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Localized prostate cancer treated with external beam radiation therapy: Long-term outcomes at a European comprehensive cancer centre

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ABSTRACT

Aims and background: To present survival and toxicity outcomes in patients with clinically localized, non-metastatic prostate cancer (PCa) treated with external beam radiotherapy (EBRT) combined with androgen deprivation therapy (ADT).

Materials and methods: Retrospective study of 849 PCa patients (pts) treated from 1996 to 2005. Until August 2000, all patients (281) were treated with conventional dose EBRT (<76 Gy); subsequent pts received ≥76 Gy (565 pts). Median age was 70 years (range, 39–82). Most pts were intermediate (353; 42.8%) or high-risk (344; 41.7%). Mean PSA was 10.1 ng/ml. Median dose to the prostate was 75 Gy. Complete ADT was administered to 525 pts (61.8%).

Results: Median follow-up was 109.6 months (range, 68.3–193.4). Overall survival (OS) was 92.5% and 81.1% at 5 and 10 years; by risk group (low, intermediate, high), 5- and 10-year OS rates were 94.3% and 85.9%, 92.3% and 79.2%, and 91.9% and 80.2% ($p = 0.728$). Five- and 10-year BRFS was 94.1% and 80.6% (low risk), 86.4% and 70.9% (intermediate), and 85.2% and 71.4% (high) ($p = 0.0666$). Toxicity included rectitis: grade 1 (G1) (277 pts; 32.6%), G2 (108; 12.7%), and G3 (20; 2.6%) and urethritis: G1 (294; 34.6%); G2 (223; 26.2%), and G3 (11; 1.3%). By dose rate (<76 Gy vs. ≥76 Gy), 5 and 10-year BRFS rates were 83.1% and 68.3% vs. 88.4% and 74.8% ($p = 0.038$).

Conclusions: Our results are comparable to other published series in terms of disease control and toxicity. These findings confirm the need for dose escalation to achieve better biochemical control and the benefits of ADT in high-risk PCa patients.

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1. Background

External beam radiation therapy (EBRT) has long been used to treat localized prostate cancer (PCa). In the past, the prescribed radiation dose ranged from 64 to 70 Gy delivered in fractions of 1.8–2 Gy, although data from clinical trials[1,2] showed that such doses were insufficient to achieve better disease control. However, it was not possible to increase the maximum doses with conventional EBRT due to toxicity risk (primarily to the bladder and rectum). The advent of three-dimensional conformal radiotherapy (3D-CRT) in the 1990s increased the accuracy of dose delivery to the target, thus enabling the use of higher, more effective doses while keeping toxicity within acceptable levels. As a result, long-term outcomes have been improved and toxicity decreased.[3]

Dose escalation can be achieved with precise radiotherapy techniques such as 3D-CRT or intensity-modulated radiotherapy (IMRT), or by adding a boost delivered with high-dose rate brachytherapy (HDRB) or IMRT.[4–7] Overall survival in high risk patients can be further improved by combining EBRT with androgen deprivation therapy (ADT).[8,9]

2. Aim

In the present retrospective study, we report long-term outcomes in a large patient cohort (849 patients) treated from 1996 to 2005 during a time period in which our treatment approach transitioned from conventional dose EBRT to high-dose 3D-CRT.

3. Materials and methods

3.1. *Patient cohort*

From 1996 to 2005, 849 patients (pts) underwent EBRT for clinically localized, non-metastatic PCa at our institution (Catalan Institute of Oncology; Barcelona, Spain). The median age was 70 years (range 39–82), with a median follow-up of 109.6 months (range, 68.3–193.4). Patient characteristics are shown in Table 1.

Up to August 2000, all patients received conventional dose EBRT, at which time 3D-CRT was implemented. Thus, 281 of the 849 pts (33.1%) were treated with EBRT at doses <76 Gy. In the year 2000, our institution switched to high-dose radiotherapy based on findings from multiple studies[10–15] and updated international guidelines.[16] Thus, all patients treated from August of that year (565 pts) were prescribed ≥76 Gy. Dose prescription data is not available for 3 cases.

The TNM-staging system of the American Joint Committee on Cancer[17] was used to classify patients. The Table shows the patient characteristics at baseline. Staging and pre-treatment work-up for all patients consisted of a complete physical examination including digital rectal examination, complete blood count with PSA determination, chest X-ray, and transrectal ultrasound. CT scan, bone scintigraphy, and pelvic MRI were performed when needed.

The risk group classification system developed by D'Amico and colleagues,[18] which includes blood PSA levels, Gleason score (GS) and tumour (T) stage, was used to assign patients to one of three risk groups: low, intermediate or high risk. Of the 849 pts in the study, data on risk group classification was available for 824 pts, as follows: 127 (15.4%) were considered low risk, 353 (42.8%) intermediate risk, and 344 (41.2%) high risk (Table 2). Mean pre-treatment prostate-specific antigen PSA was 10.1 ng/ml and Gleason score (GS) was ≤6, 7 and >7 in 389 pts (45.8%), 365 pts (43.0%), and 95 pts (11.2%), respectively. Perineural invasion was positive in 156 pts (18.4%).

In all cases, EBRT was performed with the patient in a supine position with legs and feet immobilized. Data from a CT scan performed with the patient in the treatment position were entered into the 3D treatment planning system to outline the prostate, vesicles, bladder and rectum. Regional lymph nodes were also contoured if the risk of the involvement was ≥15% (Partin tables).[19] Patients with confirmed pelvic node involvement were excluded from the study.

The EBRT treatment was delivered in daily fractions of 2 Gy, 5 days per week. All patients received EBRT alone without boost. The median dose to the prostate was 75 Gy (range, 73.9–76). Most patients (565; 66.8%) were prescribed 76 Gy with the remaining (281; 33.2%) receiving <76 Gy. Data from 3 pts are missing.

Table 1 – Patient characteristics.

Characteristic*	Value
Patients	849 (100%)
Age (years)	
Median	70
Range	39–82
Follow-up (months)	
Median	109.6
Range	68.3–193.4
Gleason score	
≤6	389 (45.8%)
=7	365 (43.0%)
>7	95 (11.2%)
Pretreatment PSA (ng/mL)	
Median	10.1
Range	1.2–300.8
T stage (DRE) (*n* = 819)	
T1	379 (46.3%)
T2	279 (34.1%)
T3	156 (19.0%)
T4	5 (0.6%)
T stage (MRI)) (*n* = 124)	
T1	14 (11.3)
T2	57 (46%)
T3	53 (42.7%)
T stage (US) (*n* = 477)	
T1	206 (43.2%)
T2	246 (51.6%)
T3	25 (5.2%)
Risk group (*n* = 824)	
Low	127 (15.4%)
Intermediate	353 (42.8%)
High	344 (41.7%)

* MRI indicates magnetic resonance imaging; US, ultrasound; DRE, digital rectal examination.