Conformal radiotherapy (3D CRT) for non-metastatic androgen-independent prostate cancer: costly and sophisticated but ineffective treatment?

Received: 11.09.2006
Accepted: 7.02.2008
Subject: original paper

[1] Department of Radiotherapy, Greatpoland Cancer Centre, ul. Garbary 15, 61-866 Poznań, Poland,
[2] Chair of Urology, University School of Medical Sciences, ul. Kurlandzka 1, 61-650 Poznań, Poland

Address for correspondence:
Piotr Milecki
Radiotherapy Department of the Greatpoland Cancer Centre
ul. Garbary 15,
w61-049 Poznań, Poland
e-mail: piotr.milecki@wco.pl

Piotr MARTENKA[1] , Piotr MILECKI[1], Małgorzata ŻMIJEWSKA-TOMCZAK[1], Zbigniew KWIAS[2]

ABSTRACT

Purpose: Patients with diagnosis of hormone-refractory prostate cancers (HRPC) present a very heterogeneous population, and therefore it has been proposed to sub-categorize them into two subgroups depending on presence or absence of distant metastases. While the former subgroup has been typically treated with palliative intention, for the latter apparently there is no standard approach. The role of three-dimensional conformal radiotherapy (3D-CRT) for this subgroup has not been well documented in the literature. Thus, the purpose of this work is to analyze the results of treatment of non-metastatic androgen-refractory prostate cancer (ARPC) with 3D-CRT and to investigate the potential prognostic factors which influenced the results.

MATERIAL AND METHODS: Of 424 patients with diagnosis of localized and locally advanced prostate cancer who were treated between 1999 and 2004 in our centre, forty-three (n=43) patients were classified as non-metastatic ARPC. Distant metastases were excluded by negative bone scan, negative chest X-ray and negative pelvic CT for lymph node metastases. The median pre-hormone therapy PSA (pre-HT PSA) level for this group was 24 ng/ml (range 1 to 120) and 5.7 ng/ml (range 0.06 to 27) at the beginning of radiotherapy (pre-RT PSA). Clinical T stage distribution, defined according to the 2002 AJCC, was as follows: T1c = 12, T2 = 23, and T3 = 8 patients, respectively. Of 44 patients, 39 had a Gleason score of 2-7 and 4 had a Gleason score of 8 -10. All patients with diagnosis of non-metastatic ARPC were treated with 3D-CRT with the daily fraction dose of 2 Gy to a median total dose of 68 Gy (range from 60 to 74 Gy). The median duration of androgen ablation therapy before RT was 26 months (range from 7 to 96). The median time of follow-up after 3D-CRT was 27 months (range from 13 to 62) and from the beginning of androgen ablation was 53 months (range from 20 to 158). The following prognostic factors were evaluated in univariate and multivariate analysis: age, pre-HT PSA, pre-RT PSA, Gleason score, total dose, PSA doubling time (PSADT< 6 months vs. PSADT > 6 months).

RESULTS: The 5-year actuarial overall survival was 82% and 5-year clinical relapse free-survival rate was 49%. During the follow-up 14 patients developed disease progression (locoregional and/or distant and/or biochemical) and two patients died of prostate cancer. The univariate analysis indicated that pre-HT PSA > 20 ng/ml, pre-RT PSA > 4ng/ml, and the high-risk group defined according to NCCN criteria (PSA >20 ng/ml and Gleason score >7) were statistically significant factors for the risk of disease progression.

CONCLUSIONS: Three-dimensional conformal radiotherapy for patients with non-metastatic ARPC is a valuable method of treatment for the subgroup of patients with pre-HT PSA<20 ng/ml and Gleason score < 8. For patients classified as the high-risk group according to NCCN criteria 3D-CRT seems to be an ineffective treatment due to the observed high incidence of distant failure, and should be viewed as costly and sophisticated yet ineffective intervention. For this subgroup a systemic modality of treatment such as chemotherapy or biological manipulation should be considered.

KEY WORDS: non-metastatic hormone-refractory prostate cancer, three-dimensional conformal radiotherapy, prognostic factors

INTRODUCTION

Optimal treatment of prostate cancer is a field of debate as a result of lack of outcomes of randomized clinical trials which would compare the efficacy of main treatment modalities such as radical prostatectomy, radiotherapy (external beam therapy, brachytherapy), and hormonal therapy (HT) [1]. Hormonal therapy, the third main method of treatment, is used for prostate cancer treatment throughout a wide range of disease presentations because of the dependence of prostate cancer on testosterone [2]. In Poland, many patients are diagnosed in an advanced stage of disease, and thus androgen deprivation therapy (ADT) has frequently been used as the first line of treatment by urologists [3]. Beside that, in some cases of localized stage of disease, treatment is started with ADT as well. The main indication for HT in the latter group of patients is lack of the patient's agreement for active methods of treatment such as surgery or radiotherapy. During hormonal treatment increase of serum PSA level only and/or local progression without clinical evidence of distant progression in many cases changes the patient's decision and gives permission to move on to more radical treatment such as radiotherapy. Generally, for patients classified as nonmetastatic androgen-independent prostate cancer (ARPC) prognosis is poor, with a median survival of approximately 20 months [4]. However, if in this group of patients we could distinguish two main subgroups - the first with occult distant metastases and/or local failure, and the second with local failure alone which is represented by biochemical relapse too - then for the latter group an efficient local therapy might have been strongly indicated and effective. Therefore, selecting the subgroup of patients for whom radiotherapy could be beneficial is a crucial point of treatment of patients classified as ARPC. The role of radiotherapy in the treatment of prostate cancer is well established, although the role of this method of treatment for patients with non-metastatic ARPC is not well documented [5]. To date, only a few studies have described the outcome of radiotherapy in hormone-refractory prostate cancer [6–8]. Moreover, in the aforementioned studies important differences in patient selection and dose fractionation existed.

The aim of this study was to analyze the results of treatment of non-metastatic ARPC with conventionally fractionated 3D CRT and to investigate the potential prognostic factors which influenced the results.

MATERIAL AND METHODS

Patient characteristics

Between May 1999 and December 2004, at the Great Poland Cancer Centre in Poznañ, 424 patients with diagnosis of prostate cancer (T1-T3N0M0) were treated with three-dimensional conformal radiotherapy (3D CRT) with curative intent. In the present study from this cohort only forty-three patients 43 (n=43) were included due to fulfilment of the criteria for non-metastatic ARPC .

The median age of patients was 71 years (range 55–79 years). Distribution of T stage was as follows: (T1c = 12, T2 = 23 patients, T3a = 8 patients). All patients had a pathologically confirmed diagnosis of adenocarcinoma, which was classified according to the Gleason scoring system. The average level of PSA before the beginning of HT (pre-HT PSA) was 25 ng/ml (range 1 to 120 ng/ml) and the average PSA prior to RT (pre-RT PSA) was 5.7 ng/ml (range 0.06 to 27 ng/ml).

Before starting HT the following initial evaluation of disease was performed: digital rectal examination (DRE), transrectal ultrasonography (TRUS), bone scan, pelvis CT, chest X-ray. During hormonal therapy at 3-month intervals DRE was performed and serum PSA level measured.

All patients referred for RT were restaged using the following examinations: physical examination with DRE, bone scan/skeletal X-ray, chest X-ray, PSA serum level. In addition all patients had pelvic lymph nodes evaluated by computer tomography (CT) or magnetic resonance imaging (MRI) or ultrasound (US). None of the patients had diagnostic lymphadenectomy of the pelvic lymph nodes performed. Additionally all patients prior to HT and then before RT had a complete blood count, biochemistry including serum BUN, creatinine, and liver enzymes.

Hormonal therapy

In the analyzed group of patients, the decision concerning HT was made before consultation