Radiotherapy and Oncology 115 (2015) 321–326

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Salvage RT in prostate cancer

Changes in lower urinary tract symptoms and quality of life after salvage radiotherapy for biochemical recurrence of prostate cancer

Makito Miyake [a], Nobumichi Tanaka [a,*], Isao Asakawa [b], Yoshihiro Tatsumi [a,c], Yasushi Nakai [a], Satoshi Anai [a], Kazumasa Torimoto [a], Katsuya Aoki [a], Tatsuo Yoneda [a], Masatoshi Hasegawa [b], Noboru Konishi [c], Kiyohide Fujimoto [a]

[a] Department of Urology; [b] Department of Radiation Oncology; and [c] Department of Pathology, Nara Medical University, Japan

ARTICLE INFO

Article history:
Received 31 August 2014
Received in revised form 29 April 2015
Accepted 30 April 2015
Available online 16 May 2015

Keywords:
Prostate cancer
Salvage radiotherapy
International Prostate Symptom Score
Health-related quality of life
Disease-specific quality of life
SF-36

ABSTRACT

Background and purpose: The aim of this study was to evaluate chronologic changes in lower urinary tract symptoms (LUTS), health-related (HR) quality of life (QOL), and disease-specific QOL during the first 12 months after salvage radiotherapy (SRT) for biochemical recurrence of prostate cancer in patients who underwent radical prostatectomy.

Materials and methods: In 81 patients who received SRT (70 Gy/35fr/7 weeks), International Prostate Symptom Score (IPSS), 36-Item Short Form scores, and UCLA-Prostate Cancer Index (UCLA-PCI) were recorded before, during, and immediately after SRT, and 1–12 months after the completion of SRT.

Results: The total IPSS and storage symptom-related sum were significantly increased following initiation of SRT, and returned to the baseline 6 months after SRT. For three of eight domains of HRQOL, and the physical component summary score showed transient deterioration in the period between completion of SRT and 1 month following SRT. The UCLA-PCI for urinary function/bother and bowel function/bother was affected until 1–6 months after SRT.

Conclusions: This is the first report to concurrently evaluate detailed chronologic changes in LUTS and QOL in patients who received SRT. Knowledge of changes in LUTS and QOL outcomes associated with SRT may influence treatment recommendations and enable patients to make better-informed decisions.

Radical prostatectomy (RP) is recommended as the initial therapy for 44% of men with localized prostate cancer in the USA [1]. Our data from the Nara Uro-Oncological Research Group (NUORG) in Japan show an RP rate of approximately 30% (40% in stage cT1–2N0M0) [2–4]. Although RP provides excellent cancer control, 15–40% of these men experience biochemical recurrence (BCR) within 5 years, presenting with increasing serum prostate-specific antigen (PSA) levels, without radiographic evidence of cancer [5–7]. Within 5 years of RP, one in four men receive salvage radiotherapy (SRT), which entails external beam radiation to the prostate bed [8]. SRT is a salvage therapy that potentially achieves long-term remission from BCR and from clinical progression.

It is well documented that most patients who receive primary radiotherapy, including brachytherapy, for prostate cancer, complain of urinary symptoms such as nocturia, and frequency, urgency, hesitancy, and decreased force of urinary stream, for several months after treatment [9,10]. Moreover, many longitudinal studies have demonstrated the impact of primary radiotherapy to the prostate on health-related quality of life (HRQOL) using several measurement tools such as the Medical Outcomes Study 36-Item Short Form health survey (SF-36) and the University of California, Los Angeles-Prostate Cancer Index (UCLA-PCI) [11–14]. Several domains such as the urinary and bowel function domains, showed transient deterioration in the first years following brachytherapy [11,12].

To date, there are few reports on HRQOL in patients undergoing SRT following RP [15–18], and knowledge on issues such as HRQOL and the effects on lower urinary tract symptoms (LUTS) during and after SRT is limited. In this prospective study, we focused on the chronologic changes in the International Prostate Symptom Score (IPSS), HRQOL, and disease-specific QOL during the first 12 months following SRT, in patients treated for BCR of prostate cancer using the IPSS, SF-36 questionnaire, and UCLA-PCI.

Materials and methods

The protocol for the study was approved by the Ethics Committee of the institution within which the study was

* Corresponding author at: Department of Urology, Nara Medical University, 840 Shijo-cho, Nara 634-8522, Japan.
E-mail address: sendo@naramed-u.ac.jp (N. Tanaka).

http://dx.doi.org/10.1016/j.radonc.2015.04.026
0167-8140/

undertaken, in accordance to the provisions of the Declaration of Helsinki (64th World Medical Association General Assembly, Fortaleza, Brazil, in October 2013). Between January 2008 and December 2012, 94 consecutive patients underwent SRT treatment for BCR of prostate cancer following RP at the Nara Medical University Hospital. SRT was defined as local radiotherapy to the prostate bed, and underwent simulation prior to treatment, using three-dimensional conformal radiotherapy (3D-CRT) techniques. The clinical target volume (CTV) was defined as local radiation to the prostate and seminal vesicle bed alone using preoperative diagnostic imaging (e.g., computed tomography and/or magnetic resonance imaging) according to the guidelines of the Japan Clinical Oncology Group (JCOG) trial 0401 which was a randomized controlled trial to evaluate the efficacy of salvage radiotherapy for PSA failure after radical prostatectomy [19]. Comprehensive irradiation of pelvic lymph nodes was not attempted. The duration of SRT is almost 2 months at our institution; per protocol, 70 Gy was delivered in daily fractions of 2 Gy. The fields were shaped to protect the small bowel, bladder, and posterior rectal wall.

The IPSS and SF-36 questionnaires were conducted at several time-points as follows: before SRT initiation (hereafter referred to as "baseline"), 1 month after SRT initiation (hereafter referred to as "during SRT", abbreviated to D-SRT), immediately after the completion of SRT (hereafter referred to as "immediately after SRT" abbreviated to I-SRT), and 1, 3, 6, and 12 months following the completion of SRT (hereafter referred to as "follow-up after SRT", abbreviated to F-SRT-1, 3, 6, and 12). We chose a 12-month assessment endpoint as the maximum change in the parameters during this interval. For IPSS assessment, the sum of questions 1, 3, 5, and 6, and the sum of questions 2, 4, and 7, were defined as the voiding symptom related-sum and the storage symptom related-sum, respectively [20]. The QOL question index (0–6) was also recorded. The SF-36 is a self-administered questionnaire includes an eight-item scale of physical function (PF), role limitation due to physical problems (RP), bodily pain (BP), general health perception (GH), vitality (VT), social function (SF), role limitation due to emotional problems (RE), and mental health (MH) [21]. The SF-36 physical component summary (PCS) and mental component summary (MCS) scores were also calculated from the mean of the scores of items related to physical and emotional health, respectively. The UCLA-PCI measures disease-specific QOL using six domains; namely, urinary function, urinary bother, bowel function, bowel bother, sexual function, and sexual bother [22]. Each domain is scaled separately from 0 to 100 with higher scores representing better outcomes. The reliability of the Japanese versions of SF-36, its summary scores, and the UCLA-PCI was previously validated in a pilot study carried out in a Japanese population [23–25].

Of 94 patients, 13 were excluded because of follow-up in other hospitals or insufficient data collection due to cessation of follow-up visit. The remaining 81 patients were analyzed in the present study. The clinicopathological characteristics of the enrolled patients are listed in Table 1. The median age was 69 years (range, 58–81 years). The median pre-SRT prostate-specific antigen (PSA) value was 0.39 ng/mL (range, 0.06–5.1 ng/mL). One pathologist (K.N.), with expertise in prostate cancer diagnosis, centrally reviewed the Gleason scores of all prostatectomies. Tumor stage was diagnosed according to the 2002 Union for International Cancer Control classification. All patients were stratified according to the National Comprehensive Cancer Network criteria (available from: http://www.nccn.org). Of the 81 patients, we conducted a subgroup analysis of 61 patients treated with SRT alone and 20 with a combination of SRT and androgen deprivation therapy (ADT), in which either luteinizing hormone-releasing hormone agonist or anti-androgen, or a combination of both was used. We compared the HRQOL domains, and the two summary scores between the SRT monotherapy group and the combination therapy group.

Table 1
Characteristics of 81 who underwent patients salvage radiotherapy.

Variables	Total (n = 81)
Age at SRT (median, [range] years)	69 (58–81)
Initial PSA (median, [range] years)	9.0 (3.0–207)
NCCN risk classification	
Low	14
Intermediate	33
High/Very high	34
Prostatectomy Gleason score	
6	7
7	33
8	14
9	20
Unknown	7
Prostatectomy pathological T stage	
T2a	13
T2b	11
T2c	18
T3a	27
T3b	8
Unknown	4
Surgical margin	
Negative	35
Positive	39
Unknown	7
Salvage treatment method	
SRT monotherapy	61
Combination of SRT and ADT	20
PSA nadir after prostatectomy (median, [range] ng/mL)	0.06 (0.003–7.9)
Pre-SRT PSA (median, [range] ng/mL)	0.39 (0.06–5.1)

SRT = salvage radiotherapy; PSA = prostate-specific antigen; NCCN = The National Comprehensive Cancer Network; ADT = androgen-deprivation therapy.

Radiation-induced toxicity was graded using the common terminology criteria for adverse events (CTCAE) version 4.0. Early and late toxicity was defined as complications occurring within three months of the completion of SRT and three months after the completion of SRT, respectively. Toxicity was categorized into genitourinary (GU) and gastrointestinal (GI) toxicity.

We evaluated the chronologic changes documented using IPSS, the 8-item scale of the SF-36, and the six domains of the UCLA-PCI. The scores were expressed as the mean ± standard deviation (SD). IBM SPSS Version 21 (SPSS Inc., Chicago, IL, USA) was utilized for statistical analyses. The Mann–Whitney U test or Wilcoxon matched paired test was used to compare time-course variations with baseline values for each parameter, and a P-value of <0.05 was considered statistically significant. This prospective study complies with the principles laid down in the Declaration of Helsinki and was approved by the institutional review board of the Nara Medical University Hospital. The aims and methodologies of this study were explained to the patients, and all patients provided informed consent.

Results

International Prostate Symptom Scores following initiation of salvage radiotherapy

The time-course changes of the seven IPSS parameters, voiding symptom-related sum, storage symptom-related sum, total IPSS and QOL question index were summarized in Table 2. Elevated scores for frequency (question 2), urgency (question 4), and nocturia (question 7) were observed between initiation and completion of SRT, resulting in a significantly elevated storage symptom-related sum (5.9 ± 3.1 at D-SRT and 7.3 ± 3.4 at I-SRT, compared to 4.4 ± 2.8 at baseline). The scores for urgency and nocturia had returned to the baseline at 6 months after completion of