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Prostate Cancer

Twenty-year Patient-reported Outcomes After Surgery, Radiotherapy, or Brachytherapy for Localized Prostate Cancer

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Abstract

Background and objective: Our objective was to compare the impact of open radical prostatectomy (RP), external beam radiotherapy (EBRT), and brachytherapy in patients with localized prostate cancer via patient-reported outcome measures up to 20 yr after treatment.
Methods: This was a prospective observational study (ClinicalTrials.gov NCT01492751) of men with localized prostate cancer (clinical stage T1–T2, low or intermediate risk). The Expanded Prostate Cancer Index Composite (EPIC-26) and Short Form-36 (SF-36) questionnaires were centrally administered via telephone interviews before treatment and then annually after treatment. Generalized estimating equation models were constructed with propensity score-based weights.
Key findings and limitations: The RP group reported gradual, statistically significant worsening for almost all EPIC-26 and SF-36 scores at most follow-up time points. Significantly lower urinary incontinence deterioration was observed in both radiotherapy groups than after RP. Urinary irritative/obstructive, sexual, bowel, and hormonal symptom patterns were similar regardless of treatment, except for less

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sexual deterioration in the brachytherapy group. The observational design is the main limitation, but propensity score weights mitigated treatment selection bias.
Conclusions and clinical implications: Our findings provide detailed novel evidence, measured over 20 yr, on the long-term impact of disease and treatment on patients with localized prostate cancer. While all treatment groups showed a general deterioration over time, important differences in urinary incontinence (highest after RP) and sexual decline (least after brachytherapy) persisted at 20 yr, and these should be incorporated into shared decision-making processes.
Patient summary: Our study provides new findings on outcomes of treatment for localized prostate cancer as reported by patients over a period of up to 20 years. There was a general deterioration over time, but worse urinary incontinence after radical prostatectomy and the lowest decline in sexual function after brachytherapy persisted over time. These findings can inform patients during shared decision-making on the most suitable treatment for localized prostate cancer.

1. Introduction

Prostate cancer is the second most frequently diagnosed noncutaneous malignancy and the fifth leading cause of cancer death among men worldwide [1]. In high-income countries, most patients are currently diagnosed with prostate cancer at a localized stage [2] and can expect to live for 15 yr or longer after diagnosis, regardless of the treatment received [3]. As a result, evaluation of the impact of treatment via patient-reported outcome measures (PROMs) is increasingly relevant.

Although PROMs have been widely documented in localized prostate cancer [4], only a limited number of studies have reported PROM data extending beyond 10 yr after treatment [5–9]. The ProtecT trial [5] and a Swedish National Prostate Cancer Register study [6] reported data at 12 yr, and three cohort studies provided follow-up 15 yr after treatment [7–9]. These studies consistently demonstrated the long-term persistence of urinary incontinence after radical prostatectomy (RP) and a gradual decline in sexual function over time, regardless of the treatment received [5–9]. However, findings on the persistence of impaired bowel function after radiotherapy have been inconsistent.

Treatments have evolved since their application in the aforementioned studies [5–9]. New modalities such as robot-assisted RP, intensity-modulated radiotherapy, and real-time brachytherapy have side effects similar to those of traditional modalities [10,11], except for better urinary continence results after Retzius-sparing robot-assisted RP [12–14]. Long-term evidence is essential for a comprehensive assessment of the trade-offs between the benefits and harms of different treatments [4] and to prevent patient regret regarding their treatment decisions [15].

As far as we are aware, the longitudinal evolution of treatment side effects beyond 15 yr in men with localized prostate cancer remains unknown. Our aim was to compare the impact of open RP, external beam radiotherapy (EBRT), and preplanned brachytherapy in patients with localized prostate cancer according to PROMs data up to 20 yr after treatment.

2. Patients and methods

The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines were followed (Supplementary Table 1). This was a prospective observational study (ClinicalTrials.gov NCT01492751) involving a cohort of men from the Multicenter Spanish Group for Clinically Localized Prostate Cancer who were diagnosed in 2003–2005 and followed over a period of 20 yr until 2023–2025. The study details have been described elsewhere [16–18]. In brief, eligible patients were those diagnosed with prostate cancer of clinical stage T1 or T2 and low or intermediate D'Amico risk and treated in one of the ten participating centers without previous transurethral resection of the prostate [19]. These inclusion criteria were in accordance with guidelines at the time of the protocol development [20,21], which recommended monotherapy treatment for these risk groups, and multimodal therapy for the high-risk group.

The decision regarding treatment was made jointly by patients and physicians. The study was approved by the ethics review boards of the participating hospitals, and written informed consent was obtained from patients at enrollment, in accordance with the 2000 revision of the Declaration of Helsinki.

2.1. PROMs

The Expanded Prostate Cancer Index Composite (EPIC) [22,23] and Short Form-36 Health Survey (SF-36) [24,25] were administered before treatment and annually after treatment. To ensure homogeneous evaluation, telephone interviews were centrally performed by trained interviewers. EPIC-26 covers urinary, bowel, sexual, and hormonal domains, with scores ranging from 0 to 100 [23]. SF-36 generates physical component summary (PCS) and mental component summary (MCS) scores standardized to have a mean of 50 and standard deviation (SD) of ten in the general US population [24,25]. For both instruments, higher scores indicate better results. In addition to EPIC scores, one key EPIC item per domain previously selected in the ProtecT

study [26] was dichotomized to reflect the proportion of men reporting any problem.

The statistical power for detection of small to moderate differences between groups (0.4 SD) in EPIC or SF-36 scores with 90 patients per treatment group was at least of 80% at a significance level of 5%.

2.2. Statistical analysis

To account for treatment selection bias, we applied a weighting approach based on the covariate balancing propensity score (CBPS) derived from a multinomial logistic regression model (c statistic 0.85; Supplementary Table 2) [27]. Covariate balance was assessed using standardized mean differences for the average treatment effect. The effective sample size for truncation at the 95th percentile was 65.7 for RP, 83.1 for EBRT, and 117.0 for brachytherapy. Multiple imputation was used to handle missing data for variables included in the model.

Unweighted and weighted summary statistics for patient characteristics at diagnosis are reported. Weighted estimates were obtained by applying CBPS-derived weights using complex survey methods. To show unweighted results before treatment and at 5, 10, 15, and 20 yr after treatment, figures were constructed for mean EPIC-26 and SF-36 scores, the percentage of men reporting key EPIC items, and 95% confidence intervals (CIs). Differences were tested using a χ^2 test or one-way analysis of variances (with a Tukey studentized range test for post hoc comparisons).

To assess PROM changes over time while accounting for correlation among repeated measures, separate generalized estimating equation (GEE) weighted models were constructed for each EPIC-26 and SF-36 score as dependent variables. Treatment (with RP as the reference group), time, and their interaction were included in the models. The bootstrapping method was used to assess uncertainty in the sampling distribution for the EPIC-26 and SF-36 mean scores. All analyses were performed using R v4.2.2 (R Foundation for Statistical Analysis, Vienna, Austria).

3. Results

Of the 704 participants (Supplementary Fig. 1), 192 were treated with open RP, 195 with EBRT, and 317 with preplanned low-dose-rate brachytherapy. At 20 yr after treatment, 387 patients had died, 230 completed PROM data, 71 were lost to follow-up, and 16 missed the interview. Among the 317 patients who survived, median follow-up was 20.1 yr (interquartile range 20.0–20.2) and the PROMs completion rate was 73%.

Table 1 shows unweighted and weighted clinical characteristics stratified by treatment. After applying propensity score–based weights, the most remarkable difference was observed for the proportion of patients with low risk group, which was 59% in the RP group, 69% in the EBRT group, and 75% in the brachytherapy group.

Fig. 1 shows EPIC-26 urinary domain results in terms of unweighted mean scores and the percentage of men reporting problems. There were statistically significant differences in urinary incontinence (Fig. 1A) among the treatment groups, with patients in the RP group reporting the greatest

Table 1 – Patient characteristics at diagnosis stratified by treatment (*n* = 704)

	Unweighted			Weighted after applying propensity scores		
	RP	EBRT	Brachytherapy	RP	EBRT	Brachytherapy
Participants (*n*)	192	195	317			
Effectiveness sample size				65.7	83.1	117.0
Age (yr)						
Mean (SD) or [SE]	64.2 (5.5)	70.1 (5.3)	67.5 (6.4)	65.8 [0.7]	67.9 [0.7]	68.3 [0.8]
Median (IQR)	64.7 (60.0–68.4)	70.9 (67.8–73.7)	68.4 (63.6–72.1)	67.2 (61.6–70.4)	69.0 (64.6–72.5)	69.6 (65.5–73.3)
PSA category, *n* (%)						
≤6 ng/ml	71 (37)	60 (31)	111 (35)	328 (43)	323 (34)	400 (39)
6–8 ng/ml	49 (26)	56 (29)	117 (37)	177 (23)	287 (30)	312 (30)
>8 ng/ml	71 (37)	79 (40)	89 (28)	260 (34)	336 (36)	326 (31)
Gleason score, *n* (%)						
≤5	15 (7.9)	49 (25)	100 (31)	165 (22)	206 (22)	256 (25)
6	99 (52)	92 (47)	208 (66)	403 (53)	563 (59)	656 (63)
7	76 (40)	54 (28)	9 (2.8)	196 (26)	177 (19)	127 (12)
cT stage, *n* (%)						
cT1	130 (68)	114 (58)	258 (81)	534 (70)	678 (72)	740 (71)
cT2	62 (32)	80 (41)	59 (19)	231 (30)	265 (28)	299 (29)
cTx	0	1 (0.5)	0	0 (0)	2 (0.2)	0 (0)
Risk group, *n* (%)						
Low risk	91 (47)	108 (55)	283 (89)	448 (59)	651 (69)	777 (75)
Intermediate risk	101 (53)	87 (45)	34 (11)	317 (41)	295 (31)	262 (25)
NAH, *n* (%)						
No	175 (91)	134 (69)	212 (67)	583 (76)	727 (77)	780 (75)
Yes	17 (8.9)	61 (31)	105 (33)	182 (24)	219 (23)	259 (25)
Number of comorbidities, *n* (%) [a]						
0	24 (19)	28 (17)	49 (18)	135 (26)	151 (19)	177 (19)
1	34 (26)	58 (34)	78 (28)	101 (19)	274 (35)	208 (23)
2	38 (29)	26 (15)	65 (24)	166 (31)	117 (15)	217 (24)
≥3	34 (26)	57 (34)	83 (30)	129 (24)	237 (30)	308 (34)

EBRT = external beam radiotherapy; NAH = neoadjuvant hormonotherapy; PSA = prostate-specific antigen; RP = radical prostatectomy; SD: =standard deviation; SE = standard error.

[a] The list of comorbidities included arthrosis, arthritis or rheumatism, chronic bronchitis, high blood pressure, diabetes, heart disease, stroke, cataracts, deafness, depression, peptic ulcer, and varicose veins.

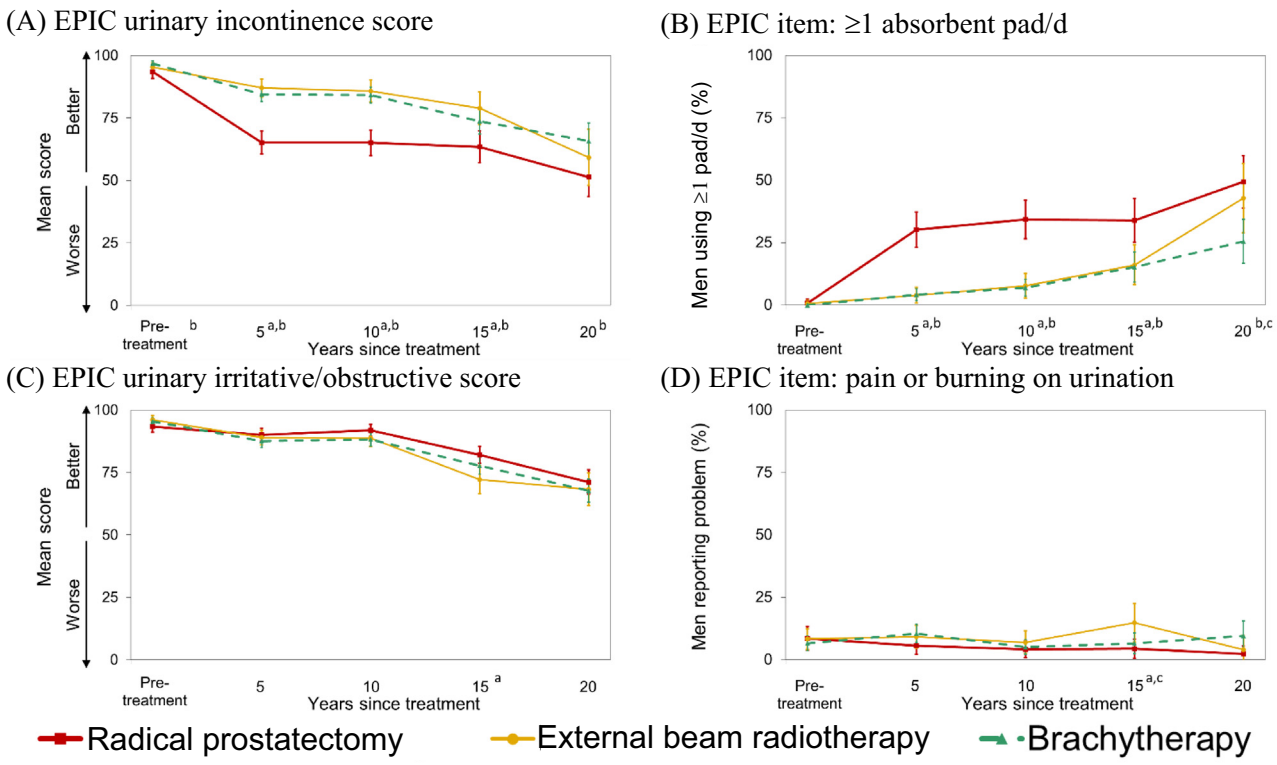

Fig. 1 – Unweighted results for EPIC-26 urinary domain. (A) Mean EPIC-26 urinary incontinence scores. (B) Percentage of men using one or more absorbent pads per day. (C) Mean EPIC-26 urinary irritative/obstructive scores. (D) Percentage of men reporting any pain or burning on urination. Superscript letters indicate $p < 0.05$ for the following comparisons: a) radical prostatectomy versus EBRT; b) radical prostatectomy versus brachytherapy; and c) EBRT versus brachytherapy. Error bars represent the 95% confidence intervals. EBRT = external beam radiotherapy; EPIC = Expanded Prostate Cancer Index Composite

deterioration. The proportion of men using absorbent pads (Fig. 1B) ranged from 15% to 34% at 15 yr, which increased to 26–49% at 20 yr. Worsening of urinary irritative/obstructive symptom scores (Fig. 1C) was similar across the groups, and the proportion of men reporting pain or burning on urination was <15% throughout the follow-up period (Fig. 1D). A detailed distribution of patient responses to EPIC items is shown in Supplementary Table 3.

Statistically significant differences in EPIC-26 sexual summary score among treatment groups disappeared beyond 10-yr follow-up (Fig. 2A). Almost all men reported erections not firm enough for intercourse at 20-yr follow-up, regardless of the treatment received (Fig. 2B). Neither the evolution of EPIC-26 bowel summary scores (Fig. 2C) nor the proportion of men reporting problems with fecal incontinence (Fig. 2D) differed among the treatment groups. Significant differences in the change in EPIC-26 hormonal summary score among treatment groups were only observed at 15 yr. The SF-36 PCS (Fig. 3A) gradually declined over time, with slight differences among groups. Fig. 3B shows the stability of the SF-36 MCS throughout the 20-yr follow-up period.

Mean EPIC-26 and SF-36 scores obtained via GEE models constructed with propensity score–based weights are shown in Table 2. Patients in the RP group experienced gradual declines that were statistically significant at most follow-up points for all EPIC-26 scores and the SF-36 PCS. Similarly, both radiotherapy groups experienced worsening of urinary incontinence throughout the follow-up period, but their deterioration was significantly lower than in the RP group at 5 yr. Significantly less sexual deterioration throughout the follow-up period was observed in the brachytherapy group. Worsening of urinary irritative/obstructive, bowel, and hormonal symptoms was similar regardless of treatment applied, except for a significantly greater hormonal decline in the EBRT group at 15 yr.

Physical and mental health declined gradually across all treatment groups. The magnitude of the deterioration was large for PCS (~20 points in 20 yr), while the MCS deterioration was small after RP, moderate after EBRT, and large after brachytherapy.

4. Discussion

This is the first 20-yr follow-up study based on PROM data to provide valuable insights into the long-term impact of open RP, EBRT, and brachytherapy on urinary, sexual, bowel, and hormonal domains and on physical and mental health. Results from weighted GEE models showed significant declines for most outcomes during the 20 yr, regardless of treatment received, but worsening of sexual and urinary incontinence scores was greatest in the RP group, while the greatest deterioration in urinary irritative/obstructive and bowel symptoms was observed in the EBRT group.

The persistent deterioration in urinary incontinence observed after RP is consistent with previous studies, where this impairment remains significant for up to 15 yr [7,9]. In

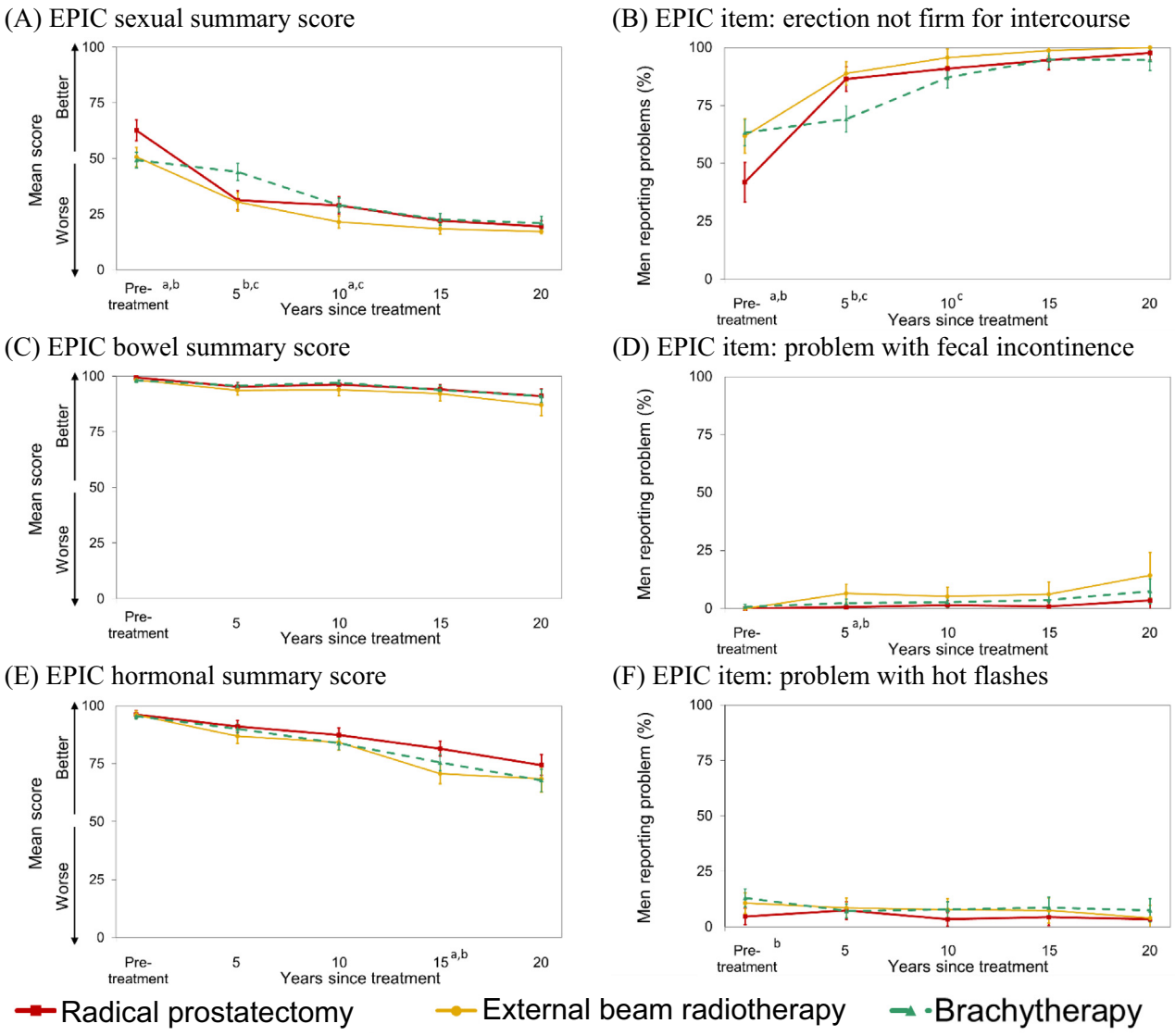

Fig. 2 – Unweighted results for EPIC-26 sexual, bowel, and hormonal domains. (A) Mean EPIC-26 sexual scores. (B) Percentage of men reporting erections not firm enough for intercourse. (C) Mean EPIC-26 bowel scores. (D) Percentage of men reporting any problem with fecal incontinence. (E) Mean EPIC-26 hormonal scores. (F) Percentage of men reporting any problem with hot flashes. Superscript letters indicate $p < 0.05$ for the following comparisons: a) radical prostatectomy versus EBRT; b) radical prostatectomy versus brachytherapy; and c) EBRT versus brachytherapy. Error bars represent 95% confidence intervals. EBRT = external beam radiotherapy; EPIC = Expanded Prostate Cancer Index Composite

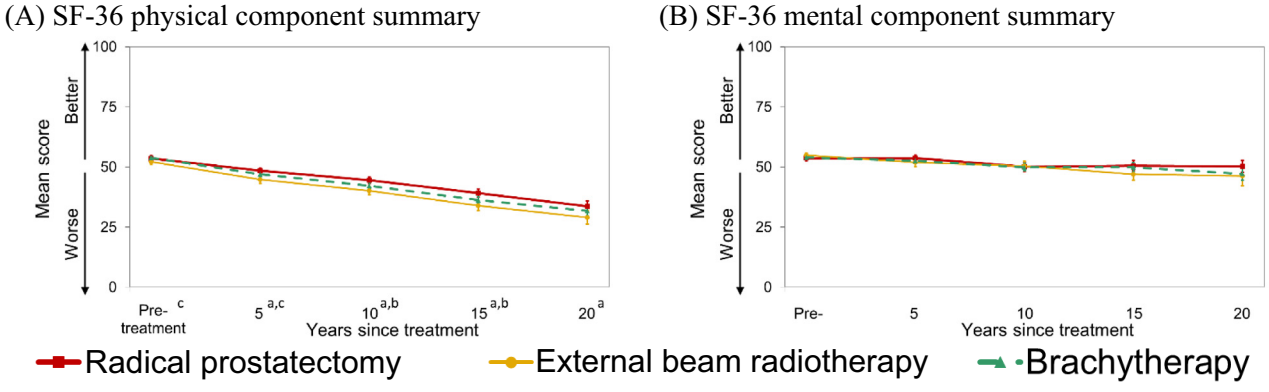

Fig. 3 – Unweighted results for the SF-36 (A) physical and (B) mental component summaries. Superscript letters indicate $p < 0.05$ for the following comparisons: a) radical prostatectomy versus EBRT; b) radical prostatectomy versus brachytherapy; and c) EBRT versus brachytherapy. Error bars represent 95% confidence intervals. EBRT = external beam radiotherapy; SF-36 = 36-item Short-Form health survey.

Table 2 – Weighted EPIC-26 and SF-36 scores over time across different treatment groups, estimated using generalized estimating equation models

Treatment and time	Mean estimated score (95% confidence interval)						
	EPIC-26 UI	EPIC-26 Urinary I/O	EPIC-26 Sexual	EPIC-26 Bowel	EPIC-26 Hormonal	SF-36 PCS	SF-36 MCS
RP							
Before Tx	90.7 (85.0–97.1)	92.2 (88.3–96.9)	65.5 (59.5–71.0)	100.6 (99.3–102.0)	96.3 (95.0–98.0)	54.6 (53.3–56.0)	53.3 (52.0–54.8)
5 yr	57.4 [a] (48.2–67.4)	83.5 [a] (78.9–88.5)	33.6 [a] (27.2–39.7)	95.5 [a] (93.6–97.5)	92.4 (89.2–96.0)	48.3 [a] (46.8–49.8)	54.0 (52.3–55.8)
10 yr	64.3 [a] (57.6–71.2)	91.6 (88.9–94.5)	32.0 [a] (25.4–37.7)	97.3 [a] (96.2–98.4)	89.0 [a] (85.2–92.9)	43.0 [a] (40.9–45.0)	51.7 (50.1–53.3)
15 yr	56.8 [a] (48.3–65.9)	80.2 [a] (76.6–83.9)	21.3 [a] (17.4–25.3)	92.9 [a] (89.6–96.7)	82.2 [a] (77.7–86.7)	39.3 [a] (36.7–41.3)	51.0 (48.3–54.0)
20 yr	49.5 [a] (40.0–59.3)	70.8 [a] (63.8–77.0)	17.4 [a] (12.9–21.6)	89.6 [a] (84.7–95.0)	74.1 [a] (69.3–78.1)	31.6 [a] (28.7–33.9)	50.9 (47.7–53.9)
EBRT							
Before Tx	98.7 [b] (95.9–101.5)	97.2 (94.9–99.4)	53.7 [b] (48.4–58.6)	99.0 (97.6–100.0)	97.2 (95.7–98.8)	52.3 [b] (51.0–53.6)	55.6 [b] (54.8–56.5)
5 yr	89.9 [a,b,c] (85.7–93.9)	91.6 [a,b] (88.6–94.5)	30.9 [a] (25.9–36.1)	94.9 [a] (92.3–97.5)	88.4 [a] (84.7–92.3)	45.6 [a,b] (43.8–47.3)	52.7 [a] (50.6–55.0)
10 yr	86.9 [a,b] (81.6–92.7)	91.4 [a] (88.2–94.3)	25.1 [a] (19.9–30.0)	92.1 [a,b] (88.2–96.1)	84.4 [a] (79.7–89.2)	39.7 [a,b] (37.6–41.7)	51.2 [a] (48.7–53.7)
15 yr	79.9 [a,b] (71.8–88.0)	75.9 [a] (69.8–81.3)	14.6 [a] (9.2–20.6)	90.6 [a] (86.4–95.0)	69.4 [a,b,c] (64.1–74.4)	33.3 [a,b] (30.8–35.6)	45.9 [a,b,c] (42.8–48.9)
20 yr	63.7 [a] (52.1–74.4)	67.0 [a] (58.4–75.3)	15.5 [a] (7.4–21.7)	84.2 [a] (77.5–91.4)	73.0 [a] (65.2–78.9)	27.1 [a] (23.3–30.3)	49.0 [a] (44.3–53.1)
BT							
Before Tx	95.6 (92.5–98.6)	94.6 (92.5–96.9)	48.7 [b] (44.4–53.0)	96.9 [b] (94.7–99.7)	94.8 (93.1–96.5)	53.9 (53.0–54.9)	53.4 (52.6–54.1)
5 yr	84.7 [a,b,c] (80.5–89.0)	84.7 [a] (81.7–88.0)	42.0 [a,b,c] (37.6–46.2)	94.6 (93.0–96.3)	88.4 [a] (85.7–91.1)	46.0 [a,b] (44.7–47.3)	51.6 (49.9–53.6)
10 yr	81.6 [a,b] (77.1–86.6)	87.0 [a,b] (83.5–90.5)	25.8 [a] (21.1–30.2)	96.4 (94.7–98.4)	85.6 [a] (82.5–88.7)	40.2 [a,b] (38.6–41.7)	49.2 [a] (47.1–51.5)
15 yr	71.4 [a,b] (64.7–79.0)	79.6 [a] (74.5–84.5)	20.7 [a,c] (14.5–26.7)	92.2 [a] (89.4–94.9)	73.8 [a,b] (69.9–77.4)	33.3 [a,b,c] (30.6–35.7)	49.5 [a] (47.2–51.6)
20 yr	60.9 [a] (51.4–71.7)	72.0 [a] (65.1–78.1)	15.9 [a,c] (8.3–22.1)	87.9 [a] (83.9–92.3)	65.6 [a,b] (58.9–71.2)	30.5 [a] (27.7–32.8)	44.8 [a,b] (41.1–49.0)

BT = brachytherapy; EBRT = external beam radiotherapy; EPIC = Expanded Prostate Cancer Index Composite; I/O = irritative/obstructive; MCS = mental component summary; PCS = physical component summary; RP = radical prostatectomy; SF-36 = Short Form-36; Tx = treatment; UI = urinary incontinence.
[a] $p < 0.05$ versus score before treatment.
[b] $p < 0.05$ versus RP (reference group).
[c] $p < 0.05$ versus change with RP (reference group).

our study, the worsening of urinary incontinence after RP was no longer significantly different from the worsening observed in the EBRT and brachytherapy groups at 10 yr because of pronounced declines in the latter groups over time. Similarly, a pronounced deterioration after EBRT was observed in an Australian study at 15-yr follow-up [9] and in a Massachusetts cohort [7]. These findings suggest that urinary incontinence emerges immediately after RP without subsequent recovery, but appears in the long term (10–15 yr) after EBRT and brachytherapy. This hypothesis is supported by the negligible differences between patients with and without additional treatments after surgery in a subsample of our cohort according to data collected up to year 10 (Supplementary Fig. 2). Finally, although a small part of this decline may be attributable to the aging process–as reported by control subjects without prostate cancer [6,9]—it should still be considered in long-term clinical follow-up.

Patients reported a mild decline in urinary irritative/obstructive symptoms during the first 10 yr after treatment, followed by gradual worsening beyond that point, especially in the EBRT group. The abovementioned studies did not report results for this domain [5,8,9], except for one study that showed a statistically significant impairment in patients treated with EBRT or brachytherapy at 15 yr after treatment, as measured using the Prostate Cancer Symptom Index [7]. Therefore, more long-term evidence on urinary irritative/obstructive symptoms is needed, particularly considering that their assessment is included in the recommended standard outcomes set for patients with localized prostate cancer [28].

In our study, large and persistent worsening of sexual function was observed, with the least impairment reported by patients in the brachytherapy group. The proportion of men reporting erections not firm enough for intercourse was >94% across all treatment groups at 15 yr after treatment and beyond. These findings align with previous studies [5,6,8,9] reporting erectile dysfunction rates at 12–15 yr of 75–87% after RP [5,8,9], 73–94% after EBRT [5,8,9], and 72% after low-dose-rate brachytherapy [9]. This deterioration in sexual function could result from an interaction between prostate cancer treatments and aging, as some studies have documented that long-term sexual dysfunction is more pronounced among men treated for prostate cancer than among control subjects [6,9].

Bowel symptoms worsened gradually, mainly in the EBRT group. Differences in most studies at 12 or 15 yr of follow-up were small [5,7–9], although the Swedish National Prostate Cancer Register study [6] reported a higher risk of bowel symptoms after external radiotherapy

in comparison to RP or the control cohort, with an odds ratio of approximately 2.5. Otherwise, the evolution of bowel symptoms after brachytherapy followed the same pattern as for RP, as also observed in the few studies assessing low-dose-rate brachytherapy [7,9].

All treatment groups in our study exhibited gradual worsening of hormonal symptoms over time up to 20 yr after treatment. To the best of our knowledge, this is a novel longitudinal finding, as previous studies that used EPIC-26 to compare outcomes of treatments for localized prostate cancer did not report results for this domain [5,8,9]. The rate of biochemical recurrence was significantly higher in the EBRT group (43%) than in the brachytherapy (29%) and RP (24%) groups [18], and the hormonotherapy rate at 10 yr after primary treatment was also higher in the EBRT group (41% vs 14% and 20%) [29], which could have contributed to hormonal impairment. However, the difference was only statistically significant at 15 yr after treatment. In the same line, changes in EPIC scores up to year 10 did not differ much between patients with and without any further treatment (Supplementary Fig. 2).

The main limitation of our study is its observational design, and assumptions under which the estimates can be interpreted on a causal basis need to be discussed [30]. A primary concern is treatment selection bias: for example, brachytherapy is preferentially prescribed for patients with lower-risk tumors. In our cohort, propensity score weights were used to mitigate this treatment selection bias, and residual confounding was explored via sensitivity analyses using untruncated CBPS weights, which showed a similar pattern to the results obtained from the main analyses (Supplementary Table 4). The balanced clinical variables before treatment obtained after applying propensity score weights and the similarities between the sensitivity and main analysis results provide assurance of exchangeability. The study inclusion criteria guaranteed positivity, as every treatment was possible for each individual at the time of diagnosis, and the therapies compared presented variations irrelevant enough to expect consistency.

Second, survivorship biases may have affected our results, as the GEE models analyzed both deaths and a lack of response to the questionnaires as missing data. However, it is important to highlight that the 20-yr weighted rates for cumulative mortality (44% vs 55% vs 56%) and non-response (72% vs 74% vs 72%) did not differ vastly for RP versus EBRT versus brachytherapy. Third, the treatments were performed 20 yr ago, and diagnostic techniques and treatments for prostate cancer have evolved since then. Comparative effectiveness research on new treatment modalities has shown similar side-effect patterns [10,11], but significantly better functional outcomes have been observed after Retzius-sparing robot-assisted RP, especially for urinary continence [12–14]. Therefore, it is important to consider this new surgical approach in the shared decision-making process. Finally, data on biochemical recurrence, disease progression, or additional treatments were not recorded beyond 10 yr after treatment, as clinical management transferred from specialists to general practitioners at that point. Data on complications such as vesicourethral anastomotic stricture and radiation cystitis or consequent procedures (urethral dilation or revision surgeries) were not collected, but PROMs can indirectly capture the impact of these complications from the patient's perspective.

5. Conclusions

Our study provides novel and detailed evidence on the long-term impact of localized prostate cancer and its treatment, with follow-up extending up to 20 yr. While all treatment groups showed a general deterioration over time, urinary incontinence was significantly greater after RP. Notably, brachytherapy appears to have the least sexual impact. To tailor strategies in accordance with each individual's needs and preferences, it is important to incorporate these longitudinal findings for traditional treatments into shared decision-making processes for patients with localized prostate cancer, together with evidence on the newer treatment modalities also available.

Author contributions: Montse Ferrer 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.

Study concept and design: Garin, Guedea, Ferrer.
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Drafting of the manuscript: Zamora.
Critical revision of the manuscript for important intellectual content: Garin, Pardo, Ferrer.
Statistical analysis: Pont.
Obtaining funding: Garin, Ferrer.
Administrative, technical, or material support: Zamora, Garin, Pont, Pardo, Gutiérrez, Castells.
Supervision: Garin, Ferrer.
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Ethics statement: This study was reviewed and approved by the institutional review board of the Hospital del Mar Medical Research Institute, in accordance with the 2000 Declaration of Helsinki. The study was also approved by the ethics committees of the participating sites: Institut Català d'Oncologia, Hospital Universitari de Bellvitge, Hospital de la Santa Creu i Sant Pau, Fundació Puigvert, Institutu Onkologikoa de Gipúzkoa, Hospital Regional Universitario de Málaga, Hospital Universitario Ramón y Cajal, Hospital Universitario y Politécnico La Fe, Centro Oncológico de

Galicia, and Hospital Universitario Virgen del Rocío. Written informed consent was provided by all subjects when they were enrolled.

Data sharing statement: The research data for this study are stored in an institutional repository and will be available to bona fide researchers on request from the corresponding authors.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2025.10.007.

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