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Overview of potential determinants of radical prostatectomy versus radiation therapy in management of clinically localized prostate cancer: results from an Italian, prospective, observational study (the Pros-IT CNR study)

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Abstract

BACKGROUND: We assessed patients and tumor characteristics, as well as health-related quality of life (HRQoL) items, associated with curative intent treatment decision-making in clinically localized prostate cancer (PCa) patients.

METHODS: Clinically localized PCa treated with either radical prostatectomy (RP) or radiation therapy (RT) within 12 months from diagnosis were abstracted from The PROState cancer monitoring in ITaly, from the National Research Council (Pros-IT CNR) database. Multivariable logistic regression (MLR) models predicting RT vs. RP were fitted, after adjustment for HRQoL items, patients and tumor characteristics.

RESULTS: Of 1 041 patients, 631 (60.2%) were treated with RP and 410 (39.8%) with RT. Relative to RT, RP patients were younger age (mean age 64.5±6.6 vs. 71.4±4.9, p<0.001) and had higher rates of D'Amico low-intermediate risk groups (31.8 vs. 21.9% low, 46.3 vs. 43.5% intermediate and 21.9 vs. 34.6% high risk, p<0.001). Overall, 93.2% of RP patients were enrolled by Urologists and 82.7% of RT patients by Radiation Oncologists. RP patients had generally higher means values of HRQoL items. In MLR models, higher RT rates were independently associated with more advanced age (odds ratio [OR] 6.14, p<0.001) and BMI $\geq$30 kg/m^2 (OR 1.78, p<0.001). Conversely, lower rates of RT were independently associated with married (OR 0.55, p=0.01) and worker status (OR 0.52, p=0.004), enrollment in academic centers (OR 0.59, p=0.005) and higher physical composite score (OR 0.88, p=0.03) and baseline sexual function (OR 0.92, p<0.001) items.

CONCLUSIONS: Most patients with clinically localized prostate cancer undergoing definitive treatment at Italian institutions receive RP instead of RT. Moreover, those who are younger,

married, working, as well as those with better physical and sexual function are more likely to undergo surgery.

Keywords: localized prostate cancer; radical prostatectomy; radiation therapy; decision-making; health related quality of life

1. Introduction

Different treatment modalities may be offered to patients diagnosed with clinically localized prostate cancer (PCa)[1–3]. Among these, treatments with curative intent include radical prostatectomy ([RP] open, laparoscopic or robotic) and radiation therapy ([RT] external beam radiation therapy [EBRT] or brachytherapy) with or without androgen-deprivation therapy (ADT). To date, none of these two treatment modalities have been definitely proven to be superior in term of oncological benefit[4–6]. Nonetheless, each treatment is associated with specific risks and side effects which may invariably impact on patients' health-related quality of life (HRQoL)[7,8].

As result of lack of specific evidences supporting the preferential use of either RP or RT among the same risk categories, decision-making process for men diagnosed with clinically localized PCa is often conditioned by patients' preferences[9,10] and features other than oncological characteristics distinctive of PCa. Indeed, several studies showed how sociodemographic characteristics[11–13], such as age, comorbidity, educational level, as well as provider facilities[14], specialist seen, as well as multimodal discussion[15,16], and social support[17], strongly influence this decision-making process.

In this population-based study, we assessed determinants of receipt of treatment with curative intent (i.e. RP or RT) in clinically localized PCa. We accounted for clinical, sociodemographic and tumor features, as well as HRQoL items, assessed through validated patient-reported outcomes measures (PROMs), prospectively collected within the PROState cancer monitoring in ITaly project from the National Research Council (Pros-IT CNR)[18].

2. Materials and Methods

2.1 Study design and population

The Pros-IT CNR project is a prospective observational longitudinal study which monitors an Italian cohort of 1 705 PCa men[18–20] through validated tools. Ninety-seven Italian public or private facilities, including 51 Urology, 39 Radiation Oncology and 7 Medical Oncology units, were involved in the Pros-IT CNR project. All the units were , identified on the basis of project Steering Committee recommendations. Patients eligible for recruitment were males aged 18 years or more willing to participate into the study and that were newly diagnosed with biopsy-confirmed PCa between September 2014 and September 2015. Each participating center was required to enroll consecutive patients. Patients were evaluated every six-months for the first year, then yearly up to five years from enrollment. The approval of the Ethics Committee of coordinating center (Sant'Anna Hospital, Como, Italy; register number 45/2014), as well as of all local Committees, were obtained. Informed consent was signed by each patient.

The aim of the present study was to examine the use of curative treatment in patients with clinically localized PCa and to identify health-related quality of life (HRQoL) items, as well as patients- and physicians-associated characteristics, to drive treatment type selection. For the present analysis, only patients with clinically localized PCa treated with curative intent were included. Specifically, clinically localized stage definition, i.e. cT1 and cT2 tumors, as well as staging work-up, followed the current guidelines[1,2]. Treatment options were categorized into two groups: (a) RP, alone or as a first step of multimodal treatment (RP plus EBRT plus/minus ADT), and (b) RT, alone or as part of multimodal treatment (EBRT plus ADT or brachytherapy plus/minus ADT). Only patients with a residual life expectancy of at least 10 years were included, according to guidelines recommendation of offering RP to patients with life expectancy of more

than 10 years. Life expectancy was calculated based on the Italian National Institute of Statistics (ISTAT) estimates for 2016. Specifically, residual life expectancy was calculated as the average number of years that a person of a specific age can expect to live, assuming that age-specific mortality levels remain constant. Further exclusion criteria consisted of lack of information of received treatment, patients treated with focal therapy, androgen deprivation therapy alone, monitoring (i.e. active surveillance or watchful waiting) and patients that did not return at least one questionnaire. These selection criteria yielded a cohort of 1 041 men with clinically localized PCa (Figure 1).

2.2 Covariates

Among patients' covariates, age at diagnosis, body-mass index (BMI), smoking status, comorbidities - assessed by the Cumulative Illness Rating Scale (CIRS) - family history of PCa, marital status, working status and area of residence were included. PROMs were assessed by validated questionnaires delivered, self-administered and returned during in-hospital visits, at diagnosis and then at 6 and 12 months after enrollment. Physical (PCS) and mental composite scores (MCS) were evaluated by the Italian versions of the Short-Form Health Survey (SF-12)[21]. Urinary, bowel and sexual functions and bothers (UF/B, BF/B, SF/B, respectively) were evaluated by the University of California Los Angeles-Prostate Cancer Index (Italian UCLA-PCI)[22]. Scores of both questionnaires ranged from 0 to 100, with higher scores indicating better outcomes. Using Gleason grade, PSA level and clinical stage, tumors were categorized according to European Association of Urology risk group as low, intermediate, or high risks. Finally, characteristics of institution where the initial prostate cancer was diagnosed (i.e. presence of Urology unit, Radiation Oncology Unit and/or Prostate Cancer Unit and type of institution – academic vs. non-academic), as well as physician that enrolled the patient, were collected.

2.3 Statistical Analysis

Number and percentages were presented for categorical variables, while means and standard deviation (SD) or medians and interquartile ranges (IQR) for continuous variables. No imputation of missing data was performed. Patient demographics, tumor characteristics and baseline PROMs were compared between RP vs. RT using chi-square or Fisher's Exact test for categorical variables, and mixed models or Wilcoxon rank-sum test for continuous variables. Additionally, to aid the interpretation of the results, the minimal clinically important difference (MID), which provides a measure of the smallest change in the PROMs of interest that patients perceive as important, was calculated for PROMs and defined as half standard deviation of the mean at baseline[23,24]. Multivariable logistic regression models predicting treatment receipt (RT vs. RP) were fitted. Adjustment variables consisted of socio-demographic characteristics (age at diagnosis, education, marital status, work conditions, geographical area of residence), lifestyle and health status (smoking status, family history of prostate cancer, comorbidities, diabetes, BMI), D'Amico risk classes and PROMs. The linearity assumption for quantitative variables was evaluated on the basis of the quartiles and interactions among covariates were also evaluated. Finally, as sensitivity analysis, multivariable logistic regression models were repeated without inclusion of PROMs.

All statistical tests were two-sided with a level of significance set at $p < 0.05$. Analyses were performed using SAS software, version 9.4 (SAS Institute).

3. Results

3.1 Baseline patients' characteristics

For the purpose of the study, 1 041 patients with clinically localized PCa were considered (Figure 1). Of these, 631 (60.3%) patients were treated with RP (509 with RP alone and 122 with RP followed by RT with or without ADT) and 410 patients (39.4%) were treated with RT (242 with EBRT alone, 150 with EBRT plus ADT and 18 with brachytherapy). Baseline sociodemographic and tumors characteristics are summarized in Table 1. When compared to RT group, RP patients exhibited younger age (mean age 64.5±6.6 vs. 71.4±4.9, p<0.001). Additionally, RP patients were more frequently married or cohabiting (89.2 vs. 81.4%, p<0.001), still working (39.6 vs. 13.0%, p<0.001) and with higher educational level (79.8 vs. 66.0%, p<0.001). Median PSA at diagnosis was lower in RP patients (6.6 vs. 7.3 ng/ml, p=0.02). D'Amico risk classification was as follows: 31.8 vs. 21.9% low, 46.3 vs. 43.5% intermediate and 21.9 vs. 34.6% high risk, for respectively RP and RT patients (p<0.001).

Additionally, 93.2% of RP patients were enrolled by Urologists, 6.5% by Radiation Oncologists and 0.3% by Medical Oncologists. Conversely, 16.6% of RT patients were enrolled by Urologists, 82.7% by Radiation Oncologists and 0.7% by Medical Oncologists (Table 2).

3.2 Baseline patients reported outcomes

There was a statistically significant difference in baseline PROMs that were higher in RP patients with the exception of MCS that was higher in RT patients (Table 3, Figure 2). However, these differences were minor. The MID did not exceed for all the PROMs with the exception of the UCLA-PCI SF. Here, the MID exceeded 0.5 SD of the baseline values (mean score of 61.4±28.6 vs. 39.0±29.9, for respectively RP and RT patients, MID 15.6 p<0.001).

3.3 Multivariable logistic regression models predicting treatment receipt

In multivariable logistic regression models predicting treatment receipt (Table 4), more advanced age (odds ratio [OR] 6.14, p<0.001) and BMI $\geq$ 30 kg/m^2 (OR 1.78, p<0.001) were independent predictors of RT treatment. Conversely, married or cohabiting patients (OR 0.55, p=0.01), workers (OR 0.52, p=0.004) and patients enrolled in academic centers (OR 0.59, p=0.005) less frequently were treated with RT. Among HRQoL items, only PCS and SF items reached the independent predictor status. Specifically, a five-point increase in both PCS (OR 0.88, p=0.03) and SF (OR 0.92, p<0.001) were independent predictors of lower RT treatments.

In sensitivity analyses, after removing PROMs, more advanced age (OR 7.26, p<0.001), BMI $\geq$ 30 kg/m2 (OR 1.91 p<0.001) and diabetes (OR 1.87, p=0.01) were independent predictors of RT treatment. Conversely, married or cohabiting patients (OR 0.51, p=0.01), workers (OR 0.45, p=0.004) and patients enrolled in academic centers (OR 0.60, p=0.005) less frequently were treated with RT.

4. Discussion

Men diagnosed with clinically localized PCa who desire treatment with curative intent face highly preference-sensitive choice between RP and RT. Indeed, both RP and RT are recognized as equivalent treatment options in patients with clinically localized PCa by both European and North-American guidelines[1,2]. Therefore, selection of either RP or RT as initial treatment in clinically localized PCa may be challenging for both physicians and patients. The present study investigated patients and tumor characteristics, as well as HRQoL items, that may be associated with treatment decision-making in a contemporary nation-based cohort with clinically localized PCa and more than ten-year life-expectancy. Our analyses resulted in several noteworthy findings.

First, in this study, 60% of patients were treated with RP, while 40% were treated with RT. This finding is in agreement with previous population and nation-based analyses[25–27], where rates of RP exceeded those of RT in clinically localized PCa patients. As those previous reports, RP patients were generally younger and with longer life expectancy. Additionally, RP patients were more frequently still working, more frequently married or cohabiting, and had higher educational level. Conversely, non-clinically meaningful differences were recorded according to comorbidity profile. Of these demographic patient's characteristics, only younger age, married or cohabiting status and still working condition were significantly associated with being treated with RP after multivariable adjustment.

Second, RP patients RP patients presented with lower D'Amico risk class. These findings suggest a more favorable tumor phenotype in RP patients. However, D'Amico risk class was not significantly associated with treatment receipt. These observations suggest that both RP and RT are equally offered based on tumor characteristics in clinically localized disease.

Third, the vast majority (93.2%) of RP patients were enrolled by Urologist, while the vast majority of RT patients (82.7%) were enrolled by Radiation Oncologist. Additionally, urologists enrolled 16.6% of RT, while radiation oncologists enrolled 6.5% of RP. Due to the wide difference in the proportions, it was not possible to test in multivariable models the effect of physician who enrolled the patient. Previous reports[15,28] consistently showed that both Radiation Oncologists and Urologists mainly prescribe the treatment modalities they offer. Moreover, if we consider the time span of the previous studies[15,28], our findings suggested that the pattern of treatment decision-making according to physician specialty have remained unchanged for the past two decades. Finally, it should be noted that in our cohort biopsy was performed by Urologists in almost all of the cases. Therefore, the Urologist was the physician who made the upfront PCa diagnosis.

Fourth, PROMs at baseline were generally higher in RP patients. Nevertheless, this difference may be considered clinically meaningful only for SF. This observation may be further confirmed by the fact that only SF item exceed the MID. However, it should be noted that these PROMs were developed before the MID concept was widespread and that use of MID was not included in the prespecified analysis plan. Therefore, MID should be use as an aid in interpretation of the results. In the present cohort, the clinically meaningful difference in PROMs was recorded for SF item that additionally exceeded the MID. Nonetheless, this difference may be attributable to the younger age of RP patients, as previously reported[24]. After adjustment for multiple covariates, only SF and PCS items were significantly associated with treatment receipt. Specifically, higher SF and PCS scores were associated with a lower likelihood of receiving a RP. Previous studies showed how patients' preference[10,29], as well as patients' bother from treatment side effects[30,31], may play an important role in treatment decision-making progress. However, to the best of our knowledge, this is the first study that investigated how HRQoL collected with

validated PROMs may be related to treatment choice. Indeed, choosing a treatment option that less negatively affects mental and physical health, as well as urinary, sexual or bowel function, may be prioritized by many patients.

In this contemporary nation-based cohort of clinically localized PCa patients treated with treatment with curative intent, the majority (60%) received RP. Higher RP rates were significantly associated with younger age, married status and still working conditions, as well as with higher baseline HRQoL items, with the biggest difference recorded for SF. It is worth of mention that those should be the subjects featured by the largest independence in choosing treatments, as well those more interested in sexual life. Therefore, it could be concluded that the expectations to achieve the more radical treatment have overcome any concern on the side effects of surgery on sexual function[32]. Alternatively, the physicians proposing surgery undermined such effects. Of interest, neither comorbidity profile nor D'Amico risk class were significantly associated with treatment receipt in our cohort, suggesting that contemporary surgical indication is not influenced by these factors due to the improvement of peri- and intra-operative care and the widening indication to more aggressive tumors. These findings offer an insight in the present Italian scenario and are of remarkable importance to further interpret the outcomes in patients treated with RP and RT that will be the matter of next future studies. Additionally, our findings further encourage the importance of a multidisciplinary approach[33], in order to provide the best tools for decision-making. Indeed, it has been demonstrated that multimodal discussion may alter management plans in 25% to 50% of PCa cases[16].

This study has several strengths and potential limitations that should be acknowledged. First of all, a strength of the study is the population-based design of contemporary patients, which

yielded a cohort that is more representative than institutional reports. However, the findings of the current study derived from exploratory analyses of an observational study design, which could have made results susceptible to confounders. Additionally, the involvement of participating centers on a voluntary basis, with almost half from the North of Italy, could have limited the representability of all Italian scenario. Second, this study is also unique in assessing patient reported HRQoL items through prospectively and systematically collected validated questionnaires. Nonetheless, patients' involvement in treatment decision-making could not be assessed. Similarly, also data on patient's income and social network could not be assessed. Therefore, we could not test the effect for these variables on treatment choice. Third, physician recommendations that may have influenced treatment choice could not be assessed. Moreover, whether multimodal discussion was performed also could not be adequately assessed. Nonetheless, we accounted for center characteristics, such as presence of Prostate Unit and academic status. Fourth, due to the low number of patients treated with active surveillance, and due to the lack of information on active surveillance strategy, in this study was not possible to investigate also active surveillance among treatment modalities.

5. Conclusions

Most patients with clinically localized prostate cancer undergoing definitive treatment at Italian institutions receive RP instead of RT. Moreover, those who are younger, married, working, as well as those with better physical and sexual function are more likely to undergo surgery.

Notes

Conflict of Interest

All the authors report no potential conflict of interest to disclose.

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Analysis and interpretation of data: all the authors

Statistical analysis: Noale

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Table 1. Baseline sociodemographic and tumors characteristics of 1 041 patients stratified according to treatment type (radical prostatectomy vs. radiation therapy) for clinically localized prostate cancer, identified within the PROState cancer monitoring in ITaly, from the National Research Council (Pros-IT CNR) study.

	Radical Prostatectomy* **(n=631, 60.6%)**	**Radiation Therapy#** **(n=410, 39.4%)**	**p**
Age at diagnosis, years, mean ± SD	64.5±6.6	71.4±4.9	<0.001
Age at diagnosis, years, median (IQR)	66 (60-69)	73 (69-75)	<0.001
Life expectancy at diagnosis, years, mean ± SD	19.7±5.4	14.3±3.8	<0.001
Education ≥ lower secondary school, n (%)	501 (79.8)	266 (66.0)	<0.001
Marital status, married or cohabiting, n (%)	563 (89.2)	333 (81.4)	<0.001
Work condition, still working, n (%)	246 (39.6)	53 (13.0)	<0.001
Geographical area of residence, n (%)			0.004
Northern regions	312 (50.7)	237 (60.8)	
Central regions	181 (29.4)	82 (21.0)	
Southern regions	122 (19.8)	71 (18.2)	
BMI, kg/m^2, mean ± SD	26.4±3.2	27.1±4.0	0.02
Smoking status, current smoker, n (%)	102 (16.5)	48 (12.0)	0.05
Diabetes mellitus, n (%)	64 (10.2)	85 (20.8)	<0.001
CIRS Comorbidities Index, median (IQR)	1 (0-2)	1 (0-2)	0.001
CIRS Severity Index, median (IQR)	1.31 (1.15-1.46)	1.31 (1.23-1.54)	0.002
Family history of prostate cancer, n (%)	129 (20.7)	53 (13.0)	0.002
Clinical T stage at diagnosis, n (%)			<0.001
cT1	378 (59.9)	187 (45.6)	
cT2	253 (40.1)	223 (54.4)	
Gleason score at diagnosis, n (%)			0.1
≤6	311 (49.8)	179 (44.1)	
3+4	151 (24.2)	96 (23.6)	
4+3	81 (13.0)	58 (14.3)	
≥8	81 (13.0)	73 (18.0)	
PSA at diagnosis, ng/mL, median (IQR)	6.6 (5.0-9.4)	7.3 (5.1-10.1)	0.02
D'Amico risk class, n (%)			<0.001
Low	198 (31.8)	89 (21.9)	
Intermediate	288 (46.3)	177 (43.5)	
High	136 (21.9)	141 (34.6)	

* Radical prostatectomy includes 509 exclusive radical prostatectomy and 122 radical prostatectomy followed by radiation therapy ± androgen deprivation therapy

Radiation therapy includes 242 external beam radiation therapy, 150 external beam radiation therapy + androgen deprivation therapy and 18 brachytherapy ± androgen deprivation therapy

Abbreviations. SD=Standard Deviation; IQR = interquartile range; BMI=Body Mass Index; CIRS=Cumulative Illness Rating Scale

Table 2. Provider and facility characteristics of 1 041 patients stratified according to treatment type (radical prostatectomy vs. radiation therapy) for clinically localized prostate cancer, identified within the PROState cancer monitoring in ITaly, from the National Research Council (Pros-IT CNR) cohort.

	Radical Prostatectomy (n=631, 60.6%)	**Radiation Therapy (n=410, 39.4%)**	**p**
Presence of Urology Unit, n (%)			<0.001
Yes	627 (99.4)	375 (91.5)	
No	4 (0.6)	35 (8.5)	
Presence of Radiation Oncology Unit, n (%)			<0.001
Yes	475 (75.3)	383 (93.4)	
No	156 (24.7)	27 (6.8)	
Presence of Medical Oncology Unit, n (%)			
Yes	551 (87.3)	399 (97.3)	<0.001
No	80 (12.7)	11 (2.7)	
Presence of Prostate Unit, n (%)			<0.001
Yes	118 (18.7)	47 (11.5)	
No	513 (81.3)	363 (88.5)	
Hospital teaching status, n (%)			
Teaching	348 (55.2)	176 (42.9)	0.02
Non-teaching	283 (44.9)	234 (57.1)	
Patient enrolled by, n (%)			<0.001
Urologist	588 (93.2)	68 (16.6)	
Radiation Oncologist	41 (6.5)	339 (82.7)	
Medical Oncologist	2 (0.3)	3 (0.7)	

Table 3. Baseline health related quality of life items of 1,041 patients stratified according to treatment type (radical prostatectomy vs. radiation therapy) for clinically localized prostate cancer, identified within the PROState cancer monitoring in ITaly, from the National Research Council (Pros-IT CNR) study.

Scores at diagnosis	Radical Prostatectomy (n=631, 60.6%)	Radiation Therapy (n=410, 39.4%)	p value	MID
UCLA-PCI scores (mean±SD)				
Urinary function	94.9±13.7	92.0±16.7	<0.001	7.5§
Urinary bother	91.1±21.5	85±25.7	<0.001	11.5§
Bowel function	95.7±10.9	92.3±15.0	<0.001	6.4§
Bowel bother	95.5±14.2	91.2±21	<0.001	8.7§
Sexual function	61.4±28.6	39±29.9	<0.001	15.6^
Sexual bother	67.4±33.6	58.9±35.6	<0.001	17.3§
SF-12 scores (mean±SD)				
Physical Component Subscale	53.2±6.1	50.3±8.1	<0.001	3.5§
Mental Component Subscale	49±9.4	50.1±9.6	0.01	4.7§

Abbreviations. SD=Standard Deviation; MID=minimal clinically important difference; SF-12=Short-Form Health Survey; UCLA-PCI=University of California Los Angeles-Prostate Cancer Index. All scores ranges from 0 to 100, with higher scores representing better quality of life.
§ the MID did exceed between groups (p>0.05)
^the MID exceeded between groups (p=0.0001)

Table 4. Multivariable logistic regression models predicting use of radiation therapy vs. radical prostatectomy as treatment with curative intent in a cohort of 1 041 patients with clinically localized prostate cancer, identified within the PROState cancer monitoring in ITaly, from the National Research Council (Pros-IT CNR) study.

	Odds ratio	95% Confidence Interval	p-value
Age at diagnosis ≥70 years	6.14	4.27-8.82	<0.001
Education ≥ lower secondary school	1.25	0.86-1.81	0.2
Marital status, married or cohabiting	0.55	0.34-0.88	0.01
Work condition, still working	0.52	0.34-0.81	0.004
Geographical area of residence			
Central vs. Northern regions	0.99	0.59-1.65	0.9
Southern vs. Northern regions	0.69	0.44-1.08	0.1
BMI ≥ 30 kg/m^2	1.78	1.13-2.81	0.01
Smoking status			
Past vs. never smoker	1.08	0.75-1.55	0.7
Current vs. never smoker	1.58	0.95-2.64	0.07
Family history of prostate cancer, yes vs. no	0.77	0.48-1.21	0.2
CIRS Comorbidity Index ≥ 2	0.72	0.48-1.06	0.1
CIRS Severity Index ≥ 1.3	0.87	0.56-1.34	0.5
Diabetes mellitus	1.46	0.91-2.35	0.1
D'Amico risk class, n (%)			
Intermediate vs. low	1.02	0.67-1.56	0.9
High vs. low	1.41	0.89-2.25	0.1
SF-12 PCS (5 points increment)	0.88	0.78-0.99	0.03
SF-12 MCS (5 points increment)	1.09	0.99-1.19	0.07
UCLA-PCI UF (5 points increment)	1.06	0.99-1.14	0.08
UCLA-PCI UB (5 points increment)	0.95	0.91-1.00	0.05
UCLA-PCI BF (5 points increment)	0.99	0.91-1.07	0.8
UCLA-PCI BB (5 points increment)	0.96	0.90-1.02	0.2
UCLA-PCI SF (5 points increment)	0.92	0.89-0.95	<0.001
UCLA-PCI SB (5 points increment)	1.00	0.98-1.03	0.8
Presence of Prostate Unit, yes vs. no	0.67	0.37-1.20	0.2
Academic centre, yes vs. no	0.59	0.41-0.86	0.005

Abbreviations. BMI=Body Mass Index; CIRS=Cumulative Illness Rating Scale; SF-12=Short-Form Health Survey; PCS=Physical Component Subscale; MCS=Mental Component Subscale. Scores ranges from 0 to 100, with higher scores representing better quality of life. UCLA-PCI=University of California Los Angeles-Prostate Cancer Index; UF=Urinary Function; UB=Urinary Bother; BF=Bowel Function; BB=Bowel Bother; SF=Sexual Function; SB=Sexual Bother. Scores ranges from 0 to 100, with higher scores representing better quality of life in relation to functions or symptoms

Figure legends

Figure 1. CONSORT flow diagram illustrating inclusion and exclusion criteria

Figure 2. Baseline health-related quality of life scores of 1 041 clinically-localized prostate cancer patients stratified according to treatment type (radical prostatectomy vs. radiation therapy), identified within the PROState cancer monitoring in ITaly from the National Research Council (Pros-IT CNR) study.
Abbreviations. RP=radical prostatectomy; RT=external beam radiation therapy; UCLA-PCI=University of California Los Angeles-Prostate Cancer Index; UF=Urinary Function; UB=Urinary Bother; BF=Bowel Function; BB=Bowel Bother; SF=Sexual Function; SB=Sexual Bother; SF-12=Short-Form Health Survey; PCS=Physical Component Subscale; MCS=Mental Component Subscale.
RP was performed either alone or as a first step of multimodal treatment (RP plus RT with/without androgen deprivation therapy). RT was performed either alone or as part of multimodal treatment (external beam RT with/without androgen deprivation therapy or brachytherapy with/without androgen deprivation therapy).
The bars represent mean values. All scores ranges from 0 to 100, with higher scores representing better quality of life.