ORIGINAL ARTICLE

SEROLOGICAL OUTCOMES OF TREATMENT WITH 3D-CRT AND IMRT IN LOCALIZED PROSTATE CANCER

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Background: Prostate cancer ranks the second most frequent cancer encountered worldwide in men. Radiotherapy has been effectively used to treat localized prostate cancer. Over the years more effective radiation techniques like 3D-Conformal Radiation Therapy (3D-CRT), Proton Therapy, Intensity Modulated Radiation Therapy (IMRT), and Brachytherapy has been evolved and effectively used to deliver radiation therapy. Herein, we compare serological outcomes of two radiation treatment techniques intensity modulated radiation therapy (IMRT) and 3- dimensional conformal radiation therapy (3DCRT) in localized prostate adenocarcinoma. **Methods:** It is a cohort study conducted at Department of Oncology, Dr Ziauddin Hospital, Karachi. Patients with localized prostate adenocarcinoma meeting the inclusion criteria were recruited from July 2016 to June 2022, underwent treatment with a total dose ≥74 Gy using two different advanced radiotherapy techniques, i.e., IMRT and 3D-CRT. Serum PSA levels were assessed prior to treatment, and 6 weeks and 12 months after treatment. Paired t-Test was applied to identify the difference in PSA levels before, and after the treatment. *p*-value less than 0.05 was taken as significant at 95% confidence interval. **Results:** A total of 78 patients with 39 in each group. The mean age of patients in 3D-CRT group was 68±10 years while in IMRT group was 68±07 years. Six weeks after initiation of treatment, we observed that both the treatment methods, i.e., 3D-CRT and IMRT reduced the PSA levels significantly *p*-value = 0.001 respectively. There was no significant difference in the mean of PSA levels on 06th week and 12th months. Furthermore, the analysis of PSA levels at 12th months when compared with the baseline PSA levels came highly significant in both the groups as depicted in paired-t teat analysis of PSA levels with acceptable toxicity. **Conclusion:** Radiation therapy modalities 3D-CRT and IMRT both showed a significant serological response with minimal or acceptable gastrointestinal and genitourinary toxicities in the 3D-CRT group in comparison to the IMRT group. Although the sample size is relatively smaller, but the results of this study are encouraging to treat those patients on 3D-CRT, who cannot afford more expansive radiotherapy treatment technique like IMRT.

Keywords: 3D-CRT (3-dimensional Conformal Radiotherapy); IMRT (Intensity-modulated radiation therapy); PSA; Prostate cancer; Outcome

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INTRODUCTION

According to the Pakistan National Cancer Registry, prostate cancer is the second most common cancer among men in the country.[1] Several factors included advance age, sedentary lifestyle, smoking are associated with risk of prostate cancer.[2,3] Its treatment modalities depend on staging and type of pathology. Based on it, the management ranges from surveillance to surgery, brachytherapy, external beam radiation therapy (3-Dimensional conformal radiotherapy, intensity modulated radiation therapy, proton therapy), hormonal therapy (Androgen deprivation therapy), chemotherapy. Initiation of treatment is in accordance with patient's preference, expected survival and risk group at the time of its diagnosis.[4]

Radiation therapy to prostate gland is considered treatment modality for the treatment of localized prostate cancer. Lately, advanced techniques have led to favorable outcomes with decrease in adverse effects. Incorporating radiation therapy to computer online monitoring optimizes therapeutic ratio, i.e., to increase dose to the target and decrease dose to organ at risks.[5] Similarly, dose escalated radiation therapy for patient prostate cancer is commonly adopted treatment method which improved tumor control and outcomes. Escalated radiotherapy dose has been supported with level I evidence for localized prostate cancer patients in all risk groups.[6] Over the past decades, external beam radiation therapy has evolved to allow higher doses of radiation to be administered safely. Three-dimensional conformal radiation therapy (3D-CRT) uses computer software to integrate CT images of the patient's internal anatomy in the treatment position, which allows higher

cumulative doses to be delivered with lower risk of late effects.[7]

The second-generation 3D technique, IMRT, has been used increasingly in practice. IMRT reduced the risk of gastrointestinal toxicities and rates of post-recurrence therapy compared to 3D-CRT in some but not all older retrospective and population studies, although treatment cost is increased.[8,9]

The preference of radiation therapy technique with diminished radiotherapy-associated adverse events (toxicity) for prostate cancer patient is substantial in improving quality of life.[10] Herein, we assessed the serological outcomes of IMRT and 3D CRT radiation techniques in localized prostate cancer.

MATERIAL AND METHODS

This is a single-institution cohort analysis to evaluate serological outcomes of two radiation techniques in localized prostate cancer between July 2016 and June 2022 at Department of Oncology, Dr Ziauddin Hospital, Karachi. This was approved by the Institutional Research Advisory Council and Ethics Committee. All patients and/or their guardians provided informed consent for all treatments, procedures, as per institutional requirements. The inclusion criteria comprised of patients with age 50 years and above, patients with histologically confirmed localized Adenocarcinoma of Prostate on either TRUS guided or TURP, patients with Performance status ECOG 0 or 2, and patients who had given informed consent after explaining both radiation modalities benefits and risks. The exclusion criteria comprised of patients who were previously treated for prostate cancer with surgery, chemotherapy or radiotherapy, and who had metastatic disease and were no-compliant. More than 90% of the Patients had received some form of hormonal treatment along with the radiotherapy. Sample size was calculated via Open-Epi, Version 3.01, in which toxicity profile/radiation induced Gastrointestinal and Genitourinary side effects. The RTOG criteria were used to evaluate acute gastrointestinal and genitourinary toxicities, while the Phoenix criteria (PSA nadir + 2ng/ml) were used for biochemical control.[11] Treatment choices and recommendations depend on several multiple aspects, including the type and stage of the disease, probable adverse effects, overall health and preference of patient. Multidisciplinary approach should be an approved plan in an MDT. The proforma was developed for the data collection tool section, that included patient's demographics, Radiation therapy technique and the toxicities (abdominal pain, loose stools, burning/painful micturition and hematuria) at observed on the defined follow-up periods of the patient undergoing Radiation treatment for Prostate cancer. Patient's themselves chose the treatment modality (3DCRT or IMRT) of their choice on their own discretion after discussing all the pros & cons of each modality with their primary Physician. After performing CT based Planning, the treatment was started. Before the initiation of radiation therapy all the patients were inquired with subsequent documentation of pretreatment symptoms (especially Gastrointestinal and Genitourinary) in a questionnaire. Prior to start of treatment, no patient from both the groups reported anorectal pain, loose stool. Serum PSA levels were assessed prior to treatment, and 6 weeks and 12 months after treatment. Paired t-Test was applied to identify the difference in PSA levels before, and after the treatment. P value less than 0.05 was taken as significant at 95% confidence interval.

All the patients were followed-up during and just after the course of radiation therapy (i.e., 02nd, 04th, 06th week during XRT, and 03rd, 06th months post XRT) for related symptoms of Genitourinary and Gastrointestinal toxicity. Data was analyzed using SPSS version 20. For categorical variables, frequency and percentages were calculated and for numerical variables, mean and standard deviation were calculated.

RESULTS

Total of 78 patients were randomly divided into two groups. Group A, 39 (50%) patients were treated with 3DCRT and similarly Group B, 39 (50%) patients were treated with IMRT. The mean age of participants in Group A was 68±10.3 years and in Group B was 68±7 years. Mean PSA levels before treatment in both groups were 41.3±5.2 and 43.4±9 ng/ml. According to risk stratification, 22 (56%), 28 (71.8%), 35 (89%) in Group A (3D-RT) and 21 (54%), 30 (77%), 36 (92,2%) patients in IMRT and had Gleason ≥ 8, T2c-T3b and High-risk features (Table 1).

Most participants 53 (68.4%) were from Karachi. There was no family history of carcinoma among 71 (89.9%) participants and no specific comorbidity among the participants except hypertension, i.e., 17 (21.7%) and Six (7.6%) were smokers.

Six weeks after initiation of treatment, we observed that both the treatment methods, i.e., 3D-CRT and IMRT reduced the PSA levels significantly *p*-value = 0.001 respectively. There was no significant difference in the mean of PSA levels on 06th week and 12th months. Furthermore, the analysis of PSA levels at 12th months when compared with the baseline PSA levels came highly significant in both the groups as depicted in paired-t teat analysis of PSA levels (Table 2). The toxicities were compared between both the groups (3D-CRT and IMRT), we found less occurrence of GI toxicity in IMRT group than 3D-CRT and same observation was seen for genitourinary toxicities.[12]

Table-1: Baseline characteristics of patients in both groups

Characteristics	3DCRT	IMRT
No. of patients	39 (100%)	39 (100%)
Age: Mean age±SD, years	68±7	68±10.36
Baseline PSA level	41.3±5.2	43.4±9
Age (years)	68±7	68±10
Weight (kgs)	70.03±10.6	67.38±10
Baseline Gleason score		
2 to 6	0	1 (2.5%)
7	17 (43.5%)	17 (43.5%)
8 to 10	22 (56.5%)	21 (54%)
Tumor Characteristics		
T1a- T2a	3 (7.6%)	3 (7.6%)
T2b	8 (20.5%)	6 (15.4%)
T2c-T3b	28 (71.8%)	30 (77%)
Risk Classification		
Low	2 (5.1%)	0
Intermediate	2 (5.1%)	3 (7.6%)
High	35 (89.8%)	36 (92.4%)

Table-2: Paired-test analysis of PSA levels in both groups

3D-CRT		*p*-value
Before treatment	Week 06	0.001*
41.3 ± 5.2	1.8 ± 1.3	
Week 06	12th Month	0.894
1.8 ± 1.3	0.38 ±1.20	
Before treatment	12th Month	0.001*
41.3 ± 5.2	0.38 ± 1.20	
IMRT		
Before treatment	Week 06	0.001*
43.4 ± 9	0.9 ± 1.5	
Week 06	12th Month	0.536
0.9 ± 1.5	0.2 ± 0.3	
Before treatment	12th Month	0.001*
43.4 ± 9	0.2 ± 0.3	

DISCUSSION

Prostate cancer is a significant health concern in Pakistan. A meta-analysis of prostate cancer in Pakistan published between 2000 and 2023 published a data of 184,384 prostate cancers from variable geographical populations of Pakistan with overall prevalence of 5.20%.[13] The findings of this local meta-analysis are almost consistent with the study from Iran, at 6.3%[14] and lower than in the study conducted in Nigeria, at 8.8%[15]. The disparity in the prevalence of prostate cancer in different provinces may be due to socioeconomic and sociocultural differences between populations. Subgroup meta-analysis by setting revealed that the prevalence of prostate cancer was significantly higher in Urban areas than in Rural areas. Similar study also found that the prevalence of prostate cancer has increased over time, with the prevalence being 3.88% from 2000 to 2010, while the prevalence from 2011 to 2023 was 5.80%.[13] Different technical advancements in radiation therapy have occurred for past few decades. The benefit of the advancements includes low radiation dose and localized approach to minimize the tissue damage and other unwanted outcome.[16] Intensity modulated radiotherapy (IMRT) has proved to be efficient in minimizing damage to surrounding tissues i.e., bladder and rectum. However, it is not economical than 3D-CRT.[17,18] The mean age at the time of diagnosis was similar to previous literatures.[19,20] The delay in diagnosis can be due to lack of awareness of different races as highlighted in literture.[21] They concluded that blacks only screen themselves when signs and symptoms of disease appear, on the other hand whites use to screen their PSA levels after age of 50 twice or thrice during the life course.[21]

The PSA findings during data collection and entry were documented as positive when it was greater than 4 ng/ml and considered negative when less than 4 ng/ml.[22]

However, there was no significant association of decline in PSA level between 3D-CRT or IMRT. The findings of our study with respect to 3D-CRT are similar but at different time interval.[23] In another study outcome of 3D-CRT and IMRT were compared and they also documented the similar findings.[24]

Out follow-up data in both groups indicated both treatment modalities revealed PSA levels compared at 6th week and 12th month no significant relation as the PSA level did not change after treatment with 3D-DRT or IMRT till 12 months. The post treatment finding with both the treatment modalities were parallel with the study with similar follow-up results.[25] Contrary to our results, it was documented that after the IMRT treatment there can be a rise in PSA levels which is not associated with tumor recurrence. They further mentioned that this rise is due to regeneration of new prostate cells.[26]

During the course of follow-up, participants were asked about anorectal pain, loose stools, burning urination and hematuria at different time intervals. After 2 weeks, participants of both groups did not complain about anorectal pain, loose stools and burning urination. So, there was no any significant difference between both the treatment modalities. Parallel to our findings, many researches have reported that the IMRT is safest treatment modality in treatment of prostate cancer when compared to 3D-CRT and there are very less chances of development of side effects after IMRT.[17,27,28]

In documented data, it is highlighted that the patients of prostate cancer have association with familial breast cancer which was not observed in our study perhaps due to small sample size.[29] Very few studies with limited approach and smaller sample size are reported that cannot show the associations between the risk factors and disease development. In our findings we cannot relate family history or ethnicity

with development of prostate cancer among our study participants.

The results of this study shows that PSA levels also decreased significantly after the completion of radiotherapy along with minimal or acceptable gastrointestinal and genitourinary toxicities in the 3D-CRT group in comparison to the IMRT group.

Although the sample size is relatively smaller, but the results of this study are encouraging to treat those patients on 3D-CRT, who cannot afford more expensive radiotherapy treatment technique like IMRT. We recommend multicenter study with larger sample size to draw evidence based inference on a larger scale and to evaluate and observe the impact and effectiveness of different hormonal regimens along with radiotherapy treatments on disease response.

Pakistan is a developing country and its healthcare system faces several challenges, such as insufficient funding, inadequate infrastructure, a shortage of healthcare professionals, and inequitable distribution of resources.[30.31]

CONCLUSION

The results of this study shows that PSA levels also decreased significantly after the completion of radiotherapy along with minimal or acceptable gastrointestinal and genitourinary toxicities in the 3D-CRT group in comparison to the IMRT group. The results of this study are encouraging to treat those patients on 3D-CRT, who cannot afford more expansive radiotherapy treatment technique like IMRT.

AUTHORS' CONTRIBUTION

SH: Conceived the idea, literature search, drafted manuscript. AHO: Literature search, drafted manuscript. JM: Overall supervision.

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