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Erectile function after stereotactic body radiotherapy for localized prostate cancer

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Objective

To elucidate the functional erection rate after prostate stereotactic body radiotherapy (SBRT) and to develop a comprehensive prognostic model of outcomes after treatment.

Patients and Methods

Between 2008 and 2013, 373 consecutive men with localized prostate cancer were treated with SBRT at a single academic institution as part of a prospective clinical trial or prospective registry. Prospective longitudinal patient-reported health-related quality of life (HRQoL) data was collected using the Expanded Prostate Cancer Index Composite (EPIC)-26 instrument. Functional erections were strictly defined as 'firm enough for intercourse' according to EPIC-26. Detailed comorbidity data were also collected. Logistic regression models were used to predict 24- and 60-month functional erection rates. Observed erection rates after SBRT were compared with those after other radiation therapies (external beam radiation therapy [EBRT] and brachytherapy) using prospectively validated models.

Results

The median (interquartile range) follow-up was 56 (37–73) months and the response rate at 2 years was 84%. For those with functional erections at baseline, 57% and 45% retained function at 24 and 60 months, respectively. On multivariable analysis for 24-month erectile function, significant variables included higher baseline sexual HRQoL (adjusted odds ratio [aOR] 1.55 per 10 points, 95% confidence interval [CI] 1.37–1.74; $P < 0.001$) and older age (aOR 0.66 per 10 years, 95% CI 0.43–1.00; $P = 0.05$). At 60 months, baseline HRQoL and age remained associated with erectile function, along with body mass index (aOR 0.45, 95% CI 0.26–0.78; $P < 0.001$). The 24- and 60-month models had excellent discrimination (c-index 0.81 and 0.84, respectively). Erection rates after SBRT were not statistically different from model-predicted rates after EBRT or brachytherapy for the whole cohort and the cohort with baseline erectile function.

Conclusions

Intermediate- to long-term post-SBRT erectile function results are promising and not significantly different from other radiotherapy techniques. Clinicians can use our prognostic model to counsel patients regarding expected erectile function after SBRT.

Keywords

erectile function, patient-reported outcomes, SBRT, sexual function, stereotactic body radiation therapy, #ProstateCancer, #PCSM

Introduction

The Prostate Testing for Cancer and Treatment (ProtecT) trial recently reported the outcomes of men with predominantly low-risk prostate cancer randomized to one of three upfront treatment strategies: nerve-sparing radical prostatectomy (RP); conventionally fractionated external beam radiation therapy (EBRT); or active surveillance [1]. Overall survival was similar in all groups, but ~50% of men in the active surveillance arm eventually underwent definitive treatment. For men who do undergo radical treatment, an understanding of its impact on health-related quality of life (HRQoL) is critically important to inform decision-making, given the equivalent efficacy demonstrated for RP and EBRT [1,2]. Among HRQoL domains, sexual function is most commonly and significantly affected by radical therapy, and

sexual function outcomes correlate closely with overall treatment satisfaction [3–5].

Much has changed, however, in the 17 years since the first patient was enrolled in ProtecT. Surgical techniques have evolved [6], and radiotherapeutic advances have allowed the advent of high-dose-per-fraction, image-guided, ultra-hypofractionated treatment to the prostate, termed stereotactic body radiotherapy (SBRT). Often delivered over five treatments, SBRT is convenient and cost-effective relative to conventional EBRT courses of 8–9 weeks [7,8], with a promising overall toxicity profile [9–11] that is currently being investigated in numerous randomized trials [12,13].

Concern remains, however, about the delayed effects of SBRT given its high-dose per fraction and mechanism of cellular injury [14]. There are few existing data on long-term functional erection outcomes after SBRT, hindering the clinical counselling of men considering this therapeutic approach. Prognostic models of functional erections have been developed after treatment with nerve-sparing RP, conventional EBRT, and brachytherapy [15], but notably absent are similar models after SBRT.

To better understand the impact of SBRT on erectile function, in the present paper, we report the results of a large prospective study using patient-reported outcomes, including a detailed set of comorbidities believed to affect sexual health to develop our models. Furthermore, we compared rates of erectile function across treatment methods using validated model-predicted rates for other radiation techniques performed at centres of excellence.

Materials and Methods

Patients

Between January 2008 and November 2013, 373 patients with localized biopsy-proven prostate adenocarcinoma were consecutively treated with SBRT as per an institutional protocol (NCT01766492) or on a prospective registry. Eligible patients included those with cT1c–T2c disease, cN0 Gleason scores 6–10, and PSA levels <50 ng/mL. Patients who had previously undergone pelvic radiotherapy or prostate surgery were excluded. Patients were staged according to National Comprehensive Cancer Center (NCCN) guidelines; high-risk patients were staged with the addition of a CT of the abdomen and pelvis and a bone scan. Prostate MRI was recommended and routinely used. All patients received baseline PSA testing prior to initiation of any therapy.

All patients were required to have baseline patient-reported HRQoL data, which consisted of the Expanded Prostate Cancer Index Composite (EPIC)-26 [16]. Additional prospective sexual health inventory data were collected, including the International Index of Erectile Function short version (IIEF-5, also known as the Sexual Health Inventory for Men [SHIM]) [17].

Treatment

Image-guided prostate SBRT was delivered using Cyberknife (Accuray, Sunnyvale, CA, USA). SBRT treatment planning and delivery have been described previously [18]. Pretreatment CT and MRI registration were used for volume delineation. CT included the prostate and the proximal seminal vesicles. The planning target volume equalled the clinical target volume expanded by 3 mm posteriorly and 5 mm in all other dimensions. Patients were treated with 35–36.25 Gy in five fractions (SBRT). Radiation was delivered every other day to a prescription isodose line of 75–80%, with a target coverage goal of ≥95%. The penile bulb was contoured with a dose–volume histogram goal of <25% receiving 29.5 Gy. Individual erectile structures, such as internal pudendal arteries, neurovascular bundles or nerve plexus, were not specifically contoured or avoided. Image guidance was applied using paired, orthogonal X-rays. Target position was verified every 1–2 min, with a minimum of three adequately separated, non-overlapping fiducials.

Beyond the 373 in the current cohort, 24 additional patients were treated during the study period with neoadjuvant androgen deprivation therapy (ADT), consisting of 3–6 months of an LHRH agonist; however, only 4/24 patients receiving ADT had baseline functional erections, limiting meaningful analysis. These patients receiving ADT were therefore not included in the present study.

Erectile Function Definition

As advocated by the National Cancer Institute Prostate Cancer Working Group, we report patient-reported sexual outcomes longitudinally [19]. The EPIC sexual function domain is a composite score of 0 to 100, comprising five questions related to sexual function and one question related to sexual bother; higher values represent improved HRQoL. 'Functional erection' was the primary metric used in the present study, and was strictly defined as the patient-reported response of having erections 'firm enough for intercourse' in the past 4 weeks, irrespective of use of sexual aids, on question 9 of the EPIC-26, in accordance with the National Institutes of Health definition of erectile function [20]. Given that SHIM scores were also collected, we also compared functional erections defined by SHIM ≥16 with those defined by EPIC.

Covariables

Age and pretreatment EPIC sexual function domain HRQoL scores were analysed as continuous variables or as a binary variable when specified. Additional patient-related variables

thought to be related to erectile function were analysed including baseline sexual medications, partner status, body mass index (BMI), diabetes, hypertension, coronary artery disease, major depression, and pretreatment testosterone. Tumour-related variables included PSA (ng/mL), T stage, and Gleason score. Treatment-related variables included prescribed SBRT dose < 36.25 or ≥36.25.

Treatment Method Comparisons

To compare rates of erectile function preservation after SBRT with other radiation therapies (EBRT and brachytherapy), our individual patient clinical characteristics were entered into validated models that have been shown to predict 24-month post-treatment erectile function for both EBRT and brachytherapy [15]. These models were generated from the Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment (PROSTQA) multicentre cohort, and validated in a Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) cohort.

Statistical Analysis

To explore differences in patients who were lost to follow-up (Table S1), logistic regression was used to predict missing data at 24 and 60 months based on a decline in sexual HRQoL in the first 12 months and the second 12 months of follow-up. Patients with decline in sexual function were more likely to have data collection at 24 months, suggesting no selection bias as a result of poor follow-up of those with significant HRQoL declines. Furthermore, analyses of missing patients at 60 months revealed no other associations with sexual function decline; thus, missing data were assumed to be missing at random and imputation was not performed.

Univariable logistic regression analysis (UVA) and multivariable logistic regression analysis (MVA) were performed to generate models of predictors of functional erections over time. The primary endpoint was at 24 months, consistent with a previous analysis of other radiation techniques [15]. Additional models were generated to predict function at 60 months. All patients were included in the modelling, including those without baseline erectile function, as 10–15% of patients who report no function at baseline regain function at later time points. Odds ratios (ORs), adjusted ORs (aORs), and 95% CIs are reported. For the logistic regression model to predict functional erections, 95% Wald CIs were calculated from the estimated covariance matrix. C-indices were calculated to determine the discriminatory performance of the model. Age was included in all MVA models, given its known association with sexual function. Variables with $P < 0.1$ on UVA, plus comorbidities known to be associated with sexual function (diabetes, hypertension, coronary artery disease and major depression), were tested in the MVA model. Stepwise backward elimination was used; two-sided P values of <0.05 were considered statistically significant. Statistical analyses were performed using SAS version 9.3.

Results

Baseline and Treatment Characteristics

The median (interquartile range [IQR]) follow-up was 56 (37–73) months. The median (IQR) age was 69 (64–73) years and 124 (33%), 233 (63%), and 16 patients (4%) were classified as low, intermediate and high risk according to the NCCN criteria, respectively. Detailed pretreatment comorbidities are shown in Table 1. Baseline EPIC sexual function domain HRQoL was available for all 373 patients. A total of 312 patients had EPIC follow-up assessment at 24 months (84% of eligible patients [Table 1]), and response rates did not vary between those with or without baseline erectile function.

Longitudinal Sexual HRQoL and Functional Erection Outcomes

The median (IQR) baseline HRQoL score was 56 (29–82). Baseline global sexual HRQoL was equally split between 182 patients (49%) with higher baseline function (HRQoL score 60–100) and 191 patients (50%) with poor function (HRQoL score < 60 [Table S2]). At 24 and 60 months after SBRT, 107/312 (34%) and 44/170 (26%) reported functional erections, respectively (Fig. 1A). A total of 184 men (49%) had functional erections at baseline and 89/157 (57%) and 39/87 (45%) retained function at 24 and 60 months, respectively (Fig. 1B). Figures 1C and D show the decline in erectile function over time by age, with older patients (age ≥65 years) having a more continual decline of erectile function over time compared with younger patients, who appeared to reach a plateau.

Baseline SHIM scores were available for 372/373 patients (99%); 182 (49%) had a baseline SHIM ≥16 which decreased to 107/311 (34%) and 51/167 (30%) at 24 and 60 months respectively. Using this SHIM definition, erectile function rates were nearly identical to those estimated by EPIC (Fig. S1).

Predictors of Functional Erections

On UVA, the following factors were associated with decreased erectile function at 24 months: older age, lower pretreatment sexual HRQoL, and T stage [all $P \leq 0.01$]; Table 2). Older age and lower pretreatment sexual HRQoL (both $P < 0.001$) remained associated with decreased function at 60 months, in addition to elevated BMI ($P = 0.005$), diabetes ($P = 0.039$) and hypertension ($P = 0.025$). On MVA, higher baseline sexual HRQoL was associated with improved

Table 1 Characteristics of the study cohort.

Patient characteristics	
Age, years	
Median (IQR)	69 (64, 73)
BMI, kg/m^2	
Median (IQR)	28 (25, 31)
BMI, *n* (%)	
<30 kg/m^2	256 (69)
>30 kg/m^2	111 (30)
>40 kg/m^2	6 (2)
Partner status	
Not married	94 (25)
Married	278 (75)
Diabetes	
Absent	295 (79)
Present	77 (21)
Hypertension	
Absent	112 (30)
Present	260 (70)
Coronary artery disease	
Absent	307 (83)
Present	65 (17)
Major depression	
Absent	343 (92)
Present	28 (8)
Pretreat testosterone	
Median (IQR)	320 (234, 437)
Baseline sexual medications	
No	223 (62)
Yes	139 (38)
Tumour and treatment characteristics, *n* (%)	
T-stage	
T1c–T2a	321 (86)
T2b–c	51 (14)
T3	1 (0)
Grade group (Gleason), *n* (%)	
1 (6)	165 (44)
2 (3 + 4)	147 (39)
3 (4 + 3)	53 (14)
4 (4 + 4)	8 (2)
5 (9 or 10)	1 (0)
Pretreatment PSA level, ng/mL	
Median (IQR)	6 (5, 9)
≤10 ng/mL	308 (83)
>10–20 ng/mL	58 (16)
>20 ng/mL	7 (2)
Risk group*	
Low	124 (33)
Favourable intermediate risk	140 (38)
Unfavourable intermediate risk	93 (25)
High risk	16 (4)
SBRT dose	
<36.25	132 (35)
≥36.25	241 (65)

**Risk group adapted from National Comprehensive Cancer Network and the Zumsteg/Spratt risk classification. Low: T1–T2a, Gleason ≤ 6, PSA <10 ng/mL; favourable intermediate: Gleason ≤ 6 with one intermediate risk factor OR Gleason 3 + 4 as only factor; unfavourable intermediate: Gleason 4 + 3 OR multiple intermediate risk factors; high risk: T3 OR Gleason 8–10 OR PSA >20 ng/mL.*

function erection rates both at 24 months (aOR 1.55 per 10-point increase [95% CI 1.37–1.74]; $P < 0.001$) and 60 months (aOR 1.54 per 10-point increase [95% CI 1.27–1.87]; $P < 0.001$). Older age was associated with decreased function at both 24 and 60 months. At 60 months, BMI was the only comorbidity independently associated with a significant decline in functional erections on MVA (aOR 0.45 [95% CI 0.26–0.78]; $P < 0.001$).

Table 3 shows the results from our MVA model-predicted functional erection rate at 24 months after SBRT (c-index 0.81 [95% CI 0.76–0.86]) and 60 months after SBRT (c-index 0.83 [95% CI 0.79–0.88]). The model predictions ranged from <10% (95% CI 4–12) for a 70-year-old man with baseline HRQoL of 25 to 80% (95% CI 68– 87) for a 60-year-old with baseline HRQoL of 100. Similar ranges are seen at 60 months, with BMI further informing predicted rates. As seen in Table 3, a decrease in BMI of 5 points increases the predicted 5-year functional erection rates by 10–20 percentage points.

Treatment Method Comparison

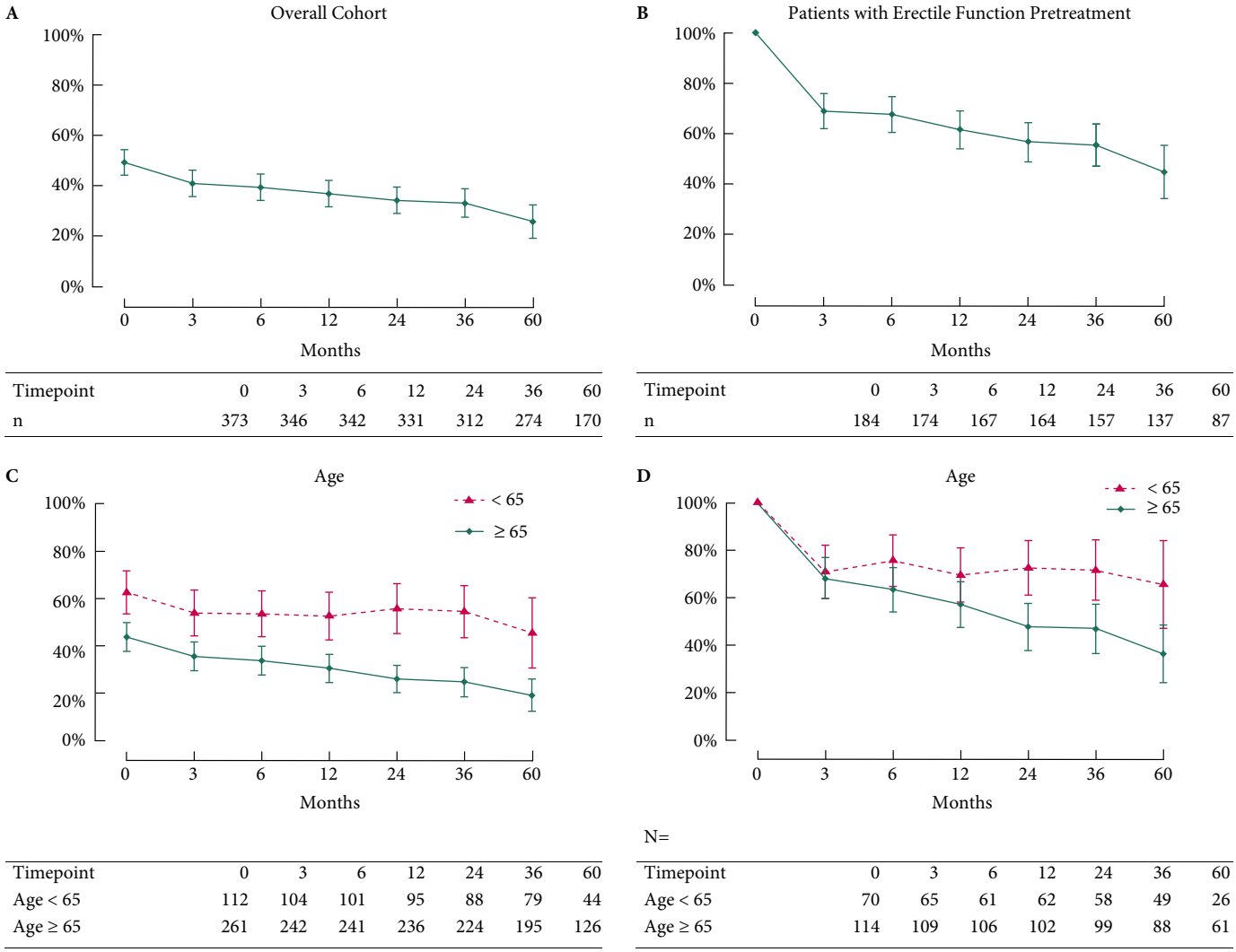
A total of 312 patients had follow-up at 24 months. Using previous prospectively validated models of 24-month functional erections after EBRT and brachytherapy [15], model-predicted rates for this cohort of men were 37% (95% CI 33–40) with EBRT and 32% (95% CI 28–35) with brachytherapy. The rate of actual functional erections after SBRT was 34% (95% CI 29–40), a rate not statistically significantly different from that after EBRT ($P = 0.31$) or brachytherapy ($P = 0.30$; Table 4). In patients with baseline erectile function, a similar lack of difference among the treatment methods was noted.

Discussion

Erectile dysfunction after treatment for localized prostate cancer is a common side effect and a major patient concern [3]. In a large cohort, broadly representative of those diagnosed with prostate cancer, we report intermediate- and long-term functional erection outcomes after high-dose-per-fraction treatment with prostate SBRT. Questionnaire response rates were robust over time (24 months: 84%), and there was substantial follow-up of up to 60 months, with no evidence of selection bias in those lost to follow-up. Among those with baseline erectile function, 57% and 45% retained erectile function at 24 and 60 months, respectively.

These results are consistent with several smaller previously reported SBRT series using similar strict EPIC-based criteria. For example, in a Stanford phase II trial of 32 patients receiving prostate SBRT, 62% of patients reported erections firm enough for intercourse at baseline, which declined to 29% at 50 months [21]. Others have obtained similar findings using different patient-reported sexual outcome measures. The HYPO-RT-PC non-inferiority trial randomized men to a seven-fraction regimen of SBRT vs standard EBRT, and

Fig. 1 Unadjusted proportions of patients reporting functional erections at each follow-up for the whole cohort (**A**), those with baseline erectile function (**B**), the whole cohort dichotomized by age 65 years (**C**), and those with baseline erectile function dichotomized by age 65 years (**D**).



Timepoint	0	3	6	12	24	36	60
n	373	346	342	331	312	274	170

Timepoint	0	3	6	12	24	36	60
n	184	174	167	164	157	137	87

Timepoint	0	3	6	12	24	36	60
Age < 65	112	104	101	95	88	79	44
Age ≥ 65	261	242	241	236	224	195	126

N=

Timepoint	0	3	6	12	24	36	60
Age < 65	70	65	61	62	58	49	26
Age ≥ 65	114	109	106	102	99	88	61

recently reported preliminary results in abstract form. Using the Prostate Cancer Symptom Scale [22], 2-year 'potency' was 34% and unchanged compared with EBRT, similar to the present results [13].

The present MVA of erectile function after SBRT identified several patient-related factors associated with functional erections. Better baseline HRQoL was strongly associated with functional erections at 24 and 60 months after treatment, consistent with findings with regard to EBRT and brachytherapy [15,23]. Older patients were more likely to experience decline in the rate of functional erections, similar to the decline experienced in older patients without prostate cancer [24,25], as well as those patients treated with RP and brachytherapy [15]. At 60 months, increasing BMI was also associated with a greater likelihood of functional erection decline, similar to those treated with brachytherapy [15]. Interestingly, while our UVA identified diabetes and hypertension as associated with declines in 60-month erectile function, these comorbidities were no longer significant after including age, baseline sexual function and BMI. Age, HRQoL and BMI are key confounders to keep in mind in any treatment method comparison, and they probably capture several other underlying comorbid contributions to sexual health, such as diabetes and hypertension.

Our sexual function outcomes after SBRT appear to be similar to EBRT and brachytherapy based on validated prediction models. These prediction models are advantageous as they were generated from treatments at centres of excellence, were externally validated, and allow patient-level comparison of treatment methods. Some may point out, fairly, that these models were based on patients treated with older, three-dimensional conformal radiation treatment techniques. Fortunately, recent efforts have provided important insights regarding sexual quality-of-life outcomes

Table 2 Univariable and multivariable models of functional erections at 24 and 60 months.

	Univariable analysis						Multivariable analysis					
	24 months (n = 312)			60 months (n = 170)			24 months (n = 312)			60 months (n = 170)		
	OR	95% CI	P	OR	95% CI	P	aOR	95% CI	P	aOR	95% CI	P
Patient factors												
Age (per 10 years)	0.44	0.30 0.64	<0.001	0.32	0.18 0.57	<0.001	0.66	0.43 1.00	0.05	0.34	0.16 0.72	0.005
Pretreat HRQoL (per 10 points)	1.58	1.41 1.79	<0.001	1.63	1.36 1.95	<0.001	1.55	1.37 1.74	<0.001	1.54	1.27 1.87	<0.001
BMI (per 5 points)	0.82	0.63 1.07	0.15	0.50	0.31 0.82	0.005				0.45	0.26 0.78	0.004
Partner status	1.037	0.60 1.80	0.90	0.87	0.40 1.89	0.73						
Diabetes	0.76	0.42 1.39	0.37	0.27	0.08 0.93	0.039						
Hypertension	0.62	0.38 1.02	0.06	0.44	0.22 0.90	0.025						
Coronary artery disease	0.75	0.38 1.47	0.40	0.27	0.06 1.20	0.09						
Major depression	0.43	0.16 1.17	0.10	–	– –	–						
Baseline sexual medication use	0.78	0.47 1.29	0.33	1.11	0.55 2.23	0.78						
Pretreatment testosterone	1.00	0.998 1.001	0.73	1.00	0.997 1.002	0.68						
Tumour and treatment factors												
T stage group*	0.33	0.14 0.76	0.01	0.72	0.25 2.07	0.54						
Gleason group†	0.84	0.62 1.14	0.25	0.67	0.41 1.09	0.11						
PSA < 4 vs PSA ≥ 4 ng/mL	1.56	0.07 3.63	0.30	1.05	0.36 3.09	0.92						
SBRT dose	1.14	0.69 1.87	0.61	0.88	0.34 2.28	0.79						

*HRQoL, health related quality of life; SBRT, stereotactic body radiotherapy; OR, odds ratio; aOR, adjusted odds ratio. At 60 month time point, no patients had major depression and erectile function, thus estimates using logistic regression are not valid. *T1–T2a, T2b–2c, T3. †(1) Gleason 6, (2) 3 + 4, (3) 4 + 3, (4) 8, (5) 9–10.*

with modern intensity-modulated radiotherapy (IMRT) [26,27]. Barocas et al. [27] used the same EPIC-based quality-of-life instrument reported in the present study, and importantly, >80% were treated with IMRT. Age and baseline sexual HRQoL was similar between the EBRT group in the Barocas study and the present study: mean age of 68 vs 69 years and mean baseline sexual HRQoL of 52 vs 55, respectively. The percentage of men with baseline erectile function who retained function at 3 years was strikingly similar between the group treated with predominantly IMRT in the Barocas study and the group in the present study treated with SBRT (56% vs 55%). Interestingly, despite younger age (mean 62 years) and better baseline sexual HRQoL (mean score 65), the erectile function preservation in those treated with nerve-sparing RP was 46%, approximately 10 percentage points lower than either radiation treatment method.

Prospective comparisons are needed to confirm these findings. The PACE trial, a phase III study, will directly compare methods by randomizing operable patients to SBRT or RP, and non-operable candidates to SBRT or EBRT [12]. Our findings lend reassurance and support for the ongoing PACE trial whose results will potentially be able to validate our model as they are collecting similar EPIC-26 data. An additional trial comparing moderate hypofractionation with SBRT is in process through the NRG Oncology cooperative group.

Several additional limitations of this study are worth discussion. No single assessment is likely to capture post-treatment sexual function both clearly and comprehensively. Beyond the validated EPIC-26 inventory, we also reported results from the commonly utilized IIEF-5 (SHIM) inventory with similar results using a threshold of ≥16. Further validation of our model should be pursued given the patients were treated at a single institution. In addition, only the penile bulb was identified as an avoidance structure in the present study. Radiation injury and erectile function is known to be complex [28], and vessel-sparing techniques have been shown to provide promising results [29], but no effort was made to spare these structures in the present study. Further, while the present study included baseline sexual aid utilization, the impact of continued or new sexual aid use on erectile function was limited given the nature of EPIC-26. Finally, unlike conventionally fractionated EBRT, where the benefit of ADT on clinically meaningful outcomes has been established in multiple phase III trials [30,31], the benefit of ADT in patients treated with SBRT is uncertain as no randomized controlled trials have been performed to date. Given the associated decline in sexual function with ADT administration, further studies should be pursued to understand the added clinical benefit of hormonal therapy in this setting.

In conclusion, long-term erectile function in men treated with prostate SBRT is promising. We provide a practical, clinically relevant model to estimate the probability of functional erections to help guide physician- and patient-shared

Table 3 Model-estimated probability of patient-reported erectile function after treatment with SBRT at 24 months and 60 months.

Age (years)	Predicted 24-month functional erections, % (95% CI)				Age (years)	BMI	Predicted 60-month functional erections, % (95% CI)			
	Baseline HRQoL score						Baseline HRQoL score			
	100	75	50	25			100	75	50	25
60	79 (68–87)	56 (45–66)	30 (21–41)	13 (7–23)	60	25	85 (70–93)	65 (49–79)	39 (22–60)	18 (6–41)
70	72 (60–81)	46 (38–54)	22 (17-29)	9 (5-14)		30	72 (54–84)	46 (33–60)	23 (12-38)	9 (3–23)
						35	53 (30–75)	28 (14–48)	12 (5–27)	4 (1–14)
					70	25	65 (49–79)	39 (31–48)	18 (11–28)	7 (3–16)
						30	46 (30–63)	23 (16-31)	9 (5–15)	3 (1–9)
						35	28 (12–52)	12 (5-24)	4 (1–11)	2 (0–5)

	Parameter Estimate (SE)	OR	95% CI	Wald chi-squared *P*		Parameter Estimate (SE)	OR	95% CI	Wald chi-squared *P*
Intercept	–0.53 (1.57)			0.74	Intercept	7.87 (3.39)			0.020
Age†	–0.42 (0.21)	0.66	0.43–1.00	0.05	Age†	–1.08 (0.39)	0.34	0.16–0.72	0.005
HRQoL‡	0.44 (0.06)	1.55	1.37–1.75	<0.001	HRQoL‡	0.43 (0.010)	1.54	1.27–1.87	<0.0001
					BMI*	–0.79 (0.28)	0.45	0.26–0.78	0.004
AUC	0.81		0.76–0.86		AUC	0.84		0.79–0.88	

*HRQoL, health related quality of life; ADT, androgen deprivation therapy; AUC, area under the curve. Individual model-estimated probability of patient-reported erectile function at 24 months can be calculated using the inverse logistic function (exp(x)/(1 + exp(x)) using the parameter estimates detailed above. *Per 5-point increase; †per 10-year increase; ‡per 10-point increase.*

Table 4 Comparison of observed erectile function at 24-months after SBRT with model-predicted outcomes after other radiation therapies.

	Total†	Baseline		SBRT			EBRT*			Brachytherapy*		
		Functional erections		Actual 24 month functional erections			Model-predicted 24-month functional erections			Model-predicted 24-month functional erections		
	n	*n*	%	*n*	%	95% CI	%	95% CI	*P* vs SBRT	%	95% CI	*P* vs SBRT
All patients	312	157	50	107	34	29–40	37	33–40	0.31	32	28–35	0.30
Baseline erectile function	157	157	100	89	57	50–64	57	54–61	0.39	54	45–64	0.38

*SBRT, stereotactic body radiotherapy; RP, radical prostatectomy; EBRT, conventional external beam radiation therapy; HRQoL, health-related quality of life. *Derived from previously validated model of erectile function after RP and EBRT, respectively (Alemozaffar JAMA 2011). EBRT model includes pretreatment HRQoL, neoadjuvant hormone treatment status (entered as no) and PSA. Brachytherapy model includes pretreatment sexual HRQoL, age, race and body mass index. †Patients with follow-up at 24 months.*

decision-making. Pretreatment age, baseline sexual domain HRQoL and BMI are powerful predictors of long-term erectile function.

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Conflict of Interest

Felix Y. Feng has served on Advisory Boards for Medivation/Astellas, GenomeDx, Celgene, Dendreon, and Sanofi, and has received grant funding from Varian, Medivation/Astellas and Celgene. Todd M. Morgan has served on Advisory Boards for Myriad Genetics, has received research funding from MDxHealth, Myriad Genetics, GenomeDx and a Prostate Cancer Foundation Young Investigator Award. Rohit Mehra is supported by a Prostate Cancer Foundation Young Investigator Award. Sean P. Collins has served as an Accuray Clinical Consultant, and grant funding from the Department of Radiation Medicine at Georgetown University Hospital and educational grant funding from Accuray. Daniel E. Spratt is supported by a Prostate Cancer Foundation Young Investigator Award.

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Abbreviations: ADT, androgen deprivation therapy; aOR, adjusted odds ratio; BMI, body mass index; EBRT, external beam radiation therapy; EPIC-26, Expanded Prostate Cancer Index Composite; HRQoL, health-related quality of life; IMRT, intensity-modulated radiotherapy; IQR, interquartile range; MVA, multivariable logistic regression analysis; NCCN, National Comprehensive Cancer Center; OR, odds ratio; ProtecT, Prostate Testing for Cancer and Treatment trial; RP, radical prostatectomy; SBRT, stereotactic body radiotherapy; SHIM, Sexual Health Inventory for Men; UVA, univariable logistic regression analysis.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1 Sexual domain health related quality of life response rate.
Table S2 EPIC sexual domain health related quality of life.
Figure S1 EPIC definition of erectile function compared SHIM ≥ 16 definition for entire cohort (A) and those with baseline EPIC defined functional erections (B).