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Quality of life after high-dose-rate brachytherapy monotherapy for prostate cancer

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ABSTRACT

Purpose: There is little information in the literature on health-related quality of life (HRQOL) changes due to high-dose-rate (HDR) brachytherapy monotherapy for prostate cancer.

Materials and Methods: We conducted a prospective study of HRQOL changes due to HDR brachytherapy monotherapy for low risk or favorable intermediate risk prostate cancer. Sixty-four of 84 (76%) patients who were treated between February 2011 and April 2013 completed 50 questions comprising the Expanded Prostate Cancer Index Composite (EPIC) before treatment and 6 and/or 12 months after treatment.

Results: Six months after treatment, there was a significant decrease ($p<0.05$) in EPIC urinary, bowel, and sexual scores, including urinary overall, urinary function, urinary bother, urinary irritative, bowel overall, bowel bother, sexual overall, and sexual bother scores. By one year after treatment, EPIC urinary, bowel, and sexual scores had increased and only the bowel overall and bowel bother scores remained significantly below baseline values.

Conclusions: HDR brachytherapy monotherapy is well-tolerated in patients with low and favorable intermediate risk prostate cancer. EPIC urinary and sexual domain scores returned to close to baseline 12 months after HDR brachytherapy.

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INTRODUCTION

Management options for patients with low or intermediate risk prostate cancer and a life expectancy of less than 10 years include active surveillance (1), radical prostatectomy (2), external beam radiation therapy (EBRT), low-dose rate (LDR) brachytherapy monotherapy (3, 4), or high-dose-rate (HDR) brachytherapy (5, 6). Since cure rates are similar among these treatment options (7), health-related quality of life (HRQOL) is an important factor in a patient's decision-making process (8).

In prostate cancer patients, physician-assessed HRQOL changes do not correlate with patient-assessed changes. Physicians under-estimate HRQOL changes and over-estimate improvement in symptoms relative to patients (9). Discrepancies are particularly large for symptoms like pain and fatigue (9). As a result, it is important to measure patient-assessed HRQOL. The Expanded Prostate Cancer Index Composite (EPIC) is a validated questionnaire used to assess HRQOL in prostate cancer patients. EPIC includes 4 domains: urinary, bowel, sexual, and hormonal (10). There are summary (i.e., overall) scores and function and bother subscale scores for each of the 4 domains. The urinary domain has 2 additional subscales: incontinence and irritative/obstructive. Domains

and subscales are scored using a 0-100 grading system, with a higher score indicating a higher quality of life.

HRQOL changes in prostate cancer patients undergoing radical prostatectomy, LDR brachytherapy monotherapy or EBRT vary significantly between treatment modalities (11). There has been only one prior report on HRQOL changes due to HDR brachytherapy monotherapy for prostate cancer (12). As a result, we studied HRQOL changes in this select group of patients.

MATERIALS AND METHODS

Recurrence risk was defined according to the National Comprehensive Cancer Network (NCCN) guidelines (13). Low recurrence risk was defined as patients with clinical T1-T2a disease, prostate-specific antigen (PSA) <10 ng/mL, and a Gleason score ≤6. Intermediate recurrence risk patients were those with clinical T2b-T2c disease, PSA=10-20 ng/mL, or a Gleason score =7. Intermediate risk patients were subdivided into "favorable" and "unfavorable" groups. Favorable intermediate risk patients were defined as those with a Gleason score of 3+4=7, ≤cT2b disease, and ≤50% positive core biopsies (5). Low risk and favorable intermediate risk patients may be treated with HDR brachytherapy monotherapy (5, 6, 12, 14). Unfavorable intermediate risk patients had a Gleason score of 4+3=7, cT2c disease, or >50% positive core biopsies (15, 16). Patients with unfavorable intermediate risk prostate cancer and patients who received intensity modulated radiation therapy (IMRT) or androgen deprivation therapy were excluded from this study.

After obtaining institutional review board approval, we treated 84 low risk and favorable intermediate risk prostate cancer patients with HDR brachytherapy monotherapy at the H. Lee Moffitt Cancer Center & Research Institute between February 2011 and April 2013. After providing informed consent, patients underwent HDR brachytherapy monotherapy to the prostate to 2,700-2,800 cGy in two 1,350-1,400 cGy fractions separated by 2-3 weeks. Over a one-year period following HDR brachytherapy, approximately half of the patients were placed on phosphodiesterase-5 inhibitors such as one sildenafil 50 mg tablet by mouth three times per week for erectile dysfunction. Use of phosphodiesterase-5 inhibitors was based upon patient preference.

HRQOL was assessed using the most recent version of EPIC. Sixty-four of 84 (76%) patients completed the 50-question form prior to HDR brachytherapy monotherapy, i.e., at baseline, and 6 and/or 12 months after treatment. Characteristics of these 64 patients are presented in Table-1. Patients who failed to complete the 50-question EPIC questionnaire commonly stated that it was too long. Mean follow-up was 9 months.

In accordance with prior reports (12, 17, 18), we calculated mean EPIC scores for each time point. Pre-treatment EPIC scores were compared to scores obtained 6 months and 12 months after treatment using a Student's t-test. Linear regression was used to analyze the relationship between patient characteristics (body mass index (BMI),

Table 1 - Patient characteristics.

Number of Patients	64
Mean Follow-up	9 months
Age at Diagnosis, mean (range)	65 years (48-83)
BMI, kg/m^2, mean (range)	29.5 (22.0-43.0)
PSA, ng/mL, median (range)	5.3 (1.0 – 16.1)
Prostate Size, cc, median (range)	54 (24-108)
AJCC Clinical T Stage	
T1c	58
T2a	5
T2b	1
Gleason Score	
3+3=6	43
3+4=7	21
NCCN Recurrence Risk Group	
Low	39
Intermediate	25

AJCC= American Joint Committee on Cancer; cc:cubic centimeters; **NCCN=** National Comprehensive Cancer Network; **PSA=** prostate-specific antigen.

age, prostate volume, PSA, Gleason score, and recurrence risk group) and EPIC scores.

RESULTS

Pre-treatment urinary overall, function, bother, incontinence, and irritative/obstructive scores were 87, 91, 85, 87, and 85, respectively (Figure-1). Six months after treatment, urinary overall, function, bother, incontinence, and irritative scores decreased to 76, 79, 75, 76, and 75 respectively ($p<0.01$). Twelve months after treatment, all urinary scores had increased and were not significantly different from baseline values.

Pre-treatment bowel overall, function, and bother scores were 95, 90, and 95, respectively (Figure-2). Six months after treatment, there was a significant decrease in bowel overall, function, and bother scores to 86, 84, and 86 respectively ($p<0.001$). Twelve months after treatment, bowel overall and bother scores increased to 88 and the bowel function score had increased to 86. These scores remained statistically below baseline values.

Pre-treatment sexual overall, function, and bother scores were 46, 43, and 53, respectively (Figure-3). Six months after treatment, there was a significant decrease in sexual overall and bother scores to 34 and 42, respectively. Twelve months after treatment, sexual overall and bother scores increased and were not statistically different from baseline values.

Pre-treatment hormonal overall, function, and bother scores were 91, 88, and 92, respectively (Figure-4). Six months after treatment, there was a non-significant decrease in sexual hormonal scores. Twelve months after treatment, hormonal scores had decreased further. However, they were not significantly below baseline.

There was no association between patient characteristics and EPIC scores.

Figure 1 - EPIC urinary overall, function, bother, incontinence, and irritative/obstructive scores before HDR brachytherapy monotherapy and 6 and 12 months after treatment.

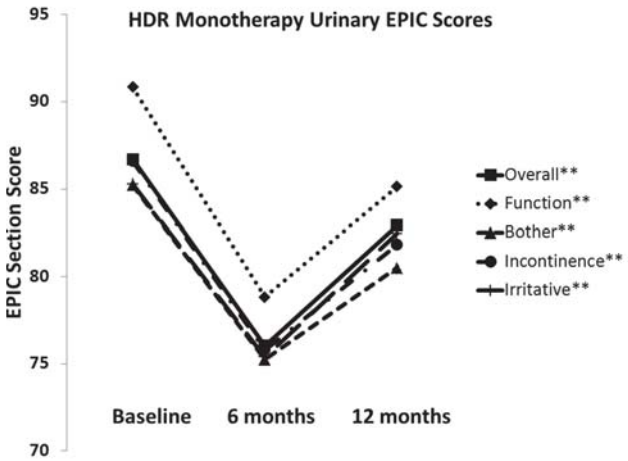


Figure 2 - EPIC bowel overall, function, and bother scores before HDR brachytherapy monotherapy and 6 and 12 months after treatment.

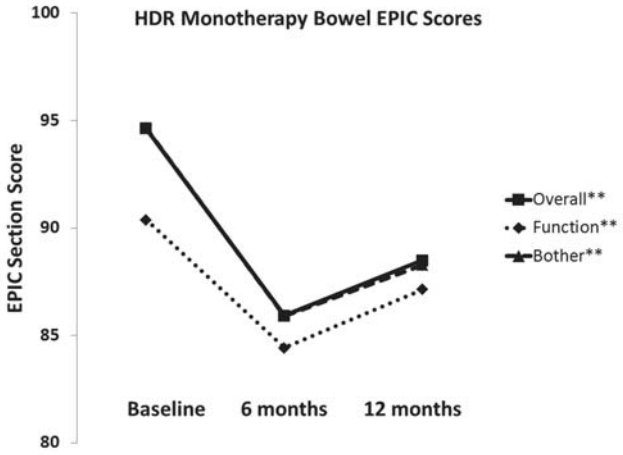


Figure 3 - EPIC sexual overall, function, and bother scores before HDR brachytherapy monotherapy and 6 and 12 months after treatment.

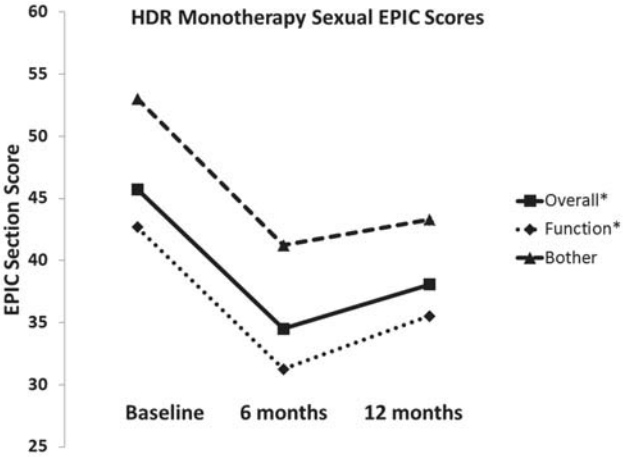
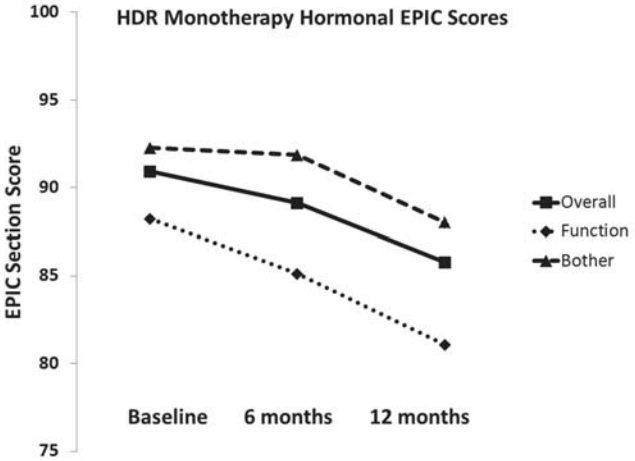


Figure 4 - EPIC hormonal overall, function, and bother scores before HDR brachytherapy monotherapy and 6 and 12 months after treatment.



DISCUSSION

Morton et al. (19) reported HRQOL changes in intermediate risk prostate cancer patients who received EBRT and an HDR brachytherapy boost without androgen deprivation therapy. Patients experienced clinically significant decreases in EPIC urinary, bowel, and sexual overall scores 12 months and 24 months after treatment. In contrast, the EPIC hormonal overall score did not change significantly due to radiotherapy. Similarly, in this study, the EPIC bowel overall score remained significantly below baseline 12 months after radiotherapy (Figure-2); however, the decrease in the EPIC hormonal overall score was not statistically significant (Figure-4).

To date, only one study has reported patient-assessed HRQOL changes in prostate cancer patients treated with HDR brachytherapy monotherapy. Barkati et al. (12) treated 79 low and intermediate risk prostate cancer patients with HDR brachytherapy monotherapy. Seven patients also received neoadjuvant androgen deprivation therapy. They observed a decline in EPIC scores across all 4 domains as early as one month after treatment. Urinary, bowel, and hormonal scores recovered 3 months after HDR brachytherapy monotherapy. This compares favorably with our findings, where EPIC urinary and sexual scores did not improve until 12 months after HDR brachytherapy (Figures 1 and 3). EPIC scores may have taken longer to improve after HDR brachytherapy in this report because we delivered a higher biologically effective dose of radiotherapy (14). Barkati et al. observed that urinary, bowel, and hormonal scores remained stable 3-48 months after treatment. Also, they reported a decline in sexual overall scores as early as one month after treatment with no recovery thereafter. Patients' ages were similar to this study. However, baseline sexual overall scores were lower in this report. As in the report by Barkati et al., baseline sexual scores in this study were considerably lower than urinary, bowel, and hormonal scores (Figures 1-4). Like Barkati et al., we observed a significant decrease in sexual overall and bother scores at 6 months (Figure-3). However, in this report, there was improvement in sexual scores at 12 months. This was probably due to early use of a phosphodiesterase-5 inhibitor after brachytherapy in approximately half of our patients (20).

Marina et al. (21) used the Common Terminology Criteria for Adverse Events v4 grading system to determine incidence rates of erectile dysfunction 3 years after HDR brachytherapy monotherapy vs. IMRT. Rates of erectile dysfunction requiring medical intervention for both HDR brachytherapy monotherapy and IMRT were low and equivalent.

In this study, 64/84 (76%) prostate cancer patients treated with HDR brachytherapy monotherapy completed 50 questions comprising the most recent version of the EPIC questionnaire. Similarly, others have reported 36-78% compliance rates (12, 22). Since men who did not complete the form commonly stated that it was too long, we have switched to a 26-item, short-form version of EPIC in an effort to improve patient compliance (23, 24).

CONCLUSIONS

HDR brachytherapy monotherapy is well-tolerated in patients with low and favorable intermediate risk prostate cancer. EPIC urinary and sexual domain HRQOL scores returned to close to baseline 12 months after treatment.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Holmberg L, Bill-Axelson A, Steineck G, Garmo H, Palmgren J, Johansson E, et al. Results from the Scandinavian Prostate Cancer Group Trial Number 4: a randomized controlled trial of radical prostatectomy versus watchful waiting. J Natl Cancer Inst Monogr. 2012; 2012: 230-3.
2. Bill-Axelson A, Holmberg L, Ruutu M, Garmo H, Stark JR, Busch C, et al. Radical prostatectomy versus watchful waiting in early prostate cancer. N Engl J Med. 2011; 364: 1708-17.
3. Sylvester JE, Grimm PD, Wong J, Galbreath RW, Merrick G, Blasko JC. Fifteen-year biochemical relapse-free survival, cause-specific survival, and overall survival following I(125) prostate brachytherapy in clinically localized prostate cancer: Seattle experience. Int J Radiat Oncol Biol Phys. 2011; 81: 376-81.
4. Taira AV, Merrick GS, Butler WM, Galbreath RW, Lief J, Adamovich E, et al. Long-term outcome for clinically localized prostate cancer treated with permanent interstitial brachytherapy. Int J Radiat Oncol Biol Phys. 2011; 79: 1336-42.
5. Ghilezan M, Martinez A, Gustason G, Krauss D, Antonucci JV, Chen P, et al. High-dose-rate brachytherapy as monotherapy delivered in two fractions within one day for favorable/intermediate-risk prostate cancer: preliminary toxicity data. Int J Radiat Oncol Biol Phys. 2012; 83: 927-32.
6. Martinez AA, Demanes J, Vargas C, Schour L, Ghilezan M, Gustafson GS. High-dose-rate prostate brachytherapy: an excellent accelerated-hypofractionated treatment for favorable prostate cancer. Am J Clin Oncol. 2010; 33: 481-8.
7. Mendenhall WM, Nichols RC, Henderson R, Mendenhall NP. Is radical prostatectomy the "gold standard" for localized prostate cancer? Am J Clin Oncol. 2010; 33: 511-5.
8. Pardo Y, Guedea F, Aguiló F, Fernández P, Macías V, Mariño A, et al. Quality-of-life impact of primary treatments for localized prostate cancer in patients without hormonal treatment. J Clin Oncol. 2010; 28: 4687-96. Erratum in: J Clin Oncol. 2011;29:779.
9. Sonn GA, Sadetsky N, Presti JC, Litwin MS. Differing perceptions of quality of life in patients with prostate cancer and their doctors. J Urol. 2009; 182: 2296-302.
10. Wei JT, Dunn RL, Litwin MS, Sandler HM, Sanda MG. Development and validation of the expanded prostate cancer index composite (EPIC) for comprehensive assessment of health-related quality of life in men with prostate cancer. Urology. 2000; 56: 899-905.
11. Ferrer M, Suárez JF, Guedea F, Fernández P, Macías V, Mariño A, et al. Health-related quality of life 2 years after treatment with radical prostatectomy, prostate brachytherapy, or external beam radiotherapy in patients with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys. 2008; 72: 421-32.
12. Barkati M, Williams SG, Foroudi F, Tai KH, Chander S, van Dyk S, et al. High-dose-rate brachytherapy as a monotherapy for favorable-risk prostate cancer: a Phase II trial. Int J Radiat Oncol Biol Phys. 2012; 82: 1889-96.
13. Mohler JL, Armstrong AJ, Bahnson RR, Boston B, Busby JE, D'Amico AV, et al. Prostate cancer, Version 3.2012: featured updates to the NCCN guidelines. J Natl Compr Canc Netw. 2012; 10: 1081-7.
14. Yoshioka Y, Yoshida K, Yamazaki H, Nonomura N, Ogawa K. The emerging role of high-dose-rate (HDR) brachytherapy as monotherapy for prostate cancer. J Radiat Res. 2013; 54: 781-8.
15. Castle KO, Hoffman KE, Levy LB, Lee AK, Choi S, Nguyen QN, et al. Is androgen deprivation therapy necessary in all intermediate-risk prostate cancer patients treated in the dose escalation era? Int J Radiat Oncol Biol Phys. 2013; 85: 693-9.
16. Huang J, Vicini FA, Williams SG, Ye H, McGrath S, Ghilezan M, et al. Percentage of positive biopsy cores: a better risk stratification model for prostate cancer? Int J Radiat Oncol Biol Phys. 2012; 83: 1141-8.
17. Pinkawa M, Fischedick K, Treusacher P, Asadpour B, Gagel B, Piroth MD, et al. Dose-volume impact in high-dose-rate Iridium-192 brachytherapy as a boost to external beam radiotherapy for localized prostate cancer--a phase II study. Radiother Oncol. 2006; 78: 41-6.
18. Sandler HM, Liu PY, Dunn RL, Khan DC, Tropper SE, Sanda MG, et al. Reduction in patient-reported acute morbidity in prostate cancer patients treated with 81-Gy Intensity-modulated radiotherapy using reduced planning target volume margins and electromagnetic tracking: assessing the impact of margin reduction study. Urology. 2010; 75: 1004-8.
19. Morton GC, Loblaw DA, Chung H, Tsang G, Sankreacha R, Deabreu A, et al. Health-related quality of life after single-fraction high-dose-rate brachytherapy and hypofractionated external beam radiotherapy for prostate cancer. Int J Radiat Oncol Biol Phys. 2011; 80: 1299-305.
20. Schiff JD, Bar-Chama N, Cesaretti J, Stock R. Early use of a phosphodiesterase inhibitor after brachytherapy restores and preserves erectile function. BJU Int. 2006; 98: 1255-8.
21. Marina O, Warner J, Ye H, Grills IS, Shah C, Wallace M, et al. An age-corrected matched-pair study of erectile function in patients treated with dose-escalated adaptive image-guided intensity-modulated radiation therapy vs. high-dose-rate brachytherapy for prostate cancer. Brachytherapy. 2014; 13: 163-8.

22. Rodrigues G, Bauman G, Venkatesan V, Ahmad B, Lock M, Sexton T, et al. Cross validation of the prostate cancer radiotherapy late toxicity (PCRT) questionnaire with the expanded prostate cancer index composite (EPIC) instrument. Can J Urol. 2011; 18: 5802-10.
23. Rnic K, Linden W, Tudor I, Pullmer R, Vodermaier A. Measuring symptoms in localized prostate cancer: a systematic review of assessment instruments. Prostate Cancer Prostatic Dis. 2013; 16: 111-22.
24. Szymanski KM, Wei JT, Dunn RL, Sanda MG. Development and validation of an abbreviated version of the expanded prostate cancer index composite instrument for measuring health-related quality of life among prostate cancer survivors. Urology. 2010; 76: 1245-50.

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