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Cancer and sexual health: The continuum of care

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Chapter 3: Sexual satisfaction in men suffering from erectile dysfunction after robot assisted radical prostatectomy for prostate cancer: an observational study

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Introduction

Prostate cancer is the second most common cancer among men(1). Robot-assisted radical prostatectomy (RARP) is one of the recommended treatment options for localized prostate cancer with a long-term survival benefit(2). Given the expected long-term survival after RARP, functional outcomes are of utmost importance(3). The most common side-effect of RARP is erectile dysfunction (ED). Reported rates of ED after RARP range between 10 and90%. These wide ranges are due to differences in patient selection, surgical approaches and heterogeneous definitions of ED(4-6). ED is an important post-operative concern for patients, which is known to negatively impact quality of life(7). Additionally, ED is associated with anxiety, depressive symptoms, low self-esteem and diminished intimate relationships with the partner(3, 8). Despite refinement of nerve-saving operative techniques, the introduction of robotic surgery and the combination with penile rehabilitation programs(9, 10), a recent study failed to show an increased likelihood of erectile function recovery after RARP, in the last decade(11). Currently, a great deal of attention is being paid to predicting ED and the chances of long-term improvement of erectile function after RARP(12-16). The overall chance of having adequate erectile function after RARP has been reported to be 35%(17). The most well-known factors for improvement of erectile function include patient's age, comorbidities, nerve-sparing status and preoperative erectile function(18, 19). Information on the probability of improvement of erectile function is important when counseling patients about their expected erectile function and so that they can be offered support if needed.

Patients who reach their baseline erectile function will not necessarily regain sexual satisfaction(20). In addition to ED, sexual changes after RARP include loss of penile length, reduced sexual desire and orgasmic dysfunction including painful orgasm and climacturia (21-23). Some men reported that they did not find sexual changes problematic or they may cope successfully with such issues(24). Whether satisfaction with sexual life improves in patients with ED due to RARP has been less frequently investigated.

Primary objective of our study was to examine if overall satisfaction with sexual life of patients without ED before RARP and with ED after RARP improved over time. As secondary objective: exploration of factors which could be correlated with overall satisfaction during long-term follow-up in this group.

Material and methods

This is an observational study. All patients treated with RARP for localized prostate cancer, at a single center, between 2006 and 2019, were evaluated. Patients who underwent a RARP for prostate cancer were asked to fill in questionnaires prior to RARP and at 6-, 12- and 24-months' follow-up. From 2013 onwards, patients were also asked to fill in an additional at 36-months' follow-up. Questionnaires were provided via email or on paper. Patient-, tumor- and surgical characteristics were available from the prospectively maintained genito-urinary database at our hospital, including treatment and follow-up data.

The following questionnaires were used: the 'EORTC core quality of life questionnaire' (QLQ-C30), 'International Index of Erectile Function 15' (IIEF-15; containing five areas: erectile function, orgasmic function, sexual desire, intercourse satisfaction,

overall satisfaction), 'International Prostate Symptom Score' (IPSS), 'International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form' (ICIQ-UISF)(25-30).

In addition, the 'International Index of Erectile Function 5' (IIEF-5) was used to describe erectile function at baseline and during follow-up(min-max: 1-25). The IIEF-5 was the score most frequently filled in by the participants during follow-up to determine erectile function. Hence the IIEF-5 was used to define and categorize ED according the validated no ED (22-25), mild ED (17-21), mild-moderate ED (12-16), moderate ED (8-11), severe ED (1-7)(31). Patients were divided into two groups: (1) patients with mild or no ED (without ED, ≥ 17) and (2) patients with mild-moderate, moderate and severe ED (with ED, < 17) (26, 29).

The 'overall satisfaction'-score (the sum of Q13 and Q14) of the IIEF-15 questionnaire was used to describe overall satisfaction with sexual life. Q13 and Q14 have a 5-point Likert-scale; 1 indicating very dissatisfied and 5 very satisfied. Satisfaction was categorized as follows, 'satisfied' (overall satisfaction ≥ 8) or 'not satisfied' (overall satisfaction < 8) (26). The scores of the other subdomains of the IIEF-15 were used according to score guideline of the IIEF-15 questionnaire (26). The score on 'quality of life' (QoL) was calculated from the QLQ-C30 according to the EORTC QLQ-C30 Scoring Manual(32).

Differences between patients with ED who were satisfied and not satisfied were calculated at 24-months and 36-months' follow-up since it is known that erectile function can still improve up to 24 months and beyond (13, 33) after surgery. Patients without ED after RARP were used as control group.

Fascia preservation score (FP score) was used as scoring system for perioperative nerve sparing(34). The score accounts for the full circular distribution of the periprostatic nerves via a 12-tier score. FP score is described as a predictor of postoperative erectile function (16).

Statistics

All analyses were conducted using IBM SPSS Statistics 25. Patient, tumor and surgical characteristics were described using demographic statistics. The means and standard deviations of questionnaire outcomes were reported. To test for differences in overall satisfaction between time-points (baseline, 6, 12, 24, 36 months) and difference between overall satisfaction of patients with ED and without ED after RARP, a mixed effect model was used with a random intercept per patient. For differences of patients who were 'satisfied' and those who were 'not satisfied' at 24-months and 36-months, the Mann-Whitney U test was used. Median and interquartile range (IQR) were reported. The variables that were significant at the 0.05 level were then used to predict the satisfaction in separate simple logistic models in the subgroups with and without ED at 24-months and 36-months. Age, quality-of-life score, IIEF-5 score, sexual desire (IIEF-15), and overall satisfaction score (IIEF-15) at baseline were entered as explanatory variables. P-value < 0.05 was considered statistically significant.

Ethics

Institutional review board (number IRBd19226) approval of the Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital was obtained.

Results

Demographics

2808 patients treated with RARP for localized prostate cancer between 2006 and 2019 were evaluated. Patients with ED before RARP (n=1281) and patients with unknown erectile function before RARP (n=643) were excluded. 884 patients reported to have no ED before RARP and were included for analysis. All were sexually active before RARP. Their characteristics are presented in **Table 1**.

Next, we divided them into a group of patients with ED due to RARP to compare to those who had no ED after RARP. Data were available for 467, 381, 333 and 189 patients with ED due to RARP at 6-mo, 12-mo, 24-mo and 36-mo follow-up. For patients without ED after RARP, data were available for 93, 124, 168 and 72 patients at 6-mo, 12-mo, 24-mo and 36-mo follow-up, respectively. All patients without ED were sexually active during follow-up. Categorization of ED by different time-points is presented in **Table 2**.

Table 1. Patient characteristics of patients without ED before RARP (n=884)

Age in years, median (IQR)	63.0 (9)
PSA-level (ng/mL), median (IQR)	8.1 (6.1)
Clinical T-stage	
- cT0 (%)	219 (25%)
- cT2 (%)	505 (57%)
- cT3 (%)	152 (17%)
- cT4 (%)	1 (0.1%)
- Missing	6 (0.9%)
Pathological Gleason sum score	
- 5-6 (%)	189 (21.4%)
- 7: 3+ 4 (%)	364 (41.2%)
- 7: 4+3 (%)	143 (16.2%)
- 8-10 (%)	103 (11.7%)
- Missing	85 (9.5%)
Pathological N-stage	
- pN0 (%)	400 (45.2%)
- pN1 (%)	90 (10.2%)
- pNx (%)	360 (40.7%)
- Missing	34 (3.8%)
Intraoperative techniques	
Fascia preservation score (mean)	4.54 (range 0-12), SD 3.0
Pelvic lymph node dissection	
Yes	501 (56.6%)
No	371 (42.0%)
Missing	11 (1.4%)
Quality-of-life data	
IIEF-5 score	22.8 (17-25), SD 2.3
Quality-of-life score	81.6 (0-100), SD 17.4
IPSS score	5.5 (0-31), SD 6.6
ICIQ incontinence score	1.3 (0-16), SD 2.6

ED=erectile dysfunction; RARP=robot assisted radical prostatectomy;
 IQR=interquartile range;
 SD=standard deviation; IIEF-5=international index of erectile function;
 IPSS=International Prostate Symptom Score; ICIQ=International
 Consultation on Incontinence questionnaire

Table 2: Categorization by timepoint of erectile dysfunction (ED) of the patients included for analysis

Categories of ED					
	No % (n)	Mild % (n)	Mild-moderate % (n)	Moderate % (n)	Severe % (n)
Timepoints (months)					
0	73.8 (652)	26.2 (232)	<i>Not applicable</i>	<i>Not applicable</i>	<i>Not applicable</i>
6	8.2 (46)	8.4 (47)	9.5 (53)	13.2 (74)	57.3 (340)
12	14.5 (73)	10.1 (51)	10.9 (55)	12.1 (61)	52.5 (265)
24	18.0 (90)	15.6 (78)	9.0 (45)	11.4 (57)	46.1 (231)
36	14.9 (39)	12.6 (33)	10.3 (27)	10.0 (26)	52.1 (136)

Satisfaction

The mean overall satisfaction of patients without ED at baseline was 8.2 (range 2-10, SD 1.7). Patients with ED due to RARP had a mean overall satisfaction of 4.8, 4.8, 4.9 and 4.6 (range 2-10, SD 1.7-2.5, $p=0.2$) at 6, 12, 24 and 36 months' follow-up, respectively. The patients without ED after RARP had a mean overall satisfaction of 8.4, 8.4, 8.1 and 8.2 (range 3-10, SD 1.4 – 1.6, $p=0.2$) at 6, 12, 24 and 36 months' follow-up, respectively (**Figure 1**). Scores of patients between patients with and without ED were significantly different ($p<0.01$). Scores of the other subdomains of the IIEF-15 (erectile function, orgasmic function, sexual desire and intercourse satisfaction) are provided in the supplemental information section (appendix 3).

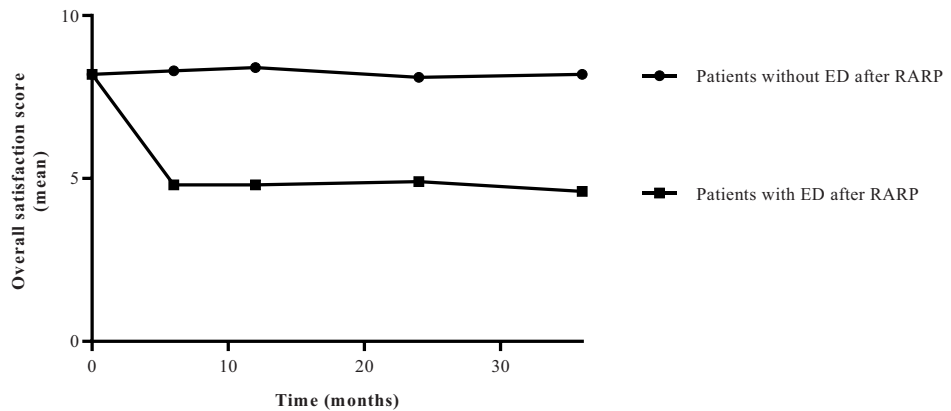


Figure 1: Sexual satisfaction score (range 2-10)

Differences between patients with ED who were satisfied and not satisfied with sexual life

Patients with ED at 24 months' follow-up, who were satisfied with sexual life at that moment, were compared to those with ED at 24 months who at that time were not satisfied with sexual life. Patients who were satisfied had a significant higher overall satisfaction score at baseline, Quality-of-life-score, IIEF-5 score and sexual desire score compared to patients who were not satisfied (**Table 3**; p-values varied between <0.01 and 0.03). Age, erectile function score at baseline, IPSS, incontinence score and FP score were not found to be associated (**Table 3**, p-values varied between 0.05 and 0.8). In a multiple logistic regression, overall satisfaction at baseline (OR 1.4, 95% CI 1.1-1.8, p=0.01) and sexual desire score at 24-mo (OR 1.7, 95% CI 1.4-2.1, p<0.01) were independent predictors of overall satisfaction in patients with ED at 24 months' follow-up (**Figure 2**).

The same was calculated at 36 months' follow-up. Patients with ED at 36 months' follow-up who were satisfied had a significantly higher overall satisfaction score at baseline, IIEF-5 score and sexual desire score compared to those who were not satisfied (**Table 3**; p-values varied between <0.01 and 0.06). In a multiple logistic regression at 36-months' follow-up, the same predictors were found as at 24-months: overall satisfaction at baseline (OR 2.3, 95% CI 1.13-4.88, p=0.02) and sexual desire score at 36-mo (OR 2.1, 95% CI 1.20-3.75, p=0.09) (**Figure 2**).

Probability of being satisfied was significantly lower in patients with ED due to RARP compared to patients without ED after RARP, both at 24 months and at 36 months' follow-up (p<0.01) (**Figure 2**).

Table 3: Differences at 24-months and 36-months follow-up

Variable	Follow-up	Satisfied mean (n, SD)	Not satisfied mean (n, SD)	p-value
Age in years	24-mo	63.1 (70, 5.6)	63.0 (254, 5.6)	0.8
	36-mo	63.6 (27, 5.7)	62.8 (158, 5.6)	0.6
IIEF-5 score at baseline (range 17-25)	24-mo	22.5 (69, 2.8)	22.6 (252, 2.2)	0.7
	36-mo	22.0 (27, 3.0)	22.7 (156, 2.4)	0.4
Overall satisfaction score at baseline (range 2-10)	24-mo	8.9 (69, 1.4)	7.8 (250, 1.8)	<0.01
	36-mo	8.6 (27, 1.7)	7.9 (154, 1.8)	0.02
QoL score (range 0 – 100)	24-mo	85.9 (57, 13.5)	78,6 (180, 16.7)	0.04
	36-mo	79.8 (12, 10.9)	77.8 (66, 15.5)	0.6
IIEF-5 score (range 17-25)	24-mo	8.5 (70, 4.8)	5,2 (254, 4.2)	<0.01
	36-mo	8.1 (27, 4.8)	5.1 (158, 4.2)	<0.01
Incontinence score (range 0-21)	24-mo	2.7 (67, 3.0)	3.9 (249, 3.9)	0.3
	36-mo	3.5 (25, 3.5)	4.0 (154, 4.2)	0.5
IPSS (range 0-35)	24-mo	3.1 (59, 4.0)	3.8 (187, 4.5)	0.5
	36-mo	3.2 (15, 4.1)	3.7 (81, 5.0)	0.6
Sexual desire score (range 2- 10)	24-mo	7.1 (70, 1.9)	5.2 (252, 1.9)	<0.01
	36-mo	7.1 (26, 1.6)	5.0 (158, 1.9)	<0.01
FP score (range 0-12)	24-mo	3.7 (70, 3.3)	3.9 (254, 2.8)	0.4
	36-mo	3.6 (27, 3.0)	4.0 (158, 2.9)	0.5

Mo=months; IQR=interquartile range; IIEF-5=international index of erectile function;

QoL= quality-of-life; IPSS = International Prostate Symptom Score; FP=fascia preservation

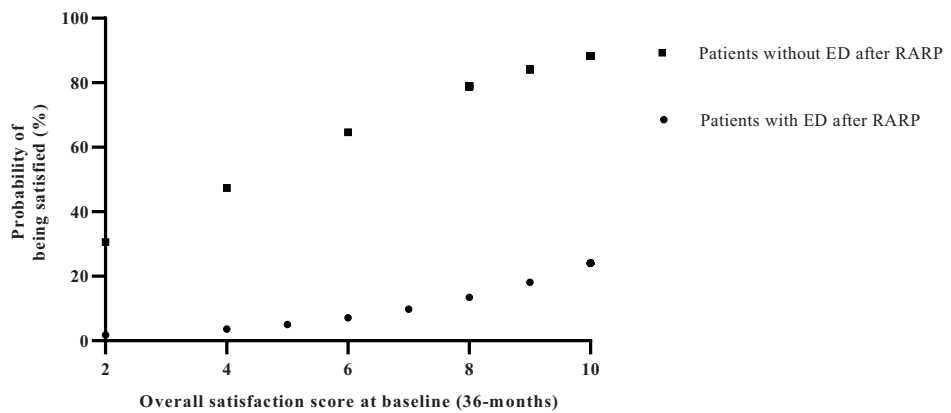
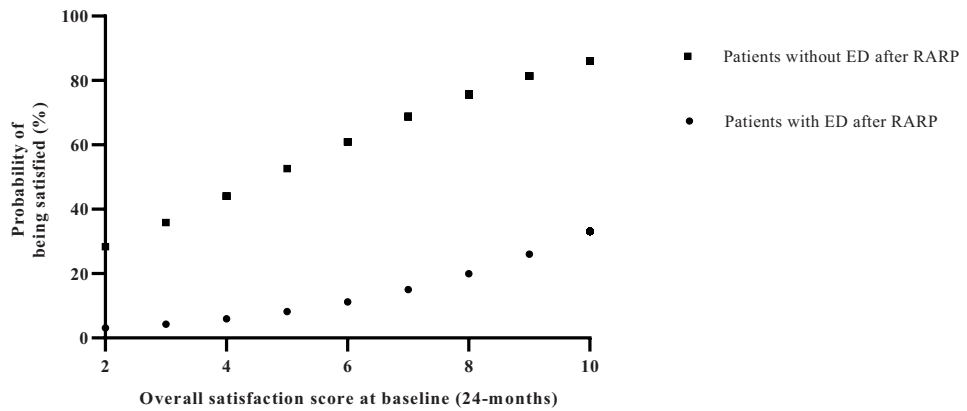


Figure 2: Probability of being sexual satisfied by overall satisfaction score at baseline (range 2-10), at 24-mo (above) and 36-mo follow-up (below)
 * Satisfaction is a subscore of the IIEF-15

Discussion

The goal of our study was to investigate if overall satisfaction with sexual life of patients with ED due to RARP improved over time, and to identify factors associated with satisfaction. We found no increase or decrease in overall satisfaction with sexual life between 6-months and 36-months' follow-up. A higher overall satisfaction score at baseline and a higher score on sexual desire were associated with satisfaction at 24- and 36 months' follow-up. Erectile function score was not correlated with overall satisfaction in this group. A high satisfaction rate was observed for men with erectile function preservation after prostatectomy.

In literature, several variables were found to be associated with sexual satisfaction: sexual desire, erectile function, sexual self-esteem, age, time since diagnoses, relationship variables and psychological variables like depression and anxiety(20, 24, 35-38). In contrast to our study, no other study evaluated satisfaction specifically in prostate cancer patients with ED due to RARP. In a study among Scandinavian prostate cancer patients who were treated with different modalities, longer time since diagnosis was associated with higher sexual satisfaction(35). The mean time since diagnosis was 6.1 years. In our study, overall satisfaction with sexual life score did not increase during follow-up. It can be argued that adjustment to or acceptance of new sexual function and sexual satisfaction may take longer than 3 years. In a prospective study, Dubbelman et al. found no significant difference between satisfaction scores 3 months and 5 years after radical prostatectomy(36). These findings indicate that improvement of sexual satisfaction of patients with ED due to RARP might occur over a long period of time. Additionally, depressive symptoms occur for a longer follow-up period postoperatively and may impact sexual functioning for a longer period of time. Depressive symptoms may contribute to delay in improvement of sexual satisfaction in patients with ED due to RARP (38, 39).

In our study, we found no relation between overall satisfaction and age in the cohort of patients with ED due to RARP. The Scandinavian study described above found that higher age was associated with an increase in sexual satisfaction in sexually active patients(35). It is known that sexual activity declines with age(40). People who are sexually active at an older age may well have continued their sexual activity because of greater sexual satisfaction and because they were able to cope with sexual changes. If this is the case, it would be the idea that the satisfaction score at baseline is important for satisfaction after treatment.

Similar to Badr et al.'s findings in their cross-sectional study among prostate cancer patients treated with different modalities, we also report that a higher score on sexual desire was associated with greater sexual satisfaction(41). In contrast, Bravi et al. found that prostate cancer patients, treated with RARP, who had a high desire, found low erectile function to be more sexually problematic than patients with lower desire(24). On the other hand, men with satisfactory erections after RARP can also experience sexual problems, and men with impotence can be satisfied with their sexual life. This may indicate that erectile function may be not the most important part of overall satisfaction with sexual life (20, 37, 42-44). We believe it might be helpful to ask patients about sexual desire and sexual satisfaction during sexual counseling, rather than counselling them only about erectile function.

Although, erectile function is associated with increased sexual satisfaction, male sexuality is not exclusively associated with erections. We found that preoperative satisfaction is more important for postoperative sexual satisfaction than erectile function at baseline or at 24-/36-months' follow-up. Besides penile rehabilitation for ED, psychological interventions focusing on adjustment to the changes in sexual functioning and other forms of (physical) intimacy might improve sexual satisfaction; especially for those men who continue to suffer from ED.

Some limitations should be considered. Our results must be interpreted within the limits of retrospectively collected, observational data. We only included patients treated by RARP and therefore our results may be not representative of other treatment modalities. Further, we did not take into account the possible negative effect of adjuvant or salvage radiotherapy and androgen deprivation. Excluding these cases would have strengthened our conclusions. However, it can be argued that, if these additional treatments affected sexual satisfaction, sexual satisfaction would decrease over time. Overall satisfaction, however, remained constant in our study. ED is known to be a predictor of depressive symptoms(38). Further research could include a questionnaire on depressive symptoms to investigate their impact on sexual satisfaction after RARP. Despite these limitations, our results add important new insights into sexual satisfaction in patients with ED due to RARP. The large sample-size, use of multiple validated questionnaires and three years' follow-up are the strengths of our study.

Conclusion

Satisfaction with sexual life in men with ED due to RARP did not improve between 6 and 36 months' follow-up, indicating improvement of satisfaction might take a long time. One could counsel patients that sexual satisfaction is based on individual baseline sexual satisfaction and the return of sexual desire after RARP. It is vital to present realistic, individualized expectations regarding both sexual satisfaction and recovery after RARP.

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