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AN INTER-INDIVIDUAL COMPARISION OF RADIOTHERAPY IN PRONE AND SUPINE POSITIONING IN PATIENTS OF CARCINOMA CERVIX – A PROSPECTIVE STUDY

Oncology

Dr. Swarnendu Biswas Medical Officer, Diamond Harbour Medical College, South 24 Parganas

Dr. Tapas Kumar Das* Associate Professor, Department Of Radiotherapy, NRS Medical College, Kolkata
*Corresponding Author

ABSTRACT

BACKGROUND: Radical radiotherapy along with concurrent chemotherapy followed by brachytherapy is the standard of care of advanced carcinoma cervix. This treatment carries a risk of inadvertent normal tissue irradiation of the small bowel, bladder and rectum. Various efforts have been made to reduce bowel toxicity by pelvic radiotherapy. Among them radiotherapy in prone position have been matter of interest for long.
OBJECTIVES : To compare the dose volume histograms of organs at risk (small bowel, bladder and rectum) and planning target volumes in supine and prone positions.
MATERIALS & METHODS: A total 60 histologically proven newly diagnosed cases of carcinoma cervix stage I – IVA, age 18 – 70 years, ECOG score 0 – 1, with informed consent were randomized in two groups (prone & supine position) for radical radiotherapy at dose 50 Gy in 25 fractions , over 5 weeks, with Concurrent cisplatin 40 mg/m2 weekly for 5 weeks followed by Intracavitory brachytherapy for all patients with 7 Gy in 3 fractions. 30 patients were treated in prone and 30 were treated in supine position with proper CTV & PTV contouring. Dosimetric analysis was done with Dose Volume Histogram and toxicity of bladder, bowel was assessed.
RESULTS & DISCUSSION: In my study I found significant less bowel volume receiving more than 20 Gy in prone position than in supine position, though no statistically significant different was seen in dose <=20 Gy. Dose received by 195 cc of bowel bag was significantly more in supine position than in prone position with a P Value of <0.001, also 45 Gy dose received by Bowel volume was more in supine position than in prone position mean V45 in prone position was 193 cc with STD.DEV of 13, and in supine position mean V45 was 216cc with STD.Dev of 12 cc,P-value <0.001. Volume of PTVmean in prone position 890.25 cc with STD.DEV. of 83.11 and in supine position PTVmean was 958 with STD Dev. Of 231.91, P-Value being 0.01.
CONCLUSION : Prone position can be used instead of supine position for Pelvic field radiation, in patients of Carcinoma Cervix for better bowel protection.

KEYWORDS

Radical Radiotherapy, Carcinoma Cervix, Prone & Supine Position, Dosimetry

INTRODUCTION:

Cervical cancer is the second most common cancer in India in women accounting for 22.86% of all cancer cases in women and 12% of all cancer cases in both men and women [1]. In India the peak age for cervical cancer incidence is 55–59 years [2]. In India Rural women are at higher risk of developing cervical cancer as compared to their urban counterparts [3].

Radical radiotherapy along with concurrent chemotherapy is the standard of care of advanced carcinoma cervix. Combination of teletherapy and brachytherapy is a conventional practice. Teletherapy includes whole -pelvic radiotherapy which consists of external beam irradiation to the primary tumor and regional lymphatics followed by brachytherapy to boost the gross tumour in the cervix [4,5,6]. However, success achieved with this treatment carries a risk of inadvertent normal tissue irradiation of the small bowel, bladder and rectum. Sixty percent of urinary adverse effects (AEs) due to RT develop more than two years following treatment, in contrast to bowel (AEs), of which 80% develop within the first two years. Annual incidence rates for urinary AEs actually increase between years three and five post-RT, from 18% to 28%, respectively [7,8,9]. In, order to cover tumour and locoregional lymph nodes adequately with 2D or 3D conformal radiotherapy technique large portions of bowel gets included in the radiation ports. Consequently, acute and chronic bowel sequels are the most important side effects of pelvic radiotherapy [7].The risk of damage to the small bowel is related to the total dose delivered to the pelvis, the fraction size, and the presence of physical factors such as multiple abdominal surgical procedures or pelvic inflammatory disease.Various efforts have been made to reduce bowel toxicity by pelvic radiotherapy. Among them radiotherapy in prone position have been matter of interest for long. Several studies [10,11,12] showed superiority of prone positioning in comparison to supine position of radiotherapy in regard to bowel protection.

Purpose of this study is to compare bowel & bladder toxicity between prone and supine positions with the help of Dose Volume Histogram, and to find out whether prone positioning results in reduced bowel toxicity.

OBJECTIVES :

To compare the dose volume histograms of organs at risk (small bowel, bladder and rectum) and planning target volumes in supine and prone positions.

MATERIALS & METHODS:

A total 60 histologically proven newly diagnosed cases of carcinoma cervix stage I – IVA, age 18 – 70 years, ECOG score 0 – 1, with informed consent were randomized in two groups (prone & supine position) for radical radiotherapy at Nilratan Sirkar Medical College and Hospital,Kolkata. Baseline complete hemogram and liver function test, urea, creatinine, Serum Electrolytes, Baseline chest x-ray, ECG.Echo Cardiogram, Baseline ultrasound abdomen and pelvis, Cystoscopy, Virtual simulation CT scan for radiotherapy planning was done.

Imaging-Treatment planning CT (Somatom emotion) scans was performed in supine position for 30 patients, and in prone position for 30 patients, without bowel or intravenous contrast.

All Patients were asked to void their bladder completely and then drink 250 ml of water 30 minutes before the stimulation and the same was followed everyday before radiotherapy on EBRT machine Theratron 780 E isocentric Cobalt 60 Teletherapy machine.
Patients were planned with four field technique in prone and supine positions , plans being optimized in terms of PTV coverage and small bowel sparing .

Clinical Target Volume(CTV) includes the gross tumor volume ,the uterus, proximal vagina,parametria and regional lymph nodes. The superior and inferior borders of the CTV was defined by bony landmarks;1 cm above L5-S1 interspace and 1cm below the obturator foramen. Planning target volume(PTV) consisted of CTV and a 1.0 cm three dimensional margin.

The external wall of rectum and bladder was contoured, so that volume included the walls and lumen. Bowel region ,defined as peritoneal cavity(excluding the rectum,bladder,uterus,vagina)was delineated up to 2cm above CTV. Individual bowel loops were not contoured

separately.

All patients were treated with External radiotherapy of 50 Gy in 25 fractions , over 5 weeks, with Concurrent cisplatin 40 mg/m2 weekly for 5 weeks followed by Intracavitory brachytherapy for all patients with 7 Gy in 3 fractions.

Patients were assessed weekly with clinical examinations, hematol ogical and biochemical parameters during the treatment for acute toxicities of skin , bladder and bowel using RTOG/CTCAE criteria, Toxicity assessment tool- National cancer Institue Common Terminology Criteria for adverse Events scale v4.0..

Treatment response evaluation was done at the end of radiotherapy and during follow up period on the first , second and third months after completion of radiation therapy.

Target volumes, volumes of organ at risk, maximal field length, dose volume histogram for organs at risk and the corresponding Quality Indices(relationship of the area under curve of the dose-volume histogram to the total area, multiplied by 100) analysis was completed.

Data was analyzed and compared according to appropriate statistical tests using SPSS V.22 software and Microsoft word-excel. Pemission of Institutional Ethical Committee was undertaken.

RESULTS :

Total 60 patients were randomized in two groups – 30 in Prone & 30 in Supine position. No statistically significant difference was seen in relation to age, ECOG, & stage (table 1).

Table 1 Dose Volume Histogram data tabulated in Dosimetric Chart.

Characteristics		Arm (Prone) n=30	Arm (Supine) n=30	p value
Age (median)		45	47	0.557
ECOG	0	4	2	0.430
	1	23	22	
	2	3	6	
Stage	Ib2	3	2	0.717
	IIB	13	16	
	IIIB	14	12	

Table 2

Dosimetry	Prone Position			Supine Position			P.value
	Mean	Median	STD.DV	Mean	Median	Std.Dev	
Urinarybladder V20	100	100	0	100	100	0	NS
UB V30	100	100	0	100	100	0	NS
UB V40	98.003	99.995	4.07	99.109	99.87	1.166	NS
UB V45	94.087	98.87	9.5027	96.78	98.13	3.272	0.9NS
UB V50.4	23	22.735	17.276	37.302	39.293	21.708	0.021
UB Dmean	98.308	100.015	3.98	98.17	100.415	12.0375	NS
Ub Total Volume In Cc	190.25	175.4	75.79	217.01	180.53	108.56	0.17 NS
Rectum V20	92.483	97.965	9.558	92.462	96.05	8.072	0.9 NS
Rectum-v30	89.187	95.76	11.669	88.756	91.195	10.778	0.87 NS
Rectum V40	85.248	91.22	13.9693	83.987	86.495	12.277	0.68 NS
Rectum V45	77.9	80.19	15.366	77.395	77.75	12.725	0.7NS
Rectum V50.4	27.672	23.645	13.102	13.739	6.31	17.594	0.004
Rectumdmean	91.994	97.495	10.417	90.289	91.76	7.793	0.18 NS
Rectum Total Volume	87.37	83.95	18.51	82.02	81.84	11.83	0.28
Bowel Bag V20	89.98	91.44	6.247	89.965	92.09	8.84	0.9
BB V30	72.011	71.09	6.358	81.743	83.235	9.076	<0.001
BB V40	46.524	44.415	11.13	66.589	67.01	12.18	<0.001
BB V45 cc	194.2596	193.94	13.344	216.358	219.5915	12.088	<0.001
BB V50.4	3.99	3.745	3.34	13.009	14.395	5.41	<0.001
BB Dmean	59.297	59.22	8.778	80.59	81.7285	10.93	<0.001
BB D195	44.83	44.73	3.08	49.92	50.623	2.78	<0.001
PTV 95	94.165	93.975	0.6474	94.046	93.9	0.829	NS,0.25
PTV Dmean	99.59	100	0.797	99.49	99.84	0.7125	Ns,0.13
PTV vol	890.25	908.2995	83.11	958.271	997.915	231.91	0.01

NS- Not Significant
UB-Urinary Bladder
BB-Bowel bag
PTV-Planning Target Volume

Table No-3 Comparison between Field size in Prone and Supine Position

Width of Field	Prone Position		Supine Position		P-Value
	Mean Width;IFD	Std Dev.	Mean Width:IFD	Std.Dev.	
AP-PA	16.60	1.16	17.4	1.22	0.034 Significant
Lateral field	14.00	0.98	14.63	0.88	0.008, Significant.

AP-PA-Anterio-Posterior -Postero-anterior.
IFD-inter field distance,Std.Dev-Standard Deviation

Bladder Toxicity 5TH WEEK

Table-4				
		ARM		Total
		PRONE	SUPINE	
UBTOXICITY5THWEEK	.00	11	3	14
	1.00	19	22	41
	2.00	0	5	5
Total		30	30	60

Chi-Square Tests

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	9.791a	2	.007
Likelihood Ratio	12.011	2	.002
N of Valid Cases	60		

BOWEL TOXICITY5TH WEEK

Table 5				
		ARM		Total
		PRONE	SUPINE	
BOWELTOXICITY5TH WEEK	.00	13	3	16
	1.00	10	2	12
	2.00	5	10	15
	3.00	2	15	17
Total		30	30	60

Table-22 Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	23.191a	3	.000

Likelihood Ratio	25.511	3	.000
N of Valid Cases	60		

DISCUSSION:

Each patient received dose of 50Gy in 25 fractions over 5 weeks with concurrent Cisplatin at 40mg/m2 weekly followed by Brachytherapy with 7 Gy X 3 fractions.

Gross tumor volume included gross disease involving cervix vagina and uterus, CTV included ovary, parametrium, pelvic nodes, up-to L4-L5, above and around external iliac vessels below. Separate Nodal contouring was not done. PTV created with 1 cm margin around CTV, excluding bones. OAR or organ at risk was contoured for Rectum,Bowel Bag, and Urinary Bladder.

In my study I found significant less bowel volume receiving more than 20 Gy in prone position than in supine position, though no statistically significant different was seen in dose <=20 Gy. Dose received by 195 cc of bowel bag was significantly more in supine position than in prone position with a P Value of <0.001, also 45 Gy dose received by Bowel volume was more in supine position than in prone position mean V45 in prone position was 193 cc with STD.DEV of 13, and in supine position mean V45 was 216cc with STD.Dev of 12 cc,P-value <0.001. Volume of PTVmean in prone position 890.25 cc with STD.DEV. of 83.11 and in supine position PTVmean was 958 with STD Dev. Of 231.91, P-Value being 0.01.

Field size in prone and supine also differs significantly .Mean lateral Width (x axis) size in supine position was 17.4 and in prone position it was 16.6, with a P-Value of 0.034, which is statistically significant, also Lateral width in Lateral field in prone position was 14.00 and in supine position 14.66, with a P-value of 0.008.

Such difference in Bowel dose may be attributable to upward displacement of bowel loops in prone position there by moving away from area near PTV, more PTV in Supine position due to anterior movement of uterus,tumour with adnexa,and this finding was consistent with finding by PINKAWA et AL[11],increased field size in AP-PA and Lateral Portal due to compression of Abdominal wall in prone position .Well filled urinary bladder also helps to keep away bowel loops ,but such change is evident on both positions [13,14].

Difference in irradiated volume of Urinary Bladder and Rectum seen only at 50.4Gy, and no statistically significant difference of irradiated volume found at 20Gy,30Gy, 40Gy and 45Gy .

Toxicity assessment was done with Chi-Square test and graded according to CTCAE-4 criterias.

Such difference in bowel dose is also reflected in development of toxicity during treatment. A significant portion of patients in supine group developed acute diarrhea, few developed Haematochezia and also some needed hospitalization in comparison to patients treated in prone position.

Bladder toxicity in the form of urgency and dysuria were observed more in patients treated in supine position and was statistically significant.

Within 3 months of follow-up period no patients developed rectal toxicity in the form of new onset rectal bleeding, tenesmus.

CONCLUSION :

Prone position can be used instead of supine position for Pelvic field radiation, in patients of Carcinoma Cervix for better bowel protection.

Volume of Urinary Bladder receiving above 50 Gy is smaller in prone position than in supine position, thus better Urinary Bladder protection was seen in higher dose in prone position.

Optimal bladder filling with bladder protocol also needed for bladder sparing and also for kee Better Bowel sparring in my observation was result of

1) Upward movement of gut loops in prone position, together with pressure effect from optimally filled urinary bladder which is also compressed in prone position.
2) Compression of abdominal wall in prone position, causes reduced anterior-posterior inter field distance in prone position(P-0.034), thus to achieve at least 93% dose at 95% of PTV lesser field dimension was needed in prone position than in supine position.

In my study I also found average PTV volume was less in prone position than in supine position and such difference is statistically significant(P-0.01).

Large scale study is required for better results.

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