

Prostate Cancer Patient Reported Outcome After Cyberknife Robotic Radiosurgery

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Abbreviations: PC: Prostate Cancer, IPSS: International Prostate Symptom Score, HRQOL: Health-Related Quality of Life, PSA: Prostate Specific Antigen

ABSTRACT

Purpose: The optimal management of localized Prostate Cancer (PC) should take account consideration of patient and clinical risk factors, as well as patient preferences. The objectives of this cohort study of men with newly diagnosed localised PC were to document side effects with the International Prostate Symptom Score (IPSS), International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF), International Index of Erectile Function Questionnaire (IIEF-5) and as well Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events Questionnaire (PRO-CTCAE) following radiosurgery with the Cyberknife.

Materials and Methods: In this cohort analysis, 20 patient with localized prostate cancer were analyzed who received Cyberknife radiosurgery (5 x 7 Gy) and completed the IPSS (1-23), ICIQ-SF (0-17), IIEF-5 (6-24) and the German validated PRO-CTCAE questionnaires.

Results: Mean IPSS score was 6.9 (mild symptomatic), mean ICIQ-SF score was 3.3 (mild impairment of incontinence), mean IIEF-5 score was 17.0 (mild erectile dysfunction). The highest score at PRO-CTCAE was for urinate frequently (one patient, 5%), achieve and maintain erection (one patient, 5%), ejaculation problems (two patients, 10%) and decreased libido (one patient, 5%). There was no significant difference at follow-up period or treated prostate volume (F/U: > 1 vs. < 1 year; Volume ml: >64 vs. < 64). Local control and overall survival were 100%. No patient developed metastasis after radiosurgery. None of our patients died until now.

Conclusion: Robotic Cyberknife radiosurgery for localized prostate cancer shows good local control and overall survival with a very mild side effect profile reported by patients.

Introduction

The optimal management of localized prostate cancer (PC) should take account consideration of patient and clinical risk factors, as well as patient preferences. Because of the high survival for localized prostate cancer [1], the long-term effects on Health-Related Quality of Life (HRQOL) are possibly the most important base for the therapy decision [2,3]. Well-documented reports of HRQoL effects are important in particular for patients to make well informed and evidence-based treatment decisions. Patient-reported outcome (PRO) is the direct report from a patient perspective about the effect of disease or treatment that has not

been interpreted by anyone else and can be easily understood from patient perspective [4]. Guidelines unfortunately do not serve the increasing interest in the potential relationship between treatment side effects and treatment decision [5]. This interest is linked to the shared decision-making paradigm, in which a "good" treatment choice is defined as one that fits the patients' values and preferences [6].

Recently, there has been a change toward the use of patient-reported outcomes (PROs), defined as the unfiltered direct report of a given symptom toxicity by a patient, and considered to be the

“gold standard” for the capture of symptomatic adverse events [7]. This change has been led by the release of the 2009 United States Food and Drug Administration (FDA) Guidance for Industry on the Use of PRO Measures in Medical Development to Support Labeling Claims [8], which subsequently led to the NCI initiative to develop a PRO version of the CTCAE (PRO-CTCAE) that will be used in future U.S.-based clinical trials in oncology [9]. The objectives of this cohort study of men with newly diagnosed localized PC were to evaluate patient-reported outcome and side effects with IPSS, ICIQ-SF, IIEF-5 and PRO-CTCAE questioner following Cyberknife radiosurgery.

Materials and Methods

The observational, retrospective, monocenter study included 20 patients with histologically confirmed localized prostate cancer treated with the Cyberknife® System (Accuray) treated after fiducial implants with 5 fractions of 7.0 Gy (35 Gy, 70 % isodose, Figure 1) every second day (treatment protocol according PACE-B study [10]). This type of stereotactic body radiotherapy (SBRT) is well established and acknowledged by international guidelines [11,12]. Patients who were treated between august 2012 and March 2020, were included in the analysis. Patients had newly diagnosed clinically localised PC (cT1–2 and/or Gleason 6-7, Prostate-Specific Antigen [PSA] < 20 ng/ml). All patients had to complete IPSS, ICIQ-SF, IIEF-5 and the PRO-CTCAE questionnaire. The questions in the IPSS questionnaire were as follows: question (Q)1, incomplete emptying; Q2, frequency; Q3, intermittency; Q4, urgency; Q5, weak stream; Q6, straining; Q7, nocturia; Q8, constancy and is utilized to measure the severity of lower urinary tract symptoms [13]. The ICIQ was developed in the early 2000s to promote use of an internationally uniform set of questionnaires [14]. The ICIQ-SF consists of 3 scored items which evaluate the frequency, volume of leakage, and overall impact of incontinence. The overall score ranges from 0 to 21, with greater values indicating increased severity.

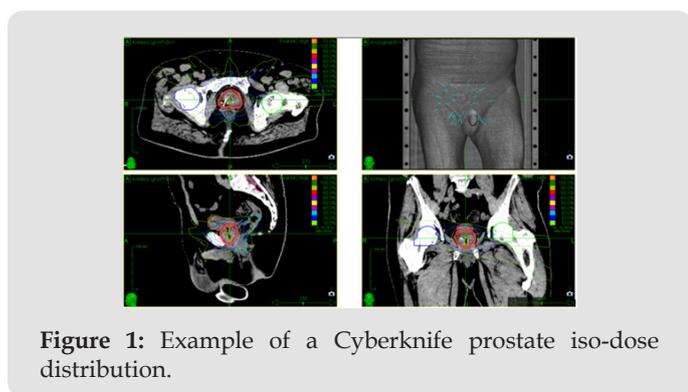


Figure 1: Example of a Cyberknife prostate iso-dose distribution.

Erectile function was prospectively assessed by a validated self-administered questionnaire IIEF-5. This questionnaire is the

simplified version of 5 items of the IIEF questionnaire, which was developed by Rosen in 1997 [15]. It is recommended as a criterion of effectiveness in clinical studies on ED. It enables to classify patients into 5 classes such as: normal EF: > 21; mild ED: 17-21; mild to moderate ED: 12-16; moderate ED: 8-11; severe ED: < 8. In total, 75 symptomatic toxicities (119 PRO-CTCAE items), corresponding to the symptomatic adverse-events profile associated with the regimens commonly used for prostate cancer treatment were selected. Patients reported symptoms on a 5-point scale. The IPSS, ICIQ-SF, IIEF-5 and PRO-CTCAE were used to evaluate patient-reported disease-specific function. Patients were treated at Strahlencentrum Hamburg and completed questionnaires at different time points after treatment. To limit study dropouts and missing data, respondents were offered to re-call or e-mail the authors for assistance, and patients received a telephone reminder 3 week after the questionnaire was sent. Study retention rates were 100% at three months.

Results

A total of 20 men were analyzed and completed the complete questionnaire and at point after therapy (median age, 73 [57-92] years). Median Age at time of therapy was 69.15 (54-79) years. Median follow-up for was 4.15 (0.5-8) years. Median initial PSA was 8.32 mg/ml (0,5-33). Median post treatment PSA was 0.58 mg/ml (0.1-4.6). Median volume of the treated volume with radiosurgery was 63.5ml (26-125). Mean Score of IPSS was 6.9 (1-23). A Score of 6.9 correlates to mild symptomatic. Mean Score of ICIQ-SF was 3.3 (0-17). A score of 3.3 shows a mild impairment of incontinence. Mean Score of IIEF-5 was 17.0 (6-24). A score of 17 shows only mild erectile dysfunction. The highest score at PRO-CTCAE was for urinate frequently (one patient, 5%), achieve and maintain erection (one patient, 5%), ejaculation problems (two patients, 10%) and decreased libido (one patient, 5%). There was no significant difference if the treatment was more or less than 1 year ago. There was no significant difference if the treated volume was greater than 64 ml or less (Table 1),

Table 1.

Results		
Number of Patients	20	
Age at follow-up	Mean: 73,25 years	From 57 - 92 years
Age at therapy	Mean: 69,15 years	From 54 - 79 years
initial PSA (0,5 – 33).	Mean: 8,32 mg/ml	From 0,5 -33 mg/ml
post treatment PSA	Mean: 0,58 mg/ml	From 0,1- 4,6 mg/ml
Follow up time	Mean: 4.1 years	From 0.5 - 8 years
Median volume Prostate	Mean: 63,5 ml	From 26- 125 ml
Response to questionnaires	100% at three months	

Local Control	100%	
Overall Survival	100%	
IPSS	Mean: 6,9 (mild)	Score: 1-23
ICIQ-SF	Mean: 3,3 (mild)	Score: 0-17
IIEF-5	Mean: 17,0 (mild)	Score: 6-24

Local Control and Overall Survival was 100% and no patient developed metastasis after radiosurgery. None of the patients died until now.

Discussion and Conclusion

Using this approach (Cyberknife, SBRT), long-term data with more than 10 years of follow-up are promising and show a biochemical freedom from recurrence of > 90% for low and intermediate-risk prostate carcinomas with significantly less than 1% local recurrences. The effectiveness (PSA control) of the radiosurgery was also with longer follow-up periods persistently very high with low toxicity. In particular, the late toxicity appears to be lower than with surgery or conventional external radiation. Recently published results show slight side effects (grade 2) for SBRT (5 treatments) below 5% in the urogenital area (GU) and below 2% in the gastrointestinal tract (GI) with very rare serious side effects (grade 3) of below 1% [10]. A German multicenter study using this Cyberknife approach is open to confirm existing international data for the national recommendations regarding long term effects (ClinicalTrials.gov NCT03795337). In this limited cohort analysis, Cyberknife radiosurgery for localized prostate cancer confirms low adverse effect profiles determined by the patients themselves with excellent local control and overall survival. The low incidence of toxicity in the PRO-CTCAE questionnaire shows a very acceptable and low adverse effect profile.

As well as with the good results of well-established scoring systems like IPSS, ICIQ-SF and IIEF-5. Since curative therapy options in man with localized prostate cancer (surgery: robotic or conventional radical prostate resection; radiotherapy: brachytherapy, conventional irradiation or radiosurgery) remain iso-effective and with regard to recent publications [16], it is very important to choose a treatment strategy with a low impact on the health-related quality of life and high cure rate. Furthermore, a short treatment interval (5 treatments only), minor side effects, good quality of life, less follow-up therapies, no absence from family and work, no hospitalization, no rehabilitation after therapy and increasing reports might be cumulative reasons to decide for Cyberknife treatment by man with localized prostate cancer acknowledged by their families, international societies and health care insurance companies.

Conflict of Interest

None.

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