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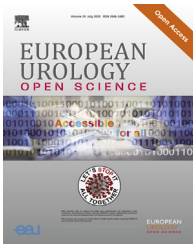

European Association of Urology

Prostate Cancer

Fear of Recurrence in Prostate Cancer Patients: A Cross-sectional Study After Radical Prostatectomy or Active Surveillance

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Abstract

Background: Fear of recurrence (FoR) is a distressing consequence of cancer. Little is known about the prevalence of FoR in different treatment groups and factors associated with FoR among prostate cancer (PCa) survivors.
Objective: To investigate the prevalence of high FoR among PCa survivors after radical prostatectomy (RP) or under active surveillance (AS) and to explore clinical and psychological factors potentially associated with FoR.
Design, setting, and participants: This is a retrospective cross-sectional study of 606 patients with PCa, treated with either RP (n = 442) or AS (n = 164) at two Norwegian regional hospitals. The 440 patients (73%) who gave consent to participate were invited in 2017 to complete a questionnaire measuring FoR, self-rated health, adverse effects, and psychological factors at a mean of 4.1 yr (standard deviation 1.7) after their treatment decision. Clinical data were retrieved from medical records.
Outcome measurements and statistical analysis: FoR was measured using the Concerns About Recurrence Questionnaire, with high FoR defined as a sum score of $\geq$12 points (range 0–40). Using multivariable logistic regression analyses, factors associated with high FoR were identified.
Results and limitations: One-third of the participants had high FoR; scores were higher in the AS group and in the RP group with treatment failure. Younger age was significantly associated with high FoR in the AS group, while high prostate-specific antigen at diagnosis, biochemical recurrence, positive surgical margin, higher

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fatigue, and a type D personality were significantly associated with high FoR in the RP group.

Conclusions: At 4 yr after a diagnosis of PCa, high FoR was common, especially among AS patients and among RP patients with treatment failure.

Patient summary: In this study, we examined fear that their disease will return or progress among prostate cancer survivors. We found that such fear was common, especially among young patients under active surveillance and among radical prostatectomy patients with treatment failure or with certain psychological features.

1. Introduction

In oncology, the consensus definition of fear of recurrence (FoR) is worry or concern about cancer returning or progressing [1]. FoR is applicable in all stages of cancer, from newly diagnosed patients to those with recurrence and progression to incurable disease [1]. High FoR is long-lasting and is associated with lower health-related quality of life, a reduced ability to plan for the future, and trauma-related and depressive mental symptoms [2–4]. FoR is considered one of the most distressing adverse effects of cancer [5] and imposes a substantial burden on patients [6].

Considering that men with localized prostate cancer (PCa) in general have a 5-yr relative survival rate of almost 100%, one might expect levels of FoR to be low [7]. However, FoR is common among men with PCa [2,3,8,9] and a recent Dutch study concluded that one-third of patients with localized PCa had high FoR [3]. Although ongoing adverse effects of cancer treatment are associated with high FoR, studies have indicated that radical prostatectomy (RP) tends to reduce FoR and that active surveillance (AS) may be associated with a higher level of FoR than RP [2,8]. A longitudinal American study showed that men with positive surgical margins after RP developed higher FoR compared to men with negative surgical margins, and that the differences in FoR increased over time [9]. Another study found that adjuvant radiotherapy (RT) and younger age were associated with high FoR after RP, while prostate-specific antigen (PSA) level and time since the last PSA test were not [3]. In a study in Sweden of low-risk PCa patients, twice as many AS patients reported that they feared they would die from PCa in comparison to patients receiving curative treatment (8% vs 3.8%) [10].

In a review of the literature, we found few studies of PCa patients that measured FoR after a known recurrence or treatment failure, and most studies were not able to identify participants with recurrence in their analyses [2,3,8]. Moreover, little is still known about factors associated with high FoR in different treatments groups of contemporary PCa patients.

With the ultimate goal of improving both pretreatment and post-treatment counseling of PCa survivors, including those with treatment failure, the aims of this study were to estimate the prevalence of FoR among patients treated with either AS or RP and to identify factors associated with high FoR in both treatment groups.

2. Patients and methods

2.1. Study design and participants

The two regional hospitals of Telemark and Vestfold Counties in south-eastern Norway provide care to all of the approximately 400 000 inhabitants. The urological departments diagnose and treat PCa according to international guidelines, and patients are involved in shared decision-making [11]. All living PCa patients aged ≤67 yr at diagnosis and treated with either RP or AS between 2010 and 2015 at these two hospitals were mailed an invitation to complete a questionnaire. A reminder was sent after 2 mo (Fig. 1). Responding RP patients who had previously been on AS (n = 34) were included in the RP group.

2.2. Primary outcome variable

FoR was self-reported using the Concerns About Recurrence Questionnaire (CARQ) [12], a five-item instrument originally developed and validated to measure FoR in breast cancer patients [12]. The items are gender neutral and have a global character that seems suitable for any cancer type (Supplementary material) [12]. On CARQ items 1–3, the patients rate the presence of different aspects of FoR over the last month from 0 (not at all) to 10 (all the time). On item four, the patients indicate their perceived absolute risk of recurrence at a value between 0% and 100%. On item five, the patients estimate their risk of recurrence in comparison to other men with PCa, with scores from 1 to 5. Psychometric testing among breast cancer patients showed satisfactory reliability and validity only for the first four items (CARQ-4) [12]. Similar testing in our sample gave the same result and therefore item 5 was omitted from the sum score (Supplementary material).

The range for the CARQ-4 sum score is 0–40, and a higher score represents higher FoR. For breast cancer patients, a score of ≥12 points was optimal for detection of clinically significant FoR [12]. In the absence of published thresholds for PCa patients, we chose the same cutoff to dichotomize high and low FoR.

2.3. Other scales and variables

Relevant clinical data were retrieved from medical records and the participants were classified according to European Association of Urology (EAU) risk groups [11]. Biochemical recurrence was defined as having two or more PSA values of >0.2 μg/l after RP [11]. We dichotomized the RP patients according to whether they had experienced treatment failure (TF) or not. TF was defined as having either

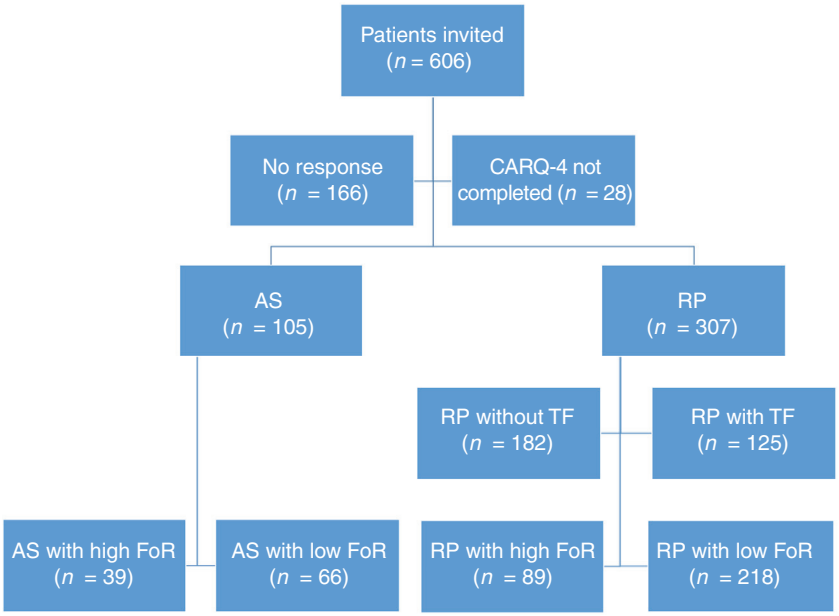

Fig. 1 – Flowchart of the study sample. CARQ-4 = Concerns About Recurrence Questionnaire-4; AS = Active surveillance; RP = Radical prostatectomy; TF = treatment failure; FoR = fear of recurrence.

biochemical recurrence, positive margin, positive surgical N status, PSA $\geq$ 0.2 μg/l at 6 wk after RP, postoperative RT, or ongoing hormonal treatment.

The EuroQoL 5D questionnaire was used for measuring self-rated health [13]. The Expanded Prostate Cancer Index Composite (EPIC-26) and Fatigue Questionnaire were used to measure physical adverse effects in relation to PCa and fatigue, respectively [14,15]. The CAGE questionnaire was used to identify patients with risky alcohol consumption [16] and the Type D Scale-14 to assess type D personality traits (a combination of high negative affectivity and social inhibition) [16,17]. Questions about marital status, educational level, occupation, and comorbidity were also included in the questionnaire. Further descriptions of the instruments are provided in the Supplementary material.

2.4. Statistical analyses

Descriptive statistics are presented as the frequency and percentage for categorical variables, and as the mean and standard deviation (SD) for continuous variables. Bivariate comparisons were made using χ^2 tests for categorical variables and independent-sample *t* tests or analysis of variance for continuous variables. We estimated bivariate and multivariable logistic regression models with high FoR as the dependent variable (low FoR as the reference). Variables previously shown to be associated with FoR or that were considered clinically relevant were included in the multivariable analyses after testing for multicollinearity using Spearman's coefficient ρ (<0.60). Results are reported as the odds ratio and corresponding 95% confidence interval. Since RP and AS patients are inherently different, all analyses were conducted separately for these two groups. In the psychometric testing of CARQ-4, bivariate correlations were estimated using Spearman's coefficient ρ. Internal consistency was measured using Cronbach's α. The level of significance was set at $p < 0.05$ and all tests were two-sided. An attrition analysis of age and clinical factors was carried out. Data analyses were performed with IBM SPSS v.25.0 (IBM, Armonk, NY, USA).

2.5. Ethics

The Regional Committee for Medical and Health Science Research of South-East Norway approved the study (#2016/925). All invited patients received written information about the study and were only included after giving written informed consent.

3. Results

3.1. Sample characteristics

Of the 606 patients invited, 440 (73%) returned the questionnaire (Fig. 1). The mean time from diagnosis to the survey was 4.1 yr (SD 1.7). The mean age was 60.9 yr (SD 4.4) at diagnosis and 65.0 yr (SD 4.2) at the time of the survey. The attrition analysis revealed no statistically significant differences between responders and nonresponders regarding age at diagnosis, distribution of risk group, or primary and postoperative treatments. Biochemical recurrence was more common among nonresponders (28% vs 14%; $p = 0.004$; Supplementary material).

3.2. Prevalence of FoR

High FoR was found for 128 patients (31%) in the total sample. Thirty-nine (37%) of the AS patients, 35 (19%) of the RP patients without TF, and 54 (43%) of the RP patients with TF had high FoR ($p < 0.001$ between these three groups). The mean CARQ-4 score was 10.1 (SD 8.8) in the AS group, 6.4 (SD 7.7) in the RP group without TF, and 11.6 (SD 10.0) in the RP group with TF ($p < 0.001$; Table 1). The RP group without TF scored all individual CARQ items significantly lower, and for item 4 their mean perceived risk of

Table 1 – Demographic and clinical characteristics, treatment groups, and CARQ–4 scores.

Variable	Patients (N = 412)	Mean CARQ-4 score (SD)	p value
Mean age at diagnosis, yr (SD)	60.9 (4.2)	8.9 (9.0)	
Mean age at survey, yr (SD)	65.0 (4.4)	N/A	
Paired relationship, *n* (%)			0.72
No	57 (14)	9.3 (9.6)	
Yes	355 (86)	8.9 (8.9)	
Level of education, *n* (%)			0.78
≤12 yr	227 (55)	9.1 (9.1)	
>12 yr	184 (45)	8.8 (8.9)	
Work status, *n* (%)			0.90
Employed	200 (49)	9.0 (8.8)	
Unemployed	45 (11)	9.3 (9.4)	
Retired	161 (39)	8.7 (9.1)	
Body mass index class, *n* (%)			0.51
<25 kg/m^2	111 (27)	8.1 (8.6)	
25–30 kg/m^2	244 (59)	9.3 (9.0)	
>30 kg/m^2	56 (14)	9.3 (9.8)	
Comorbidities, *n* (%)			0.16
0–1	300 (73)	8.5 (8.7)	
2 or more	112 (27)	10.0 (9.6)	
EAU risk group, *n* (%)			0.08
Low	109 (26)	9.6 (8.9)	
Intermediate	208 (51)	7.9 (8.6)	
High	94 (23)	10.3 (9.7)	
Treatment group, *n* (%)			<0.001
Active surveillance	105 (26)	10.1 (8.8)	
Radical prostatectomy without TF	182 (44)	6.4 (7.7)	
Radical prostatectomy with TF	125 (30)	11.6 (10.0)	

CARQ-4 = Concerns About Recurrence Questionnaire-4; EAU = European Association of Urology; N/A = not applicable; SD = standard deviation; TF = treatment failure (defined as having any of the following: biochemical recurrence, positive margin, positive surgical n–status, prostate-specific antigen ≥0.2 μg/l at 6 wk postoperatively, postoperative radiotherapy, or ongoing hormonal treatment).

recurrence was 14%, compared to 31% in both the AS group and RP group with TF ($p < 0.001$; Supplementary material).

3.3. *Factors associated with high FoR among AS patients*

Univariate analyses revealed that AS patients with high FoR were younger, had poorer self-rated health, a worse incontinence score, more fatigue, and more often had sleep problems and a type D personality in comparison to those with low FoR (Table 2). Cancer-related factors, such as EAU risk groups, were not significantly associated with high FoR. In the multivariable analysis, only lower age remained associated with high FoR (Table 3).

3.4. *Factors associated with high FoR after RP*

RP patients with high FoR more often had PSA > 10 μg/l at diagnosis, high-risk PCa, TF, poorer self-rated health, worse incontinence scores, more fatigue, sleep problems, and a type D personality in comparison to those with low FoR (Table 4). On multivariable analysis, PSA > 10 μg/l at diagnosis, positive surgical margin, biochemical recurrence, high fatigue score, and type D personality remained significantly associated with high FoR (Table 5).

3.5. *Psychometric testing*

Interitem correlation and internal consistency for CARQ-4 in our sample was at least as good as those for breast cancer patients. Correlation analysis to validated instruments

Table 2 – Comparison of groups reporting high and low FoR among the active surveillance patients.

Variable	High FoR (n = 39)	Low FoR (n = 66)	p value
Mean age at survey, yr (SD)	63.7 (4.2)	65.8 (4.3)	0.016
Mean follow-up time, yr (SD)	3.5 (1.5)	3.9 (1.8)	0.23
Body mass index class, *n* (%)			0.08
<25 kg/m^2	16 (41)	18 (27)	
25–30 kg/m^2	21 (54)	35 (53)	
≥30 kg/m^2	2 (5)	13 (20)	
Prostate-specific antigen at diagnosis, *n* (%)			0.53
<10 μg/l	36 (92)	57 (86)	
≥10 μg/l	3 (8)	9 (14)	
Clinical T stage, *n* (%)			N/A
cT1–T2c	39 (100)	66 (100)	
≥cT3a	0	0	
Gleason score at biopsy, *n* (%)			0.60
6	26 (67)	50 (76)	
7a	12 (31)	15 (23)	
≥7b	1 (3)	1 (1)	
EAU risk group, *n* (%)			0.49
Low risk	24 (62)	45 (68)	
Intermediate risk	15 (38)	21 (32)	
High risk	0 (0)	0 (0)	
Self-rated health, mean (SD)	75.2 (16.0)	84.2 (10.4)	0.001
Incontinence score, mean (SD)	87.3 (14.4)	92.4 (10.8)	0.041
Sexual domain, mean (SD)	64.6 (25.4)	70.5 (24.2)	0.24
Total fatigue score, mean (SD)	12.9 (4.0)	10.6 (2.8)	0.002
Current sleep problems, *n* (%)	15 (39)	12 (18)	0.022
Hazardous alcohol consumption, *n* (%)	8 (21)	7 (11)	0.17
Type D personality, *n* (%)	8 (21)	3 (5)	0.018

FoR = fear of recurrence; EAU = European Association of Urology; N/A = Not applicable; SD = standard deviation.

Table 3 – Bivariate and multivariate logistic regression analyses of the active surveillance patients with various independent variables and high FoR as the dependent variable and low FoR as the reference.

Variables	Bivariate analyses			Multivariable analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age at survey	0.89	0.81–0.98	**0.019**	0.89	0.80–0.98	0.025
Body mass index ≥25 kg/m^2	0.54	0.23–1.24	0.15			
PSA at diagnosis ≥10 μg/l	0.53	0.13–2.08	0.36			
Gleason score at biopsy ≥7a	1.56	0.68–3.28	0.32			
Intermediate EAU risk group	1.34	0.59–3.01	0.49	1.01	0.38–2.66	0.99
Self-rated health	0.95	0.91–0.98	**0.002**	0.96	0.93–1.01	0.08
Incontinence score	0.97	0.94–1.00	**0.049**	0.98	0.95–1.02	0.42
Sexual domain score	0.99	0.97–1.01	0.24			
Total fatigue score	1.25	1.08–1.45	**0.003**	1.12	0.95–1.32	0.19
Current sleep problems	2.81	1.15–6.91	**0.024**	1.66	0.55–5.01	0.37
Hazardous alcohol consumption	2.14	0.71–6.45	0.18			
Type D personality	5.42	0.34–21.86	**0.018**	2.02	0.38–10.77	0.41

CI = confidence interval; EUA = European Association of Urology; FoR = fear of recurrence; OR = odds ratio; PSA = prostate-specific antigen.

Table 4 – Comparison of groups reporting high and low FoR among the radical prostatectomy patients.

Variable	High FoR (*n* = 89)	Low FoR (*n* = 218)	*p* value
Mean age at survey, yr (SD)	64.4 (4.7)	65.3 (4.3)	0.09
Mean follow-up time, yr (SD)	4.3 (1.7)	4.2 (1.7)	0.68
BMI, N (%)			0.17
<25 kg/m^2	16 (18)	61 (28)	
25–30 kg/m^2	59 (66)	129 (59)	
≥30 kg/m^2	14 (16)	27 (13)	
Previously on active surveillance, *n* (%)	6 (7)	28 (13)	0.12
PSA at diagnosis, *n* (%)			0.002
<10 μg/l	43 (48)	146 (67)	
≥10 μg/l	46 (52)	72 (33)	
Clinical T stage, *n* (%)			0.20
cT1–T2c	73 (83)	191 (88)	
≥cT3a	15 (17)	25 (12)	
Gleason score at biopsy, *n* (%)			0.006
6	14 (16)	40 (18)	
7a	20 (22)	85 (39)	
≥7b	55 (68)	93 (43)	
EAU risk group, *n* (%)			0.022
Low risk	12 (13)	28 (13)	
Intermediate risk	40(45)	132 (61)	
High risk	37 (42)	57 (26)	
Pathological T–stage, *n* (%)			0.08
pT1–2c	42 (47)	127 (58)	
≥pT3a	47 (53)	91 (42)	
Treatment failure, *n* (%)	54 (61)	71 (33)	<0.001
PSA ≥ 0.2 μg/l at 6 wk postoperatively, *n* (%)	11 (12)	9 (4)	0.019
Positive surgical margin, *n* (%)	33 (37)	49 (23)	0.009
Biochemical recurrence, *n* (%)	26 (29)	19 (9)	<0.001
Postoperative radiation therapy, *n* (%)	30 (34)	31 (14)	<0.001
Ongoing hormonal treatment, *n* (%)	11 (12)	7 (3)	0.002
Self-rated health, mean (SD)	73.8 (16.7)	80.8 (13.9)	<0.001
Incontinence score, mean (SD)	60.0 (30.4)	71.1 (26.3)	0.003
Sexual domain, mean (SD)	19.5 (18.8)	24.2 (22.0)	0.08
Total fatigue score, mean (SD)	14.3 (4.6)	11.7 (3.9)	<0.001
Current sleep problems, *n* (%)	28 (32)	41 (19)	0.016
Hazardous alcohol consumption, *n* (%)	21 (24)	31 (14)	0.049
Type D personality, *n* (%)	30 (35)	31 (14)	<0.001

FoR = fear of recurrence; EAU = European Association of Urology; N/A = Not applicable; PSA = prostate-specific antigen; SD = standard deviation.

measuring fatigue, anxiety, and depression implied good discriminant validity of CARQ-4. (Supplementary material).

4. Discussion

4.1. Main findings

According to our definition, approximately one-third of the participants had high FoR, and FoR was more common among AS patients and among RP patients with TF. High FoR was associated with low age among AS patients, and with high PSA at diagnosis, biochemical recurrence, positive surgical margin, fatigue, and type D personality among RP patients.

4.2. FoR prevalence

The FoR prevalence in our sample supports findings from previous studies indicating that FoR is common among PCa patients [3,18].

AS patients and RP patients with TF had a higher CARQ-4 score than RP patients without TF. Considering the excellent cancer-specific survival for low-risk PCa and the fact that AS patients do not experience surgery-related adverse events, we expected lower FoR levels in this group. Some studies have indeed shown that anxiety among AS patients is low or comparable with that of RP or RT patients [19–21]. Conversely, AS patients had higher FoR than RP patients in an Irish study [8], and Swedish AS patients more often thought they would die from PCa when compared to their RP counterparts [10]. PSA screening and early detection of PCa are controversial, as they carry a risk of overdiagnosing many patients [11]. The high FoR levels among AS patients in this study is an important finding in this context, as diagnosing more low-risk PCa might subject more patients to FoR [11,22]. The low FoR among successfully treated RP patients was expected, and might reflect the patients' wish

Table 5 – Bivariate and multivariate logistic regression analyses of the radical prostatectomy patients with various independent variables and high FoR as the dependent variable and low FoR as the reference.

Variable	Bivariate analyses			Multivariable analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age at survey	0.95	0.90–1.01	0.09	0.94	0.88–1.00	0.06
Body mass index ≥25 kg/m^2	1.78	0.96–3.30	0.07	1.71	0.82–3.38	0.16
PSA at diagnosis ≥10 μg/l	2.17	1.31–3.59	**0.003**	2.32	1.26–4.26	0.007
Clinical T stage ≥cT3a	1.57	0.78–3.14	0.20			
Gleason score at biopsy						
6	1.00	Reference	–			
7a	0.67	0.31–1.47	0.31			
≥7b	1.69	0.84–3.38	0.14			
EAU risk group						
Low risk	1.00	Reference	–			
Intermediate risk	0.71	0–33–1.52	0.37			
High risk	1.51	0.69–3.35	0.31			
Pathological stage ≥pT3a	1.56	0.95–2.56	0.08	0.76	0.38–1.49	0.42
Treatment failure	3.19	1.92–5.33	<**0.001**			
PSA ≥0.2 μg/l at 6 wk postoperatively	3.26	1.30–8.17	**0.012**	3.78	0.95–15.00	0.059
Positive surgical margin	2.02	1.18–3.45	**0.01**	2.12	1.08–4.14	0.029
Postoperative radiotherapy	3.07	1.71–5.48	<**0.001**	0.98	0.41–2.51	0.98
Biochemical recurrence	4.32	2.24–8.33	<**0.001**	4.65	1.74–12.42	0.002
Ongoing hormonal treatment	4.25	1.59–11.36	**0.004**	1.76	0.48–6.49	0.40
Self-rated health	0.97	0.96–0.99	<**0.001**	1.00	0.97–1.02	0.80
Incontinence score	0.99	0.98–0.99	**0.002**	0.99	0.98–1.00	0.12
Sexual domain score	0.99	0.98–1.00	0.08			
Total fatigue score	1.16	1.09–1.23	<**0.001**	1.11	1.02–1.21	0.020
Current sleep problems	1.98	1.13–3.48	**0.017**	1.10	0.52–2.32	0.80
Hazardous alcohol consumption	1.85	1.00–3.44	0.051	1.72	0.80–3.72	0.17
Type D personality	3.16	1.76–5.66	<**0.001**	2.14	1.01–4.56	0.048

CI = confidence interval; EUA = European Association of Urology; FoR = fear of recurrence; OR = odds ratio; PSA = prostate-specific antigen.

to be “free of cancer” at any cost. In addition, having chosen an active treatment procedure could make RP patients feel more in control over their own health when compared to AS patients.

4.3. *Factors associated with high FoR*

The main finding in the AS group was that younger patients reported the highest levels of FoR, and there was a similar tendency among the RP patients. The association between young age and high FoR is well known from both studies of PCa survivors and cancer survivors in general [3,6,23,24]. Younger patients may feel that they have more “life to lose” and are more vulnerable to life events caused by the cancer in terms of their working life and financial responsibilities, for example. Among breast cancer survivors, the intrusiveness (physical, social, and economic consequences) of the disease seemed to mediate the higher FoR among younger patients [23]. The same could be true for young RP patients, although adverse effects such as urinary incontinence did not remain significant in our multivariable analysis.

Among the AS patients, 36 (34%) had intermediate-risk PCa, mostly because of their Gleason score. The risk of progression and metastasis is significantly higher when Gleason 4 pattern is present in biopsies, but risk group was still not associated with high FoR among the AS patients [25]. We speculate that this might be explained by AS patients with intermediate-risk PCa being better informed about their risk and therefore more certain about their treatment choice.

TF after RP implied higher FoR. This finding was not surprising and has also been demonstrated by Hong et al [9]. However, the relationship between TF and actual worse prognosis is not always clear. A large systematic review found that a positive surgical margin showed no clear correlation with hard endpoints such as distant metastases and PCa-specific mortality [26]. Another review indicated that biochemical recurrence is of prognostic importance only to a subgroup of patients with a PSA doubling time of <1 yr or a Gleason score ≥8 [27]. FoR might be higher among these patients because they are troubled by the impression that the cancer is not completely gone, and perhaps better information about the often low impact on prognosis could reduce this fear.

Interestingly, even though the group who had received postoperative RT arguably had the worst prognosis in our sample, no association was found between postoperative RT and high FoR. These findings contradict those of van de Wal et al [3], but in our study we adjusted for variables such as biochemical recurrence and positive surgical margin status, which might explain the different findings. It might be that these variables are what increases fear rather than the salvage treatment itself.

We found that RP patients with high FoR more often had a type D personality and fatigue. In a similar vein, van de Wal et al [3] reported that psychological factors such as anxiety, depression, distress, and post-traumatic symptoms were more common among RP patients with high FoR. A previous study of AS patients from the Netherlands reported an association between neuroticism and FoR,

while a longitudinal study using the CaPSURE database showed that mental health was an important predictor of FoR after RP [2,20]. The association with psychological factors in this study further highlights the need to focus more on the mental health of PCa patients.

4.4. Clinical implications

With many PCa patients experiencing FoR, health care personnel should be aware of these concerns, especially among young patients and those with positive surgical margin status or biochemical failure. The FoR level among AS patients was higher than we expected and could be due to misunderstanding or a lack of knowledge among the patients about their actual disease risk. The AS group would probably benefit from education and more emphasis on the nature and good prognosis of favorable-risk PCa during counseling. The same is probably true for patients with a positive surgical margin or biochemical recurrence, and we suspect that these patients too are being unnecessarily pessimistic about their prognosis. A recent multicenter study from the Netherlands showed that well-informed PCa patients who are active in decision-making are more content after treatment, which further underlines the importance of educating patients about their disease [28]. RP patients without TF had the lowest FoR, but the present study design cannot address the question of whether surgery reduces FoR levels. Longitudinal studies are needed to predict which patients are at risk of developing high FoR during or after a treatment decision to establish causality to associated factors and examine long-term consequences of high FoR. Follow-up interventional studies could explore possible treatment strategies to decrease FoR.

4.5. Strengths and limitations

The strengths of this study are the high response rate, the attrition analysis, and the identification of patients with TF.

The CARQ is only validated for breast cancer patients and the cutoff value might not be correct for identification of clinically significant FoR among PCa patients. However, we believed that CARQ is the best short FoR scale (<10 items) available, which was supported by the results from the psychometric analyses performed.

The value of comparing FoR levels between the different treatment groups is limited. While an AS patient may primarily fear progression to radical treatment, an RP patient with treatment failure may fear progression to metastatic disease or death. Moreover, there may be unknown selection biases between the treatment groups, and psychological features might already be different at diagnosis. Statistically, a larger sample size would be beneficial, although differences found between smaller groups may still be clinically relevant.

Biochemical recurrence was more common among non-responders. If we assume that nonresponders with biochemical recurrence have higher FoR compared to nonresponders without biochemical recurrence, the prevalence of FoR and the importance of biochemical recurrence might be underestimated in our study.

5. Conclusions

FoR is common among PCa survivors, especially among AS patients and RP patients who have experienced treatment failure. Lower age, biochemical recurrence, positive surgical margin, and psychological factors such as fatigue and type D personality were associated with high FoR. Longitudinal studies on PCa survivors are needed to identify those at risk of developing high FoR.

Author contributions: Rasmus Nilsson 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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Acquisition of data: Nilsson, Haug.
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Drafting of the manuscript: Nilsson, Næss-Andresen, Bernklev, Kersten, Myklebust, Haug.
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Appendix A. Supplementary data

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