

Comparison of quality of life after radical treatment in prostate cancer: radical prostatectomy versus external radiotherapy

Comparación de la calidad de vida tras el tratamiento radical en cáncer de próstata: prostatectomía radical frente a radioterapia externa

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Abstract

Objective: To assess and compare the functional and quality of life results in patients treated with curative intent for localized prostate cancer during 2015 in our hospital. **Method:** 77 patients treated by radical prostatectomy or external radiotherapy with androgen deprivation were prospective enrolled. Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) questionnaire at 3-year follow-up and Spanish Questionnaire on Quality of Life in Patients with Prostate Cancer (CAVIPRES-30) at diagnosis and at 3-year follow-up were registered. **Results:** 68 patients were included, 39 patients treated by radical prostatectomy and 29 received external radiotherapy with androgen deprivation. Among the operated patients, 61.5% were dry and 17.9% use three or more daily pads, compared to 72.4% and 6.8%, respectively, in the radiotherapy group. 48.7% of prostatectomized patients reported very poor or no capacity to have a sufficiently rigid erection, compared to 69% of the radiated group. After surgery, 43.6% considered bad or very bad quality-of-life, compared to 68.9% in the radiotherapy group. In the comparison of the data of the preand post-treatment questionnaire can be seen that the patients had a superior perception before the procedure. **Conclusions:** Patients treated by surgery have a better perception of quality-of-life compared to those treated by radiotherapy.

Keywords: Prostate cancer. Radical prostatectomy. External radiotherapy. Quality of life. Questionnaire.

Resumen

Objetivo: Determinar y comparar los resultados funcionales y de calidad de vida de pacientes con cáncer de próstata tratados con intención curativa durante el año 2015 en nuestro centro. **Método:** Se incluyeron 77 pacientes sometidos a prostatectomía radical (PR) o radioterapia externa con terapia de privación androgénica (TDA). Se realizaron el Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) tras 3 años de seguimiento y el Cuestionario Español de Calidad de Vida en Pacientes con Cáncer de Próstata (CAVIPRES-30) al diagnóstico y a los 3 años. **Resultados:** Se incluyeron 68 pacientes, 39 con PR y 29 con radioterapia más TDA. De los pacientes intervenidos, el 61.5% están secos y el 17.9% usan tres o más compresas, diarias frente al 72.4% y el 6.8%, respectivamente, en el grupo de radioterapia. El 48.7% de los prostatectomizados refieren erecciones muy malas o ninguna, frente al 69% de los radiados. Tras la cirugía, el 43.6% refieren mala o muy mala calidad de vida, frente al 68.9% de los radiados. En la comparación de los datos del cuestionario pre y postratamiento, los pacientes tenían una percepción superior antes del procedimiento. **Conclusiones:** Los pacientes tratados mediante cirugía tienen una mejor percepción de su calidad de vida relacionada con la salud que los radiados.

Palabras clave: Cáncer de próstata. Prostatectomía radical. Radioterapia externa. Calidad de vida. Cuestionario.

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Introduction

Prostate cancer (PC) is the second most common type of cancer and the fifth leading cause of cancer-related death among men¹. Its incidence rate has increased in recent years, and it is expected that its high prevalence will make the treatment of this tumor a significant challenge due to the decrease in quality of life (QoL) it causes in patients with favorable overall and cancer-specific long-term survival².

The average life expectancy for organ-confined PC is 13.8 years, making QoL assessment crucial due to the prolonged time patients may suffer from treatment sequelae such as urinary incontinence, bleeding, GI toxicity, and erectile dysfunction, among others³.

Evaluating functional outcomes is essential to understanding the situation of men living with PC. Currently, several validated questionnaires are available for assessing general QoL and health-related QoL (HRQoL) in PC patients, such as the FACT-P⁴, the EORTC-QLQ-PR25⁵, the UCLA-PCI⁶, the EPIC-CP⁷, the ROSQOLI⁸, the QOLM-P⁹, and the CAVIPRES¹⁰. We should mention that the correct interpretation of these test results is impacted by the different clinical significance of the measured parameters, as well as by the limited training of physicians in using these tools. Additionally, many are adaptations of the original English versions, and there may be differences in translation.

The Spanish Quality of Life Questionnaire for Prostate Cancer Patients (CAVIPRES-30), developed and validated in Spain, is a manageable, sensitive, and specific tool for assessing QoL in PC patients¹⁰. The Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) is a specific questionnaire for evaluating the impact of treatments on the QoL of PC patients. Its Spanish version is validated and shows excellent sensitivity to language change, making it useful in our setting⁷.

The objective of this study was to determine the functional and QoL outcomes after radical treatments for localized PC in our center by applying specific questionnaires and comparing their results across each treatment group.

Method

We conducted a prospective non-randomized study, recruiting 77 patients with localized PC undergoing radical prostatectomy (RP) or external radiotherapy

with androgen deprivation therapy (RT + ADT) from January through December 2015. Out 39 patients who underwent surgery, 18 underwent open surgery (retropubic RP) while 21 underwent laparoscopic surgery by the same team of surgeons in both cases. No patient underwent lymphadenectomy. Patients treated with RT (29) received 46 Gy in 23 fractions of 2.00 Gy per day on the prostate volume, seminal vesicles, and pelvic lymph nodes with a safety margin, using 6 MV photons from a TrueBEAM linear accelerator and the VMAT technique (RapidArc) with 2 dynamic arcs shaped with a multileaf collimator, combined with a high-dose-rate brachytherapy boost in a single 15 Gy fraction. Radiated patients received ADT for 6 months (intermediate risk) or 2 years (high risk). No patient received exclusive brachytherapy. Six patients were excluded due to subsequent oncological recurrence requiring salvage treatment, while 3 were excluded due to loss to follow-up.

Data mining was performed through a direct structured interview using the EPIC-CP and CAVIPRES-30 questionnaires. Each patient signed an informed consent form beforehand. Both questionnaires were administered 3 years after the completion of treatment, and CAVIPRES-30 was also administered at the time of diagnosis.

The EPIC-CP includes 50 items covering 4 specific domains: urinary, intestinal, sexual, and hormonal. Each domain contains 3 questions with response options on a scale of 0 to 4 points (lower score indicates better HRQoL perception). In this study, each question was used as a variable to allow result comparison in each group⁷.

The CAVIPRES-30 consists of 30 questions with 5 domains: psychological aspects, hope and future, social support and partner, sexual life, and information and communication (higher score indicates better HRQoL perception)¹⁰.

Both questionnaires have a recall period of 4 weeks.

Data were analyzed using the R package, version 3.4.4 (R Development Core Team 2018). Percentages were compared using the chi-square test, means were compared using the Student t-test, while medians were compared using the Wilcoxon test for independent data. For the numerical CAVIPRES variable, the Wilcoxon test for paired data was used. Statistical significance was set at $p < 0.05$.

Results

A total of 68 patients were included: 39 underwent RP and 29 underwent RT + ADT. The median age in

the RP group was 62 years, and in the RT + ADT group, 69 years. Regarding risk, the RP group included 14 low-risk patients, 21 intermediate-risk patients, and 4 high-risk patients, compared to 2, 16, and 11, respectively, in the RT + ADT group ($p < 0.01$) (Table 1).

Regarding urinary habits according to the EPIC-CP questionnaire (Table 2), in the RP group, 61.5% did not use pads, 17.9% used 1 per day, 2.6% used 2 per day, and 17.9% used 3 or more per day vs 72.4%, 17.4%, 3.4%, and 6.9%, respectively, in the RT + ADT group ($p = 0.68$).

In the RP group, 84.6% did not have dysuria problems, while in the RT + ADT group, 48.2% had moderate (17.2%) or major problem (31%) with dysuria ($p < 0.01$). No prostatectomy patients reported problems with hematuria vs more than half in the RT + ADT group, where 24% considered hematuria a moderate problem ($p < 0.01$).

In the RP group, 48.7% reported very poor or no ability to have a quality erection vs 69% in the RT + ADT group ($p = 0.27$).

In the RP group, 53.8% did not consider any reduction in their QoL concerning current urinary habits, vs 31% in the RT + ADT group. Regarding sexual activity, 23.1% of RP patients considered it a major problem vs 17.2% in the RT + ADT group.

HRQoL determined by the CAVIPRES-30 questionnaire before radical treatment in the RP group was considered very poor in 2.56%, poor in 12.82%, fair in 76.92%, and good in 7.69%; for the RT + ADT group, the rates were 0%, 27.59%, 68.97%, and 3.45%, respectively ($p = 0.36$).

After treatment, HRQoL in the RP group was poor or very poor in 43.6%, fair in 53.8%, and good in 2.6% vs 68.9%, 31%, and 0%, respectively, in the RT + ADT group ($p < 0.05$).

When comparing CAVIPRES-30 values pre- and post-treatment within each group, statistically significant differences were reported ($p < 0.01$) in both the RP and RT groups, with a positive difference in both cases, indicating that patients had a better perception of QoL before the procedure.

The relationship between risk group and presence or absence of comorbidities, such as type 2 diabetes mellitus and ischemic heart disease, with the use of pads and the ability to achieve an erection in each treatment group was studied (Tables 3 and 4). No worse functional outcomes were observed between different risk groups or in patients with comorbidities in each treatment group.

Table 1. Sample description

	Overall (n = 68)	RP (n = 39)	RT + ADT (n = 29)	p-value
Age, years	64 (59-69)	62 (56-66)	69 (64-72)	< 0.0001
PSA				0.03
< 10	55 (80.9%)	35 (89.7%)	20 (69.0%)	
10-20	10 (14.7%)	4 (10.3%)	6 (20.7%)	
> 20	3 (4.4%)	0	3 (10.3%)	
TPB				0.01
Gleason < 7	23 (33.8%)	19 (48.7%)	4 (13.8%)	
Gleason 7	36 (52.9%)	17 (43.6%)	19 (65.5%)	
Gleason > 7	9 (13.2%)	3 (7.7%)	6 (20.7%)	
Risk groups				0.003
Low	16 (23.5%)	14 (35.9%)	2 (6.9%)	
Intermediate	37 (54.4%)	21 (53.8%)	16 (55.2%)	
High	15 (22.1%)	4 (10.3%)	11 (37.9%)	

TPB, transrectal prostate biopsy; RP, radical prostatectomy; PSA, prostate-specific antigen; RT + ADT, external radiotherapy with androgen deprivation therapy.

Discussion

Since the 1990s, the incidence of PC has increased due to the widespread use of prostate-specific antigen (PSA) testing, leading to higher rates of diagnosis and early treatment.

There are various therapeutic options for organ-confined PC, and the final decision should be made based on clinical stage, PSA levels, Gleason score, chronological age, and the patient's functional status. Treatment should be approached from a multidisciplinary perspective to provide the patient with the best available alternatives in each case. The patient should actively participate in decision-making, as reflected in the European Association of Urology clinical guidelines¹¹.

The complex choice of final treatment is justified by the high survival rate and the significant impact on quality of life (QoL) that can be experienced in the following years.

The term "quality of life" first appeared as a researchable concept in the United States National Library of Medicine in 1966, in an article published by Elkinson entitled "Medicine and the quality of life." In clinical practice, we understand QoL as the maintenance of physical functions along with acceptable symptomatic control. However, its assessment remains a subjective perception, and consideration should be given not only to symptoms or organ functions derived from the disease but also to information about psychological and social influences and their impact. The scientific

Table 2. Results to the EPIC-CP u

	RP (n = 39)	Urinary habits					RT + ADT (n = 29)	p			
How often do you have urine leakage?											
More than once a day	11 (28.21%)						3 (10.34%)	0.29			
Once a day	4 (10.26%)						2 (6.9%)				
More than once a week	1 (2.56%)						0				
Once a week	7 (17.95%)						6 (20.69%)				
Never/Occasionally	16 (41.03%)						18 (62.6%)	0.08			
No control	2 (5.13%)						2 (6.9%)				
Frequent leakage	8 (20.51%)						2 (6.9%)				
Occasionally	17 (43.59%)						8 (27.59)				
Total control	12 (30.77%)						17 (58.62%)				
How many pads or adult diapers have you used per day to control urine leakage?											
None	24 (61.54%)						21 (72.41%)	0.68			
Once a day	7 (17.95% %)						5 (17.24%)				
Twice a dat	1 (2.56%)						1 (3.45%)				
Three or more times a day	7 (17.95%)						2 (6.9%)				
Have any of the following aspects been a problem for you?											
Leakage	18 (46.5%)	4 (10.26%)	5 (12.82%)	6 (15.38%)	6 (15.38%)	19 (65.52%)	4 (13.79%)	1 (3.45%)	3 (10.34%)	2 (6.90%)	0.39
Pain or itch when urinating	33 (84.62%)	2 (5.13%)	2 (5.13%)	2 (5.13%)	2 (5.13%)	12 (41.38%)	1 (3.45%)	2 (6.9%)	5 (17.24%)	9 (31.03%)	< 0.01
Blood in urine	39 (100%)	0	0	0	0	16 (55.17%)	1 (3.45%)	2 (6.9%)	7 (24.14%)	3 (10.34%)	< 0.01
Weak streamline or incomplete emptying	28 (71.79%)	3 (7.69%)	4 (10.26%)	3 (7.69%)	3 (7.69%)	11 (37.93%)	2 (6.9%)	3 (10.34%)	5 (17.24%)	8 (27.59%)	< 0.01
Need to urinate frequently	26 (66.67%)	3 (7.69%)	3 (7.69%)	5 (12.82%)	2 (5.13%)	10 (34.48%)	3 (10.34%)	2 (6.9%)	6 (20.69%)	8 (27.59)	0.05
Bowel habits											
Have any of the following aspects been a problem for you?											
Urgent need to have bowel movement	35 (89.74%)	2 (5.13%)	0	1 (2.56%)	1 (2.56%)	11 (37.93%)	3 (10.34%)	5 (17.24%)	9 (31.03%)	1 (3.45%)	< 0.01
More frequent bowel movement	37 (94.87%)	0	0	1 (2.56%)	1 (2.56%)	15 (51.72%)	2 (6.90%)	3 (10.34%)	8 (27.59%)	1 (3.45%)	< 0.01

(Continues)

Table 2. Results to the EPIC-CP (continued)

	RP (n = 39)				RT + ADT (n = 29)				p	
	Bowel habits									
Control loss (no defecation)	38 (97.44%)	0	0	0	1 (2.56%)	22 (75.86%)	4 (13.79%)	0	3 (10.34%)	0.01
Defecation with blood	37 (94.87%)	0	1 (2.56%)	0	1 (2.56%)	20 (68.97%)	6 (20.68%)	0	3 (10.34%)	< 0.01
Rectal, pelvic, or lower belly pain	35 (89.74%)	2 (5.13%)	1 (2.56%)	1 (2.56%)	0	13 (44.83%)	5 (17.24%)	5 (17.24%)	1 (3.45%)	< 0.01
Sexual activity										
How would you rate each of the following aspects?										
Ability to have an erection	19 (48.72%)	7 (17.95%)	10 (25.64%)	3 (7.69%)	0	20 (68.97%)	3 (10.34%)	3 (10.34%)	0	0.27
Ability to achieve orgasm	15 (38.46%)	1 (2.56%)	9 (23.08%)	13 (33.33%)	1 (2.56%)	18 (62.07%)	3 (10.34%)	3 (10.34%)	5 (17.24%)	0.09
Quality of erections										
No quality	22 (56.41%)					19 (65.52%)				0.84
Not rigid enough for any type of sexual activity	5 (12.82%)					3 (10.34%)				
Rigid enough for masturbation	7 (17.95%)					3 (10.34%)				
Rigid enough for intercourse	5 (12.82%)					4 (13.79%)				
Hormonal function										
Have any of the following aspects been a problem for you?										
Hot flashes	37 (94.87%)	0	1 (2.56%)	1 (2.56%)	0	15 (51.22%)	4 (13.79%)	4 (13.79%)	2 (6.9%)	< 0.01
Breast tenderness or pain/enlargement	39 (100%)	0	0	0	0	19 (65.52%)	1 (3.45%)	5 (17.24%)	1 (3.45%)	< 0.01
Feeling depressed	33 (84.62%)	1 (2.56%)	3 (7.69%)	2 (5.13%)	0	17 (58.62%)	4 (13.79%)	0	3 (10.34%)	< 0.01
Lack of energy	34 (87.18%)	0	1 (2.56%)	3 (7.69%)	1 (2.56%)	18 (62.07%)	3 (10.34%)	0	3 (10.34%)	0.013
Weight change	38 (97.44%)	0	1 (2.56%)	0	0	21 (72.41%)	1 (3.45%)	2 (6.9%)	3 (10.34%)	< 0.01

Table 3. Relationship between incontinence and erectile dysfunction with comorbidity and tumor risk in the prostatectomy group

RP	Age, median (years)	p	Risk groups			p	Comorbidity			
			Low	IntermmEDIATE	High		T2DM (p = 0.71)		IDH (p = 1)	
							Yes	No	Yes	No
0-1 pad	62.50	0.50	11 (45.8%)	11 (45.8%)	2 (8.3%)	0.3	5 (20.8%)	19 (79.2%)	2 (8.3%)	22 (91.7%)
> 2 pads	60		3 (20%)	10 (66.7%)	2 (13.3%)		4 (26.7%)	11 (73.3%)	1 (6.7%)	14 (93.3%)
							T2DM (p = 1)		IHD (p = 0.25)	
							Yes	No	Yes	No
Poor or very poor erection	61.23	0.43	7 (26.9%)	16 (61.54%)	3 (11.5%)	0.2	6 (23.1%)	20 (76.9%)	1 (3.9%)	25 (96.1%)
Good or very good erection	59.54		7 (53.9%)	5 (38.5%)	1 (7.7%)		3 (23.1%)	10 (76.9%)	2 (15.4%)	11 (84.6%)

IHD, ischemic heart disease; T2DM, type 2 diabetes mellitus; RP, radical prostatectomy.

Table 4. Relationship between incontinence and erectile dysfunction with comorbidity and tumor risk in the external radiotherapy group with androgen deprivation therapy

RT + ADT	Age, median (years)	p	Risk groups			p	Comorbidity			
			Low	Intermmediate	High		T2DM (p = 0.71)		IDH (p = 1)	
							Yes	No	Yes	No
0-1 pad	69	0.25	2 (9.52%)	9 (42.86%)	10 (47.62%)	0.12	6 (28.57%)	15 (71.43%)	1 (4.76%)	20 (95.24%)
> 2 pads	72		0	7 (87.5%)	1 (12.5%)		4 (50%)	4 (50%)	0	8 (100%)
							T2DM (p = 0.07)		IDH (p = 1)	
							Yes	No	Yes	No
Poor or very poor erection	71	0.12	0	12 (52.17%)	11 (47.83%)	< 0.01	10 (43.5%)	13 (56.5%)	1 (4.35%)	22 (95.65%)
Regular or good erection	65			2 (33.3%)	4 (66.7%)		0	6 (100%)	0	6 (100%)

IHD, ischemic heart disease; RP, radical prostatectomy; T2DM, type 2 diabetes mellitus; RT + ADT, external radiotherapy with androgen deprivation therapy.

community has faced the difficulty of the absence of a standard method to interpret the various aspects of QoL¹².

Specific QoL measurement instruments for PC patients focus on 5 health domains that are repeated in validated questionnaires: urinary symptoms, sexual and intestinal activity, and social and relational aspects of the patient. In the present study, we investigated the deterioration of QoL resulting from each treatment based on these 5 items, in addition to comparing different therapies to support decision-making with the most objective data possible.

Regarding the two most relevant side effects attributed to surgery, urinary incontinence and erectile dysfunction, in our series, despite not achieving statistical

significance, 61.5% were dry and 17.9% used three or more pads at 3 years after RP vs 72.4% and 6.9%, respectively, from the RT + ADT group. Additionally, in the RP group, 48.7% reported very poor or no ability to have an erection, and 7.7% reported good ability, while in the RT + ADT group, 1 year after the completion of ADT, 69% had very poor or no erections, while 10.3% considered them good.

Compared with the available literature, considering continence as not using pads, our results are consistent with published data for RP, which ranges from 60.5% up to 93% at 1 year¹³⁻¹⁹. The best figures are achieved by high-volume reference center with experienced surgeons; as they indicate, experience and the surgeon are fundamental factors in surgical outcomes²⁰.

This fact is further highlighted in the analysis of erectile dysfunction data. Kundu et al.¹³ describe that, when evaluating the results of RPs performed between 1983 and 2003, in the first 1000 patients, erectile function recovery was 68%, while in patients 1000 to 3000, it was 78% ($p < 0.01$). The subjectivity in assessing sexual potency makes inter-series comparison very complex.

Of note that, when specifically asked about the impact of these items on their lives, 53.8% of RP patients did not consider any reduction in their QoL regarding their current urinary habits vs 31% from the RT + ADT group. However, regarding sexual activity, 23.1% of RP patients considered it a major problem vs 17.2% from the RT + ADT group.

In the analysis of the items most frequently associated with RT + ADT, no RP patient reported hematuria-related problems vs 10.3% of radiated patients who considered it a major problem.

Additionally, in line with the study by Litwin et al.²⁰, urinary discomfort was notably worse after 2 years of radiation vs surgery. In our series, up to 31% considered dysuria as a major problem in their lives, while none of the RP group described it this way ($p < 0.01$).

Regarding digestive symptoms, the incidence is very low in RP patients, who practically did not report urgency, bowel movement frequency, blood in stool, fecal incontinence, or abdominal pain. This is not the case in the RT + ADT group, where up to 17.2% considered digestive disturbances a moderate problem and 3.4% as a major problem. As reported by Wei et al.²¹ and Potosky et al.²², diarrhea, rectal tenesmus, and rectal bleeding are significantly more frequent after radiation.

Given that patients undergoing external radiotherapy require ADT, and despite all patients included in the study having been off ADT for, at least, 1 year, up to 27.5% of patients in this group reported despondency as a moderate or major problem vs 5.1% from the RP group.

From all these data, we can conclude that, in our series, urinary incontinence and erectile dysfunction are more frequent in patients undergoing RP. Still, in terms of QoL, the most significant impact comes from the adverse effects of RT + ADT. Results are consistent with those published by Resnick et al.²³, who compared long-term functional outcomes after RP or RT and concluded that operated patients tended to have worse results in terms of urinary incontinence and erectile dysfunction at 2 and 5 years, with no differences at 15 years, and were less likely to experience bowel urgency at 2 and 5 years²³.

Notably, in the overall assessment of HRQoL using the CAVIPRES-30 questionnaire, RP patients had a

better perception of their QoL vs the RT + ADT group, with statistically significant differences.

In the evaluation of HRQoL before and after radical treatments, both the RP and RT + ADT groups showed better perceptions before the procedure ($p < 0.01$); hence, the importance of multidisciplinary evaluation and joint decision-making with the patient for the final therapeutic decision.

A limitation of this study is the subjective nature of evaluating functional aspects, which increases the variability of results. It is necessary to establish a standard definition, evaluation method, and time frame for assessing these items. Meanwhile, using validated questionnaires allows for comparison. Additionally, the study has limitations inherent to a small sample size and being a non-randomized series, with data extracted from clinical practice, making the patients directed to one or another treatment non-homogeneous groups.

Conclusions

Patients with a poorer perception of their HRQoL after receiving radical treatment for organ-confined PC are those who undergo RT + ADT vs RP. Hematuria, digestive symptoms, and urinary discomfort were more common in the radiotherapy group. Urinary incontinence and erectile dysfunction are more frequent in the RP group, although not statistically significant.

The evaluation of HRQoL before and after both treatments shows a deterioration in both cases, highlighting the impact of decision-making on PC management.

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Conflicts of interest

The authors declare no conflict of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments on humans or animals have been performed for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their center for the protocols on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the approval of the

Ethics Committee for the analysis and publication of routinely collected clinical data. The informed consent of the patients was not informed consent of the patients was not required as this was a retrospective observational study.

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