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ORIGINAL ARTICLE

Erectile function following brachytherapy, external beam radiotherapy, or radical prostatectomy in prostate cancer patients

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Abstract
Background and purpose For localized prostate cancer, treatment options include external beam radiotherapy (EBRT), radical prostatectomy (RP), and brachytherapy (BT). Erectile dysfunction (ED) is a common side-effect. Our aim was to evaluate penile erectile function (EF) before and after BT, EBRT, or RP using a validated self-administered quality-of-life survey from a prospective registry.
Material and methods Analysis included 478 patients undergoing RP ($n=252$), EBRT ($n=91$), and BT ($n=135$) with at least 1 year of follow-up and EF documented using IIEF-5 scores at baseline, 6 weeks, 6 months, 1 year, and annually thereafter.
Results Differences among treatments were most pronounced among patients with no or mild initial ED (IIEF-5 ≥ 17). Overall, corrected for baseline EF and age, BT was associated with higher IIEF-5 scores than RP (+7.8 IIEF-5 score) or EBRT (+3.1 IIEF-5 score). EBRT was associated with better IIEF-5 scores than RP (+4.7 IIEF-5 score). In patients undergoing EBRT or RP with bilateral nerve sparing (NS), recovery of EF was observed and during follow-up, the differences to BT were not statistically significant. Overall age had a negative impact on EF preservation (corrected for baseline IIEF).
Conclusion In our series, EF was adversely affected by each treatment modality. Considered overall, BT provided the best EF preservation in comparison to EBRT or RP.

Keywords Quality of life · Erectile dysfunction · Brachytherapy · Prostatectomy · Radiotherapy

Erektile Funktion nach Brachytherapie, externer Radiotherapie oder radikaler Prostatektomie bei Prostatakrebs-Patienten

Zusammenfassung
Hintergrund und Ziel Die externe Radiotherapie (EBRT), die radikale Prostatektomie (RP) sowie die Brachytherapie (BT) stellen Behandlungsoptionen für das lokalisierte Prostatakarzinom dar. Die erektile Dysfunktion (ED) ist eine häufige Nebenwirkung dieser Therapien. Unser Ziel war es, die penile erektile Funktion (EF) vor und nach BT, EBRT und RP mit Hilfe eines validierten, vom Patienten ausgefüllten Lebensqualitätsfragebogens aus einer prospektiven Datenbank zu beurteilen.
Material und Methoden Mit einer minimalen Nachbeobachtungszeit von einem Jahr wurden 478 Patienten analysiert, die eine RP ($n=252$), EBRT ($n=91$) oder BT ($n=135$) erhalten hatten und deren EF mit dem IIEF-5-Score vor Therapie sowie nach 6 Wochen, 6 Monaten, nach einem Jahr und danach jährlich ermittelt worden sind.
Ergebnis Die größten therapiebedingten Unterschiede wurden bei Patienten ohne oder nur mit milder initialer ED beobachtet (IIEF-5 ≥ 17). Korrigiert für die EF und das Alter bei Therapie, war die BT mit höherem IIEF-5-Score

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assoziiert als die RP (+7,8 IIEF-5-Score) oder die EBRT (+3,1 IIEF-5-Score). Die EBRT war mit einem besseren IIEF-5-Score assoziiert als die RP (+4,7 IIEF-5-Score). Bei Patienten mit bilateraler nervenschonender RP oder einer EBRT wurde eine Erholung der EF beobachtet; im Verlauf war der Unterschied zur BT nicht mehr statistisch signifikant. Insgesamt hatte ein höheres Alter einen negativen Einfluss auf die Erhaltung der EF (korrigiert für Ausgangs-EF).
Schlussfolgerung In unserer Serie verschlechterte sich die EF durch alle Therapieformen. Insgesamt bot die BT die beste EF-Erhaltung verglichen mit der EBRT oder RP.

Schlüsselwörter Lebensqualität · Erektile Dysfunktion · Brachytherapie · Prostatektomie · Radiotherapie

Prostate cancer remains the most common nondermatologic cancer affecting men in the Western world [1]. The optimal management strategy for patients with newly diagnosed clinically localized prostate cancer remains a matter of debate. Because of a lack of definitive evidence demonstrating superiority in cure rates of one local treatment over another [2, 3], quality-of-life (QoL) parameters are even more important [4–6]. Functional and oncological outcomes should be considered in the evaluation of treatment success [3, 7]. Despite improvements in radiotherapy and prostatectomy, erectile dysfunction (ED) among other adverse effects, is still common [8–11]. Although local treatments focus on cure, there is a need to include ED and possible recovery of potency in their assessment [7, 12], especially since patients' decisions are driven by many factors other than cancer cure [13].

Our aim was to perform an intention-to-treat analysis from prospectively collected data from a single institution on the functional results associated with three different treatment modalities for localized prostate cancer. Patients underwent permanent I-125 low dose rate prostate brachytherapy (BT), external beam radiotherapy (EBRT), or radical prostatectomy (RP). In our study, we evaluated penile erectile function (EF) at baseline, and after treatment with a minimum follow-up of 12 months using a validated self-administered patient quality-of-life survey; we subsequently determined the impact of clinical and treatment parameters. The five-item version (IIEF-5) of the 15-item International Index of Erectile Function (IIEF; [14]) was used to quantify ED [15].

Materials and methods

A total of 478 patients with at least 12 months of follow-up and assessment of pretreatment EF determined using the IIEF-5 (range 1–25; [15, 16]) underwent LDR I-125 BT with a prescribed dose of 145 Gy, EBRT with a median dose of 72 Gy (70–78 Gy; the target of treatment being the prostate and the base of the seminal vesicles) in 3D conventional four-field technique or RP between 2005 and 2013 for mostly low–intermediate risk prostate cancer based on eligibility to these treatments and treatment decision was based on patient preference. Of the 252 radical prostatectomies, 65 were robot-assisted and the others were open. Follow-up data were collected in a prospective registry at 6 weeks, 6 months, 12 months, and annually thereafter. As a part of their follow-up patients were asked to complete an IIEF-5 questionnaire. The median follow-up was 2 years.

The IIEF-5 score was graded as very severe (1–4), severe (5–7), moderate (8–11), mild to moderate (12–16), mild (17–21), and no ED (22–25) based on the published classification [14]. In addition, a cut-off score of 17 was used to differentiate no-to-mild ED and worse ED. An age of 65 years, the median of our cohort, was used to differentiate younger from older patients.

Statistical analysis

Multinomial regression was used to explore the relationship between age, EF, and the choice of treatment. To examine the relationship between treatment and EF, linear mixed models with a random slope and intercept were used, adjusted for baseline EF and current age (<65 vs. ≥ 65 years). Linear models were used to examine the effect of treatment on EF scores at 1, 2, and 3 years. Adjusted confidence intervals for differences between the treatments were computed from the regression models, and adjusted using the Holm correction [17].

All analyses were performed in the R programming language (version 3.0.2; [18]). The package lme4 [19] was used to estimate the mixed models, while the multcomp package [20] was used to compute the *p*-values and confidence intervals. Box-and-whisker plots were used to represent the distribution of variables. Median values were denoted by a thick line, the box represented the upper and lower quartile. The vertical lines denote maximum and minimum values, excluding outliers. Outliers were defined as more than 3/2 of upper quartile or less than 3/2 of lower quartile and were denoted as points. The database was approved by the local ethics committee (Ethics Committee St. Gallen).

Results

A summary of baselines characteristics is provided in Table 1. Younger patients and patients with better baseline EF were more likely to undergo BT than RP and more likely to undergo RP than EBRT. There was no statistically significant interaction between age and baseline IIEF-5 score in terms of treatment choice (data not shown). Androgen

Table 1 Summary statistics at baseline by type of treatment

Variable	RP	BT	EBRT	All
n	252	135	91	478
Age, years (median, range)	64.5 (43.6–77.1)	63.3 (48.8–76.4)	72.0 (52.7–84.0)	65.0 (43.6–84.0)
PSA, ng/ml (median, range)	8.8 (0.2–59.0)	6.2 (0.1–20.6)	4.9 (0.1–36.0)	7.1 (0.1–59.0)
Gleason score (median, range)	7 (4–9)	6 (4–7)	7 (4[a]–9)	6 (4–9)
T stage, *n* (%)				
T1	131 (52.0%)	89 (65.9%)	37 (41.1%)	257 (53.9%)
T2	121 (48.0%)	46 (34.1%)	45 (50.0%)	212 (44.4%)
T3	0 (0%)	0 (0%)	8 (8.9%)	8 (1.7%)
IIEF-5 score (median, range)	19.0 (1.0–25.0)	21.0 (1.0–25.0)	10.0 (1.0–25.0)	19.0 (1.0–25.0)

n number of patients, *BT* brachytherapy, *RP* radical prostatectomy, *EBRT* external beam radiotherapy. *IIEF-5* international index of erectile function.

[a]In four patients Gleason score could not be determined because prostate cancer was diagnosed based on cytology.

deprivation therapy was registered in less than 5 patients per treatment group during the first year after treatment, a few of these patients had started ADT before treatment (neoadjuvant, leading to low pre-treatment values). Only 17 patients were taking medication for ED during the whole follow-up period; 12 in the radical prostatectomy group and 5 in the brachytherapy group. The available IIEF-5 entries were 429, 358, and 275 at 1, 2 and 3 years, respectively, with similar drop-out rates across all patients groups and treatments.

While all treatment modalities were associated with a decrease in EF, the course of EF scores over time revealed a divergent effect (Fig. 1). Even after adjusting for baseline EF and age, the course of EF differed significantly depending on treatment modality. BT resulted in higher EF scores compared to RP and EBRT, while EBRT yielded higher EF scores compared to RP (Table 2 and 3).

Age was an important clinical predictor regarding the preservation of potency; thus, increasing age was associated with lower EF scores (Fig. 2). However, when analyzed separately for patients with no or mild ED at baseline (IIEF-5 ≥ 17) or worse, age was a significant predictor only for patients with worse ED (IIEF-5 < 17; Table 2).

For patients with mild to no ED (IIEF-5 ≥ 17) at baseline, differences in EF according to treatment modality persisted. Patients who received BT had IIEF-5 scores that were on average 9.1 points higher than those treated with RP, while patients treated with EBRT had IIEF-5 scores that were on average 6.9 points higher than those who received RP. We also observed a small, slightly nonsignificant difference between the BT and EBRT patients favoring the BT patients (Table 2).

Differences between treatments were smaller but nonetheless significant among patients with worse ED (IIEF-5 < 17) at baseline. Thus, those treated with BT had an IIEF-5 that was on average 4.6 and 2.7 points higher during overall follow-up than that in patients treated with RP and EBRT, respectively. Patients treated with EBRT had an IIEF-5 that was on average 1.8 higher than that in patients treated with RP (Table 2).

Nerve sparing (NS) was used in 45% of radical prostatectomies. Among patients treated with RP, there were no statistically significant differences in IIEF-5 between those receiving unilateral or no NS, even after adjusting for IIEF-5 at baseline and age (Table 2). However, patients receiving bilateral NS had a significantly higher IIEF-5 than patients receiving both no or unilateral NS. For patients with mild to no ED at baseline, we observed a 0.7 point higher IIEF-5 among those receiving unilateral vs no NS, and a 4.4 point higher IIEF-5 comparing patients receiving a bilateral and no NS. Among patients with a poor EF, there were no significant differences between any of the nerve sparing strategies (Table 2; Fig. 3).

For younger RP patients undergoing bilateral NS, recovery at 3 years after treatment was comparable to recovery for younger patients undergoing EBRT (Fig. 2). Thus, compared to baseline, younger RP patients undergoing bilateral NS had a mean decrease in EF of −4.4 (95% CI −8.1 to −0.8), compared to younger BT patients with a decrease of −5.3 (95% CI −6.9 to −3.6) and younger EBRT patients with a decrease of −3.8 (95% CI −13.2 to 5.6). Generally, in patients with moderate to very severe posttreatment ED no improvement was observed (Fig. 3).

When 1-, 2-, and 3-year IIEF-5 scores were compared with baseline scores a stronger preservation of EF was observed among patients undergoing EBRT or BT as compared with RP without bilateral NS, even after adjusting for baseline EF and age. At the 3-year follow-up EBRT and RP with bilateral NS were associated with worse EF than BT, but this difference was not statistically significant (Table 3).

Discussion

Our study results revealed that in a large proportion of men who undergo therapy with curative intent for localized prostate cancer, ED will occur as an adverse effect. In our series, ED was more frequent after RP relative to EBRT or BT, with a proportion of younger patients showing recovery, independent of treatment modality. Overall, the best erectile function preservation throughout follow-up, independent of age, was provided by BT. RP with bilateral NS and EBRT were associated with good recovery in young patients with good baseline EF.

Table 2 Linear mixed model with random slope and intercept for erectile function (*EF*) at 1.5–36 months for all patients (*upper part* of table) and RP patients only (*lower part* of table). Confidence intervals for differences between the three treatments were adjusted using the Holm correction. Values show estimate and 95 % confidence interval (*95% CI*)

Predictor	All		No or mild ED (IIEF-5≥17)		Worse ED (IIEF-5<17)	
	Estimate	95 % CI	Estimate	95 % CI	Estimate	95 % CI
Baseline EF	0.411	0.346–0.476	0.650	0.410–0.890	0.315	0.209–0.422
Age (≥65)	−1.446	−2.411 to 0.482	−0.961	−2.250 to 0.327	−1.866	−3.068 to −0.665
BT vs. RP	7.799	6.564–9.034	9.092	7.506–10.677	4.573	2.877–6.269
EBRT vs. RP	4.740	3.226–6.254	6.929	4.459–9.398	1.845	0.271–3.419
BT vs. EBRT	3.059	1.348–4.771	2.163	−0.419 to 4.745	2.728	0.767–4.690
Intercept	−0.888	−0.699 to 2.155	−7.036	−12.274 to −1.797	1.9564	0.487–3.426
Predictor	**All RP**		**No or mild ED (IIEF-5≥17)**		**Worse ED (IIEF-5<17)**	
	Estimate	**95 % CI**	**Estimate**	**95 % CI**	**Estimate**	**95 % CI**
Baseline EF	0.174	0.092–0.257	0.058	−0.238 to 0.354	0.213	0.081–0.345
Age (≥65)	−1.358	−2.454 to −0.263	−1.114	−2.610 to 0.382	−1.764	−3.100 to −0.428
unilateral vs. no NS	0.370	−1.226 to 1.966	0.683	−1.452 to 2.818	0.013	−2.118 to 2.143
bilateral vs. no NS	3.302	1.527–5.076	4.391	2.016–6.766	0.983	−1.296 to 3.262
bilat. vs. unilateral	2.932	0.870–4.993	3.708	1.005–6.411	0.971	−1.775 to 3.716
Intercept	2.503	0.804–4.202	4.596	−1.705 to 10.898	2.707	0.913–4.501

BT brachytherapy, *RP* radical prostatectomy, *EBRT* external beam radiotherapy. *IIEF-5* international index of erectile function, *ED* erectile dysfunction, *EF* erectile function, *NS* nerve sparing.

The optimal treatment for men with newly diagnosed clinically localized prostate cancer remains up for debate, which is due to a lack of contemporary prospective randomized studies comparing efficacy and side effects incorporating different therapies. Besides active surveillance for low-risk prostate cancers, EBRT, BT, and RP are all associated with good long-term cancer control in early stage disease [21]. During the last decade increasing attention has focused on the relative toxicities of treatments in an effort to decrease treatment-related morbidity. Patient decisions are often driven not by a focus on cancer cure, but by side effects and personal perceptions, including fear [13, 21]. This underlines the importance of outcomes beyond survival. In addition to our investigation, several studies have shown, albeit in retrospective nonrandomized series, a negative influence on sexual function after completion of prostate cancer treatment.

Sanda et al. [22] conducted a prospective multicenter evaluation assessing outcomes from 1201 patients and 625 spouses or partners before and after RP, BT, or EBRT. They noted that sexual QoL was adversely affected after each treatment as compared with baseline [22]. Besides being modality dependent, the etiology of posttreatment ED is considered to be multifactorial. The wide ranges of reported ED likely reflect differences in follow-up, patient selection, treatment technique, and the mode of data collection. However, even within trials the range of outcomes can vary considerably, in a population-based analysis by Carlsson et al. [11], odds ratios favored radiotherapy over RP for erectile dysfunction (1.56 vs. 2.29), however with an overlap in confidence intervals. Unfortunately, similar to cancer outcomes, little information exists in terms of randomized trial data for the evaluation of sexual QoL measures following RP, BT, or EBRT.

RP is known to cause immediate ED, after which recovery of potency typically occurs slowly or not at all [23, 24]. Unilateral nerve-sparing was performed in 21 % of our patients undergoing surgery and 24 % received bilateral NS. The high incidence of ED after RP in our study is in accordance with data from a large randomized trial conducted by Wilt et al. [25] who reported an incidence of 81.1 % ED after nerve sparing surgery relative to 44.1 % in the observational arm. In a recent paper, Montorsi et al. [26] reported data from a randomized trial regarding the effects of tadalafil treatment on recovery of EF following bilateral nerve-sparing RP. After bilateral nerve-sparing RP, 20.9, 16.9, and 19.1 % of patients (mean age 57.9 years; follow-up 9–13.5 months) in the tadalafil once daily, on demand, and placebo groups, respectively, achieved IIEF-5 scores ≥22 after a 6-week drug-free washout. An adjuvant radiotherapy trial (South Western Oncology Group 8794; [9]) indicated that only 7 % of men had intact EF function postprostatectomy and preradiotherapy. Summarizing these trials, it can be assumed that about 80–95 % of patients may suffer from ED immediately after RP.

ED is also a common sequelae of RT for prostate cancer, affecting approximately 35–55 % of patients after EBRT [27–29] and 25–50 % after BT [30–33]. Using a patient-administered validated QoL instrument, Merrick et al. [31] showed that BT-induced ED occurred in 50 % of patients

Table 3 Linear model adjusted for baseline erectile function (*EF*) and age with EF at 12, 24, and 36 months as dependent variables. Values show estimate and confidence intervals (*CI*) for differences between the treatments, which were adjusted using the Holm correction

Comparison	EF at 12 months estimate (95% CI)	EF at 24 months estimate (95% CI)	EF at 36 months estimate (95% CI)
BT vs. EBRT	3.568 (1.167–5.969)	3.021 (0.300–5.743)	1.035 (−2.580 to 4.651)
BT vs. No NS	8.901 (6.927–10.876)	7.811 (5.696–9.926)	6.456 (3.775–9.138)
BT vs. unilateral NS	8.334 (5.688–10.980)	7.106 (4.044–10.168)	7.664 (3.533–11.796)
BT vs. bilateral NS	4.522 (1.427–7.617)	3.271 (−0.151 to 6.694)	2.923 (−1.459 to 7.305)
EBRT vs. no NS	5.333 (3.078–7.587)	4.790 (2.259–7.320)	5.421 (2.058–8.784)
EBRT vs. unilateral NS	4.766 (1.795–7.736)	4.085 (0.567–7.603)	6.629 (1.792–11.467)
EBRT vs. bilateral NS	0.953 (−2.462–4.369)	0.250 (−3.616–4.116)	1.888 (−3.107–6.882)

BT brachytherapy, *RP* radical prostatectomy, *EBRT* external beam radiotherapy. *IIEF-5* international index of erectile function, *NS* nerve sparing.

at 3 years. In 2014, Ong et al. [33] reported outcomes for 366 potent (IIEF ≥17) patients undergoing BT with EF measured by IIEF-5. At 2 and 5 years, the prevalence of moderate–severe ED was 46 and 53%, respectively. Following permanent prostate BT, Taira et al. [34] reported a 7-year actuarial rate of potency preservation of 55.6%, with a median postimplant IIEF of 22 in potent patients. Potent patients were statistically younger, had a higher pre-implant IIEF, were less likely to be diabetic, and were more likely to report nocturnal erections [34]. A matched-pair study compared erectile dysfunction between patients undergoing dose-escalated image-guided radiotherapy (IMRT) and high dose-rate interstitial brachytherapy (HDR) revealed no overall difference in erectile function with a 2-year median follow-up [35].

Few prospective series, comparing different treatment modalities, have been reported using validated QoL instruments and incorporating pretreatment functional data. For example, Litwin et al. [36] evaluated 580 men with clinically localized prostate cancer who were undergoing RP ($n=307$), EBRT ($n=78$), or BT ($n=90$). These investigators found that men who underwent RP had worse sexual function than either radiation cohort. However, beyond 8 months after treatment the proportion of men reporting severe sexual bother did not differ significantly among treatment groups, largely due to an improvement in the sexual bother score among RP patients over time. Data from the Spanish Multicentric Study of Clinically Localized Prostate Cancer [37] showed that sexual deterioration was greater among surgical patients. Few studies have reported on long-

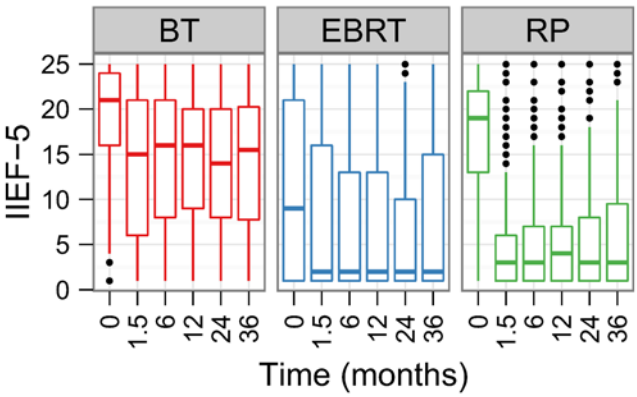

Fig. 1 Boxplots of IIEF-5 scores at baseline and follow-up for different treatment modalities. *RP* radical prostatectomy, *BT* brachytherapy, *EBRT* external beam radiotherapy

term functional outcomes involving >10 years follow-up after different treatment modalities. In 2013, the Prostate Cancer Outcomes Study [8] reported on data from a cohort comprising 1655 men in whom localized prostate cancer had been diagnosed in 1994 or 1995, between the ages of 55 and 74 years, and who had undergone either surgery (1164 men) or EBRT (491 men). Patients undergoing RP were more likely to have ED at 2 years (OR 3.46) and 5 years (OR 1.96), but no significant between-group difference was noted at 15 years. Treatment-related long-term effects on ED should be discussed with caution. The Massachusetts Male Aging Study [38] showed that the incidence rate of ED in the normal male population between 60 and 69 years of age was 4.6% per year.

In concordance with previous trials [39–41], in our study age at diagnosis was found to be an important clinical predictor for potency preservation; however, when adjusted for a baseline IIEF-5 of at least ≥17 (no/mild ED), age was no longer an adverse factor (Table 2). We demonstrated that preservation of EF based on baseline IIEF scores was dependent on treatment modality. At the 1-year follow-up, the treatment-related difference in occurrence of ED was most pronounced in patients with good baseline EF, favoring BT and EBRT relative to RP.

There were a number of limitations associated with the current study. First, although the data were collected prospectively, it was not a randomized trial. Second, the sample size of this prospective, single-center study was limited as compared with the sample sizes evaluated in other series, especially those with single arms. Third, the follow-up in this investigation was limited and a reliable estimation regarding EF beyond the limited follow-up time was impossible.

Improvements and developments in treatments including modern IMRT techniques and prostatectomy techniques, including their learning curves, are not addressed in this report.

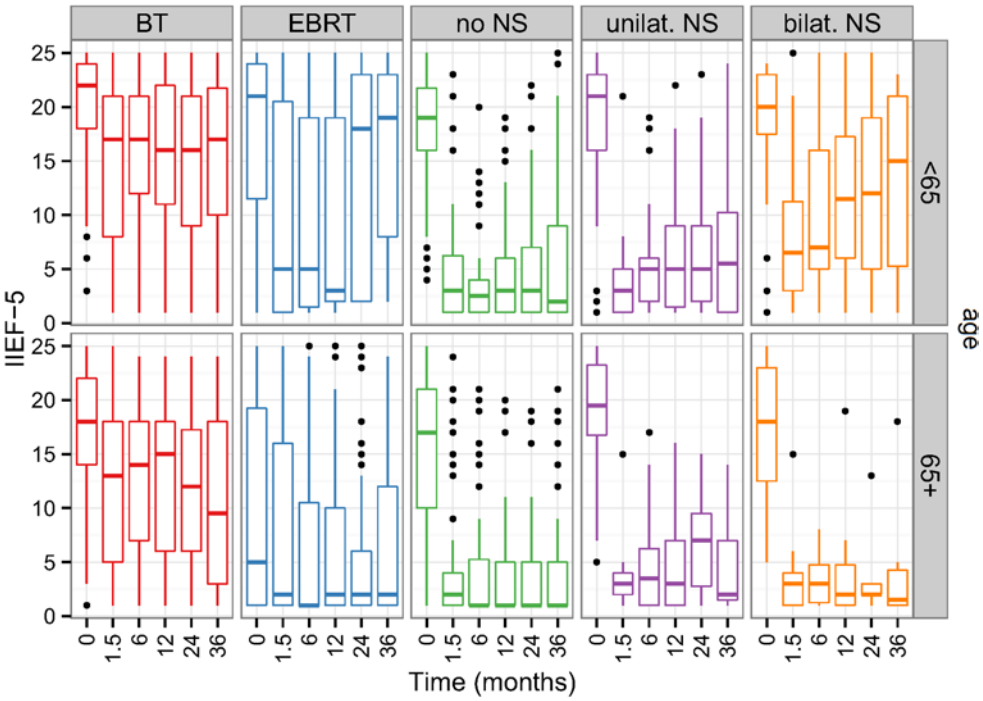

Fig. 2 IIEF-5 -scores for baseline (preoperative) EF and during follow-up for the different treatment modalities and nerve sparing strategies. Generally, the best EF preservation was observed in patients undergoing BT. Young patients undergoing EBRT or bilateral NS RP displayed partial EF recovery during follow-up. *EF* erectile function, *RP* radical prostatectomy, *BT* brachytherapy, *EBRT* external beam radiotherapy, *NS* nerve sparing

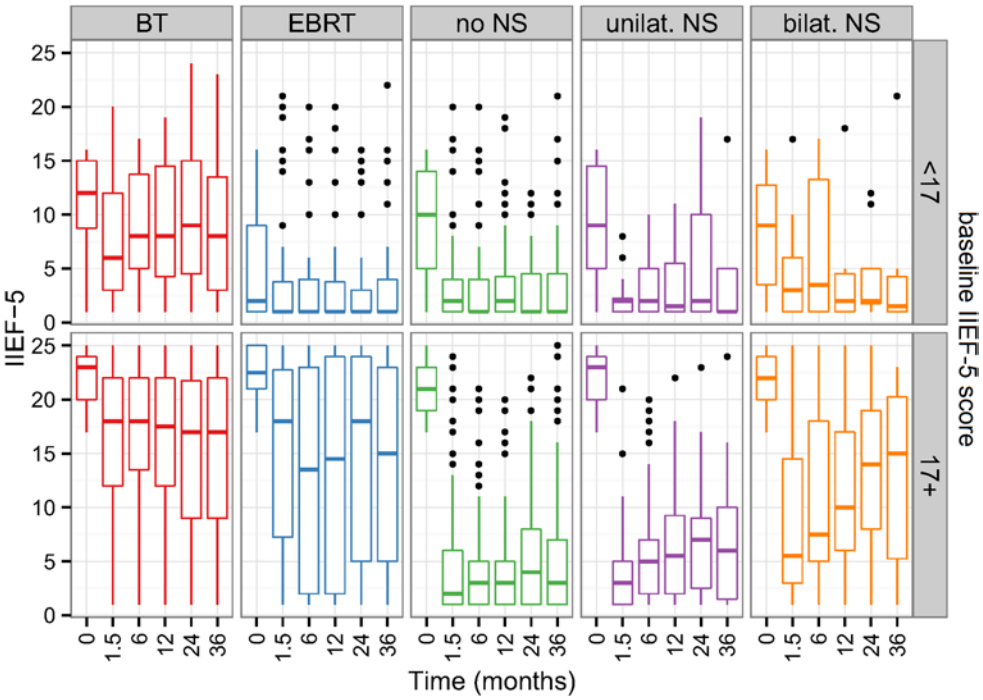

Fig. 3 Boxplots of IIEF scores for baseline (preoperative) erectile function and during follow-up for different treatment modalities. Patients with worse baseline EF generally did not recover. *EF* erectile function, *RP* radical prostatectomy, *BRA* brachytherapy, *EBRT* external beam radiotherapy, *unilat*. unilateral, *bilat*. bilateral, *NS* nerve sparing

In addition, prospective data collection did not include other risk factors that may be associated with erectile function, such as smoking history, concomitant medication, diabetes mellitus, or other comorbidities [42–45]. Patient expectations and fears are also relevant for decision making and subjective outcome evaluation; these were not addressed [13]. Details of dose distribution known to be relevant, such as the dose to the penile bulb were also not included [46]. Currently many centers are implementing IMRT in prostate cancer [47] which has been shown to be associated with better long-term erectile function [48]. Considering all these shortcomings, a risk for bias cannot be excluded; unknown factors may have influenced treatment decision, baseline ED as well the effect of individual treatments on EF.

Our current study also had a number of notable strengths. First, evaluation was performed using a validated QoL instrument and incorporated pretreatment functional data. In comparison to many other series we were able to include

three treatment modalities (BT, EBRT, and RP). The median follow-up was 24 months. According to the literature the follow-up should be about 24 months, after which time the development of ED tends to stabilize, at least for the following few years [8, 27, 29, 49]. Both surgical and radiotherapy patients were evaluated during the same time period with the same standardized questionnaire at the same institution.

Conclusion

In our series, relative to baseline, EF was adversely affected by each treatment modality. EF was best preserved after BT, remaining superior to EBRT and RP during 36 months of follow-up. EBRT had slightly better outcomes when compared with RP, this difference being most pronounced when patients undergoing RP did not receive bilateral nerve sparing. The treatment-related differences in occurrence of ED was most pronounced in younger patients (<65 years of age) with a good baseline EF favoring BT over other modalities. Independent of age, patients with good baseline function had the best EF preservation with BT. Although not conclusive, these data enhance our existing understanding of treatment-induced ED, which is essential when counselling patients on their treatment options.

Compliance with ethical guidelines

Conflict of interest P.M. Putora, D. Engeler, S.R. Haile, N. Graf, K. Buchauer, H.P. Schmid, and L. Passwilm state that there are no conflicts of interest.

All studies on humans described in the present manuscript were carried out with the approval of the responsible ethics committee and in accordance with national law and the Helsinki Declaration of 1975 (in its current, revised form).

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