Three-Dimensional Conformal versus Intensity Modulated Radiation Therapy in Treatment of Nasopharyngeal Carcinoma

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ABSTRACT

Background: Nasopharyngeal carcinoma is an endemic disease of Southeast Asia with incidence rates of between 15 and 50 per 100 000. There is an intermediate incidence in North Africa and Far Northern hemisphere while in the West the disease occurs sporadically. In Egypt the incidence rate is low and the peak at age (50-54) is 3.4%, and other age varying between 0.3 and 0.4 per 100 000**.**

Aim of the Work: The aim of this study was to evaluate and compare both techniques as regard their efficacy on tumor response, local control, overall survival and progression free and treatment related toxicity between both techniques.

Patients and Methods: This retrospective analysis included 54 patients diagnosed with primary nasopharyngeal carcinoma recruited from the clinical oncology department, Ain Shams University and the International Medical Center during 3 years (January 2014 -December 2016). They were divided into 2 groups, group A was treated using 3D conformal radiotherapy (CRT) whereas group B was treated using intensity modulated radiation therapy (IMRT).

Results: In general, acute toxicity was tolerable and complete healing was the rule. As a whole, group A showed a higher toxicity profile as compared to group B. IMRT was able to decrease xerostomia and spare at least part of the parotid gland excretory function which was shown in the salivary gland scintigraphy. Results of the dosimetric comparison between both techniques showed that IMRT had a better tumor coverage and conformity index. Homogeneity index was similar in the two groups. Also, doses received by the risk structures, particularly parotids, was significantly less in the IMRT plans than those of 3D-CRT. **Conclusion:** IMRT is considered as a more advantageous radiation treatment technique as it can deliver high-dose irradiation to defined tumor targets while minimizing the dose delivered to the surrounding normal organs and tissues, thereby improving the therapeutic ratio of radiation therapy. IMRT has been shown to offer superior dose conformity to the tumor target and better sparing of critical organs in the treatment of NPC.

Keywords: three-dimensional ultrasound conformal, intensity modulated radiation therapy, nasopharyngeal carcinoma.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a rare malignancy with an extraordinarily skewed geographic distribution worldwide. It is more prevalent in Southern China, Southeast Asia and Northern Africa. Nasopharyngeal carcinoma is strongly associated with the Epstein-Barr virus [(1)].

There were an estimated 86,700 new cases of NPC and 50,800 deaths. Although this disease may be considered one of the rarer forms of cancer globally, it is notable for its high incidence in select geographic and ethnic populations, Nasopharyngeal carcinoma is more common in male than female with a ratio of 2.3:1.

Three subtypes of NPC are classified into: (type 1: squamous cell carcinoma, typically found in the older adult population, type 2: non-keratinizing carcinoma, type 3: undifferentiated carcinoma). Other malignant tumors of the nasopharynx include nasopharyngeal papillary adenocarcinoma, plasmacytoma, minor salivary gland tumors, melanoma, rhabdomyosarcoma, and chordoma. The majority of lymphoma of the nasopharynx is non-Hodgkin's lymphoma, diffuse large B cell [(3)].

Nasopharyngeal carcinoma is highly radiosensitive and chemo sensitive. Radiation therapy (RT) is the mainstay of treatment and is an essential component of curative-intent treatment of non-disseminated NPC. Stage I disease is treated by RT alone, while stage III, IVA, IVB disease are treated by RT with concurrent chemotherapy. Concurrent chemotherapy is recommended for stage II disease [(4,5)].

Tumor control for carcinoma of the nasopharynx has been highly correlated with the dose delivered to the tumor. A total dose of 70 Gy is needed for eradication of gross tumor and either 50–60 Gy or 46–60 Gy for elective treatment of potential risk sites [(4)].

Conventional or so-called 2-dimensional RT (2D-RT) has proven effective in the control of NPC. However, complications associated with irradiation of sensitive normal structures, such as the glands and inner ears in the path of the irradiation, are notable and often lifelong. Common toxicities with this technique, particularly with concurrent chemotherapy, included: xerostomia, occurring in over 90 % of patients and 70 % have

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reported moderate or severe symptoms, mucositis, and dysphagia [6].

To address these challenges 2D-RT was replaced by three-dimensional conformal radiotherapy (3DCRT). CT scan based planning provides better delineation of tumor target and organ at risk with clearer radiologic visualization of their spatial relation, more optimization of beam orientation, beam weighting and beam shaping. However, the problem of dose inhomogeneity and suboptimal coverage is still unresolved because of highly infiltrative growth pattern with a propensity to spread through skull base foramina to the intracranial structures [7].

Intensity-modulated RT (IMRT) represents an advanced form of 3D-CRT. It employs inverse planning algorithms and iterative, computer-driven optimization to generate treatment fields with varying beam intensity. Combinations of intensity-modulated fields produce custom-tailored, conformal, dose distributions around the tumor with steep dose gradients at the transition to adjacent normal tissues [8].

Several institutions have shown an unquestionable diametric benefit of IMRT for NPC over conventional techniques. When compared to 2D and 3DCRT techniques, IMRT lowered doses to the critical structures such as spinal cord, mandible, temporal lobes, optic nerve, optic chiasm and brain stem while increasing coverage to the retropharynx, skull base, and nodal regions [9].

Two phase III trials compared IMRT vs. conventional RT for early-stage NPC. IMRT was significantly better than conventional RT in regards to parotid sparing and improved quality of life. The incidence of observer-rated xerostomia was 39.4 % with IMRT compared to 82.1 % with conventional RT ($p<0.01$) ([10,11].

In radiation therapy oncology group (RTOG) 0225, which was a phase II study of IMRT with or without chemotherapy for NPC of all stages, the investigators were able to demonstrate the feasibility of delivering IMRT in a multi-institutional setting with reproducible excellent outcomes. Also, 90 % of patients received the planned 70 Gy and 88 % with locally advanced disease received three cycles of concurrent cisplatin [10]. This compliance rate compared favorably to 63 % in the Intergroup 0099 trial, 52 % in the Hong Kong NPC-9901 trial, and 71 % in the Singapore randomized trial all of which used non IMRT techniques [12,13].

The treatment of patients with IMRT led to a significant improvement in the local recurrence-free survival and overall survival of NPC patients [14].

AIM OF THE WORK

This retrospective study analysis aims to compare 3D conformal radiation therapy and intensity modulated radiation therapy in treating nasopharyngeal carcinomas, evaluation, and comparison between both techniques as regard their dosimetric variations, response rate, PFS and treatment related toxicity as well.

PATIENTS AND METHODS

Study design

Retrospective analysis

Site of the study

Patients diagnosed with primary nasopharyngeal carcinoma recruited from the Clinical Oncology Department, Ain Shams University and the International Medical Center during 3 years (January 2014 -December 2016). **The study was approved by the Ethics Board of Ain Shams University.**

Study population:

The patients were divided into 2 groups:

Group (I): IMRT group (N24)

- Patients who were treated by intensity modulated radiation therapy (IMRT)

Group (II): 3DCRT group (N30)

- Patients who were treated by 3D conformal external beam radiotherapy

Inclusion criteria:

1. Biopsy proven carcinoma (by histopathology previously proved to be nasopharyngeal squamous cell carcinoma).
2. Age between 18-70 years.
3. Stage II to IVB and receiving concurrent chemotherapy.

Exclusion criteria:

1. Evidence of distant metastasis.
2. Previous treatment for head and neck tumor or previously treated with radiotherapy
3. Patients with other malignancy.
4. Poor performance status that can't tolerate treatment (ECOG 3).

Methods: all patients in both groups were subjected to:

The files of patients were reviewed and data were extracted including:

- Personal data (age, sex, performance status, comorbid disease, EBV infection, smoking ..).
- Base line laboratory results (CBC, LFT, KFT), radiological findings and pathological data (grade, stage,..).
- The planning physical data (dose, dose volume histogram to clinical target volume and organs at risk)
- Follow up data to assess treatment toxicity, event free survival and overall survival.

Radiotherapy

Pre-radiation therapy preparation: Fixation was done with a thermoplastic mask (while patient was lying supine with fully extended neck in the treatment position) over the head and shoulders, a lead marker was used to delineate the site of involved lymph nodes. CT scan of the head and neck with IV contrast was taken with 5 and 3 mm sections for the 3-D conformal and IMRT respectively down to the infraclavicular region. CT was then transferred to the planning system (Eclipse) for volume definition. Simulation was done after plan approval to identify the laser marks for the isocenter of treatment.

Treatment planning: 5 to 7 fields isocentric technique using isotropic gantry angles which are adjusted when a risk organ could be avoided for adequate target coverage.

Target volumes:

GTV: gross disease including the primary tumor and enlarged lymph nodes as demonstrated on imaging modalities.

CTV1 (high risk disease) : includes the entire nasopharynx, sphenoid sinus, cavernous sinus, base of skull posterior ½ of nasal cavity and posterior 1/3 of maxillary sinuses, pterygoid fossa, lateral and posterior pharyngeal walls to the level of mid-tonsillar fossa, the retropharyngeal nodes and bilateral upper cervical nodes including level V and supraclavicular nodes.

CTV2 (low risk disease) includes low risk nodal regions.

PTV high risk: margin around CTV high risk (3-5mm),

PTV low risk: If N0 neck or low neck (levels IV and VB).

Dose prescriptions in IMRT: GTV: 70Gy/2.12 per fraction, CTV1: 60/1.8 per fraction and CTV2: 54Gy/1.64 per fraction in 33 fractions.

Dose prescriptions in 3D conformal RT: By conventional fractionation, 200c Gy up to 50 Gy over 25 fraction to all target volume then cone down to CTV high risk till 60 Gy. Further cone down is then made to GTV + 2 cm margin to 70 Gy and positive LND. For the neck lower anterior, N0 = 50 Gy.

Dose limitation to risk organs: Partial brain 60 Gy, brainstem 50-54 Gy, spinal cord 45-50 Gy, optic chiasma 50-54 Gy, lens 10 Gy, and parotid mean dose < 26 Gy in at least one gland or 20 cc of both < 20 Gy, cochlea V55 < 5 %.

Quality Assurance (QA):

For pretreatment patients specific QA, the direct measurement of the IMRT dose distribution was checked using a special phantom. This treatment plan used the beam fluencies and energies, MUs, gantry angles and other delivery parameters that were selected for the patient plan and calculated the dose to the CT scan of the phantom. The phantom is subsequently irradiated and the measured dose was compared against the calculated dose distribution. During radiation delivery, the accelerator MLC position readout and the record and verify system were checked to verify the start and stop leaf positions of each field for the daily treatments. Off-line electronic portal image device (EPID) was done once a week for the 3-D conformal group, and twice weekly for the IMRT group. An isocenter shift of 5 mm and 3 mm was accepted for the 3-D conformal CRT and IMRT respectively.

Treatment delivery machine: Linear accelerator, 6 MV photon beam, step and shoot technique were used for the IMRT treatment delivery.

Dosimetric comparison between 3D conformal and IMRT planning:

A) Dose homogeneity within the target volume. Comparison between V95 % (volume of PTV planning target volume receiving 95 % of the prescribed dose) and V107 % (volume of PTV receiving ≥ 107 % of prescribed dose) for each technique and volume receiving D min. Homogeneity index and conformity index was calculated for each case.

B) Dose received by organs at risk (OARs) was compared for each contoured structure in terms of mean dose and D max (volume).

Treatment Verification:

The patient's setup was verified using an electronic portal imaging device. At the first treatment session, portal images of the treatment fields were acquired and compared with the treatment plan digitally reconstructed radiographs in 3DCRT in IMRT adding con beam CT weakly and portal image daily. At the same time, a reference surface image of the mask was recorded.

Concurrent systemic therapy

- For, the 3D and IMRT, cisplatin 100 mg/m^2 D1, 22 and 43 or cetuximab weekly with initial dose of 400 mg/m^2 one week before start of radiotherapy then 250 mg/m^2 day 1 weekly week 1 to 7.
- Post-radiotherapy cisplatin 80 mg/m^2 on day 1 and 5-flurouracil (5FU) 1000 mg/m^2/d continuous infusion day 1 to day 4 for 3 cycles were offered to all patients in the inpatient ward.

Evaluation of response, toxicity and follow up

a) During radiation course:

All patients were seen weekly for assessment and management of treatment related toxicity. Acute toxicity during radiation therapy was scored and graded according to the EORTC/ RTOG toxicity criteria.

b) Post-radiation therapy

Physical examination and full labs (CBC, LFT, and KFT) were done every 3 weeks for assessment of the patient's condition before giving chemotherapy. Toxicity during chemotherapy administration was recorded and collected during both concurrent and adjuvant phase. Acute toxicities were scored according to morbidity criteria of RTOG.

c) Post-treatment follow-up

The first visit was started 6 weeks after completion of the described treatment, every 2 months in the first year, every 3 months during the second year and third year, every 6 months in the fourth and fifth year then yearly for life. In each visit, complete clinical examination, endoscopy and biopsy was done for complete responders. CT/ MRI of the head and neck were done every 3 months.

Data management and analysis

The collected data were revised, coded, tabulated and introduce to PC using statistical package for social science (SPSS 15.1 for windows, PSS inc, Chicago, IL, 2001). Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

i. ***Descriptive analysis***

-Mean.

- Standard deviation.
- Minimum and maximum values (range) for numerical data.
- Frequency and percentage of non-numerical data.

ii. Analytic statistics:

1. **Independent-sample T test:** was used to assess the statistical significance of difference between two study group means.
2. **Chi-square test:** was used to examine the relationship between two qualitative variables.

P-value: level of significance:

- P>0.05: Non-significant (NS).
- P<0.05: Significant(S).
- P<0.01: Highly significant (HS).
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RESULTS

The current retrospective study was done in Clinical Oncology Department, Ain Shams University and International Medical Center in Egypt between January 2014 and December 2016. The study included fifty four eligible locally advanced nasopharyngeal carcinoma patients distributed between two arms, twenty four patients were treated with intensity modulated radiation therapy (IMRT) and thirty patients were treated with three dimensional conformal radiation therapy (3D-conformal RT) , both arms had received concurrent systemic therapy either standard of care cisplatin 100 mg/m2 D1, 22 and 43 or cetuximab weekly with initial dose of 400 mg/m^2 one week before start of radiotherapy then 250 mg/m^2 day 1 weekly week 1 to 7.

Regarding clinic-pathological data, T- stage assessment for both groups was done. For patients in IMRT group T1, T2, T3, T4 stages were represented in 5 (20.8%), 9 (37.5), 5 (20.8%) and 5 (20.8%) patients respectively while 3D conformal RT group T1, T2, T3, T4 stages were represented in 3 (10%), 10(33.3%), 11 (36.7%) and 6 (20%) patients respectively as shown in table 1.

Regarding N-stage, patients number in IMRT group presented with N0, N1, N2 and N3 was 4 (16.7%), 13 (54.2%), 6 (25%) and 1(4.2%)\ respectively and in 3DCRT group nodal staging was N0, N1, N2, N3, in 3 (10%), 14 (46.7%), 10 (33.3%), 3 (10%) patients respectively as show in table 1.

Table (1): Clinic-pathological data for both groups

		IMRT N= 24		**3D CRT N= 30**	
T	**T1**	5	20.8%	3	10%
	T2	9	37.5%	10	33.3%
	T3	5	20.8%	11	36.7%
	T4	5	20.8%	6	20%
N	**N0**	4	16.7%	3	10%
	N1	13	54.2%	14	46.7%
	N2	6	25%	10	33.3%
	N3	1	4.2%	3	10%
Differentiation	**Well**	2	8.3%	3	10%
	Moderate	7	29.2%	4	13.3%
	Poor	1	4.2%	2	6.7%
	Undifferentiated	14	58.3%	21	70%

Tumor differentiation in 3DCRT was well, moderate, poor, and undifferentiated in 3 (10%), 4 (13.3%), 2 (6.7%), and 21 (70%) patients respectively, while tumor differentiation in IMRT group was well, moderate, poor, and undifferentiated in 2 (8.3%), 7 (29.2%), 1 (4.2%), 14 (58.3%) patients respectively as show in table 1.

As regard the stage of both studied groups, in IMRT stage II was 7 (29.2%), stage III 13 (54.2%), and stage IV A 3 (8.3%), stage IV B 3 (8.3%) while 3D was stage II was 12 (40%), stage III 10 (33.3%),and stage IV A 4(13.3%), stage IV B 4(13.3%) as shown in table 2.

Table (2): Shows distribution of pathological stages in both groups

	IMRT N= 24		**3D CRT N= 30**	
Stage II	7	29.2%	12	40%
Stage III	11	45.8%	10	33.3%
Stage IV A	3	12.5%	4	13.3%
Stage IV B	3	12.5%	4	13.3%

Patients in IMRT group had suffered acute radiation toxicities less than the group received 3DCRT with significant difference in regard to skin toxicity, mucositis, and xerostomia toxicity grades as shown in table 3.

More patients in the IMRT group suffered G2 skin toxicity compared to the 3DCRT group (63.3% vs 26.7%), while more patients in the 3DCRT suffered G3 skin toxicity (16.7% vs 73.3%).

No G4 toxicity was reported in both groups.

Similarly, G2 toxicities of mucositis, dysphagia, and xerostomia were higher in the IMRT group compared to the 3DCRT group (29.2% vs 3.3%), (25% vs 6.7%), and (50% vs 3.3%) respectively. On the contrary, high grade toxicities (G3 and 4) of mucositis, dysphagia, and xerostomia were significantly lower in the IMRT group compared to the 3DCRT group (70.8% vs 90%), (75% vs 90%), and (50% vs 86.7%) respectively.

Table (3): Shows acute tolerance and feasibility in both study groups

		IMRT N= 24		**3D CRT N= 30**		**p-value**
Skin toxicity	**G2**	19	79.2%	8	26.7%	0.001 °*
	G3	5	20.8%	22	73.3%	
Mucositis	**G2**	7	29.2%	1	3.3%	0.01 °*
	G3	17	70.8%	27	90%	
	G4	0	0%	2	6.7%	
Dysphagia	**G2**	6	25%	2	6.7%	0.096 °NS
	G3	18	75%	27	90%	
	G4	0	0%	1	3.3%	
Xerostomia	**G2**	12	50%	1	3.3%	0.0050 °*
	G3	12	50%	26	86.7%	
	G4	0	0%	3	10%	

*: Statistically significant difference NS: no statistically significant difference

No significant difference was found between both groups regards drug toxicity; however group of IMRT had fewer cases who received cisplatin than the group of 3D CRT. There were 2 patients in each group who received cetuximab due to history of kidney transplantation as shown in table 4.

Table (4): Shows distribution of radiosensitizer in both study groups

		IMRT N= 24		**3D CRT N= 30**		**p-value**
Sensitivity	**Cisplatin**	22	91.7%	28	93.3%	0.818 [b]NS
	Cetuximab	2	8.3%	2	6.7%	

NS: no statistically significant difference

[b]:Chi-square test

IMRT group had significantly better tolerance doses regarding cochlea, parotid and spinal cord affection than the group of 3D CRT. Spinal cord Dmax in the IMRT group was 41.1±6.2 versus 49.9±2.6 in the 3DCRT group with p-value 0.001. Parotid mean dose was 24.04±2.4 versus 48.6±5.2 in the IMRT and 3DCRT groups respectively with p-value 0.001. Cochlea mean dose in IMRT was 39.2±3.01 versus 42.6±7.06 in the 3DCRT group with p- value 0.035 as shown in table 5.

Table (5): Shows dose distribution for organ at risk in the both study groups

			IMRT N= 24	**3D CRT N= 30**	**p-value**
Spinal cord	**Dmax (Gy)**	**Mean ±SD**	41.1±6.2	49.9±2.6	0.001 [a] *
Parotid	**Mean dose (Gy)**	**Mean ±SD**	24.04±2.4	48.6±5.2	0.001 [a] *
Cochlea	**Mean dose (Gy)**	**Mean ±SD**	39.2±3.01	42.6±7.06	0.032 [a] *

[a]: student t test

*: statistically significant difference

Mean PTV dose coverage was significantly higher in the IMRT group compared to the 3DCRT group in IMRT mean 97.22±4.57 versus 3DCRT 92.81±2.45 with p value 0.001 as shown in table 6.

Table (6): Shows dose distribution to PTV in the both study groups

		IMRT N= 24	3D CRT N= 30	p-value
PTV	**Mean ±SD**	97.22±4.57	92.81±2.45	0.001 [a] *
	Range	90 - 110	86 - 96	

[a]: student t test

*: statistically significant difference

Complete response in 3D conformal RT group was achieved in 86.7% of cases and the remaining 13.3% had partial response. All patients in the IMRT group had complete response. There was no statistically significant regarding response rate between both groups as shown in table (7 and 8).

Table (7): Comparison between 3DCRT arm and IMRT arm regarding primary and secondary efficacy endpoint

	IMRT arm No. (%)	3DCRT arm No. (%)	Test	p-value (Sig.)
Response	(N=24)	(N=30)		
Complete response	24 (100%)	26 (86.7%)	3.456*	0.120 (NS)
Partial response	0 (0%)	4 (13.3%)		

Table (8): Comparison between 3DCRT arm and IMRT arm regarding disease free survival, local recurrence free survival, regional recurrence free survival, locoregional recurrence free survival, distant metastasis free survival and overall survival

	IMRT arm (N=24)	3DCRT arm (N=26)	Test*	p-value (Sig.)
Disease Free Survival (DFS)				
1-year DFS	95.8%	76.9%	4.105	0.043 (S)
2-year DFS	83.9%	57.7%		
3-year DFS	83.9%	57.7%		
Median DFS	NR	NR		
Local Recurrence Free Survival (LRFS)				
1-year LRFS	100%	84.6%	3.980	0.046 (S)
2-year LRFS	93.3%	70.5%		
3-year LRFS	93.3%	70.5%		
Median LRFS	NR	NR		
Regional Recurrence Free Survival (RRFS)				
1-year RRFS	100%	100%	0.833	0.361 (NS)
2-year RRFS	100%	94.4%		
3-year RRFS	100%	94.4%		
Median RRFS	NR	NR		
Distant metastasis Free Survival (DMFS)				
1-year DMFS	95.8%	85.7%	0.185	0.667 (NS)
2-year DMFS	89.4%	85.7%		
3-year DMFS	89.4%	85.7%		
Median DMFS	NR	NR		
Overall Survival (OS)				
1-year OS	100%	80%	6.044	0.014 (S)
2-year OS	100%	75.8%		
3-year OS	100%	75.8%		
Median OS	NR	NR		

NR: Not reached yet

Both groups were compared as regard efficacy and survival end points. The analyzed end points with statistically significant values were local recurrence free survival (LRFS), disease free survival (DFS), overall survival (OS). Neither regional recurrence free survival (RRFS) nor distant metastasis free survival (DMFS) showed a statistically significant difference between both groups.

DISCUSSION

In our study, we assessed the difference between 3D conformal radiation therapy and intensity modulated radiation therapy in treating nasopharyngeal carcinomasas regards efficacy and toxicity.

Out of 54 studied patients, male gender constituted 75% of IMRT arm while constituted 70% of 3DCRT arm, which was consistent with most data from the literature that agrees about the male predominance of this disease [(15)].

In our study mean age in IMRT and 3DCRT were 49.9 and 44.9 years respectively. This is similar to the study conducted by **Chen *et al.*** [(16)], where the median age of their study population was 49 years.

In our study, 60% of patients in the 3DCRT arm, and 70.8% of patients in the IMRT arm had stage III or IV disease at presentation which differs from the trial conducted by **Moon *et al.*** [(14)], in which their study population had 72.6% and 76.1% of patients had stage III or IV disease in 3DCRT and IMRT arms respectively. Another study by **Chen and colleagues**[(16)] showed also higher proportion of patients of stage III or IV disease than our study. The percentage of patients with stage III/IV disease in their study population was 92 % and 75.9% in 3D and IMRT arms respectively. Our suggestion for this variation is that due to the fact that our study population size is considerably smaller than that of the previous two studies.

As regard dosimetric comparison, this study showed that IMRT had statistically significantly better PTV coverage as well as better sparing of organ at risk as evidenced by lower mean cochlea and parotid dose and lower spinal cord D-Max. This was in concordance with **El-Ghoneimy *et al.*** [(9)] results that showed that IMRT delivered fewer doses to organs at risk including brainstem, spinal cord, chiasma, temporal lobes and cochleae compared to 3D-CRT technique.The incidence of grade 3 skin toxicity was lower in IMRT than 3DCRT arms (16.7% and 73.3% respectively) in this study and this is supported by **Moon *et al.*** [(14)] study who documented grade 3 skin toxicity (2% and 2.3% respectively) in lower in IMRT than 3DCRT groups **.**

In our study grade 4 mucositis was observed in lower number in IMRT than 3DCRT arms (0% and 6.7% respectively), this differed from **Moon *et al.*** [(14)] study as grade 4 mucositis was observed in insignificantly higher number in IMRT than 3DCRT groups (0.4% vs 0%, respectively). This was due to higher number of 3DCRT than IMRT in their study. Also in our study grade 4 xerostomia was observed only in 3 patients treated in 3DCRT group, but no patient developed grade 4 xerostomia in IMRT group (0% and 3.3% respectively), while in the results of the same study no grade 4 xerostomia was observed in both groups.

Compared to study conducted by **Ozdemir *et al.*** [(17)] on 695 nasopharyngeal carcinoma patients treated using IMRT, there was no reported grade 4 toxicity in patients as regards mucositis, xerostomia and skin toxicity which was similar to our study.

Complete response was achieved in 100% of IMRT arm in our study while achieved in 86.7% of 3DCRT arm without a significant statistical difference. Similar to our study, **El-Ghoneimy *et al.*** [(9)] results showed complete response in IMRT arm which was100%, compared to 95% in 3DCRT arm which was also statistically non-significant. Both studies suggested better efficacy of intensity modulated radiotherapy even if the difference is not evident statistically.

In a study conducted by **Peponi *et al.*** [(18)] to estimate survival rates of patients with nasopharyngeal carcinoma treated with 3D conformal radiation therapy (3DCRT), the results showed that 4-year disease-free survival (DFS) and overall survival (OS) were (80 and 82%) with median follow up 4-year. This differed from the results obtained from our study which showed disease-free survival (DFS) and overall survival (OS) (56.7%, 67.7%) respectively. The poorer outcome in our study may be attributed to the difference in study population radiotherapy technique or difference in the supportive care available for the treatment- related toxicity. Another study conducted by **Ozdemir *et al.*** [(17)] assessed the outcome of intensity modulated radio-therapy (IMRT) in treatment of primary nasopharyngeal cancer, showed 5-year disease free survival (DFS) and overall survival (OS) (70.9%, 79.1%) respectively, which is lower than the obtained from our study which was (87.5%, 100%) respectively. We expect similar result rate of DFS, OS in our study compared to wang trial [(6)] after longer follow up.

As regard disease free survival, our present study showed statistically significant difference in 3-year disease free survival DFS in favor of the IMRT arm compared to the 3DCRT arm (83.9% vs 57.7 %, respectively) which was not consistent with the study conducted by **Moon *et al.*** [(14)] in which there was no statistically significant difference between intensity modulated radiotherapy IMRT and three dimensional conformal radiotherapy (3DCRT) as regard 5-year disease free survival DFS (67.2% and 65.1%, respectively).

Similarly our study showed statistically significant difference in 3 year overall survival OS in favor of the IMRT arm compared to 3DCRT arm (100% vs 75.8%, respectively) which also was not evident in the study conducted by **Moon *et al.*** [(14)] where there was no statistically significant difference in 5-year OS (76.7 % versus 73.6%, respectively). We attributed the difference in DFS and OS obtained in our study compared to Moon study to possible difference in the duration of follow up. Also it may be explained by the excess number of deaths in 3DCRT arm in our study due to treatment-related toxicity.In our study, 3-year distant metastasis free survival was statistically insignificant in IMRT arm than in 3DCRT arm (89.7% and 85.7% respectively), this is going with the results obtained by **Moon *et al.*** [(14)] study, 5-year distant metastasis free survival was statistically insignificant in IMRT arm than in 3DCRT arm (79.5% and 78.81% respectively). In the present study, disease control rate was significantly higher in IMRT arm than in 3DCRT arm (87.5% and 61.5% respectively). Local control rate was statistically insignificant in IMRT arm than in 3DCRT arm (95.8% and 73.1% respectively), and this was similar towas similar to **Lee et al. 2014**where 5 year local control rate in T3-4 patients was 83 and 84% in 3DCRT and IMRT patients, respectively.

CONCLUSION

IMRT is considered as a more advantageous radiation treatment technique as it can deliver high-dose irradiation to defined tumor targets while minimizing the dose delivered to the surrounding normal organs and tissues, thereby improving the therapeutic ratio of radiation therapy. IMRT has been shown to offer superior dose conformity to the tumor target and better sparing of critical organs in the treatment of NPC.

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