups 0-7 "mild", 8-19 "moderate", and 20-35 "severe" are shown in Figure 2b, Figure 2c, and Figure 2d, respectively.

GEE models demonstrate a significant difference in IPSS score between RP and IMRT at nearly all time points. RP patients reported an improvement in their obstructive urinary symptoms following prostatectomy, while patients treated with IMRT had stable scores over time. This trend was true for the entire cohort and for those patients with baseline scores 0-7 and 8-19. Patients with baseline IPSS scores of 20-35 reported improved obstructive urinary symptoms following IMRT as well as RP, with patients undergoing RP noting a more dramatic improvement in their score. LDR was associated with an initial large increase in IPSS score, followed by normalization towards baseline. LDR scores were significantly higher than IMRT until 34 months, after which this difference was no longer significant. The PPRT group showed no significant overall difference in symptom scores compared to the IMRT group.

For urinary quality of life score, the majority of patients treated had a baseline score of 0-2 ("delighted," "pleased," or "satisfied," respectively) for all treatment modalities (71% of IMRT patients, 83% of LDR patients, 72% of PPRT patients, and 70% of RP patients). Within this favorable baseline quality of life group, there were no significant differences by treatment modality in average QOL scores at and beyond 28 months by treatment. For

TABLE 1. **Patient characteristics**

	IMRT		LDR		PPRT		RP only	
Total N	**n = 2372**	**%**	**n = 308**	**%**	**n = 414**	**%**	**n = 435**	**%**
Analytic cohort								
AUA	2371		308		411		425	
QOL	2261		295		395		334	
SHIM	376		80		145		256	
Age at end of treatment								
Median (range)	69 (36-91)		63.5 (41-83)		62 (42-76)		59 (38-80)	
Mean (std dev)	68.3 (7.9)		63.2 (7.3)		61.7 (6.7)		59 (6.9)	
Race								
White	1944	82.0	260	84.4	345	83.3	375	86.2
Black	326	13.7	39	12.7	57	13.8	41	9.4
Other/unknown	102	4.3	9	2.9	12	2.9	19	4.4
Gleason score								
4-6	1131	47.7	296	96.1	74	17.9	201	46.2
7	829	35.0	5	1.6	242	58.5	207	47.6
8-10	390	16.4	0	0.0	96	23.2	25	5.8
Missing	22	0.9	7	2.3	2	0.5	2	0.5
T stage								
T1	1515	63.9	264	85.7	0	0.0	0	0.0
T2	638	26.9	35	11.4	189	45.7	388	89.2
T3	112	4.7	0	0.0	212	51.2	45	10.3
T4	6	0.3	0	0.0	7	1.7	0	0.0
Missing	101	4.3	9	2.9	6	1.4	2	0.5
N stage								
N0	2161	91.1	282	91.5	319	77.1	346	79.5
N1	33	1.4	0	0.0	16	3.9	3	0.7
Missing	178	7.5	26	8.4	79	19.0	86	19.8
Pre-treatment PSA								
< 10 ng/mL	1869	78.8	300	97.4	303	73.2	387	89.0
>= 10-< 20 ng/mL	336	14.2	7	2.3	47	11.4	23	5.3
>= 20 ng/mL	155	6.5	1	0.3	20	4.8	3	0.7
Missing	12	0.5	0	0.0	44	10.6	22	5.1

IMRT = intensity modulated radiation therapy; LDR = low dose rate brachytherapy; PPRT = post-prostatectomy IMRT; RP = radical prostatectomy. Note, nearly all characteristics differ significantly by treatment.
Note: All distributions differ by treatment, $p < 0.0001$, except for race, where Chi-squared p value = 0.17

patients with > 28 months of follow up, 91% achieved a post treatment quality of life score of satisfied or better, 0-2 (by treatment: 92% IMRT, 87% LDR, 88% PPRT-IMRT, and 88% RP patients, respectively, $p = 0.055$). A chart of urinary QOL scores over time for this group of patients with a baseline score of 0-2 is shown in Figure 3.

The GEE model assessing differences in QOL scores between treatment groups demonstrates a significant initial worsening in urinary QOL at 1.5 and 5 month follow up for both RP and LDR when compared to IMRT. At the 1.5 month follow up time point, RP mean quality of life score increased by 1.9 points, and LDR mean quality of life score increased by 1.6 points, while IMRT mean score increased 0.3 points, and PPRT mean score increased 0.4 points. Patients undergoing RP then had a return towards baseline, with quality of life score no different than IMRT by 10 months. LDR patients had a slower return to baseline, but again had scores no different than IMRT from 34 months of follow up onward. The trends in urinary quality of life for the largest subgroup of patients, those with baseline score 0-2, are depicted in Figure 3.

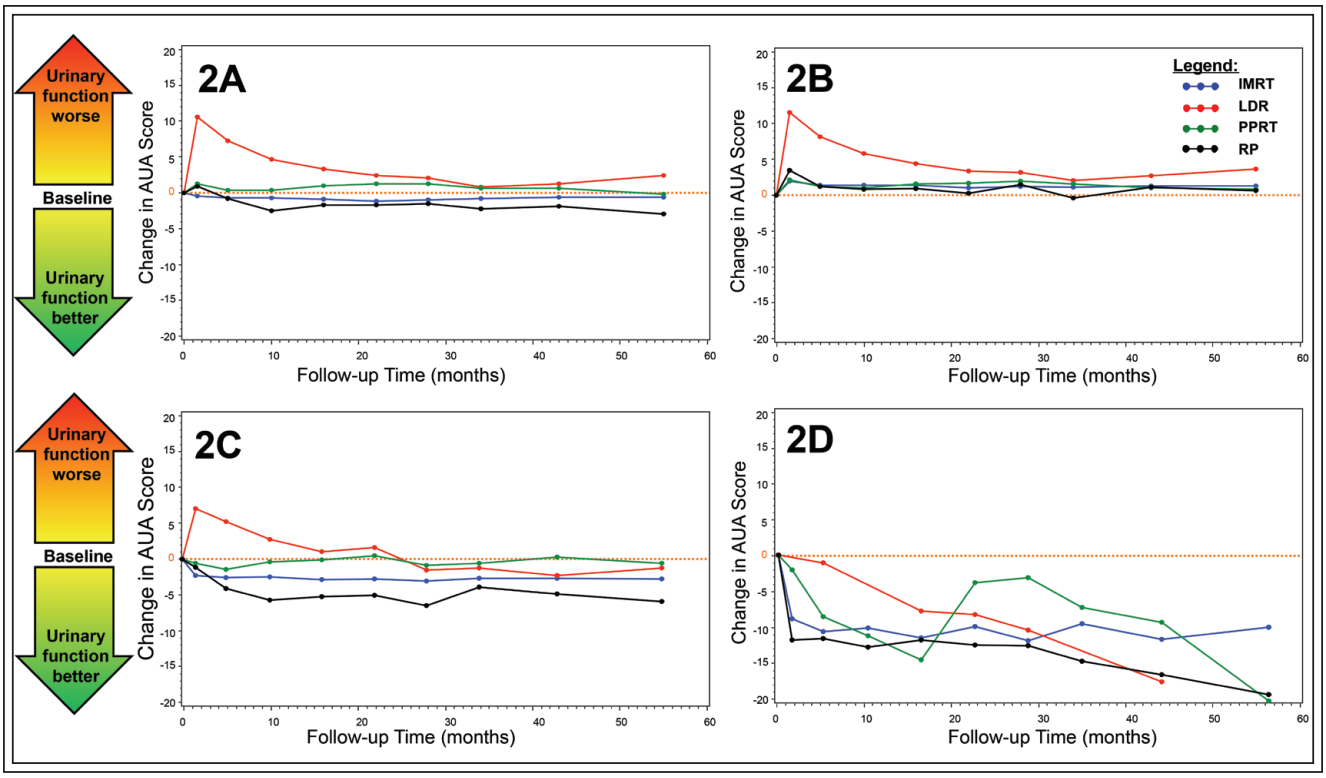


Figure 2. IPSS score change from baseline. **A)** entire cohort. **B)** baseline IPSS 0-7: mild. **C)** baseline IPSS 12-21: moderate. **D)** baseline IPSS 22-25: severe. Note: patient QOL scores have been normalized to 0, as described in the methods.

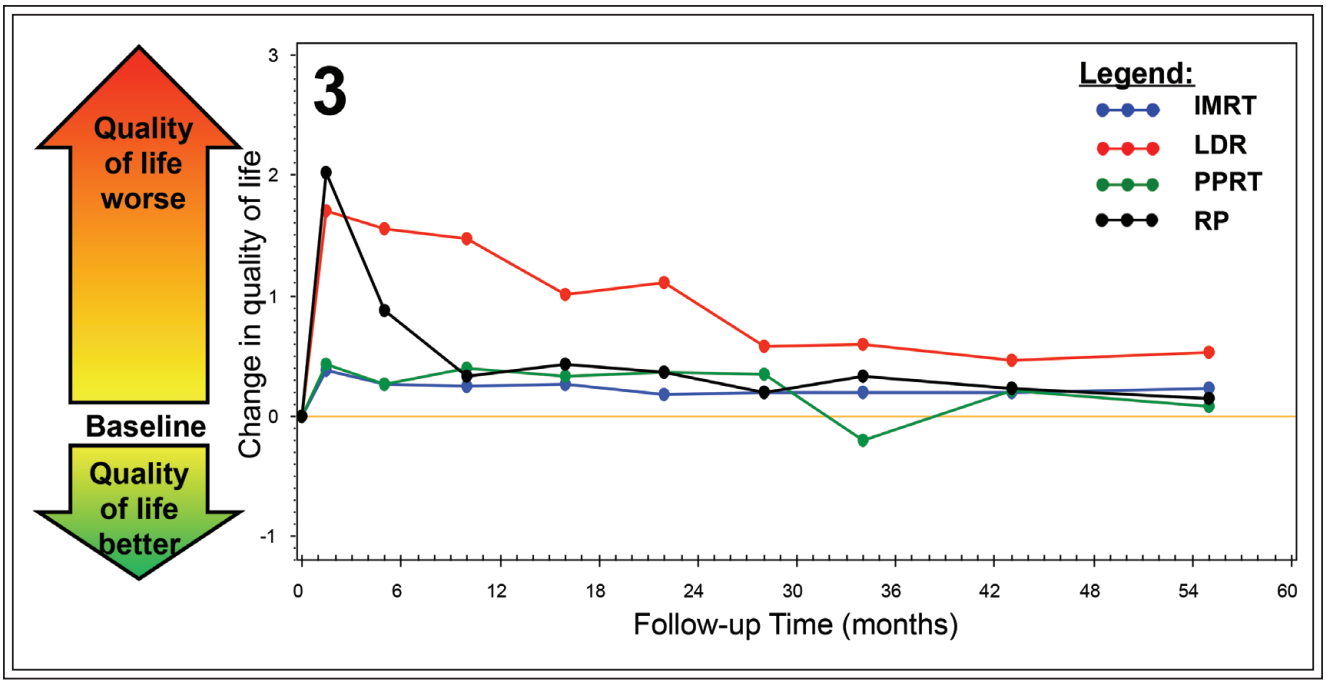


Figure 3. Urinary QOL score change from baseline for patients with baseline QOL score 0-2. Note: patient QOL scores have been normalized to 0, as described in the methods.

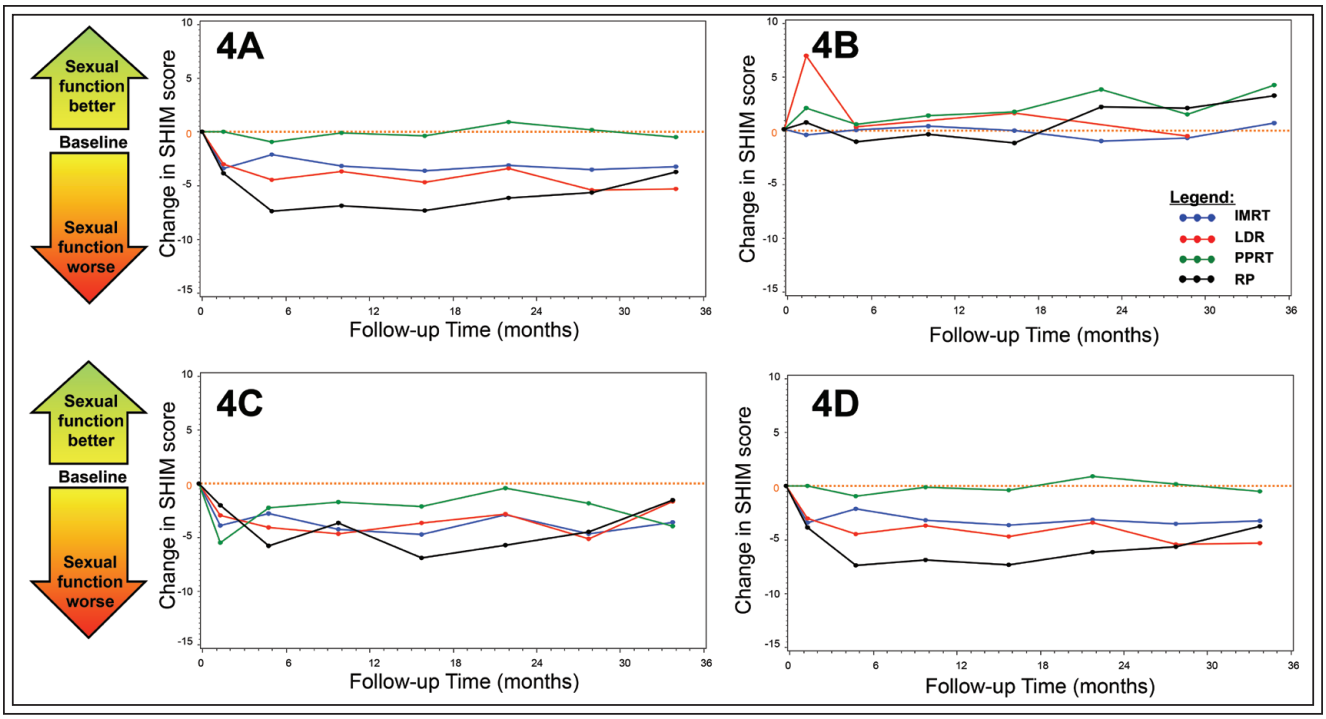


Figure 4. SHIM score change from baseline. **A)** entire cohort. **B)** baseline SHIM 1-11: moderate ED/severe ED. **C)** baseline SHIM 12-21: mild ED/mild to moderate ED. **D)** baseline SHIM: 22-25 no ED.
Note: patient SHIM scores have been normalized to 0, as described in the methods.

SHIM score changes from baseline for the entire cohort are shown in Figure 4a. SHIM score change from baseline for the subgroups 1-11 "moderate ED"/"severe ED", 12-21 "mild ED"/"mild to moderate ED", and 22-25 "no ED" are shown in Figure 4b, Figure 4c, and Figure 4d, respectively.

For the entire SHIM cohort, the GEE model demonstrates no significant difference in SHIM trends between LDR and PPRT when compared to IMRT. Patients treated with RP reported significantly worse sexual function between 5 and 16 months after surgery. There was no difference between RP and IMRT SHIM score change from baseline after 22 months. Patients undergoing RP had a rapid decrease in SHIM score over the first 6 months following treatment after which point sexual function stabilized, while patients treated with IMRT experienced a slower decline. For patients with moderate to severe ED at baseline, there was little change from baseline regardless of treatment modality, with the exception of an initial improvement in SHIM score 1.5 months after LDR. For men with a SHIM baseline score of 22-25 "no ED," all treatment modalities result in a decline in SHIM score, with the exception of the group of men who retained good sexual function after RP, 20% in this series, who experienced no change from baseline after undergoing PPRT.

Discussion

This large, NCI-designated comprehensive cancer center experience demonstrates significant differences in the post-treatment patient-reported urinary and sexual function outcomes across various treatment modalities. The results complement those of the CaPSURE registry and the results from Harvard.[10,11] This builds upon the existing published data of patient-reported outcomes by providing longer follow up data exceeding the 1[36,37] or 2[38-40] years which is most commonly reported. We believe this presents the largest single-institution comparison across multiple treatment modalities, compared to the existing multi-institutional series reported by Resnick and colleagues.[41]

LDR was associated with significant worsening of obstructive urinary symptoms during the early months following treatment. IPSS scores peak at 1.5 months, then decline back towards baseline. Although this change is no longer significantly different than that seen after IMRT at and beyond 34 months after treatment, the magnitude of change compared to baseline was most pronounced of all treatment modalities studied. Our results are consistent with the meta-analysis of randomized trials that shows < 3% severe toxicity among patients treated with IMRT.[42] A similar trend in overall urinary quality

of life score was seen, with an initial worsening of score, with return towards baseline over 12-18 months. This trend may be due to the radioactive decay of the Iodine-125 seeds, since half of the total dose is delivered in the first 60 days. This trend of acute worsening of obstructive urinary symptoms with slow return toward baseline is consistent with other published data,[43-45] and underscores the importance of close monitoring of patients' urinary function in the first 6 months following LDR. This also supports the recommendation to not offer LDR to patients with high baseline IPSS scores.[46]

The majority of patients in this series reported good baseline urinary function (IPSS 0-7, QOL 0-3). With the exception of the LDR trend, discussed above, there is little change in IPSS score from baseline over time for patients undergoing IMRT, RP, or PPRT. This is in contrast to the urinary QOL score trend, which demonstrates a nearly 2-point worsening of patients at the first follow up point for patients who were treated with RP. This variance is likely secondary to the fact that the IPSS score does not capture incontinence, which can occur in the time period following RP, while patients may account for incontinence in their rating of global urinary quality of life. It is important to note that urinary quality of life scores return towards baseline relatively quickly after RP.

Interestingly, patients with a baseline IPSS score of 20-35, consistent with "severe" obstructive symptoms, uniformly experienced improvement in urinary function during follow up, regardless of the treatment modality. Patients receiving RP and IMRT experienced relatively rapid improvement in their urinary function, with IPSS scores improving by approximately 10 points at 1.5 months. This improvement appears to be durable over time, out to 55 months of follow up. This is expected for patients undergoing RP, as removal of the prostate would intuitively improve obstructive urinary symptoms. However, we saw a similar improvement in IPSS scores in the first few months following external beam radiation for patients with severe obstructive GU symptoms. This is in agreement with data from the University of Chicago. Their study of 368 men with baseline IPSS ≥ 15 demonstrated that external beam radiation was associated with a mean improvement in IPSS score of 6.9 points at a median follow up of 44 months.[47]

It is important to note that PPRT did not seem to have a significant impact on urinary or sexual function scores over time. There was no significant worsening of urinary function seen in the entire cohort or in any baseline subgroup for patients treated with PPRT. Additionally, in the subgroup of men who retained good sexual functioning after prostatectomy (pre-PPRT baseline score 22-25), there was no significant change in median SHIM scores following PPRT. This is consistent with published data examining patient-reported outcomes for men undergoing IMRT which demonstrated no decline in urinary or sexual quality of life at 24 months follow up.[48]

There are several limitations of this study. The instruments used in our methods are imperfect. The IPSS is an instrument derived from the AUA intended to evaluate men with BPH. Although IPSS was used to compare urinary outcomes between IMRT and RP, the IPSS score does not capture urinary incontinence, which is more commonly seen following RP. However, incontinence bother may be accounted for in the patient's overall urinary quality of life score. The SHIM was designed by the industry to evaluate therapies for ED. Many prostate cancer registries instead use the University of California Los Angeles Prostate Cancer Index (UCLA PCI) or the Expanded Prostate Cancer Index Composite (EPIC)-26,[49] as recently recommended by the International Consortium for Health Outcomes Measurement.[50]

Additionally, the patient groups were not well balanced among treatment modalities for each of the descriptives examined. This is likely due to patient selection, as this is an observational study and treatment modality was not randomized. Two examples of this are that patients age 70 or older are unlikely to undergo RP, and patients with high baseline IPSS scores may not be offered LDR. We attempted to mitigate some of the imbalance between baseline scores among the treatment modalities by examining subgroups of patients by baseline score, however, this cannot completely account for this imbalance. Additionally, we sometimes recommend multimodal therapy to patients with high-risk disease,[35] and we may recommend RT to men with bulky (i.e. T3-4) unresectable tumors for local control.[51] Our physicians typically avoid LDR for patients with large prostate gland volumes (i.e. > 70 cc), although this may not be a contraindication at other institutions.[52] We did not look into quality of life as a function of ethnic background, which has been shown to impact quality of life.[5] We were also unable to report outcomes for other prostate cancer therapies, such as hypofractionated RT,[26] stereotactic body RT[27] and high dose rate brachytherapy[28-30] secondary to inadequate follow up.

Conclusion

IPSS and SHIM score patterns differed among prostate cancer treatment modalities. These data can be used to predict changes in urinary and sexual function over time based on treatment modality and baseline score and are useful for counseling patients regarding treatment selection. □

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