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Prostate RT in young patients

The curative role of radiotherapy in adenocarcinoma of the prostate in patients under 55 years of age: A rare cancer network retrospective study

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Abstract

To determine whether radiation therapy could be an acceptable alternative to surgery in young patients with adenocarcinoma of the prostate, we analysed the outcome of 39 patients aged under 55 with organ confined tumours who received external radiation therapy in a curative intent. Our results suggest that similar local control in younger and older patients can be expected from either external beam radiotherapy or radical prostatectomy.

Keywords: Prostate cancer; Young patients; Radiotherapy

Prostate cancer is especially a disease of older men and rare below the age of 55. Therefore, few papers concerning prostate cancer in younger patients are currently available. The reported literature consists of small series and provides conflicting clinical data: early prostate cancer may be seen as a more virulent disease [8,16,17], while others studies [2,4,6,15,20] provide data supporting the contrary. In Europe, as far as treatment is concerned, radical prostatectomy is generally preferred for younger patients [12,13,15,16,18]. Direct comparisons between surgery and radiotherapy are not available in any age group [19]. Because we did not find sufficient data in the literature on young patients treated by high dose radiotherapy to the prostate, information were collected through the different databases of 14 departments of radiation oncology affiliated to the Rare Cancer Network to retrospectively analyse the outcome of patients irradiated with a curative intent. This study aimed to provide a basis for further discussions on prognosis and treatment choices.

Materials and methods

From January 1990 to August 2001, data on symptoms at presentation, family history of cancer, histological grade, clinical and pathological stage, treatment modality and clinical outcome, were reviewed.

Thirty-nine patients fulfilled the inclusion criteria: absence of nodal involvement, curative high dose radiation therapy to the prostate and no adjuvant endocrine therapy. The Gleason grading system was used to score the histological grade. The staging classification was carried out using the TNM-UICC classification (5th edition). The tumour staging was established by combining digital rectal examination, prostatic ultra sound, and in few cases only, MRI of the prostate. The nodal staging was determined by CT scan and/or bilateral lymphadenectomy. The absence of distant metastases was assessed by bone nuclear imaging and chest X-rays. The patients in this series did not accept surgery for personal reasons or were not eligible for radical prostatectomy according to the medical and/or tumoral

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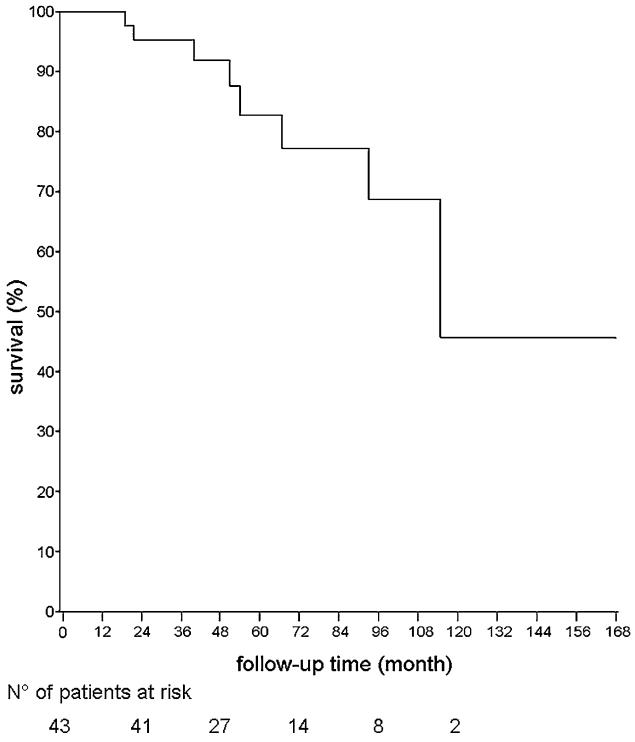

Fig. 1. Mean actuarial survival curve.

criteria used in the participating centres. External radiotherapy consisted of a four field box technique using megavoltage equipments (energy $\geq$10 MV) to deliver a median dose of 70 Gy (65–78 Gy) in 7–9 weeks to the prostate. The pelvis was irradiated in those patients whose PSA level was $\geq$10 μg/l and/or stage was T3. Hormonal therapy (androgen deprivation) was only given in cases of biological or local/distant failures. Definition of local failure was any clinical progression inside the pelvis whether or not documented by a biopsy. The criteria for biological failure were those proposed by the American Society for Therapeutic Radiation and Oncology i.e. three consecutive rising PSA values after the nadir.

The Kaplan–Meier method was used to estimate the survival. Comparisons between survival curves were made with the log rank test. Cox proportional hazards were used for the multivariate analysis and to assess the relation of NED status to stage, PSA level and Gleason score.

Results

Median age was 52 (range 28–55). The minimal follow up was 36 months; the median follow-up was 60 months. The clinical and pathological characteristics appear in Table 1. Among the 39 patients of the series, 16 patients were offered a prostate biopsy after a screening PSA checking. Voiding difficulties were the second most frequent symptom leading to the diagnosis. At the time of diagnosis only 4 patients had a PSA value $\leq$4 μg/l. All the others had a pathologic PSA ranging from 6 to 458 μg/l. Within 6–9 months after the end of radiotherapy, the PSA was normalized in all except two patients who eventually had a tumour progression within the pelvis. Out of the 37 remaining patients two clinical failures and four distant failures were observed (5 and 10%, respectively). The mean time to local and distant failure was 81 and 77 months, respectively. In the multivariate analysis we did not find any significant and independent factor predicting local and/or distant recurrence. Thirty-three patients were alive with no evidence of disease and one patient was alive with metastases. Five patients died due to prostate cancer and two patients died due to another cause (gastric carcinoma and myocardial infarction). The 5-year actuarial disease free survival was 88% (Fig 1). The median survival was 124 months. As far as late complications are concerned, we observed one case of urethral stricture necessitating repetitive dilatations and three cases of grade 3 proctitis. No case of incontinence was reported. No data were available concerning the sexual potency and the quality of life of the patients.

Table 1
Clinical and pathological characteristics

	N	%
Family history		
Prostate cancer[a]	**3**	**9**
Other cancers	7	19
No cancer	29	72
Gleason score		
$\leq$6	25	60
$>$7	14	40
T stage		
T1	7	18
T2	22	57
T3	10	25

[a] Prostate cancer in one first degree relative.

Discussion

This study is of limited value because of its retrospective multicentric design. Whether the modalities of diagnosis and treatment were homogenous enough to pool the patients into a single analysis is also questionable. To address this issue, a questionnaire sent to the different participating centres contained numerous items on the methods of diagnosis, staging and treatments. In case of inadequate or imprecise answer, a direct contact (TDN) was always organised with the responsible physician. The definition of young men in prostate cancer remains unclear. Freedman et al. [3] and Kupelian et al. [10] selected patients aged less than 65 Ruska et al. [16] reported in 1999 on 23 patients younger than 40. Aprikian et al. [2] in 1994, Wherthman et al. [19] in 1992 and Masood et al. [12] in 2003 reported on patients under 50 of age. All these authors did not provide a particular explanation for their age selection. In our series, age was set at 55 because this threshold was 10 years before the highest peak of incidence for prostate cancer and 20 years before the mean male life expectancy in Europe.

Definitive radiotherapy in our series cannot be considered as homogenous as theoretically expected in a single institution and within a short time period. The period of our analysis was however settled (1990–2001) to increase the radiation