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Patient-reported outcomes after curative treatment for prostate cancer with prostatectomy, primary radiotherapy or salvage radiotherapy

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ABSTRACT

Background: Trials reporting adverse health outcomes (AHOs) in terms of patient-reported outcome measures (PROMs) after contemporary curative treatment of prostate cancer (PC) are hampered by study heterogeneity and lack of new treatment techniques. Particularly, the evidence regarding toxicities after radiotherapy (RT) with the volumetric arc therapy (VMAT) technique is limited, and comparisons between men treated with surgery, primary radiotherapy (PRT) and salvage radiotherapy (SRT) are lacking. The aim of the study was to evaluate change in PROMs 3 months after treatment with robotic-assisted laparoscopic prostatectomy (RALP), PRT and SRT administered with VMAT.

Material and methods: A prospective cohort study of men with PC who received curative treatment at the University Hospital of North Norway between 2012 and 2017 for RALP and between 2016 and 2021 for radiotherapy was conducted. A cohort of 787 men were included; 406 men treated with RALP, 265 received PRT and 116 received SRT.

Patients completed the validated PROM instrument EPIC-26 before (pre-treatment) and 3 months after treatment. EPIC-26 domain summary scores (DSSs) were analysed, and changes from pre-treatment to 3 months reported. Changes were deemed clinically relevant if exceeding validated minimally clinically important differences (MCIDs).

Results: Men treated with RALP reported clinically relevant declining urinary incontinence DSS (−41.7 (SD 30.7)) and sexual DSS (−46.1 (SD 30.2)). Men who received PRT reported worsened urinary irritative DSS (−5.2 (SD 19.6)), bowel DSS (−8.2 (SD 15.1)) and hormonal DSS (−9.6 (SD 18.2)). Men treated with SRT experienced worsened urinary incontinence DSS (−7.3 (SD 18.2)), urinary irritative DSS (−7.5 (SD 14.0)), bowel DSS (−12.5 (SD 16.1)), sexual DSS (−14.9 (SD 18.9)) and hormonal DSS (−23.8 (SD 20.9)).

Conclusion: AHOs 3 months after contemporary curative treatment for PC varied according to treatment modality and worsened in all treatment groups, although most in SRT.

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Introduction

For men with localised or locally advanced prostate cancer (PC), curative treatment options include surgery or primary radiotherapy (PRT) in combination with endocrine therapy [1,2]. There are no randomised trials comparing prostatectomy with radiotherapy for men with high-risk disease, and survival differences has not been shown [3]. Consequently, until data from the ongoing trial by the Scandinavian PC Group (SPCG-15) [4] become available, patient treatment decisions are made based on knowledge about the treatment's impact on adverse health outcomes (AHOs).

RALP is a minimally invasive technique that has shown less peri-operative complications than open surgery and is safe in the long run (similar functional and oncological

outcome) [5,6]. At the University Hospital of North Norway (UNN), robotic-assisted laparoscopic prostatectomy (RALP) was established in 2012. However, 17–31% experience a biochemical failure after treatment and are offered salvage radiotherapy (SRT) as a second curative treatment [7,8]. In November 2016, our radiotherapy department implemented volumetric arc therapy (VMAT) and simultaneous integrated boost (SIB) in the curative treatment of PC, with delivery of a precisely sculptured three-dimensional dose distribution to facilitate improved treatment precision while further limiting the doses to healthy tissue [9]. Toxicity within 3–6 months after radiotherapy is defined as acute or subacute toxicity. The pathophysiology of radiation-induced toxicity involves an acute inflammatory response and tissue oedema [10].

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Patient-reported outcomes (PROs) are collected through various patient-reported outcome measures (PROMs) and are powerful tools to inform clinicians and policy-makers about AHOs. EPIC-26 is an internationally validated tool for evaluating PROs in men with PC. The instrument focuses on the same five domains as the original EPIC questionnaire; urinary incontinence, urinary irritative/obstructive, bowel, sexual, and hormonal [11]. Most published studies addressing potential side effects after radical treatment for PC during the last decades have used EPIC-26 [12].

Available studies reporting PROMs after curative treatment of PC are limited by heterogeneous study populations and/or lack of details regarding radiotherapy doses and techniques [13–16]. Particularly, the evidence regarding toxicities after RT with the VMAT technique is limited [17], and comparisons between men treated with surgery, PRT and SRT are lacking. Both surgical and radiation techniques have improved the recent years, hence updated information on both short-term and long-term AHOs after treatment is warranted.

In this prospective population-based cohort study, the aim was to evaluate the impact of RALP, PRT and SRT (both with VMAT) on AHOs measured by EPIC-26 before and 3 months after treatment, with a special emphasis on change in AHOs.

Patients and methods

Patients

Together with implementing new curative treatment techniques of prostate cancer at our hospital, prospective registries for registration of PROs were established. A quality registry for men treated with RALP at UNN was established in September 2012 after the implementation of RALP as a standard procedure. A quality registry for men treated with curative radiotherapy for PC was established at UNN in November 2016 after the implementation of new radiotherapy techniques including VMAT and SIB. In both registries, PROMs were evaluated by the questionnaire EPIC-26. The first EPIC-26 was filled out at the first patient visit at UNN, immediately before surgery or radiotherapy, but after initiation of endocrine treatment (for primary irradiated patients, endocrine treatment was initiated at local hospital). Patients completed EPIC-26 before treatment and 3 months after treatment and returned the questionnaire by mail. All men who completed EPIC-26 before and/or 3 months after treatment were included in this study.

The study was approved by the data protection officer (0637 and 0345) and the Regional Committee for Medical and Research Ethics North (2018/1849 and 2018/369) and informed written consent was obtained from all participants.

Medical and treatment characteristics

The study obtained information about disease, treatment characteristics and comorbidity from medical records. Prostate specific antigen (PSA) was reported at start of primary treatment and at start of RT. International Society of

Urological Pathology (ISUP) 2014 grade [18] and American Joint Committee of Cancer TNM-classification, as well as risk group stratification [19] was registered (Table 1). Most high-risk patients were screened using bone scintigraphy or MRI scan of the spine.

Curative surgical treatment in terms of RALP included removal of the prostate gland, seminal vesicles and in high-risk patients, pelvic lymph nodes [20]. Curative radiotherapy was administered with the VMAT and SIB techniques and applied in combination with endocrine treatment (Supplementary Table 1) [4,21–24].

Outcomes

The Norwegian version of EPIC-26 has shown acceptable reliability and validity in psychometric testing [25]. EPIC-26 covers five domains (urinary incontinence, urinary irritative/obstructive, bowel, sexual and hormonal; Supplementary Table 3) [26]. Further, EPIC-26 comprises three questions on overall problem; urinary, bowel and sexual. Except for overall urinary problem, the problem scores are included as an item in the domain summary scores (DSSs), but as they are of high clinical relevance, several studies report problem scores in addition to DSSs.

DSSs and problem scores were computed by the standardised EPIC-26 scoring instructions in which individual items are transformed linearly to a 0-100 scale and high scores represent better function or lower problems [27]. Corresponding DSSs were not calculated if $\geq 20\%$ of the items were missing, and g [27] missing data were not imputed. Number of patient replies for each EPIC-26 DSS is presented in Supplementary Table 2. For patients who completed EPIC both pre-treatment and 3 months after treatment, change in DSS and problem score were calculated as the score 3 months post-treatment minus the pre-treatment score.

Minimally clinically important differences (MCIDs) are thresholds for clinically relevant differences. Previously published validated cut-off values of MCIDs for each EPIC-26 domain are: 6 points for urinary incontinence, 5 points for urinary irritation, 4 points for bowel function, 10 points for sexual function, and 4 points for hormonal function [28].

Statistical analysis

Categorical variables are presented as counts (proportion) and continuous variables are presented as median (interquartile range [IQR]) or mean (standard deviation [SD]). Categorical variables were compared using the chi-square test and continuous variables were compared using one-way ANOVA or t -tests depending on the number of groups being compared. EPIC-26 problem-scores were compared between time points using paired t -tests. Two-sided p -values of < 0.05 were considered statistically significant. Data were analysed using IBM SPSS version 27.

Table 1. Patient characteristics according to type of curative treatment.

	Radical prostatectomy <i>n</i> = 406	Primary radiotherapy <i>n</i> = 265	Salvage radiotherapy <i>n</i> = 116
Age at start of treatment (median (IQR), years)	65.1 (60.6–69.6)	73.5 (70.3–76.7)	66.3 (61.0–71.6)
PSA ^a (median (IQR), µg/mL)	8.9 (5.6–12.2)	11.0 (5.8–16.3)	10.3 (9.6–14.9)
PSA at start of RT (median (IQR), µg/mL)		0.2 (0–0.5)	0.4 (0–0.9)
ISUP grade group ^b			
1	142 (35.0)	18 (6.8)	16 (13.8)
2	142 (35.0)	56 (21.1)	26 (22.4)
3	58 (14.3)	86 (32.5)	23 (19.6)
4	45 (11.1)	69 (26.0)	36 (31.0)
5	19 (4.7)	36 (13.6)	15 (12.9)
T stage ^c			
T1a-c	4 (1.0)	10 (3.8)	0
T2	280 (69.1)	119 (44.9)	43 (37.1)
T3a	79 (19.5)	87 (32.8)	40 (34.5)
T3b	40 (9.9)	43 (16.2)	31 (26.7)
T4	2 (0.5)	0	2 (1.7)
N stage ^d			
N0	388 (95.6)	261 (98.5)	112 (96.7)
N1	18 (4.4)	2 (0.8)	3 (2.6)
Prostate cancer risk group at treatment ^e			
Low risk	23 (5.7)	4 (1.5)	6 (5.2)
Intermediate risk	205 (50.6)	61 (23.0)	36 (31.0)
High risk	177 (43.7)	200 (75.5)	74 (63.8)
Comorbidity			
Hypertension	117 (28.8)	120 (45.3)	37 (31.2)
Coronary disease	41 (10.1)	64 (24.2)	11 (9.5)
Diabetes mellitus	18 (4.4)	42 (15.8)	5 (4.3)

n: number; IQR: interquartile range; RT: radiotherapy; PSA: prostatic specific antigen; ISUP: International Society of Urological Pathology. Data are presented as *n* (%) unless otherwise stated.

^aPSA reported at start of primary treatment.

^bThe ISUP grade system classifies patients into five groups based on Gleason score: grade 1 Gleason score = 6; grade 2 Gleason score 3 + 4 = 7; grade 3 Gleason score 4 + 3 = 7; grade 4 Gleason score 8 and grade 5 Gleason scores 9–10 [18].

^cFor men treated with surgery (radical prostatectomy and salvage radiotherapy) pathological T-stage is reported. Data missing for one patient treated with radical prostatectomy who had no tumour material in the resected specimen, all tumour tissue probably removed at biopsy. For men treated with primary radiotherapy, radiological T stage is reported (missing data for 6 patients; no MRI scan due to ICD/pacemaker/claustrophobia (*n* = 4), previous transurethral resection of prostate (*n* = 1), not reported (*n* = 1)).

^dFor men treated with radical prostatectomy, pathological N stage is reported when lymph node removal was performed. For remaining patients and for men treated with radiotherapy, radiological N stage is reported. For 3 men (2 primary radiotherapy, 1 salvage) radiological N stage is missing as MRI was not performed due to ICD/pacemaker.

^eRisk group according to European Association of Urology (EAU) guidelines: High risk patients had American Joint Committee of Cancer (AJCC) clinical T stage ≥ 2c, or PSA level > 20 ng/mL or ISUP grade 4/5. Intermediate risk patients had AJCC clinical T stage 2b, or PSA level 10–20 or ISUP grade 2/3. Low risk patients had AJCC clinical T stage ≤ 2a, PSA level < 10 ng/mL and ISUP grade 1 [19]. Based on radiological T stage when available, otherwise clinical T stage.

Results

Patient characteristics

Between September 2012 and October 2017, 533 men with PC treated with curative surgery were enrolled in the surgical registry of whom 127 were excluded (Figure 1), Between November 2016 and March 2021, 463 men with PC were treated with curative radiotherapy, of whom 422 (91%) were included in the radiotherapy registry, and among them 41 men were excluded (Figure 1). Overall, 406 patients who underwent RALP and 381 patients who received radiotherapy, including 265 who received PRT and 116 who received SRT, were included in the study, for a total of 787 patients.

Men treated with PRT were older (median age 73.5 years) than men treated with RALP (median age 65.1 years) and SRT (median age 66.3 years, Table 1), with both differences being statistically significant, $p < 0.001$). Men treated with PRT or SRT had higher ISUP grade group, higher T stage and a larger proportion were high-risk patients compared to men treated with RALP. Hypertension, coronary disease and diabetes mellitus were more prevalent among men treated with PRT ($p < 0.001$). Overall, 27.5% of men treated with PRT and

56.6% of men treated with SRT received pelvic lymph node irradiation (Table 2).

Urinary function and problem

Pre-treatment urinary incontinence DSSs were similar for men treated with RALP and PRT (90.2 (SD 17.8) and 88.8 (SD 17.0) respectively), while men treated with SRT had lower scores (69.4 (SD 27.2), $p < 0.001$, Table 3, Figure 2). Men treated with RALP and SRT reported clinically important changes in DSS (mean change RALP −41.7 (SD 30.7), mean change SRT −7.3 (SD 18.2), Figure 3).

Pre-treatment urinary irritative DSS was significantly higher for men treated with SRT compared with RALP and PRT (mean 87.9 (SD 13.3) vs 80.0 (SD 16.8) and 80.1 (SD 16.5), $p < 0.001$). After RALP there was a small improvement, with no significant change in DSS. For patients treated with radiotherapy, the urinary irritative DSS was decreased (mean changes PRT −5.2 (SD 19.6); SRT −7.5 (SD 14.0)).

Mean overall urinary problem score before treatment was similar across treatment groups (Table 3, Supplementary Table 3). Mean overall urinary problem scores changes were

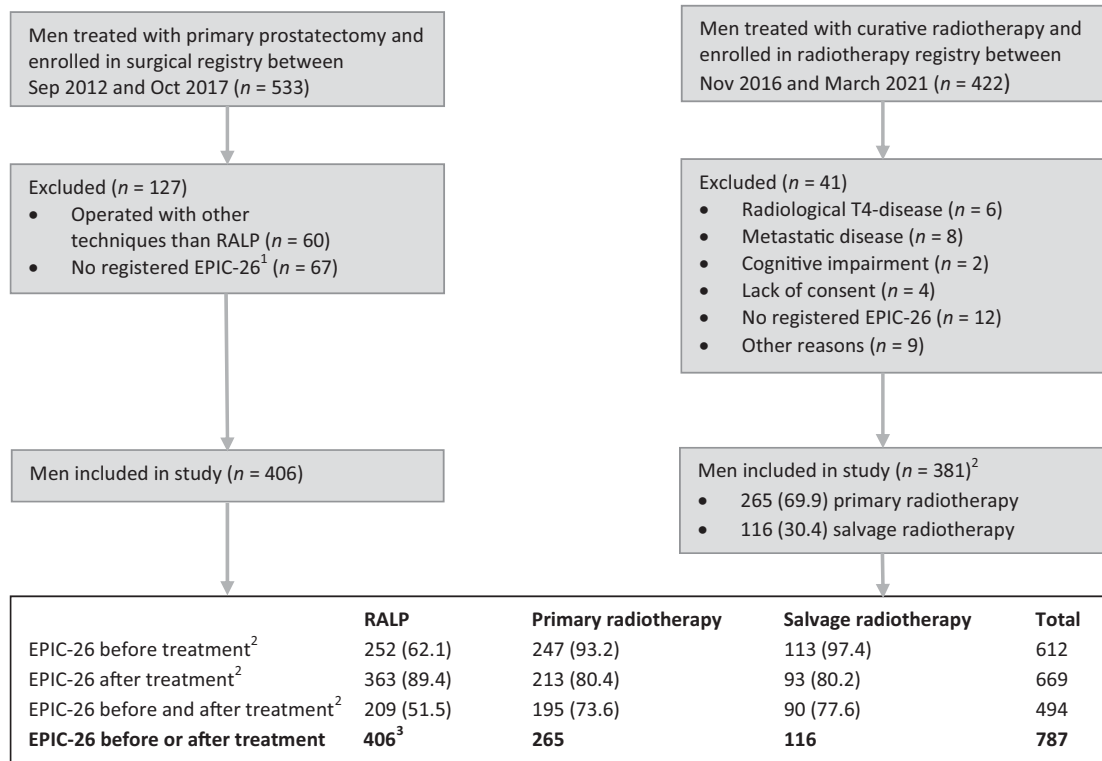


Figure 1. Flow chart presenting the study population.

RALP = Robotic-assisted laparoscopic prostatectomy; n = number; EPIC-26 = Expanded Prostate Cancer Index Composite 26-item.

¹The database for surgical patients were administered by different personnel than the radiotherapy database and information about reasons for exclusion is missing.

²Data are presented as n (%).

³49 of the RALP patients were later included in the radiotherapy registry as they received salvage radiotherapy.

Table 2. Treatment details.

	Radical prostatectomy $n = 406$	Primary radiotherapy $n = 265$	Salvage radiotherapy $n = 116$
Surgery:			
Type of surgery			
RALP	406 (100)		96 (82.8)
Open retropubic			19 (16.4)
Laparoscopic			1 (0.9)
Lymph node removal ^a	145 (35.7)		81 (69.8)
Limited	57 (14.0)		38 (32.8)
Expanded	88 (21.7)		42 (36.2)
Nerve sparing ^b	197 (48.5)		58 (50.0)
Unilateral	118 (29.1)		40 (34.5)
Bilateral	79 (19.5)		18 (15.5)
Positive margins	73 (18.0)		58 (50.0)
Time from surgery to salvage radiotherapy (median (IQR), months)			20.1 (0–50.2)
Radiotherapy:			
Radiotherapy regimen ^c			
60 Gy		79 (29.8)	
77 Gy		186 (70.1)	
70 Gy			116 (100) ⁴
Pelvic lymph node irradiation		73 (27.5)	54 (56.6)
Androgen deprivation therapy		259 (97.7)	107 (92.2)

n : number; RALP: Robotic assisted laparoscopic prostatectomy; IQR: interquartile range. Date are presented as n (%) unless otherwise stated.

^{a,b}Missing data on type of lymph node removal and nerve sparing for one salvage patient operated abroad.

^cFourteen men with high risk disease were treated as intermediary risk patients with a total radiotherapy dose of 60 Gy. For 7 of these a shorter regimen was chosen due to the covid epidemic, while for the other 7 a lower radiotherapy dose was chosen due to comorbidity/high age/less aggressive disease.

^d17 patients received adjuvant radiotherapy due to affected surgical margin ($n = 14$) or measurable PSA ($n = 3$).

Table 3. EPIC-26 domain summary scores and problem scores.

	RALP (n = 406)			Primary radiotherapy (n = 265)			Salvage radiotherapy (n = 116)		
	Pre-treatment	3 months	Change ^a	Pre-treatment	3 months	Change ^a	Pre-treatment	3 months	Change ^a
Urinary incontinence DSS	90.2 (17.8)	48.2 (28.5)	-41.7 (30.7)*	88.8 (17.0)	86.8 (19.6)	-1.9 (17.5)	69.4 (27.2)	61.3 (31.2)	-7.3 (18.2)*
Urinary irritative DSS	80.0 (16.8)	81.0 (15.8)	1.6 (19.5)	80.1 (16.5)	73.8 (20.0)	-5.2 (19.6)*	87.9 (13.3)	81.3 (16.6)	-7.5 (14.0)*
Urinary problem	79.1 (27.7)	56.9 (31.0)	-21.8 (34.7)	72.9 (29.0)	64.6 (30.6)	-8.3 (22.3)	75.0 (28.1)	58.2 (32.3)	-15.5 (29.3)
Bowel DSS	90.4 (13.9)	89.0 (14.6)	-0.7 (14.5)	92.9 (10.6)	84.5 (17.2)	-8.2 (15.1)*	91.7 (11.9)	78.7 (21.1)	-12.5 (16.1)*
Bowel problem	89.8 (19.7)	87.3 (21.3)	-2.8 (21.7)	88.4 (19.3)	77.7 (25.6)	-10.8 (26.4)	86.9 (20.1)	70.9 (30.2)	-17.1 (25.4)
Sexual DSS	67.6 (26.9)	22.4 (23.9)	-46.1 (30.2)*	23.0 (19.0)	16.7 (16.5)	-5.9 (15.9)	29.1 (26.3)	14.7 (17.3)	-14.9 (18.9)*
Sexual problem	66.8 (32.1)	28.3 (31.9)	-39.3 (42.7)	50.5 (36.2)	46.4 (40.5)	-3.0 (32.9)	42.8 (34.6)	36.1 (35.0)	-8.7 (33.1)
Hormonal DSS	84.2 (15.9)	83.4 (16.1)	-1.0 (13.9)	74.3 (18.4)	63.9 (19.4)	-9.6 (18.2)*	85.7 (14.8)	60.8 (23.8)	-23.8 (20.9)*

EPIC-26: Expanded Prostate Cancer Index Composite 26-item; RALP: Robotic assisted laparoscopic prostatectomy; n: numbers; DSS: domain summary score. Data are presented as mean (standard deviation).

^aChange in domain score was calculated for patients who completed EPIC-26 both pre-treatment and at three months after treatment; 209 men treated with RALP, 195 men treated with primary radiotherapy and 90 men treated with salvage radiotherapy.

*Clinically relevant (exceeding minimally clinically important differences).

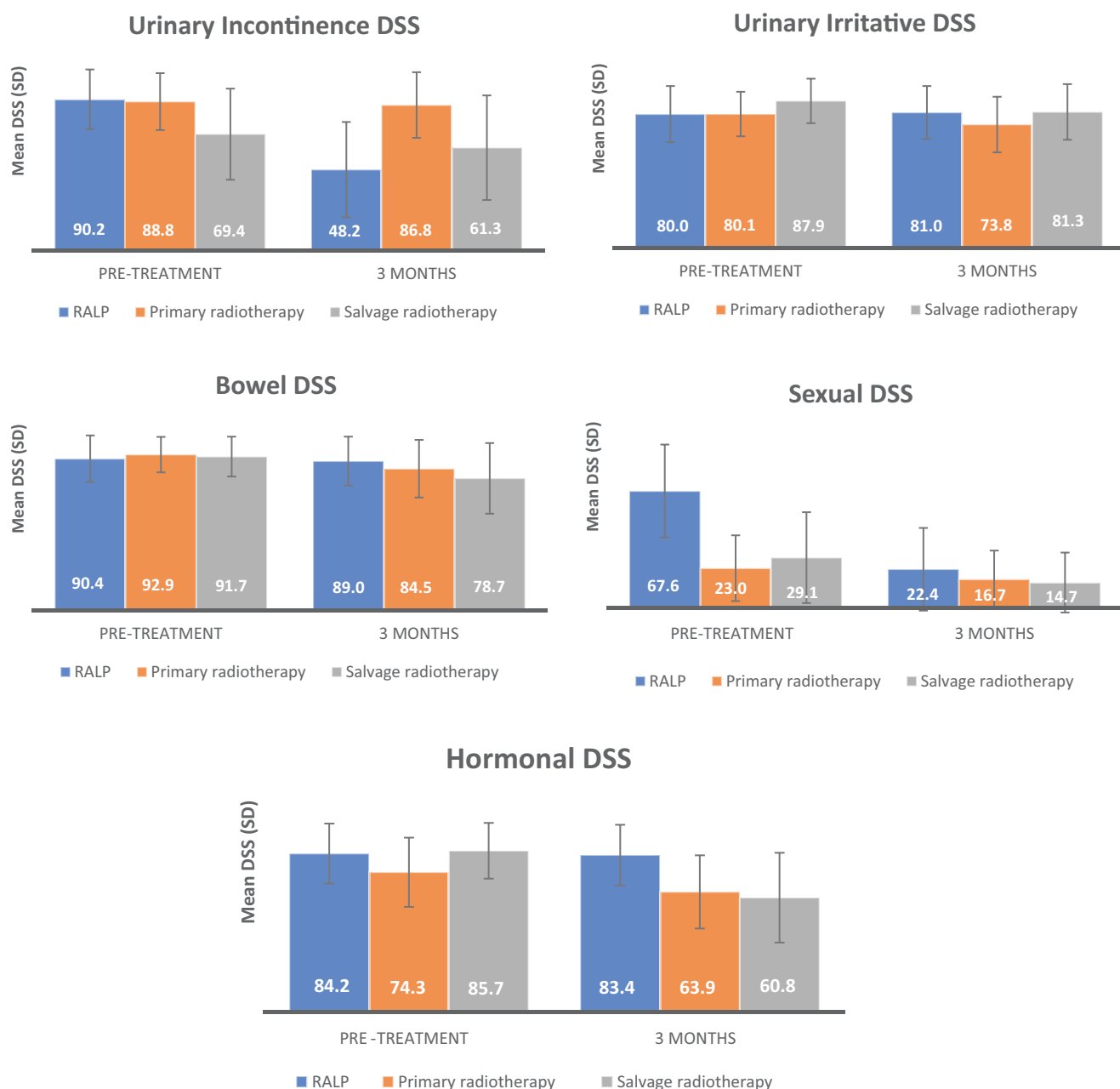


Figure 2. EPIC-26 mean domain summary scores across treatment groups before and 3 months after treatment. EPIC-26 = Expanded Prostate Cancer Index Composite 26-item; SD = standard deviation.

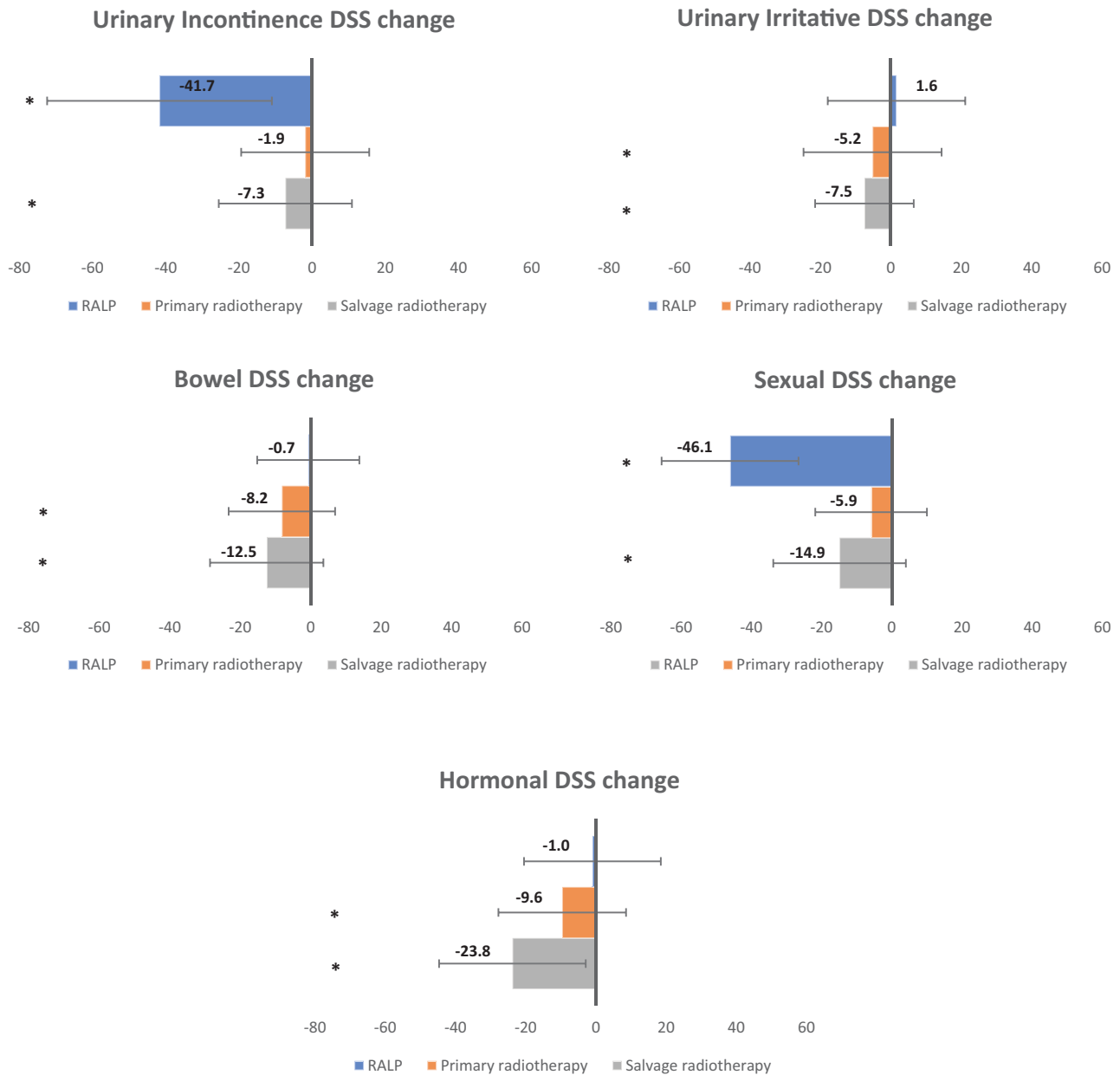


Figure 3. EPIC-26 mean domain summary score changes across treatment groups from pre-treatment to 3 months after treatment.

EPIC-26 = Expanded Prostate Cancer Index Composite 26-item.

Brackets indicate standard deviation.

*indicate change exceeding the minimally clinically important differences. Changes in domain score was calculated for patients who completed EPIC-26 both pre-treatment and at three months after treatment

statistically significant ($p < 0.001$) for RALP (-21.8 (SD 34.7)), PRT (-8.3 (SD 22.3)) and SRT (-15.5 (SD 29.3)).

Bowel function and problem

Mean bowel DSSs before treatment were similar across treatment groups (Table 3, Figure 2). Men treated with PRT and SRT reported clinically important declines in bowel function (mean DSS changes of -8.2 (SD 15.1) and -12.5 (SD 16.1), respectively, Figure 3).

Overall bowel problem score before treatment was similar across treatment groups (Table 3, Supplementary Table 3). Mean overall bowel problem score changes were statistically

significant ($p < 0.001$) for all treatment groups, most pronounced for men treated with PRT and SRT (-10.8 (SD 26.4) and -17.1 (SD 25.4), respectively, $p < 0.001$).

Sexual function and problem

Mean pre-treatment sexual DSS for men undergoing RALP was 67.6 (SD 26.9), compared to 23.0 (SD 19.0) and 29.1 (SD 26.3), for PRT and SRT respectively ($p < 0.001$, Table 3, Figure 3). Mean sexual DSS changes for men treated with RALP and SRT were clinically important; -46.1 (SD 30.2) and -14.9 (SD 18.9), respectively Figure 3).

Overall pre-treatment sexual problem varied across treatment groups, with the lowest bother before RALP (Table 3, Supplementary Table 3). Mean score changes for overall sexual problem for patients treated with RALP and SRT were statistically significant ($p < 0.001$) and were -39.3 (SD 42.7), and -8.7 (SD 33.1), respectively.

Hormonal function

The mean DSS before treatment for PRT was 74.3 (SD 18.4) compared to 84.2 (SD 15.9) and 85.7 (SD 14.8) for RALP and SRT respectively, $p < 0.001$, Table 3, Figure 2). The mean hormonal DSS changes for PRT and SRT were -9.6 (SD 18.2) and -23.8 (SD 20.9), respectively, Figure 3).

Discussion

In this prospective cohort study, we report PROMs in terms of EPIC-26 DSSs immediately before and 3 months after contemporary curative treatment for PC with RALP, PRT or SRT. Men treated with RALP experienced reduced urinary continence and sexual function. Men treated with PRT reported reduced urinary irritative, bowel and hormonal function. Men treated with SRT experienced worsening of all five functional domains. Studies reporting EPIC-26 DSSs following radiotherapy with VMAT are scarce. To the best of our knowledge, there are no other studies reporting PROs after SRT using the VMAT technique, and no studies which compare PROs after RALP, primary and salvage radiotherapy with VMAT.

Urinary incontinence DSS after RALP was reduced, in line with other studies [15,29] (Supplementary Table 4A). Urinary continence function after PRT was not reduced herein, while other studies are diverging [15,29–32] (Supplementary Table 4B). For men treated with SRT, we observed a low pre-treatment urinary incontinence DSS as could be expected due to previous surgery. In contrast to other studies, we noted reduced urinary incontinence DSS after SRT [33–36] (Supplementary Table 4C).

Urinary irritative function was not changed after RALP, in line with the unfavourable risk group of Hoffman et al. [15], but in contrast to Sanda et al. [29] and the favourable risk group of Hoffmann [15], reporting improved function. We observed a decline in urinary irritative function after PRT and SRT, in contrast to comparable studies reporting a stable [29,30,32–34] or improving irritative function [15,35]. Overall urinary problem worsened in all treatment groups, most for men treated with RALP, consistent with Stensvold et al. [37]. We observed worsened urinary problem after PRT in line with Caumont et al. [31]. In contrast to previous studies [34,36] we also noted worsened urinary problem after SRT.

Bowel function for men treated with RALP was not altered, consistent with other studies [6,15,29]. Our reduced DSS after PRT is in line with most comparable studies [15,29,31,32], however Ischii et al. [30] observed a stable bowel function. In our study, bowel DSS was reduced after SRT, while other studies reported a smaller but clinically relevant decline [34] or a stable bowel function [33,35,36]. We observed a worsened bowel problem after both PRT and

SRT, which was more pronounced than comparable studies [31,34,36].

We observed a decline in sexual function after RALP, consistent with other studies [15,29]. Pre-treatment sexual DSS were low for patients treated with PRT most probably due to older age, more comorbidity and ongoing neoadjuvant ADT. Pre-treatment sexual function for men treated with SRT was low, probably related to the previous prostatectomy with impact on erectile function and corroborate results from other studies. We observed a clinically relevant reduced sexual function after SRT, in contrast to other studies [33–36]. The reduced sexual function after SRT could partly be explained by hormonal treatment, as LHRH-agonist was initiated at start of radiotherapy, whereas comparable studies applied neoadjuvant ADT. Sexual problem worsened in all treatment groups, in agreement with most other studies [31,34,37].

Hormonal function was not changed after RALP, in line with Hoffman et al. [15] and Sanda et al. [29]. Pre-treatment hormonal DSS was lower for patients treated with PRT compared to SRT and RALP, probably due to ongoing treatment with neoadjuvant ADT. Still we observed further reduction of hormonal function after PRT, in line with other studies [15,29]. The large decline in hormonal function after SRT, is probably related to treatment with LHRH-agonist initiated at start of radiotherapy.

In contrast to comparable studies [33–36], we observed clinically reductions of EPIC-26 DSSs after SRT in all five functional categories. Comparisons are challenging due to heterogeneity of patient inclusion (e.g., high-risk patients) as well as treatment regimens (e.g., radiation techniques and doses). Others have used lower prostate bed doses (66–68 Gy) compared to our study, while doses to elective pelvic nodes varied (50.4–56 Gy). Our study comprises a high number of SRT patients receiving pelvic nodal irradiation (57%) compared to van Gysen (15.6%) [36]. The percentage of SRT patients receiving concomitant/adjuvant ADT was high in our study (92.2%). Some of the reported toxicity discrepancy could be due to a larger proportion of more heavily treated patients than in other studies. The reduction of bowel function is especially worrying, but also a reduced urinary and sexual function is of note, since previous surgery already has influenced these functions. The number of men eligible for treatment with SRT will probably increase, as more patients with high-risk disease undergo surgery [38]. EAU has proposed a risk stratification for biochemical recurrence of PC after prostatectomy into low-risk and high risk based on PSA-doubling time and ISUP grade [39,40]. For some patients with low-risk biochemical recurrence, the risk of side effects probably outweighs the potential benefit of SRT.

When advising men with PC on curative treatment options, knowledge of PROs after treatment is important. Our study adds important information, especially regarding the decline in all five domains in the SRT group. Thorough information about AHOs to be expected may increase patient acceptance of symptoms. However, we observed large inter-individual differences of AHOs, which also must be communicated to the patient.

Strengths of our study include the prospective and longitudinal design and the relatively large number of patients treated in a consistent manner throughout the study period. Of note, the contemporary radiotherapy technique VMAT was applied in all irradiated patients. Furthermore, the pre-treatment PROMs available enables us to calculate changes for the individual patient and compare treatment groups. Limitations include variation in the completion rates of the EPIC questionnaire, lack of data before start of neoadjuvant endocrine treatment and the reporting of PROMs only 3 months after treatment. One should also be careful to directly compare our results to the other mentioned studies, since several studies lack calculation of the individual DSS changes. An example is the Hoffmann study [15], which is older with different pre-treatment staging, differences in surgical and radiotherapy techniques, however their strength is reporting of data with a longer follow-up (5 years). Contemporary information on long-term AHOs and especially longitudinal assessment of patients treated with prostatectomy and subsequent SRT is warranted.

Conclusions

Contemporary curative PC therapy is associated with significant and specific AHOs according to treatment modality. The combined treatment of prostatectomy and SRT is especially associated with short-term reduced urinary, bowel, sexual and hormonal function. The risk of increased symptom burden must be communicated to the patient when making decisions on primary treatment modality, especially when discussing surgery in patients with high-risk disease.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Data availability statement

The data are not available due to restrictions from the data protection officer and the Regional Committee for Medical and Research Ethics.

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