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ACUTE TOXICITY IN HYPOFRACTIONATED RADIOTHERAPY OF PROSTATE CANCER: VMAT *VERSUS* 3DCRT WITH DAILY IGRT

UNIVERSITÀ DEGLI STUDI DE L'AQUILA

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BACKGROUND/AIM

Radiation therapy (RT) is a curative treatment modality for localized prostate cancer. Randomized trials suggest that in men with pre-RT genitourinary (GU) and gastrointestinal (GI) morbidity, some hypofractionated regimens giving fewer fractions with higher dose may be associated with increased toxicity. Today, intensity-modulated RT (IMRT) is considered standard, where radiation beams of different shapes and intensities can be delivered from a wide range of angles, thus further decreasing doses to normal organs and likely reducing treatment-related toxicity. At the same time, IMRT with or without image-guided RT (IGRT) seems to decrease post-RT GI and GU toxicity. A limited number of clinical data are available about the incidence of GU and GI toxicity in men undergoing hypofractionated RT (HyRT) and treated by volumetric-modulated arc therapy (VMAT) and IGRT. This study aims to compare the acute GI and GU toxicity of men undergoing HyRT and treated by three-dimensional conformal radiation therapy (3DCRT) or VMAT with daily IGRT.

PATIENTS AND METHODS

A retrospective cohort of 91 men with low/intermediate risk prostate cancer (Pca) was selected according to the National Comprehensive Cancer Network (NCCN) criteria between July 2015 and July 2018. Patients underwent a moderate HyRT with a cumulative dose of 60 Gy delivered in 20 daily fractions. An IGRT strategy based on daily cone-beam CT was adopted in all treated patients according to the latest clinical indications (NCCN guidelines). A weekly clinical assessment during radiation treatment was arranged for the detection of any early toxicity. Men were treated with VMAT (n=21) or with 3DCRT (n=70). The post treatment follow-up visits were performed at 1, 4 and 12 weeks after the end of radiotherapy. The acute GI and GU toxicities were rated according to the Radiation Therapy Oncology Group (RTOG) scale for early side effects (1). Differences in the incidence of toxicities between the two groups were evaluated by the Fisher's exact test. A *p*-value lower than 0.05 was considered statistically significant.

RESULTS

One week after RT, a decrease in the rate of Grade 2 or greater acute toxicity was recorded in the group of men treated by VMAT. Interestingly, Grade 2 or more GI and GU toxicity were observed in 41.4 % *vs.* 4.7% (p=0.0012) and in 40% *vs.* 9.5% (p=0.0087) in men treated by 3DCRT and VMAT, respectively. At four weeks after RT, the reduced toxicity in the study group treated with VMAT was also confirmed. The incidence of Grade 2 or greater GI and GU toxicity was 27.2% and 20% after 3DCRT and 0% after VMAT. The decreased Grade 2 or more GI and GU toxicity observed between the two treatments achieved the statistical significance (GI toxicity VMAT *vs*. 3DCRT: p=0.005; GU toxicity VMAT *vs*. 3DCRT: p=0.034) (Tables I and II).

TABLE I

	RTOG GI Acute Toxicity				
	3DCRT		VMAT		p value*
	No.	%	No.	%	
1 week post RT					
Grade ≤ 1	41/70	58.6	20/21	95.3	0.0012
Grade ≥ 2	29/70	41.4	1/21	4.7	
4 weeks post RT					
Grade ≤ 1	51/70	72.8	21/21	100	0.005
Grade ≥ 2	19/70	27.2	0/21	0	
12 weeks post RT					
Grade ≤ 1	67/70	95.7	21/21	100	1.0
Grade ≥ 2	3/70	4.3	0/21	0	

TABLE II

	RTOG GU Acute Toxicity				
	3DCRT		VMAT		p value*
	No.	%	No.	%	
1 week post RT					
Grade ≤ 1	42/70	60	19/21	90.5	0.0087
Grade ≥ 2	28/70	40	2/21	9.5	
4 weeks post RT					
Grade ≤ 1	56/70	80	21/21	100	0.034
Grade ≥ 2	14/70	20	0/21	0	
12 weeks post RT					
Grade ≤ 1	65/70	92.8	21/21	100	586
Grade ≥ 2	5/70	7.2	0/21	0	

CONCLUSION

Men undergoing HyRT with image-guided VMAT experienced a significantly lower GI toxicity 1 and 4 weeks after RT with respect to men treated by 3DCRT. An identical trend was found for GU toxicity one week and 4 weeks after RT. This advantage was not maintained 12 weeks after RT. The early results are encouraging and guarantee the continuation of the study. Advanced radiotherapy techniques like VMAT with daily IGRT should therefore be considered to reduce acute toxicity profile in treatment of low or intermediate risk prostate cancer (2, 3). Our results must be considered preliminary and more powered studies will be necessary to investigate this understudied topic.

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