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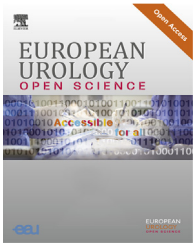

European Association of Urology

Prostate Cancer

The Longitudinal Course of Prospectively Recorded Patient-reported Outcomes in Prostate Cancer Patients Treated with Surgery and Salvage Radiotherapy

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Abstract

Background: Patient-reported outcome measures (PROMs) after prostate cancer (PC) treatment, including both radical prostatectomy (RP) and salvage radiation therapy (SRT), are under-reported.
Objective: To investigate PROMs longitudinally from before SRT until 18 mo after SRT for men treated with contemporary treatment modalities.
Design, setting, and participants: This prospective, longitudinal cohort study included 120 men (whole cohort) treated with SRT administered with volumetric modulated arc radiotherapy from 2016 to 2021 at the University Hospital of North Norway. The whole cohort was followed from before SRT until 18 mo after SRT. A subcohort of 48 men was followed from before RP until 18 mo after SRT.
Outcome measurements and statistical analysis: PROMs were collected with the Expanded Prostate Cancer Index-26 (EPIC-26), covering symptoms of urinary incontinence, urinary irritative, bowel, sexual, and hormonal domains. The domain scores were inquired before RP, 3 mo after RP, before SRT, at SRT termination, and 3 and 18 mo after SRT. We used linear mixed models with repeated measurements design to assess changes in PROMs throughout the treatment period.
Results and limitations: The median age before SRT was 63 yr. For the whole cohort, all five domains worsened at 3 and 18 mo after SRT compared with those before SRT. The estimated mean changes from before SRT to 18 mo after SRT are as follows: urinary incontinence –13.1, urinary irritative function –10.4, bowel –16.8, sexual function –9.1, and hormonal function –20.2 (at clinically important levels for all domains but sexual). For the subcohort, the mean urinary incontinence, bowel, sexual, and hormonal functions were significantly worsened 3 and 18 mo after SRT compared with those before RP at clinically important levels.

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Conclusions: Men treated for PC report particular increased severity of urinary, bowel, sexual, and hormonal symptoms after SRT compared with baseline status.
Patient summary: For men with prostate cancer, the treatment combination of surgery and salvage radiotherapy worsens urinary incontinence and bowel, sexual, and hormonal functions.

1. Introduction

Prostate cancer (PC) represents the most common male cancer in Europe [1]. During the past decade, robot-assisted laparoscopic prostatectomy (RALP) has been implemented as a standard treatment for localized PC, with excellent long-term PC-specific survival [2]. This procedure has improved short-term complication rates compared with retropubic radical prostatectomy (RP) [2].

Approximately 20% of patients treated with RALP will develop a biochemical recurrence (BCR) within 7 yr after surgery, and for men with high-risk features, the risk of recurrence is higher [3]. Men experiencing a BCR can be offered salvage radiotherapy (SRT), often combined with androgen deprivation therapy (ADT), as a second curative treatment attempt [4]. Side effects after SRT include erectile dysfunction, urinary symptoms, bowel dysfunction, and eventually ADT-associated adverse effects [5].

To evaluate the side effects after PC treatment, patient-reported outcome measures (PROMs) are considered reliable [5], and can provide important information to clinicians and their PC patients with BCR when deciding on further treatment. The Expanded Prostate Cancer Index-26 (EPIC-26) is an international, well-validated questionnaire including urinary, bowel, sexual, and hormonal symptoms for evaluating PROMs in men with PC [6]. Earlier publications reporting on late effects in patients receiving SRT often lack clinical information before surgery to longitudinally elucidate the impact from both surgery and subsequent radiation therapy on adverse health outcomes (AHOs) [5–10].

In this prospective population-based cohort study, we aimed to investigate the longitudinal course of urinary, bowel, sexual, and hormonal problems according to PROMs in PC patients treated with SRT, with measurements spanning from before surgery at the earliest until 18 mo after SRT.

2. Patients and methods

2.1. Patients

In 2012, a quality registry for men treated with RALP at the University Hospital of North Norway (UNN) was established. In 2016, a quality registry was established for men treated curatively for PC with new radiotherapy techniques including volumetric modulated arc therapy (VMAT) and simultaneous integrated boost (SIB). The participants filled out the EPIC-26 at the hospital before surgery and radiotherapy, as well as at the last radiotherapy fraction. Furthermore, they were asked to return mailed questionnaires 3 and 18 mo after completed treatment in a prepaid envelope.

In this study on mostly Caucasian men, the majority (87%) of those who received SRT between December 2016 and February 2021 participated in the radiotherapy quality registry (whole cohort, n = 120). Of these men, 48 were registered with EPIC-26 forms in the surgical quality registry (subcohort, n = 48), and their questionnaires could therefore be analyzed with respect to the entire treatment course from before surgery until 18 mo after SRT.

All eligible men received oral and written study information and gave written informed consent before the start of treatment. Both registries are approved by the data protection officer at the UNN. The current study was approved by the Regional Committee for Medical Research Ethics (2018/1849 and 2018/369).

2.2. Treatment characteristics

Clinical data regarding blood samples, comorbidity, histopathology, and cancer treatment details were retrieved from the medical records. Detailed information about the radiation treatment was retrieved from databases at the radiotherapy unit.

The clinical staging of PC was devised from the American Joint Committee on Cancer tumor, node, metastasis (TNM) system. Risk stratification was based on the European Association of Urology (EAU) guidelines according to clinical tumor stage, Gleason score, International Society of Urological Pathology grade, and pretreatment prostate-specific antigen (PSA) level [11,12]. The majority of patients with high-risk features were screened by bone scintigraphy or a magnetic resonance imaging scan of the spine before both surgery and SRT.

All participants had been treated with RP (n = 23) or RALP (n = 97) during January 2003 through August 2020, reflecting the gradual change in surgical technique. For most high-risk patients (n = 66), the pelvic lymph nodes were sampled [12].

SRT was delivered to the prostate bed with the VMAT and SIB techniques (Supplementary material) [13–15]. Adjuvant/concomitant ADT was administered from early 2017 (Supplementary material) [16,17].

2.3. Outcomes

The EPIC-26 questionnaire includes questions for assessing five domains according to urinary incontinence and urinary irritative, bowel, sexual, and hormonal symptoms during or after treatment for PC [6]. According to the scoring manual, the original questions were transformed to a scale from 0 to 100 points, with higher scores indicating better outcomes [18]. If ≥20% of answers composing a domain were missing, the domain summary score (DSS) was not computed.

Scores for the individual questions and the five DSSs were retrieved before RP, 3 mo after RP, before SRT, at the end of SRT, and 3 and 18 mo after SRT, with the last questionnaire used to evaluate long-term effects after treatment [19].

For the evaluation of clinical relevance, estimated values for minimally clinically important differences (MCIDs) of the EPIC-26 domains have been calculated previously [20]: 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.

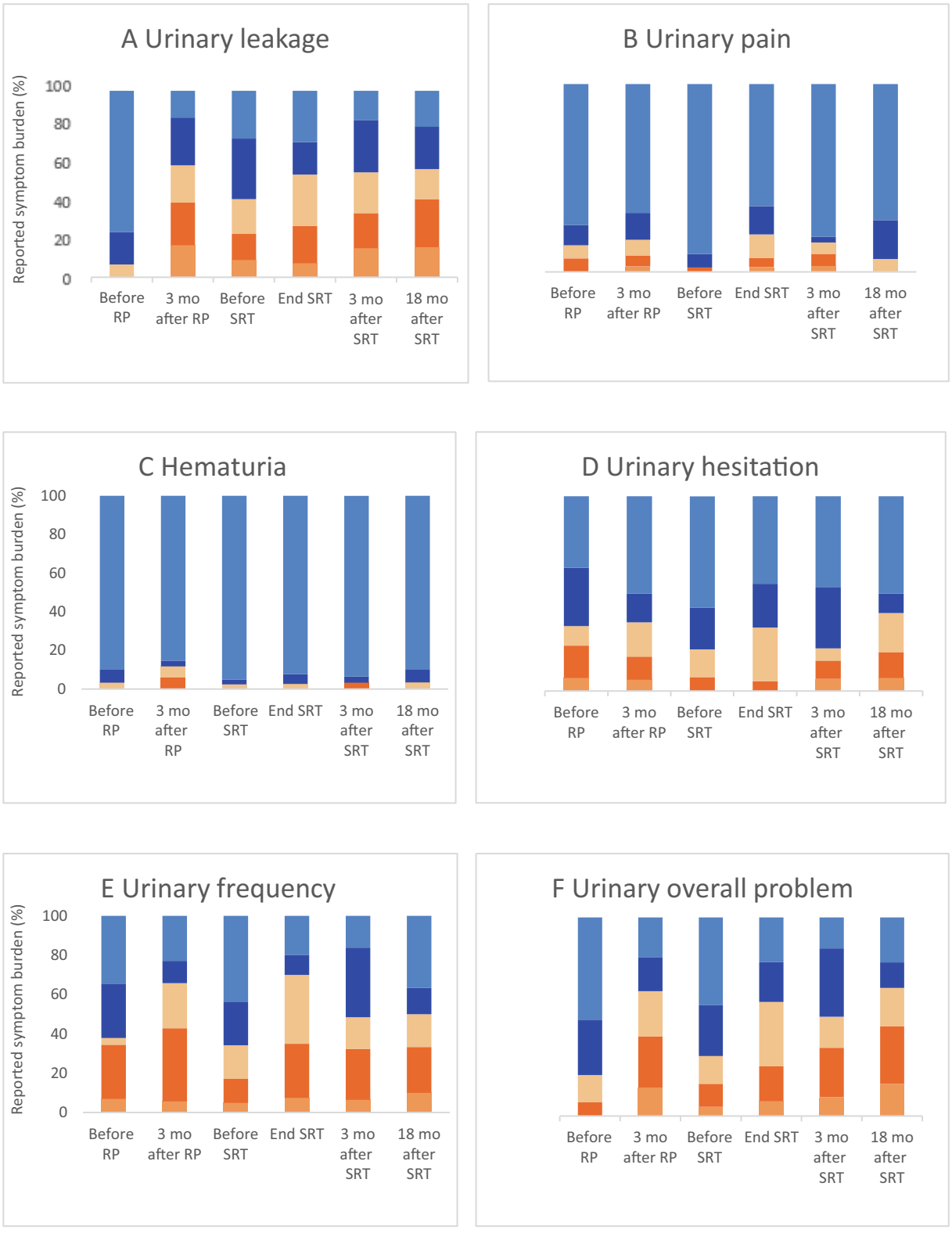

Fig. 1 – Distribution of reported severity of urinary functional problems for the subcohort (*n* = 48) according to time. The darkest orange color represented the most severe symptom, and dark blue represented the least severe symptom. RP = radical prostatectomy; SRT = salvage radiation therapy.

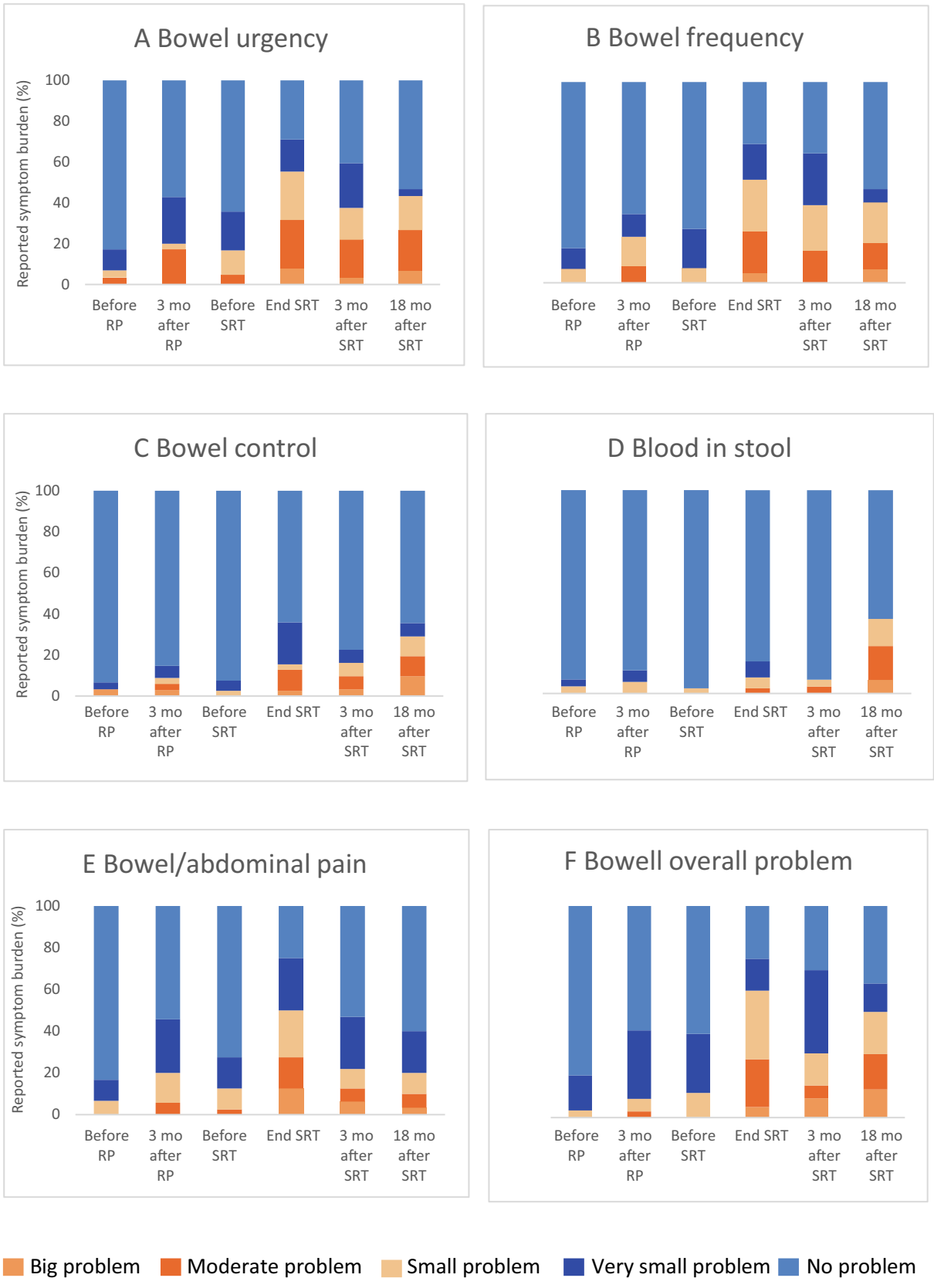

Fig. 2 – Distribution of reported severity of bowel functional problems for the subcohort (*n* = 48) according to time. The darkest orange color represented the most severe symptom, and dark blue represented the least severe symptom. RP = radical prostatectomy; SRT = salvage radiation therapy.

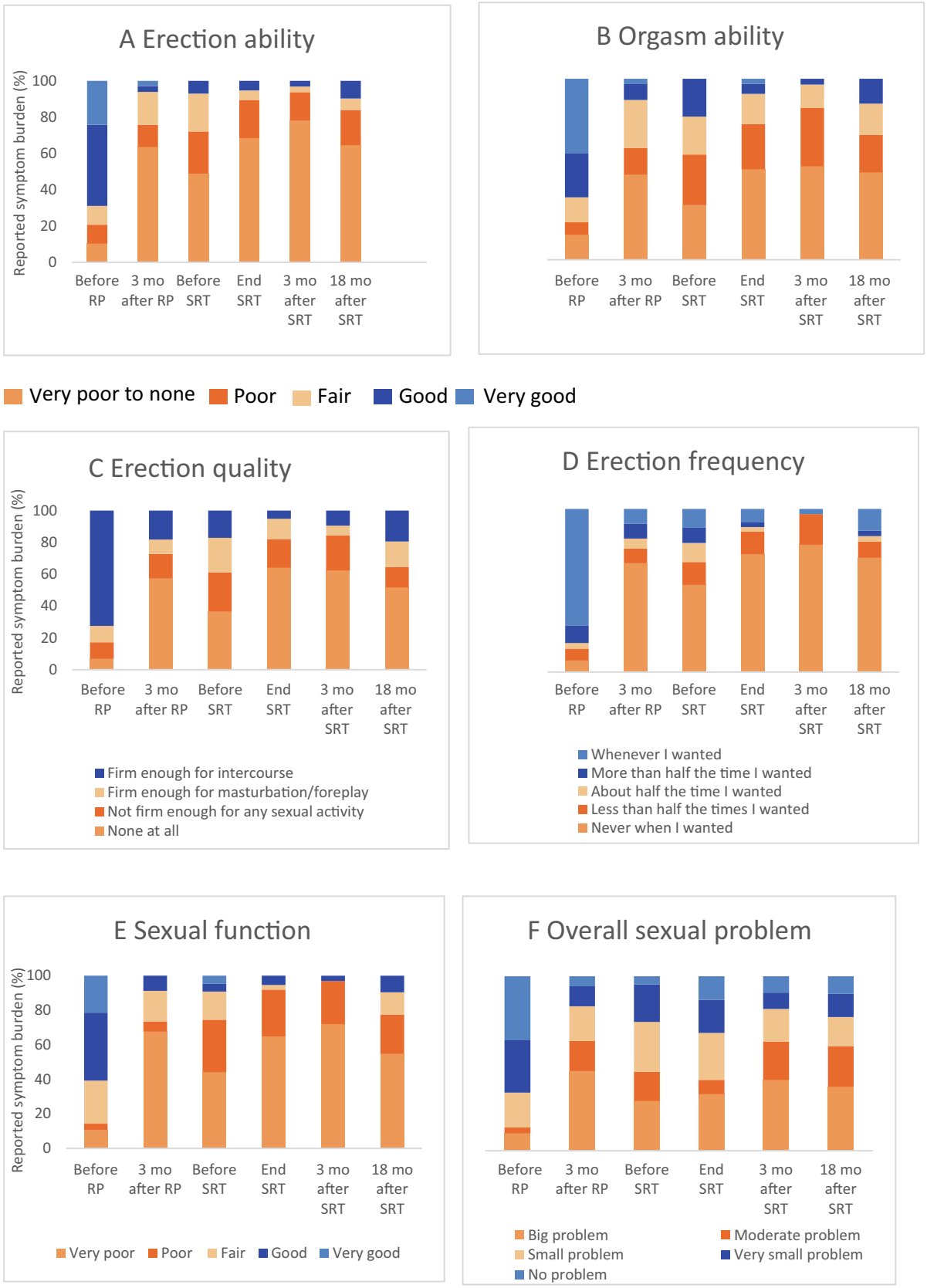

Fig. 3 – Distribution of reported severity of sexual functional problems for the subcohort (*n* = 48) according to time. The darkest orange color represented the most severe symptom, and dark blue represented the least severe symptom. RP = radical prostatectomy; SRT = salvage radiation therapy.

Answers in our study are described as severe if they were reported as a moderate or a big problem to the patient, and are presented in Figures 1–3 and Supplementary Figure 1 for the subcohort. The mean DSS and mean scores for the specific EPIC questions for the whole cohort are presented in Supplementary Table 1. Supplementary Table 2 presents the number of submitted EPIC-26 forms according to follow-up group and time.

2.4. Statistical analysis

Continuous variables are presented as median (range) or mean (standard deviation), and categorical variables as absolute numbers with percentages. The mean changes in DSS at the various times retrieved were compared with baseline (before SRT for the whole cohort and before RP for the subcohort) and were determined using linear mixed models. The analyses were carried out with time as the only variable to determine the mean change in toxicity scores at the different time points throughout the treatment course compared with baseline. Indicator variables of each time point were included as the exposure. In separate analyses, "age", "time from RP to SRT" (categories: <1, 1–3, and >3 yr), "nerve sparing (yes or no)," and "ADT duration" (categories: 0, 1–11, ≥12 mo) as potential confounding factors were added to the models. No imputations were made for missing values. All tests were two sided, and the significance level was defined as $p < 0.05$. The statistical analyses were performed in IBM SPSS, version 27 (Chicago, Illinois, US).

3. Results

3.1. Patients and treatment characteristics

The two cohorts of interest (whole cohort [$n = 120$] and subcohort [$n = 48$]) are presented in Table 1.

The median age at diagnosis was 63 yr in both cohorts of interest. Fewer men had high-risk disease (62% vs 71%) and fewer men were operated with RALP in the whole cohort (81% vs 96%) than in the subcohort.

3.2. Urinary function and problem

Figures 1A–E present urinary function item severity for the subcohort according to time. More than 40% of patients in the subcohort reported a severe degree of urinary leakage 18 mo after SRT (Fig. 1A). At the end of follow-up, 20% were reporting on severe urinary hesitance (Fig. 1D).

Before RP, 6.9% reported severe overall urinary problem. Before SRT, 16% reported severe overall urinary problem, and it was increasing at all time points throughout SRT follow-up until a maximum level of 45% 18 mo after SRT (Fig. 1F).

The linear mixed models for the whole cohort from before SRT until 18 mo after SRT revealed clinically relevant worsening of urinary DSS for incontinence and irritation, with −13.1 and −10.4 ($p < 0.001$), respectively, in mean changes at 18 mo after SRT (Table 2) [20]. Compared with men with >3 yr between RP and SRT, men with <1 yr between RP and SRT had considerable worsening of urinary incontinence (estimated change −17.4 [$p = 0.004$]) and urinary irritation (estimated change −8.2 [$p = 0.01$]).

The estimated mean urinary incontinence DSS in the subcohort was 90.7 before RP (Table 2) and was significantly worsened for all later time points compared with baseline ($p < 0.001$). The estimated mean urinary irritative

Table 1 – Patient and treatment characteristics according to treatment cohort

	Whole cohort ($n = 120$)	Subcohort ($n = 48$)
Age at diagnosis (yr), median (range)	63 (45–74)	63 (48–74)
PSA (μg/ml), median (range)		
At diagnosis	10.0 (2.7–110)	10.2 (2.7–104)
Before SRT	0.4 (<0.1–6.3)	0.5 (<0.1–6.3)
Men with PSA <0.1 μg/ml after RP	80 (67)	35 (71)
Men treated with adjuvant RT	16 (13) [a]	7 (15)
ISUP grade group [b]		
1 + 2 + 3	76 (64)	30 (62)
4+ 5	43 (36)	18 (38)
T stage		
T2	46 (38)	17 (35)
T3a	41 (34)	20 (42)
T3b	31 (26)	10 (21)
T4	2 (2)	1 (2)
N1 stage	22 (18)	8 (17)
Prostate cancer risk group before RP [c]		
Low risk	7 (6)	1 (2)
Intermediate risk	39 (33)	13 (27)
High risk	74 (62)	34 (71)
Time from RP to SRT (yr)		
<1	41 (34)	14 (29)
1–3	41 (34)	18 (38)
>3	38 (32)	16 (33)
Surgery [d]		
RALP	97 (81)	46 (96)
Open retropubic	22 (18)	2 (4)
Laparascopic	1 (1)	
Nerve sparing		
Unilateral	44 (37)	23 (48)12
Bilateral	19 (16)	4 (8)
Nodal lymphadeneectomy	83 (69)	40 (83)
Positive margins	61 (50)	21 (44)
Androgen deprivation therapy	108 (90)	40 (83)
LHRH alone	43 (36)	19 (40)
AA alone	19 (16)	10 (21)
LHRH + AA	46 (38)	11 (23)
ADT duration (mo)		
0	12 (10)	8 (17)
0–11	47 (39)	20 (42)
≥12	61 (51)	20 (42)
Radiotherapy; preparation and regimen		
PSMA-PET before radiotherapy	60 (50)	18 (38)
Prostatic bed, 70 Gy	120 (100)	48 (100)
Pelvic nodal irradiation, 56 Gy	51 (43)	12 (25)
Boost to macroscopic disease, 73 Gy	20 (17)	5 (10)
Comorbidity		
Hypertension	38 (32)	17 (38)
Coronary disease	11 (9)	4 (8)
Diabetes	5 (4)	2 (4)

AA = antiandrogen therapy; ADT = androgen deprivation therapy; ISUP = International Society of Urological Pathology; LHRH = luteinizing hormone releasing hormone agonist; n = number; PSA = prostate-specific antigen; PSMA-PET = prostate-specific membrane antigen positron emission tomography; RALP = robot-assisted laparoscopic prostatectomy; RP = radical prostatectomy; RT = radiotherapy; SRT = salvage radiotherapy; TNM = tumor, node, metastasis.

Data are presented with number (%) unless otherwise specified.

[a] Sixteen men in the whole cohort received adjuvant RT (within 6 mo after surgery) due to positive surgical margins.

[b] The ISUP grade system divides patients into groups based on Gleason score: grade 1 has Gleason score ≤6; grade 2 has Gleason score 3 + 4; grade 3 has Gleason score 4 + 3; grade 4 has Gleason score 8, and grade 5 has Gleason scores 9–10 [20].

[c] The European Association of Urology guidelines classification is based on TNM classification, PSA level, and ISUP grade. The low-risk group has American Joint Committee on Cancer (AJCC) clinical T stage ≤2a, PSA level <10 ng/ml, and ISUP grade 1. The intermediate-risk group has AJCC clinical T stage 2b or PSA level 10–20 ng/ml or ISUP grade 2/3. The high-risk group has AJCC clinical T stage ≥2c or PSA level >20 ng/ml or ISUP grade 4/5 [21]. Risk groups are based on radiological T stage when available, otherwise clinical T stage.

[d] Data are missing for one patient operated abroad in the whole cohort group.

Table 2 – Mean estimates of change for the five domain summary scores according to mixed models of repeated measurement analyses for the whole cohort (*n* = 120, compared with before SRT as baseline) and subcohort (*n* = 48, compared with before RP as baseline)

	Mean estimates of change (95% CI) and *p* value					
	Before RP	3 mo after RP	Before SRT	End of SRT	3 mo after SRT	18 mo after SRT
Whole cohort						
Urinary incontinence			68.7 (63.3, 74.0)	0.5(−3.5, 4.5) 0.81	−7.9 (−12.1, −3.7) **<0.001**	−13.1 (−17.9, −8.2) **<0.001**
Urinary irritative			88.0 (85.0, 91.0)	−9.6 (−12.7, −6.5) **<0.001**	−7.0 (−10.3, −3.8) **<0.001**	−10.4 (−14.1, −6.7) **<0.001**
Bowel			91.5 (87.7, 95.3)	−22.1 (−26.2, −7.9) **<0.001**	−12.9 (−17.2, −8.6) **<0.001**	−16.8 (−21.8, −11.8) **<0.001**
Sexual			29.6 (25.5, 33.7)	−8.6 (−11.9, −5,3) **<0.001**	−14.2 (−17.6, −10.8) **<0.001**	−9.1 (−13.1, −5.1) **<0.001**
Hormonal			85.4 (81.7–89.1)	−12.3 (−16.2, −8.3) **<0.001**	−24.1 (−28.2, −20.1) **<0.001**	−20.2 (−24.9, −15.5) **<0.001**
Subcohort						
Urinary incontinence	90.7 (80.8, 100.6)	−44.6 (−54.3, −35.0) **<0.001**	−25.6 (−34.5, −16.7) **<0.001**	−29.8 (−38.7, −20.8) **<0.001**	−33.1 (−42.7, −23.5) **<0.001**	−35.3 (−45.1, −25.6) **<0.001**
Urinary irritative	79.1 (72.8, 85.3)	−3.9 (−11.1, 3.4) 0.3	8.0 (1.2, 17.7) **0.02**	−0.3 (−7.2, 6.5) 0.93	1.4 (−6.0, 8.7) 0.72	2.6 (−4.8, 10.0) 0.49
Bowel	94.1 (87.6, 100.7)	−7.2 (−14.5, 0.1) 0.054	−3.2 (−10.1, 3.8) 0.37	−24.2 (−31.2, −17.2) **<0.001**	−15.9 (−23.3, −8.5) **<0.001**	−19.3 (−26.8, −11.8) **<0.001**
Sexual	70.6 (62.0, 79.2)	−45.7 (−55.6,−35.7) **<0.001**	−39.2 (−48.5, −30.0) **<0.001**	−49.5 (−59.1, −39.9) **<0.001**	−55.0 (−64.9, −45.1) **<0.001**	−46.0 (−56.3, −35.7) **<0.001**
Hormonal	83.7 (77.4, 89.9)	−2.4 (−9.5, 4.6) 0.5	−1.6 (−8.2, 5.0) 0.63	−12.2 (−19.1, −5.4) **<0.001**	−22.2 (−29.3, −15.2) **<0.001**	−16.7 (24.0, −9.4) **<0.001**

CI = confidence interval; RP = radical prostatectomy; SRT = salvage radiotherapy.
Statistically significant values ($p < 0.05$) are highlighted in bold. In the whole cohort, there is one missing for all domain summary scores for urinary irritative and bowel analyses, and two missing for all domain summary scores for sexual analyses. In the subcohort, there is one missing for all domain summary scores for sexual analyses.

DS was 79.1 before RP, with improvement before SRT (8.0, $p = 0.02$). Age, time between RP and SRT, and ADT usage were not confounding factors in the mixed models' analyses for the subcohort. Nerve sparing was positively associated with urinary irritative DSS with an estimate of 8.8 ($p = 0.02$).

3.3. Gastrointestinal function and problem

For the subcohort, all bowel functional problems were reported with higher severity at all time points after SRT, compared with that before RP and before SRT (Fig. 2A–E). Severe bowel urgency, loss of control, and blood in stools were reported by ≥20% 18 mo after SRT.

The proportion of severe overall bowel problem increased dramatically from before SRT to the end of SRT, from 0% to 27%. This high severity in overall bowel problem was maintained until 18 mo after SRT (Fig. 2F).

The mean DSS estimates for the whole cohort decreased significantly at all time points, with clinical relevance after receiving SRT versus before SRT ($p < 0.001$; Table 2). The estimated mean bowel DSS for the sub-cohort decreased significantly at all time points after completing SRT (Table 2). None of the covariates of interest were associated with bowel DSS.

3.4. Sexual function and problem

A considerable proportion of the subcohort reported severe symptoms according to all sexual function items at all time points after RP (Fig. 3A–E). After SRT, all function items had worsening of symptom severity, with a maximum of reported problems at the end of SRT and 3 mo after SRT. Overall sexual problem (Fig. 3F) was reported with somewhat less severity compared with the specific sexual function items.

The mean sexual DSS estimates for the whole cohort decreased significantly at all time points after receiving SRT ($p < 0.001$, all; Table 2). Age and ADT duration (≥12 mo) was negatively associated with sexual DSS, with an estimate of −0.7 per year ($p = 0.01$) and −14.4 ($p = 0.03$), respectively. Nerve sparing was positively associated with sexual DSS, with an estimate of 8.5 ($p = 0.03$).

For the total subcohort, the estimated mean sexual DSS decreased significantly and had very low and clinically relevant estimated mean scores at all time points after completing RP ($p < 0.001$; Table 2). Age was negatively associated with sexual DSS, with an estimate of −1.1 per year ($p = 0.01$). Nerve sparing was positively associated with sexual DSS, with an estimate of 16.8 ($p = 0.002$).

3.5. Hormonal function and problem

For the subcohort, severe hot flashes or breast tenderness was not reported after RP, but were reported by 13.4% 18 mo after SRT (Supplementary Fig. 1). High degrees of depression and lack of energy were reported by a substantial proportion of men at all time points, with more severe problems 18 mo after SRT (33.4% and 56.7% reporting depression and lack of energy, respectively; Supplementary Fig. 1C and 1D).

The mean change of hormonal DSS for the subcohort was not significantly reduced after RP, but had clinically relevant decreases at all time points after SRT ($p < 0.001$; Table 2). Age was positively associated with hormonal DSS, with an estimate of 0.8 per year ($p = 0.006$).

For the whole cohort, the estimated mean change of hormonal DSS decreased with clinical relevance at all time points after SRT ($p < 0.001$; Table 2). Age was positively associated with hormonal DSS, with an estimate of 0.7 per year ($p = 0.03$). ADT duration (≥12 mo) was negatively associated with hormonal DSS, with an estimate of −9.8 ($p = 0.08$).

4. Discussion

In this prospective cohort study on PC patients, we report PROMs and estimated mean change of EPIC DSS from before surgery at the earliest until 18 mo after SRT. We have showed that urinary incontinence, bowel, hormonal, and sexual DSSs were significantly reduced 18 mo after SRT compared with those before surgery. As far as we know, there are few equivalent longitudinally studies comparing PROMs with data before surgery.

The mean urinary incontinence DSSs reported before RP and before SRT among our cohorts are in line with earlier reported baseline functions [8–10,21,22]. We observed a considerable, clinically relevant increase of urinary incontinence 3 and 18 mo after SRT, which contrasts with the findings of several previous studies that reported long-term stable or improving urinary continence symptoms for SRT-treated men [7,8,22].

In the whole cohort, we observed clinically important worsening of urinary irritative function 18 mo after SRT compared with pre-SRT levels. Comparable studies show stable urinary irritative function 12–72 mo after SRT [8,10], although Braide et al [5] reported an increased impact of SRT on urinary symptoms compared with patients with prostatectomy only. In our study, timing of SRT impacted long-term urinary function, significantly worsening problems for men receiving SRT <1 yr after RP compared with men receiving SRT >3 yr after RP. Earlier studies regarding adverse effects of SRT with respect to timing after RP are conflicting and originated from retrospective data [23].

The improved estimated urinary irritative DSS in our subcohort from before RT to before SRT is in line with a report by Hoffman et al [21], and is expected as many patients suffer from irritative and obstructive symptoms before RP due to an enlarged prostate. Our subcohort had stable urinary irritative symptoms at 18 mo after SRT compared with that before RP.

Both our cohorts report high levels of bowel symptoms after SRT, exceeding MCID threshold levels for bowel function significantly [20]. In our subcohort, bowel function was reduced temporarily at 3 mo after RP, but with stabilized levels before SRT, in agreement with previous studies [21,24]. Our findings are in line with those of Braide et al [5], who have recently reported long-term relative risks for SRT-treated patients compared with those treated with RP only, ranging from 1.7 to 6.5 concerning rectal symptoms, whereas other studies report long-term stable bowel functions after SRT [7–9]. Worth noticing is the particularly

high increase of symptoms and lack of recovery of bowel on long-term follow-up.

In line with other studies reporting on PROMs during and after RP, we found a substantial decline in sexual function 3 mo after RP and before SRT [21,24]. The further clinically relevant decline in sexual function noted 3 mo after SRT is probably due to ongoing adjuvant ADT in the majority of patients. A significant decline in sexual function was observed at 18 mo after SRT for the whole cohort, but the estimated change did not reach clinically important threshold levels, equivalent with comparable research [5,8,9].

Hormonal function did not change from before RP to before SRT for the subcohort, with levels corroborating prior studies [21,25]. However, the hormonal function decreased significantly 3 mo after SRT and remained at low levels 18 mo after SRT for both cohorts. This abrupt change of hormonal function is presumably caused by ADT. A particular matter of concern in our study is the high levels of severe depression and lack of energy reported 18 mo after SRT. This can be due to ADT use, although many men in our study have probably returned to normal testosterone levels at 18 mo after SRT, since a previous study showed a median testosterone recovery at 6.8 mo after ADT treatment for <18 mo [26]. Distress because of serious illness and worries about lack of recovery could influence the patient's global perception of health and well-being.

Published studies on SRT report on different treatment regimens, both according to prostate bed doses, and whether they give pelvic nodal irradiation and/or ADT treatment. According to the SAKK 09/10 study, comparing 64 with 70 Gy to prostate bed, the higher dose increased gastrointestinal side effects without improving biochemical progression freedom [27]. GETUG-AFU 16 showed increased toxicity only in the form of hot flushes when comparing between SRT with and without short-term ADT (goserelin 6 mo) [16]. Thus, some of the reported toxicity discrepancy could be due to our more heavily treated cohort, with more high-risk patients than in other studies. Nevertheless, our treatment is in line with a recently published trial demonstrating biochemical progression–free advantage for men receiving SRT with ADT treatment and nodal irradiation [4].

For men experiencing a BCR after RALP, the main concern is often related to their possibility of curation and overall survival, but only a subgroup of these will proceed to metastatic progression [28]. As more patients with advanced PC are offered RALP, the number of patients accepted for SRT will increase as it currently is the only possible curative treatment option for BCR after RP [29]. A recent, validated EAU BCR risk stratification (low and high risk), based on PSA doubling time and pathological Gleason score, has been proposed to help guide clinicians and patients to well-informed decisions concerning SRT [30]. Herein, we present information on treatment-related symptoms that should also impact these treatment decisions.

The major advantages of our study include the prospective and longitudinal design with EPIC questionnaires before treatment, and treatment that was administered with contemporary techniques.

Limitations in our study include that few patients were available from the surgical quality registry, hampering the power of the longitudinal analyses for the subcohort. To further assess long-term AHOs of patients treated with SRT, we need studies with longer follow-up time, including PROMs evaluated before RP, and specific information on impact of the radiotherapy. Details on how radiotherapy techniques and dose constraints influence the AHOs will be published later by this group.

5. Conclusions

SRT decreases urinary, bowel, and sexual functions. Advising patients regarding the risk of AHOs is necessary to increase the possibility of patients taking part in shared decision-making before SRT. We suggest that selection of patients for SRT should be balanced carefully with the potential benefits, and patients with high levels of AHOs after SRT should be offered more extensive support after treatment.

Author contributions: Hege S. Haugnes had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Appendix A. Supplementary data

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