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Original Article

Studying the efficacy of escalated dose conformal radiation therapy in prostate carcinoma − Pakistan experience

Asad Zamir [a], Ahmad Farooq [b], Hasan Nisar [c], Ismat Fatima [b], Irfan Ullah Khan [b,*], Misbah Masood [b], Abubaker Shahid [b]

[a] *Bannu Institute of Nuclear Medicine, Oncology & Radiotherapy (BINOR), Bannu, Pakistan*
[b] *Institute of Nuclear Medicine and Oncology (INMOL), New Campus Road, Lahore, Pakistan*
[c] *Pakistan Institute of Engineering and Applied Sciences (PIEAS), Islamabad, Pakistan*

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Abstract

Background: Our objective in this study was to evaluate the role and benefits in terms of local toxicity and biochemical disease-free survival (bDFS) following escalated-dose conformal radiation therapy in prostate adenocarcinoma.
Methods: The study population was composed of 53 patients with histologically proven T1b-T4, NO, MO prostate adenocarcinoma, having any Gleason score with prostate-specific antigen (PSA) of less than 50 ng/mL at diagnosis, given escalated dose EBRT (74 Gy) during the period between January 2011 and December 2013, retrospectively and evaluated for a period of 2 years post-radiation. Patients were followed up for a period of 2 years, beginning after completion of escalated dose external beam radiotherapy (EBRT) for biochemical failure as defined in ASTRO consensus committee guidelines 1996 and investigated for gastrointestinal, genitourinary skin toxicity.
Results: Out of 53 patients, 35 showed no biochemical failure at the end of 2 years following the completion of definitive escalated dose conformal radiotherapy while 18 were observed to have biochemical relapse. Acute gastrointestinal grade 1 toxicity was found in 26 patients, grade 2 in 24, and grade 3 only in 3 patients. Late gastrointestinal grade 0 toxicity was found in 16 patients, grade 1 in 28, grade 2 in 7 and grade 3 only in 2 patients. Grade 1 acute genitourinary toxicity was the highest in frequency observed in 28 of the total population followed by grade 2 in 21, grade 0 and grade 3 each, only in 2 patients. Late genitourinary Grade 0 toxicity was observed in 32 patients, grade 1 in 19, grade 2 and 3 only in 1 patient of the total population, respectively.
Conclusion: Our data were comparable to international studies of dose escalation using 3D and beneficial as compared to conventional radiation therapy delivered by 2D in terms of biochemical failure rate and treatment related toxicity.

Keywords: Biochemical failure; Conformal radiotherapy; Prostate cancer; Prostate-specific antigen; Toxicity

1. Introduction

Radiation therapy plays a vital role in the management of prostate cancer. Radical prostatectomy with pelvic lymph node dissection is only a standard option for T1 or T2 lesions if nodes are clinically negative, PSA is less than or equal to 20 ng/mL and Gleason score is less than or equal to 7. Even in these cases, carefully planned external beam radiotherapy (EBRT) leads to equivalent oncologic outcomes as compared with radical prostatectomy. In all other cases, EBRT with or without hormone therapy for localized prostate cancer is standard of care.[1] However, total dose of EBRT plays a critical role in treatment response, as does the fractionation protocol. Modality-specific toxicity profile and logistics should be

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Irfan Ullah Khan, Institute of Nuclear Medicine and Oncology (INMOL), New Campus Road, Lahore 54600, Pakistan.
E-mail address: drirfankhan69@gmail.com (I.U. Khan).

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incorporated into the decision-making process of the individual patient.[2−6]

Conventional radiotherapy (RT) of 66 Gy in 2-Gy fractions was practiced up till 2010 in our set up and is still used in most radiotherapy institutes in our country. In leading radiotherapy institutes in the world, practice has long been changed to prescribing escalated doses of radiation by means of IMRT.[7−11]

We have studied escalated-dose conformal radiotherapy of 74 Gy in 2-Gy per fraction with the aim of observing the biochemical progression-free survival and treatment-related gastrointestinal and urinary tract toxicities of escalated dose-conformal radiation of 74 Gy, which is currently being practiced in our setup. The efficacy data for escalated-dose treatment are weighed against the increase in acute and late toxicities associated with the escalated dose and emphasize the importance of using appropriate modern radiotherapy methods to reduce side-effects and provide maximum dose to cure the disease.

Objective

To evaluate escalated-dose conformal radiotherapy in localized prostate cancer in terms of biochemical failure as well as escalated EBRT-related acute toxicities.

Operational definitions

Treatment-related side effects were characterized as acute and late bowel and urinary side effects using the RTOG/EORTC Acute and Late Radiation Morbidity Scoring Schema. Biochemical failure was defined using the American Society for Therapeutic Radiology and Oncology (ASTRO) published Consensus Panel Guidelines 1996, for testing prostate-specific antigen (PSA) levels following radiation therapy. These guidelines define biochemical failure as three rises in PSA value over three consecutive readings following radiotherapy or any rise great enough to provoke initiation of treatment ($\geq$2 ng/mL rise in our study) with the date of failure being the midpoint between the PSA nadir and the first PSA rise. Later ASTRO consensus guidelines were not used in our study as for them to be applicable, the patient population is not supposed to receive ADT, which is impractical when treating locally advanced disease. Conventional fractionation is delivery of external beam radiotherapy to a total dose of 66 Gy in 2 Gy per fraction. Dose escalation in our study is defined as dose delivery of 74 Gy at 2 Gy per fraction.

2. Methods

2.1. Sample selection

Radically treated cases of prostate cancer randomly selected from January 2011 to December 2013.

Inclusion criteria:

- Histologically proven prostate adenocarcinoma either on transrectal ultrasound (TRUS) guided biopsy or on transurethral resection of prostate chips (TURP).
- Radiologically staged T1b-T4, N0, M0 disease with the help of MRI of pelvis with contrast, along with CT abdomen with contrast and MDP-Tc^{99m} Bone scan.
- No previous pelvic radiotherapy.
- Any age
- Performance status ECOG 0−1

Exclusion criteria

- PSA >50 ng/dL due to high probability of occult distant metastases
- Moderate to severe ischemic heart disease
- Renal insufficiency
- Uncontrolled diabetes Mellitus (DM)
- Uncontrolled hypertension

2.2. Study design

The study was carried out retrospectively to evaluate the role of escalated-dose conformal radiation therapy in patients who fulfilled the above-mentioned criteria. Neo-adjuvant, adjuvant or concurrent ADT was not part of the exclusion criteria. Since 96.2% of patients fell into either the intermediate or high risk group of patients, all such patients were offered hormone therapy for three months in neoadjuvant setting before definitive RT. Furthermore, patients in the intermediate risk group were planned for hormone therapy for an additional 3 months during and post RT, while those in the high-risk group were planned for hormone therapy for an additional 21 months during and post RT. The hormone therapy offered in each case was a subcutaneous depot injection of Leuprolide (22.5 mg) administered once every 3 months in the anterior abdominal wall.

No formal stopping rules were specified.

2.3. Data collection

Data were collected at Institute of Nuclear Medicine and Oncology (INMOL) Hospital, Lahore which serves as catchment cancer care centre for Punjab in particular and all of Pakistan, in general. Sampling was carried out from amongst patients registered for treatment from January 2011 to December 2013 in order to ensure a minimum follow-up record of 2 years post EBRT completion. All data were collected with informed consent from all participating adult subjects and from parents or legal guardians for minors or incapacitated adults, together with the manner in which informed consent was obtained (e.g., oral or written). Data regarding the variables of interest were collected through the patient's medical record. Risk grouping was done on the basis of T stage, PSA levels and Gleason scoring.

2.4. Data analysis

For data entry and analysis, (version 16, SPSS, Inc., Chicago, IL) software was used.