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Full Length Article

Hypofractionated Volumetric Modulated Arc Radiotherapy with simultaneous Elective Nodal Irradiation is feasible in prostate cancer patients: A single institution experience

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KEYWORDS

Prostate cancer;
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Abstract *Purpose:* To assess feasibility, toxicity and biochemical relapse-free survival (b-RFS) for a group of organ confined (OC) Saudi prostate cancer patients treated by hypo-fractionated Volumetric Modulated Arc Radiation Therapy (VMAT) Simultaneous Integrated Boost (SIB) Elective Nodal Irradiation (ENI) whole pelvic radiotherapy (WPRT).

Patients and methods: Between March 2009 and January 2014, 29 OC prostate cancer patients; median age 64 years, PS 0–1 were treated in King Faisal Specialist Hospital – Riyadh, Kingdom of Saudi Arabia using VMAT–SIB–ENI–WPRT, to a total dose of 70 Gy in 28 fractions. Twenty Four patients (83%) were treated with neo-adjuvant; concurrent androgen deprivation therapy (ADT). Median follow-up (FU) was 42 months (range: 18–72 months).

Results: The 3-year actuarial b-RFS for low/intermediate and high risk groups were 100%, and 48%, respectively ($p = 0.09$) with a median FU period of 34 months (range: 14–53 months). Gleason Score ($p = 0.02$), and pretreatment PSA ($p = 0.01$) were predictive for biochemical failure on univariate analysis; with no observed prostate cancer-related deaths. Grade 2 acute/late GI and GU toxicities were 28%/0% and 17%/10% respectively with no reported grade 3/4 toxicities. Four

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(50%) out of the 8 patients with baseline partial potency, retained sexual function on long term follow-up.

Conclusions: Hypo-fractionation dose escalation VMAT–SIB–ENI–WPRT using 2 arcs is a feasible technique for intermediate/high risk OC prostate cancer patients, with acceptable rates of acute/late toxicities, much favorable planning target volume (PTV) coverage, and shorter overall treatment time. Prospective randomized controlled trials are encouraged to confirm its equivalence to other fractionation schemes.

Introduction

Prostate cancer is the second most common solid tumor diagnosed in men in the United States and Western Europe [1]; a situation which is different in the middle east with reported incidence ranging from 4.7% to 6.4% of all cancers [2–3].

Treatment of localized prostate cancer has been proven by clinical trials including hypofractionation radiation therapy (RT) dose escalation with Elective Nodal Irradiation (ENI) [4,5] and androgen deprivation therapy (ADT) combined with RT [6,7]. Radiation therapy related toxicities is attributed to high total RT doses, short recovery time, and the volume of neighboring organs at risk [OARs] normal tissues (rectum and bladder) even in prostate-only RT [4–6]. Volumetric-modulated arc therapy (VMAT); a relatively new rotational radiation therapy intensity modulated radiotherapy (IMRT) technique delivering RT using continuous dynamic modulation of the dose rate, field aperture, and gantry speed in the treatment of whole pelvis (WPRT) or prostate only (±seminal vesicles) has been reported to be equal or better for target volume coverage and normal tissue sparing than IMRT [8]. One additional strategy to optimize the therapeutic ratio is hypofractionation, with the advantage of the assumption that prostate cancer is more sensitive than normal surrounding tissues to fractionation (low α/β ratio) [9]. Data from 7 databases (~6000 patients) evaluating prostate cancer clinical outcomes in relation to radiobiology confirmed the relatively low α/β ratio for prostate cancer control (range: 0.9–2.2 Gy); a ratio which is lower than the corresponding α/β ratios for late-responding tissues (3–5 Gy), with hypo-fractionation benefiting all risk groups with or without pelvic node irradiation [10]. Confirmatory meta-analysis supported prostate cancer low α/β ratio of $\leqslant$4 Gy [11]. Hypofractionation RT to the prostate only is now an accepted therapeutic alternative for high risk (HR) group of patients, with a weak evidence supporting concomitant pelvic node irradiation (retrospective phase I–II trials). Careful use of modern RT technologies with hypofractionation is a challenge to allow treatment of smaller volumes of critical structures (bowel, rectum, and bladder) [12].

To our knowledge; this study is the first experience in the Middle East Region using hypofractionated VMAT–SIB–ENI–WPRT technique with daily Image guided radiotherapy (IGRT) for a group of OC prostate cancer Saudi patients to assess its feasibility, toxicity and long-term b-RFS and to compare these outcomes with internationally published data.

Patients and methods

Between March 2009 and January 2014, 29 newly diagnosed, non-metastatic, biopsy-proven adenocarcinoma localized prostate cancer patients with no prior therapy; referred to radiation Oncology service – King Faisal Specialist Hospital (KFSH) – Riyadh, Kingdom of Saudi Arabia-KSA were treated with definitive Volumetric Modulated–Simultaneous Integrated Boost–Elective Nodal Irradiation–Whole Pelvis Radiotherapy (VMAT–SIB–ENI–WPRT) to a total dose of 70 Gy in 28 fractions (250 cGy/Fx). Patients with distant metastases or recurrent disease and those who did not complete their treatment, in addition to those treated with palliative intent were excluded from the study.

All Patients underwent pre-treatment trans-rectal ultrasound prostate biopsy; median number of cores collected was 9 [6–12]. Pre-treatment work-up included: MRI pelvis to evaluate extraprostatic extension, pelvic lymph node metastases and prostate volumetric assessment, CT scan of the chest–abdomen and pelvis and nuclear medicine (NM) bone scan. Patients were stratified to risk groups based upon current NCCN prognostic risk groupings (www.nccn.org). Baseline demographics and clinical characteristics of the treated group are shown in Table 1. Due to the small numbers of low risk (5 patients) and intermediate risk patients (4 patients), both groups were merged together as one group for statistical analysis.

Among the 29 patients; 24 (83%) were treated by androgen deprivation therapy (ADT): a total of 6-months for intermediate-risk patients (14%) and 2–4 months prior to VMAT–SIB–WPRT. While for high-risk patients (69%) ADT was continued to a total duration of $\geqslant$24–36 months. Biochemical failure was defined as per the Phoenix-Radiation Therapy Oncology Group (RTOG) criteria: nadir prostate-specific antigen (PSA) post radiotherapy concentration plus 2 ng/mL [13].

Written informed consent was obtained from all patients

Patients were clinically assessed during treatment on a weekly basis. Acute (during RT) and late ($\geqslant$90 days post treatment) GU and GI toxicities were documented based on Radiation Therapy Oncology Group (RTOG) Criteria for Adverse Events (www.RTOG.org). The maximum toxicity suffered was recorded.

Post treatment follow-up visits were performed by the treating radiation oncologist every 3 months for the first 2 years, followed by every 4–6 months for the next 3 years and yearly