Quality of Life in Patients with Low-Risk Prostate Cancer. A Comparative Retrospective Study: Brachytherapy Versus Robot-Assisted Laparoscopic Prostatectomy Versus Active Surveillance

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Abstract

Purpose: To investigate the quality of life (QoL) after different treatment modalities for low-risk prostate cancer, including brachytherapy, robot-assisted laparoscopic prostatectomy (RALP), and active surveillance (AS) with validated questionnaires.

Materials and Methods: From a prospective database, we selected a total of 144 men with low-grade localized prostate cancer including 65 (45.1%) patients with RALP, 29 (20.2%) with brachytherapy, and 50 (34.7%) whose cancer was managed with AS. QoL was routinely evaluated with validated questionnaires: The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30), EORTC-QLQ-Prostate Module (PR)25, International Index of Erectile Function (IIEF)-15, International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) with a minimum follow-up of 1 year.

Results: In comparison with baseline scores, the brachytherapy group showed a significant decrease of QoL domain scores of voiding complaints ($P=0.010$), use of incontinence aids ($P=0.011$), sexual functioning domain ($P=0.011$), and erectile function ($P\leq 0.001$). In the RALP group, sexual function ($P\leq 0.001$), incontinence ($P\leq 0.001$), and erectile function were significantly affected. A decrease in sexual function was observed in 71% of men after RALP and 59% after brachytherapy. In 30% of men under AS, a decrease of erectile function score during follow-up was reported. Overall, no significant decrease in general QoL was observed neither for men under AS nor for men treated by brachytherapy or RALP. Clinical factors such as age, prostate size, prostate-specific antigen level, and nerve preservation during RALP were nonpredictive of overall QoL after treatment for the individual patient ($P=0.676$).

Conclusion: Patients with low-risk prostate cancer who are treated with brachytherapy or RALP report deterioration of QoL of specific domains such as voiding, continence, and sexual functioning in comparison with AS patients. A decrease of erectile function was also observed during AS. Overall QoL was similar for all three treatments options.

Introduction

CANCER-SPECIFIC SURVIVAL IN MEN with low-risk prostate cancer is good. In men over age 70, the risk of dying from a newly diagnosed low-risk (prostate-specific antigen [PSA] level <10 ng/mL, Gleason score [GS] <7) prostate cancer is less than 10%.¹

For low-grade localized prostate cancer, there are different kinds of treatment modalities including brachytherapy, radical prostatectomy, and active surveillance (AS). Radical

prostatectomy and brachytherapy are known to have effects on quality of life (QoL) in psychological and physical domains.² Many studies have described side effects of radical prostatectomy and brachytherapy, including sexual functions or urinary and bowel problems.^{3,4}

Men with low-risk prostate cancer are five times more likely to die of other diseases, and recent data from the randomized Prostate Cancer Intervention Versus Observation Trial show that 12-year survival in this group of men is not improved by local treatment such as prostatectomy compared

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with AS.⁵ QoL in men after local treatment may deteriorate in particular, because most are asymptomatic from their prostate cancer at baseline. Many men therefore opt for AS.

AS may cause side effects, mostly psychological, such as anxiety and distress, and at least 30% of men will be treated with progressive disease during the initial years of AS.^{6,7} For the decision-making process, consulting the patients about the possible outcomes of treatment alternatives in localized prostate cancer and comparison of all aspects of current treatments are required. Hayes and associates⁸ estimated that AS may provide the most quality adjusted life years when compared with surgery or brachytherapy.

In the current study, the general and disease-specific prospectively sampled QoL between three different approaches to low-risk localized prostate cancer including brachytherapy, robot-assisted laparoscopic prostatectomy (RALP), and AS in patients from a single institute were compared.

Materials and Methods

Setting

This study was performed at the urology department of the Antoni van Leeuwenhoek (AvL) Hospital in Amsterdam, the Netherlands. The eligible patients records were extracted from the prospective prostate cancer database at the AvL Hospital.

Study design and participants

From the original database of the AvL hospital for patients with prostate cancer, which consisted of 2615 patients with prostate cancer since 2004, men with low-risk localized prostate cancer according to the D'Amico risk classification of prostate cancer (PSA level <10 ng/mL, cT_{1-2a}, and GS ≤6, number of positive biopsy core ≤2) were selected. Men who filled out the questionnaires pre- and post-treatment with a follow-up period of at least 1 year were included. After diagnosis, these patients had three different treatment options: Brachytherapy, RALP, or AS. For the QoL analysis, patients treated with external beam radiation therapy (EBRT) were excluded, because only a small number of low-risk patients were available. Selection of treatment options was based on the following aspects: Tumor characteristics, level of serum PSA, size of the prostate, number of positive biopsies, Gleason score, age of the patient, voiding complaints, levels of anxiety of the patient concerning the prostate cancer diagnosis, and comorbidity.

Among a total of 144 patients, 65 (45.1%) patients treated with RALP, 50 (34.7%) with AS, and 29 (20.2%) with brachytherapy were eligible for the analysis. A flowchart of patient selection according to eligibility criteria is shown in Figure 1. The QoL outcome measures of patients with localized prostate cancer with their baseline QoL measures before treatment were compared.

Data collection

Patients with localized prostate cancer completed validated questionnaires between 2004 and 2011. These questionnaires were routinely sent by regular mail or e-mail before patients visited the hospital for the first time. After treatment, the patients completed the same questionnaires again at regular intervals of 6 months. To evaluate QoL, the overall QoL

questionnaire (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 [EORTC-QLQ-C30]), prostate-specific QoL questionnaire (EORTC-QLQ-Prostate Module [PR]25), sexual functioning questionnaire (International Index of Erectile Function [IIEF]-15), and the incontinence questionnaire (International Consultation on Incontinence Questionnaire Short Form [ICIQ-SF]) were used.

Questionnaires

EORTC-QLQ-C30/PR25 questionnaires. EORTC-QLQ-C30 is a questionnaire used to evaluate the overall QoL of cancer patients. Questions are grouped as domains of QoL including the physical, social, emotional, and cognitive functions, vitality/fatigue, pain, general health status, overall QoL, and life satisfaction. The last two questions (29th and 30th questions) are used for the evaluation of overall QoL.

EORTC-QLQ-PR25 is a questionnaire based on prostate cancer-specific QoL. It constitutes 25 questions. This form is composed of six domains to evaluate the voiding complaints, problems from incontinence, bowel problems, metabolic and endocrinologic effects, sexual activity, and sexual functions of the patients.

IIEF-15 questionnaire. Sexual functions of the patients were evaluated under the components of erectile function (EF), intercourse satisfaction (IS), orgasmic function (OF), overall satisfaction (OS), and sexual desire (SD) with IIEF-15. Patients with an IIEF-EF score of 19 and above are defined as having a normal or mildly affected erectile function.

ICIQ-SF questionnaire. ICIQ-SF is a questionnaire composed of four questions evaluating the severity of incontinence and QoL.

Statistical analysis

The questionnaires were checked for completeness, and baseline QoL questionnaires were compared with follow-up QoL questionnaires. Patient characteristics and questionnaire scores among the three groups were compared with the nonparametric Kruskal-Wallis test, followed by a Mann-Whitney analysis to specify differences among groups. To examine the relationship between baseline QoL domains and the independent variables, age, and size of the prostate, we used the nonparametric Spearman correlation coefficient test. The nonparametric Wilcoxon signed rank test was used to test whether there were significant differences between baseline QoL and follow-up QoL within the three groups. To observe significant differences in QoL domains of individual patients, we used the chi-square test to compare patients who had a decline of specific QoL domains with patients who had an improvement or equal score of specific QoL domains. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 20.0. The level of significance is accepted as $P < 0.05$.

Results

Median follow-up of the brachytherapy group was 40 months (12.3–169.1 months); the RALP group was 21 months (12–54.4 months) and the AS group was 29.7 months (12–75.5 months) ($P = 0.001$). A statistical significance was observed

FIG. 1. Flowchart of patient selection of the Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital (NKI-AvL) Hospital prostate cancer database. BT = brachytherapy; RALP = robot-assisted laparoscopic prostatectomy; AS = active surveillance; iPSA = initial prostate-specific antigen.

between the follow-up periods of RALP and brachytherapy ($P=0.001$) groups and also between the RALP and AS groups ($P=0.007$).

Patient characteristics at diagnosis according to treatment groups are shown in Table 1. The mean age of the entire population was 61.9 ± 6.6 (range 44–85) years. The mean age of the brachytherapy and AS group was higher than for the RALP group ($P=0.002$).

The mean initial prostate-specific antigen (iPSA) level of the entire population was 6.3 ± 2.2 ng/mL. There was no significant difference between the three groups for iPSA ($P=0.087$) and number of positive biopsies ($P=0.501$).

The mean prostate volume of the entire population was 50.5 ± 22.7 (range 16–165) cc. The mean prostate volume in the brachytherapy group was not significantly different from the RALP group ($P=0.629$), but was higher for the AS group ($P=0.008$).

Baseline QoL

At baseline, the only significant differences in sexual function QoL scores were observed between the RALP and AS group: Men in the RALP group had a significantly higher IIEF-15 ($P=0.015$), IIEF-erectile function (EF) ($P=0.006$), IIEF-orgasmic function (OF) ($P=0.023$), and IIEF-intercourse satisfaction (IS) score ($P=0.025$) (Table 2). There were no significant differences seen among groups for PR25 domains and overall QoL between the groups.

Correlation between age and prostate size vs QoL measures

There was a significantly inverse relation between age and QoL measures including sexual functions (PR domain 5), sexual activity (PR domain 6), IIEF-15 and its subdomains of IIEF-EF, IIEF-OF, and IIEF-IS in all groups. A positive relation was observed between the age and overall QoL (EORTC-QLQ-C-30 domain 15). No relation was found between prostate size and any domain score.

Comparison of baseline QoL measures with follow-up

The graphic representation of the differences (%) of the QoL domains according to the patient groups is shown in Figure 2. The values and comparisons of QoL measures during follow-up are shown in Table 2.

RALP. In the RALP group, there was significant deterioration in the domains of sexual function and use of incontinence aids (PR domains 2 and 6). A significant decrease was found in the domain scores of IIEF-15 total, IIEF-EF, IIEF-OF, IIEF-IS, IIEF-OS, and ICIQ-SF total score.

Brachytherapy. In the brachytherapy group, a significant deterioration in the domain scores of voiding complaints, the use of incontinence aids, metabolic and endocrinological effects, and sexual functioning (PR domains 1, 2, 4, and 6) was

TABLE 1. PATIENT CHARACTERISTICS AT DIAGNOSIS BY TREATMENT GROUP

Characteristics total (n = 144)	BT (n = 29)	(%)	RALP (n = 65)	(%)	AS (n = 50)	(%)	Total	P value ^a
Age ± SD (years)	63.8 ± 5.5 (49–76)		59.5 ± 6.1 (44–73)		63.8 ± 6.9 (49–85)		61.9 ± 6.6 (44–85)	0.000
Initial PSA ± SD (ng/ml)	6.8 ± 1.9 (1.7–9.6)		6.4 ± 2.1 (1.80–10)		5.8 ± 2.4 (1.10–9.70)		6.3 ± 2.2 (1.10–10)	0.087
Size prostate ± SD (cc)	44.1 ± 13.6 (25–68)		46.7 ± 19.6 (16–107)		59.3 ± 27.8 (20–165)		50.5 ± 22.7 (16–165)	0.008
Number of positive biopsies							1.4 (1–2)	0.501
1 biopsy	17	(58.6)	29	(44.6)	30	(60)	76	
2 biopsies	10	(34.5)	28	(43.1)	18	(36)	56	
Missing	n = 2	(6.9)	n = 8	(12.3)	n = 2	(4)	n = 12	
Gleason-score	n = 29	(%)	n = 65	(%)	n = 50	(%)		
Grade 6	29	100	65	100	50	100		
Clinical stage (cT-stage)							Total (%)	
cT _{1c}	14	(48.3)	35	(53.8)	33	(66)	82 (56.9)	
cT _{2a}	15	(51.7)	30	(46.2)	17	(34)	62 (43.1)	

^aKruskal-Wallis test ($P < 0.05$).

BT = brachytherapy; RALP = robot-assisted laparoscopic prostatectomy; AS = active surveillance; SD = standard deviation; PSA = prostate-specific antigen.

found as well as measures of sexual functioning including IIEF-15 total, IIEF-EF and IIEF-SD impaired during follow-up.

AS. In the AS group, there was only a significant decrease in QoL for the domain score of use of incontinence aids during follow-up compared with baseline (PR domain 2).

There was no significant difference in the percent of patients with a decrease in overall QoL among treatment groups (38% for AS, 32% for RALP, and 30% for brachytherapy, $P > 0.05$). Significant decreases were found in terms of sexual functioning in 30% of the AS group, 71% of the RALP group, and 59% of the brachytherapy group ($P = 0.004$). The deterioration of lower urinary tract symptoms in AS, RALP, and brachytherapy was 43%, 40%, and 58% of the patients, respectively ($P < 0.005$).

Clinical factors such as age, prostate size, PSA level, and nerve preservation during RALP were nonpredictive of overall QoL after treatment for the individual patient ($P = 0.676$).

Discussion

The prognosis for patients with low-risk prostate cancer is good even when an initial AS management is considered.⁷ In particular in low-risk disease, AS was shown to maintain QoL without compromising disease-specific survival.^{5,8} In addition, QoL may be negatively affected by treatment options such as brachytherapy and RALP. We hypothesized that patients in the AS group would have a better QoL outcome after an initial period of expectant management compared with the QoL of patients treated with brachytherapy or RALP.

In the current study, a nonsignificant (-1%) decrease was observed in the general health-related QoL of the AS group after treatment with at least a 1-year follow up. A mild increase in overall QoL was found in the brachytherapy and RALP groups compared with baseline values (1.5% and 3.4%, respectively).

Several studies addressed general QoL after management for localized prostate cancer. All reported little impact on overall QoL by local treatment,^{2,9–11} although some reported temporary effects that normalized within 1 year of treatment.¹¹

AS may lead to psychological problems that may affect patients' health-related QoL. Van den Bergh and associates¹² found limited involvement of the patient in the decision of AS, a low score of pretreatment physical health, high anxiety score, and high PSA values as predictive factors of poor outcome of general QoL in an AS population. According to the results of a multicentered international prostate cancer AS study, health-related QoL and patients' anxieties were stable at the first 9 months of AS.¹³ Studies with long follow-up are needed to evaluate the proper effects of AS on health-related QoL. In our study, some of the baseline QoL domains were significantly different between the groups rendering comparison difficult. These differences, however, existed only between men in the RALP and AS groups. Men in the RALP group were younger and had better IIEF-15, IIEF-EF, IIEF-OF, and IIEF-OS scores compared with the AS group. We also found a significant inverse correlation between age and sexual functions. This may explain the low sexual function scores in the AS group. Selection bias to treatment instead of AS in younger men expecting to maintain erectile function with nerve sparing RALP may affect outcome.

TABLE 2. COMPARISON OF BASELINE QoL MEASURES WITH FOLLOW-UP QoL*

Domain	n	Mean baseline QoL (%)	SD	Mean follow-up QoL (%)	SD	% difference	P value ^a
<i>BT</i>							
PR domain 1	27	10.47 (89.7%)	2.92	12.37 (81.8%)	5.14	-7.9%	0.010
PR domain 2	7	0.00 (100%)	0.00	1.14 (71.4%)	0.38	-28.6%	0.011
PR domain 3	28	4.25 (97.9%)	0.44	4.43 (96.4%)	0.69	-1.5%	0.166
PR domain 4	26	6.41 (97.7%)	0.63	6.88 (95.1%)	1.03	-2.6%	0.043
PR domain 5	28	4.15 (64.1%)	1.28	4.07 (65.5%)	1.27	+1.4%	0.562
PR domain 6	19	12.74 (72.8%)	2.21	11.16 (59.6%)	2.93	-13.2%	0.011
IIEF-15	8	52.88 (68.4%)	18.2	42.75 (53.9%)	20.3	-14.5%	0.028
IIEF-EF	10	18.6 (60.7%)	10.4	14.6 (46.9%)	10.2	-13.8%	0.013
IIEF-OF	10	6.90 (69.0%)	3.35	5.40 (54.0%)	3.57	-15%	0.063
IIEF-SD	12	6.92 (61.5%)	2.43	5.25 (40.6%)	1.76	-20.9%	0.035
IIEF-IS	11	6.82 (45.5%)	4.85	5.82 (38.8%)	4.94	-6.7%	0.078
IIEF-OS	11	6.82 (60.2%)	2.52	5.73 (46.6%)	2.72	-13.6%	0.088
ICIQ-SF total	6	0.00 (100%)	0.00	2.00 (90.5%)	4.43	-9.5%	0.180
QLQ-C30-domain 15	28	80.25% (11.63)	16.29	81.77% (11.81)	14	+1.5%	0.568
<i>RALP</i>							
PR domain 1	65	11.42 (85.7%)	3.45	10.94 (87.8%)	2.79	+2.1%	0.372
PR domain 2	26	0.00 (100%)	0.00	1.42 (64.4%)	0.64	-35.6%	0.000
PR domain 3	64	4.42 (96.5%)	0.79	4.34 (97.1%)	0.65	+0.6%	0.536
PR domain 4	60	6.80 (95.6%)	1.73	6.92 (94.9%)	0.98	-0.7%	0.174
PR domain 5	63	4.73 (54.5%)	1.19	4.52 (57.9%)	1.09	+3.4%	0.134
PR domain 6	51	13.53 (79.4%)	2.61	11.73 (64.4%)	2.40	-15%	0.000
IIEF-15	27	55.15 (71.6%)	19.0	41.11 (51.6%)	22.5	-20%	0.000
IIEF-EF	28	24.32 (80.4%)	8.60	16.61 (53.8%)	11.4	-26.6%	0.000
IIEF-OF	28	8.04 (80.4%)	3.26	6.11 (61.1%)	3.52	-19.3%	0.001
IIEF-SD	28	6.71 (58.9%)	1.67	6.21 (52.7%)	2.25	-6.2%	0.176
IIEF-IS	28	9.29 (61.9%)	4.47	7.11 (47.4%)	4.85	-14.5%	0.013
IIEF-OS	27	7.15 (64.4%)	2.68	5.96 (49.4%)	2.99	-15%	0.014
ICIQ-SF total	25	0.68 (96.8%)	1.41	2.4 (88.6%)	3.42	-8.2%	0.038
QLQ-C30-domain 15	65	78.17% (11.38)	16.24	81.57% (11.79)	13.1	+3.4%	0.090
<i>AS</i>							
PR domain 1	40	11.19 (86.7%)	2.89	11.5 (85.4%)	3.49	-1.3%	0.440
PR domain 2	14	0.00 (100%)	0.00	1.07 (73.2%)	0.27	-26.8%	0.000
PR domain 3	40	4.38 (96.8%)	1.17	4.48 (96.0%)	1.06	-0.8%	0.182
PR domain 4	37	6.63 (96.5%)	1.32	6.92 (94.9%)	1.30	-1.6%	0.053
PR domain 5	39	4.36 (60.7%)	1.23	4.33 (61.1%)	1.15	+0.4%	0.850
PR domain 6	33	12.58 (71.5%)	3.49	12.64 (72.0%)	2.79	+0.5%	0.939
IIEF-15	24	42.88 (54.1%)	22.5	41.00 (51.4%)	21.8	-2.7%	0.639
IIEF-EF	25	17.63 (57.3%)	10.7	16.36 (53.0%)	10.5	-4.3%	0.420
IIEF-OF	24	6.28 (62.8%)	3.90	6.04 (60.4%)	3.82	-2.4%	0.637
IIEF-SD	26	5.94 (49.2%)	2.21	5.92 (49.0%)	2.35	-0.2%	0.876
IIEF-IS	25	7.04 (46.9%)	4.85	7.04 (46.9%)	4.74	-0.0%	0.826
IIEF-OS	26	6.41 (55.1%)	2.68	6.00 (50.0%)	2.65	-5.1%	0.431
ICIQ-SF total	28	1.79 (91.5%)	3.72	1.64 (92.2%)	3.59	+0.7%	0.721
QLQ-C30-domain 15	40	83.00% (11.6)	15.27	82.02% (11.84)	16.1	-1.0%	0.647

*The QoL scores are recorded so that 100% reflects the highest and best QoL score and 0% the lowest score. The column % difference shows the % change of QoL score at follow-up.

^aP value: Wilcoxon test ($P < 0.05$). All the significant differences show a decrease in quality of life (QoL).

BT=brachytherapy; SD=standard deviation; QoL=quality of life; PR domain 1: voiding complaints; PR domain 2: use of incontinence aids; PR domain 3: bowel complaints; PR domain 4: metabolic and endocrinological effects; PR domain 5: sexual activity; PR domain 6: sexual functioning; International Index of Erectile Function (IIEF)-15: overall sexual function; IIEF-EF: erectile function; IIEF-OF: orgasmic function; IIEF-SD: sexual desire; IIEF-IS: intercourse satisfaction; IIEF-OS: overall satisfaction; International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF)-total: domain of severity of urine incontinence and quality of life; QLQ-C30 domain 15: Overall quality of life according to the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 questionnaire; RALP=robot-assisted laparoscopic prostatectomy; AS=active surveillance.

FIG. 2. (a–d) Differences (%) in QoL outcome among three treatment groups for each QoL domain. The difference (%) is indicated by decline or by improvement of QoL (X axis). * indicates significant differences of each treatment group per QoL domain. EORTC-QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC-QLQ-PR25=EORTC-QLQ-Prostate Module (PR)25; IIEF=International Index of Erectile Function; ICIQ-SF=International Consultation on Incontinence Questionnaire Short Form.

Randomized controlled trials need to overcome this selection bias. Recently, Crook and colleagues¹⁴ reported health-related QoL of 168 patients who were randomized to radical prostatectomy and brachytherapy in the American College of Surgeons Oncology Group phase III Surgical Prostatectomy Versus Interstitial Radiation Intervention Trial (SPIRIT) with a mean follow-up of 5.3 years. The authors stated that brachytherapy has better functional outcomes (urinary and sexual) and good patient satisfaction. Another study emphasized that the patients who had high expectations about functional outcome had reduced satisfaction.¹⁵ These aspects may affect QoL outcome in particular, considering the fact that even a randomized study can never be conducted in a double-blind fashion.

All studies seem to agree to the point that overall QoL is only marginally affected by treatment choice in patients with low-risk prostate cancer. Functional outcome, however, may differ considerably between treatments.^{2,9–11,14,16} Radical

prostatectomy has negative effects on several aspects of specific QoL including sexual and urinary functions. Technical improvements such as nerve-sparing techniques and robot assistance may help reduce the side effects related to erectile and voiding functions.^{17,18} In a prospective longitudinal study, some domains of QoL including score for cognitive, emotional, and interpersonal relations returned to baseline in the first year after surgery in 71 men who were treated with RALP. The decrease in sexual desire, sexual confidence, and self-esteem, however, was permanent.¹⁹

In the current study, RALP affected many domains of QoL with a mean follow-up period of 1.9 years. The use of incontinence aids and sexual functioning were prominently reduced in the EORTC-PR25 questionnaire. RALP had negative effect on overall sexual functions in IIEF-15 as well IIEF-EF, IIEF-OF, IIEF-IS, and IIEF-OS despite the use of phosphodiesterase-5 inhibitors for penile rehabilitation in the majority of men. In addition, 71% of patients treated with RALP had a decrease in

sexual function scores. Compared with AS and brachytherapy, men in the RALP group showed a higher postoperative ICIQ-SF incontinence score, but fewer men in the RALP group had deterioration of lower urinary tract symptoms.

Radiation therapy (EBRT and brachytherapy) for prostate cancer has detrimental effects on urinary, sexual, and intestinal functions.²⁰ It may cause irritative voiding symptoms (urgency, pollakiuria, and urge incontinence), bowel and rectal symptoms (tenesmus, hematochesia).^{4,21} These symptoms may be observed either during or immediately after treatment. In a retrospective observational study of 143 patients with localized prostate cancer, after brachytherapy 13.2% of patients reported fecal incontinence symptoms affecting daily activities during 2 years of follow-up.²²

Roeloffzen and coworkers²³ demonstrated that the patients treated with brachytherapy have significantly severe urinary symptoms, intestinal symptoms, and pain as well as impaired physical functionality and sexual activity in a 6-year follow-up. They noted that only the changes in emotional and sexual functions were clinically important. Most of the men returned to their baseline health-related QoL within 1 year.²⁴ Sanda and colleagues⁴ prospectively compared the QoL changes of radical prostatectomy, brachytherapy, and EBRT in 1201 prostate cancer patients. In the brachytherapy group, a significant deterioration in urinary symptoms (irritation or obstruction and incontinence) was reported when compared with baseline values. Incontinence after brachytherapy was reported by 4% to 6% of patients at 1 to 2 years after treatment. Eighteen percent of patients in the brachytherapy group reported moderate or worse distress from overall urinary symptoms at 1 year.

In the current study, prostate cancer-specific QoL (PR25 domains) in the brachytherapy group were significantly affected. Significant differences were observed in voiding symptoms, use of incontinence aids, metabolic and endocrinological effects, and sexual functions in the EORTC-PR25 questionnaire. Brachytherapy also had a negative impact on sexual functions according to scores of IIEF-15, IIEF-EF, and IIEF-SD, and 59% of patients had a decrease in sexual function after brachytherapy whereas this percentage was 71% after RALP. No significant difference, however, was noted in terms of gastrointestinal side effects in the brachytherapy group (PR domain 3). These observations support data from the SPIRIT trial that brachytherapy may affect sexual functions to a lesser degree than RALP does.

There are several limitations in our study. The non-randomized setup causes a treatment selection bias. Second, it is important to note that 80% of all patients were referred to our tertiary oncology center. This implies that in the study group, all patients were aware of the diagnosis of prostate cancer at the time they filled in the questionnaires. This may have affected their QoL score. Because all groups were equally informed of the diagnosis of low-risk prostate cancer, we considered the AS group as the control group. The sample size of patients in our analysis was small. Not all patients were eligible, and the response rate to mailed questionnaires was 63%. Another limitation was the fact that comorbidities and age may have affected treatment choice. Men in the AS group were older. Permanent pathologic findings after RALP and different profiles of progression of the disease may affect the QoL and satisfaction. Secondary treatments including adjuvant hormonal therapy or radiotherapy have a negative im-

pact on QoL. Therefore, patients who received adjuvant therapy were excluded from the study for both the brachytherapy as well as the RALP group. Furthermore, no data on QoL effects of delayed local treatment in the AS group were collected. Because an expected 30% of men will need local treatment during the initial years of AS, longer follow-up in the AS group may show alterations in QoL from this treatment.

Conclusion

At baseline, patients treated with AS showed lower physical QoL domains, especially erectile function, compared with men selecting brachytherapy or RALP. Patients selecting AS were also older than patients who received RALP. No difference in overall QoL score changes for men treated with AS, brachytherapy, or RALP were observed. The patients on AS showed relatively stable scores on physical QoL domains during follow-up, while the patients receiving brachytherapy or RALP showed decreasing scores on different measures, especially erectile function and incontinence. In addition, 30% of AS patients had a decrease in sexual functions during the follow-up compared with 59% and 71% for brachytherapy and RALP treated patients, respectively. Deterioration in voiding complaints was not more frequent after brachytherapy (58%) compared with AS (43%) or RALP (40%). The effects of secondary delayed treatments on QoL need further study.

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References

1. Lu-Yao GL, Albertsen PC, Moore DF, et al. Outcomes of localized prostate cancer following conservative management. *JAMA* 2009;302:1202–1209.
2. Brandeis JM, Litwin MS, Burnison CM, Reiter RE. Quality of life outcomes after brachytherapy for early stage prostate cancer. *J Urol* 2000;163:851–857.
3. Johansson E, Steineck G, Holmberg L, et al. Investigators SPCG-4 Investigators. Long-term quality-of-life outcomes after radical prostatectomy or watchful waiting: the Scandinavian Prostate Cancer Group-4 randomised trial. *Lancet Oncol* 2011;12:891–899.
4. Sanda MG, Dunn RL, Michalski J, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. *N Engl J Med* 2008;358:1250–1261.
5. Wilt TJ, Brawer MK, Jones KM, et al. Radical prostatectomy versus observation for localized prostate cancer. *N Engl J Med* 2012;367:203–213.
6. Bergman J, Litwin MS. Quality of life in men undergoing active surveillance for localized prostate cancer. *J Natl Cancer Inst Monogr* 2012;2012:242–249.
7. Bul M, Zhu X, Valdagni R, et al. Active surveillance for low-risk prostate cancer worldwide: The PRIAS study. *Eur Urol* 2013;63:597–603.
8. Hayes JH, Ollendorf DA, Pearson SD, et al. Active surveillance compared with initial treatment for men with low-risk prostate cancer: A decision analysis. *JAMA* 2010;304:2373–2380.

9. Litwin MS, Hays RD, Fink A, et al. Quality-of-life outcomes in men treated for localized prostate cancer. *JAMA* 1995;273:129–135.
10. Lubeck DP, Litwin MS, Henning JM, et al. Changes in health-related quality of life in the first year after treatment for prostate cancer: Results from CaPSURE. *Urology* 1999;53:180–186.
11. Bradley EB, Bissonette EA, Theodorescu D. Determinants of long-term quality of life and voiding function of patients treated with radical prostatectomy or permanent brachytherapy for prostate cancer. *BJU Int* 2004;94:1003–1009.
12. van den Bergh RC, Essink-Bot ML, Roobol MJ, et al. Anxiety and distress during active surveillance for early prostate cancer. *Cancer* 2009;115:3868–3878.
13. van den Bergh RC, Vasarainen H, van der Poel HG, et al. Short-term outcomes of the prospective multicentre 'Prostate Cancer Research International: Active Surveillance' study. *BJU Int* 2010;105:956–962.
14. Crook JM, Gomez-Iturriaga A, Wallace K, et al. Comparison of health-related quality of life 5 years after SPIRIT: Surgical Prostatectomy Versus Interstitial Radiation Intervention Trial. *J Clin Oncol* 2011;29:362–368.
15. Messaoudi R, Menard J, Ripert T, et al. Erectile dysfunction and sexual health after radical prostatectomy: Impact of sexual motivation. *Int J Impot Res* 2011;23:81–86.
16. Downs TM, Sadetsky N, Pasta DJ, et al. Health related quality of life patterns in patients treated with interstitial prostate brachytherapy for localized prostate cancer—data from CaPSURE. *J Urol* 2003;170:1822–1827.
17. Porpiglia F, Morra I, Lucci Chiarissi M, et al. Randomised controlled trial comparing laparoscopic and robot-assisted radical prostatectomy. *Eur Urol* 2013;63:606–614.
18. Asimakopoulos AD, Pereira Fraga CT, Annino F, et al. Randomized comparison between laparoscopic and robot-assisted nerve-sparing radical prostatectomy. *J Sex Med* 2011;8:1503–1512.
19. Thornton AA, Perez MA, Oh S, Crocitto L. A prospective report of changes in prostate cancer related quality of life after robotic prostatectomy. *J Psychosoc Oncol* 2011;29:157–167.
20. Wei JT, Dunn RL, Sandler HM, et al. Comprehensive comparison of health-related quality of life after contemporary therapies for localized prostate cancer. *J Clin Oncol* 2002;20:557–566.
21. Dandapani SV, Sanda MG. Measuring health-related quality of life consequences from primary treatment for early-stage prostate cancer. *Semin Radiat Oncol* 2008;18:67–72.
22. Lamb MN, Trabinino L, Hackford A. Patients' perspectives on fecal incontinence after brachytherapy for localized prostate cancer. *Dis Colon Rectum* 2011;54:615–621.
23. Roeloffzen EM, Lips IM, van Gellekom MP, et al. Health-related quality of life up to six years after (125)I brachytherapy for early-stage prostate cancer. *Int J Radiat Oncol Biol Phys* 2010;76:1054–1060.
24. Lee WR, McQuellon RP, Harris-Henderson K, et al. A preliminary analysis of health-related quality of life in the first

year after permanent source interstitial brachytherapy (PIB) for clinically localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2000;46:77–81.

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Abbreviations Used

AS	= active surveillance
AvL	= Antoni van Leeuwenhoek
EBRT	= external beam radiation therapy
EORTC-QLQ-C30	= The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30
EORTC-QLQ-PR25	= The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Prostate Module 25
GS	= Gleason score
ICIQ-SF	= International Consultation on Incontinence Questionnaire Short Form
IIEF	= International Index of Erectile Function
IIEF-EF	= International Index of Erectile Function erectile function
IIEF-IS	= International Index of Erectile Function intercourse satisfaction
IIEF-OF	= International Index of Erectile Function orgasmic function
IIEF-OS	= International Index of Erectile Function overall satisfaction
IIEF-SD	= International Index of Erectile Function sexual desire
iPSA	= initial prostate-specific antigen
PSA	= prostate-specific antigen
QoL	= quality of life
RALP	= robot-assisted laparoscopic prostatectomy