International Journal of Cancer Therapy and Oncology
www.ijcto.org

Involved-site radiation therapy by volumetric modulated arc therapy versus 3D- conformal radiotherapy for treatment of stages I and II supra-diaphragmatic Hodgkin's lymphoma

Mohamed Daoud[1], Engy Aboualnaga[1], Mohamed Mahfouz[2], Samah Elkhaiate[3], Ahmed Shehata[2]

[1]*Department of Clinical Oncology and Nuclear Medicine, Mansoura University, Mansoura, Egypt*
[2]*Department of Radiation Oncology, King Abdullah Medical City, Jeddah, Saudi Arabia*
[3]*Department of Pediatric Oncology, King Faisal Specialist hospital, Jeddah, Saudi Arabia*

Received February 26, 2016; Revised July 16, 2016; Accepted August 01, 2016; Published Online August 07, 2016

Original Article

Abstract

Purpose: Based on the observation that recurrences of Hodgkin's lymphoma (HL) typically occur in sites of initial nodal involvement the need to concise radiotherapy to only involved nodes that was termed as involved nodal radiotherapy (INRT) or of involved site lymph nodes, involved-site radiation therapy (ISRT) is starting to be widely accepted to use in early stage HL. We aimed in our study to compare between volumetric modulated arc therapy (VMAT) and 3D-conformal radiotherapy (3D-CRT) in radiation of early stage supra-diaphragmatic HL. **Methods:** The clinical and dosimetric data of 34 patients affected with stages I and II supra-diaphragmatic HL, treated between January 2011 and September 2015 with combined modalities therapy in a single institution were analyzed. Patients received 2-8 cycles of combination chemotherapy ABVD (Adriamycin, Bleomycin, Vinblastine & Dacarbazine) on days 1 and 15 repeated every 28 days. The clinical target volume (CTV) was contoured based on the pre-chemotherapy CT and PET-CT scans. Modification of the CTV was done according to post-chemotherapy anatomical changes. The radiation dose given was 30 Gy/15 fractions. **Results:** After a median follow up period of 30 months, the progression free survival (PFS) and overall survival (OS) in both groups were 100%. Oropharengeal mucositis was the commonest toxicity in both groups. There was no statistically significant deference between the acute radiation toxicities in both groups. The D_{mean} value for lung was higher in 3D-CRT than VMAT (12.0 ± 6.1 Gy vs. 9.9 Gy ± 8.6 Gy). For the breasts volume, the V_{5Gy} was slightly higher for 3D-CRT compared with VMAT at, 7.6% and 6.5% respectively. For the heart, V_{5Gy} and V_{10Gy} values were higher for the RA than for 3D-CRT accounting for (51.9 ± 28.9%) and (41.0 ± 24.6%) versus (40.0 ± 25.9% and 30.7 ± 22.5%) respectively. Thyroid gland mean dose was lower for VMAT (21.8 ± 7.7 Gy) than for 3D-CRT (26.8 Gy ± 4.1 Gy) but did not reach statistically significant value (P = 0.06). **Conclusion:** Involved-site VMAT technique is safe and effective in term of providing excellent local control and survival following ABVD-based chemotherapy.

Keywords:Hodgkin's lymphoma, Supradiaphragmatic, Radiation Therapy Involved site

1. Introduction

This study compares the dosimetric parameters and clinical outcomes of involved-site volumetric modulated arc therapy (IS-VMAT) versus 3D-conformal radiation therapy (3D-CRT) following chemotherapy for patients with early stage Supradiaphragmatic Hodgkin's lymphoma. With larger clinical target volume (CTV), IS-VMAT could yield perfect target volume coverage and sparing of normal tissue. ABVD chemotherapy and IS by either VMAT or 3D-CRT resulted in a favorable outcome and minimal toxicity to organs at risk specially the lung.

Corresponding author: Mohamed A Daoud; Department of Clinical Oncology and Nuclear Medicine, Mansoura University, Mansoura, Egypt.

***Cite this article as**: Daoud M, Aboualnaga E, Mahfouz M, Elkhaiate S, Shehata A. Involved-site radiation therapy by volumetric modulated arc therapy versus 3D- conformal radiotherapy for treatment of stages I and II supra-diaphragmatic Hodgkin's lymphoma. Int J Cancer Ther Oncol. 2016; 4(3):4313. **DOI**: 10.14319/ijcto.43.13*

ISSN 2330-4049

Radiation therapy is a major component in the treatment of Hodgkin's lymphoma (HL)[1]; However significant morbidities and increased incidence of second malignancies were detected in long-term survivors with using of radiation therapy[2,3]. Based on the observation that recurrences of HL typically occur in sites of initial nodal involvement[4], the need to concise radiotherapy to only involved nodes that was termed as involved nodal radiotherapy (INRT) or of involved site lymph nodes, involved-site radiation therapy (ISRT) is starting to be widely accepted to use in early stage HL[5,6]. The shifting from IFRT to INRT or ISRT decreased the volumes of lungs, breasts and thyroid that receiving high-dose radiation, giving the potential to reduce long-term second malignancy risks without effect on local control.[7] More recently, there has been some interest in arc-based or rotational therapies in an attempt to overcome some of the limitations associated with fixed field intensity modulated radiation therapy (IMRT).

In arc therapy the radiation is delivered a continuously rotating X-ray source allowing a wide beam angle.[8, 9] VMAT is an evolving radiotherapy technique using radiation by arcs and inverse planning to deliver highly conformal radiotherapy, to allow reducing the volumes of organs exposed to high-dose radiation.[10] Also, VMAT can delivers the radiation dose in a precise and accurate way in addition to the short delivery time as compared to the conventional fixed-field IMRT.[1, 9] The clinical worldwide use of VMAT is increasing significantly for patients having a pre-existing heart disease to minimize further cardiac toxicity risks.[7, 9]

The superiority of dose conformity and sparing of organ at risk (OAR) are the advantages of VMAT compared with conformal radiotherapy (CRT). On other side, in comparing with fixed field IMRT equivalent outcomes were obtained. However, OAR sparing is improved in treatment of special sites as prostate or cervical cancer with VMAT.[11] The treatment delivery time and reduction of monitor units (MU) are significantly differing between VMAT and fixed field IMRT.[9] Evaluation of VMAT for early HL was reported in planning studies and revealed improvement of planning target volume (PTV) dose uniformity with reduction of the irradiated volume of heart and lung and allowing sparing of OAR. [10, 12]

We aimed in our study to compare between VMAT and 3D conformal radiotherapy (3D-CRT) in radiation of involved site lymph nodes in cases of early stage supra-diaphragmatic HL.

2. Methods and Materials

The clinical and dosimetric data of 34 patients affected with stages I and II supra-diaphragmatic HL, treated between January 2011 and September 2015 with combined modalities therapy in a single institution were analyzed. Study inclusion criteria were, age ≥15 years, patients with classic HL, prior chemotherapy containing Adriamycin, Bleomycin, Vinblastine and Dacarbazine (ABVD) chemotherapy, complete response after chemotherapy, involved site radiation volumes, and RT dose of 30 Gy/15 fractions delivered with 3D-CRT or VMAT. The choice between 3D-CRT and VMAT was made for each patient, considering clinical presentation and specific needs related to dosimetric plan evaluation. Pre- and Post-chemotherapy assessment by both CT and FDG-PET- CT was done for all patients.

2.1. Chemotherapy

Patients with low risk factors received 2-3 cycles of ABVD chemotherapy on days 1 and 15 repeated every 28 days. Patients with unfavorable prognostic factors are treated with 4-8 cycles of ABVD. Radiation therapy was initiated within 4 weeks after chemotherapy for all patients.

2.2. CT simulation

Patients were positioned supine with arms along the body or arms up using special device. The thermoplastic masks used for immobilization of head and shoulders. Non-contrast CT simulation with a slice thickness of 3mm was done.

2.3. Clinical target volumes

CT simulation images were fused with images of pre-chemotherapy CT and PET-CT images using the Varian planning system Eclipse. Drawing of both CTV and PTV was done according to INRT guidelines.[6,13,14] The CTV was contoured based on the pre-chemotherapy CT and PET-CT scan. Modification of CTV was done according to post-chemotherapy anatomical changes. Organs at risk like heart, lung, spinal cord, and thyroid were delineated. We used slandered CT window (0) and width (500) level for the glandular tissue of the breast. Also, the heart was determined from the root of great vessels down to the tip of the organ, including the four cardiac chambers.

2.4. Dosimetric parameters and treatment planning

Patients were given 30 Gy as 2 Gy/fraction over 3 weeks period. The PTV received ≥ 95% and maximum dose ≤ 115% of the prescribed dose. The 3-DCRT plans consisted of two parallel opposing fields that are shaped with Multileaf Collimator (MLC). The VMAT plans consisted of either single full arc (360 °) plan or double – arc plan of 60° angle with starting angles at 150° and 330°. The Anisotropic Analytical Algorithm (AAA), Eclipse version 10.0.28.2, photon algorithm was use for all patients. It allows optimization according to biologic coast functions. Plans were optimized in order to spare OAR as much as possible (particularly lungs, breasts, and heart). Dose constraints for organs at risk are shown in Table 1. Image guidance protocols consisted of daily kilovoltage images or cone beam CT (CBCT) at the first

three days of treatment followed by weekly imaging thereafter.

Table 1: Dose constrains for organs at risk.

Variable	Factors	Objectives
PTV	D_{Mean}	30 Gy
	V<95%	<5%
	V>107%	<4%
Breast	V5 Gy	<40%
	V10 Gy	<25%
Lung	D_{mean}	<14 Gy
	V5 Gy	<50%
	V10 Gy	<35%
	V20 Gy	≤20%
Esophagus	D_{mean}	<25 Gy
	D_{Max}	<35 Gy
Heart	D_{mean}	<20 Gy
	V5 Gy	<66%
	V10 Gy	<50%
Parotids	D_{mean}	<24 Gy
Thyroid	D_{mean}	18 Gy
	V30 Gy	<20%

The cumulative Dose Volume Histograms (DVHs) were used for quantitative analysis of the treatment parameters. These parameters include for PTV (D_{mean}, V95 and V107) and for OAR, the mean dose and representative Vd according to the dose constrains of each organ.

2.5. Follow up

During radiation, therapy patients were seen weekly for assessment of acute radiation toxicities. Following radiotherapy patients were checked every 2 months in the first year and every 4 months after that for three years. PET-CT was performed every 6 months. Toxicities were scored according to radiation therapy oncology group (RTOG) scoring criteria.[15] Relapse was defined as the clinical or radiological appearance of new disease sites outside radiation fields or the reappearance of initially involved lymph nodes on CT scans and/or PET-CT scans.

2.6. Statistical analysis

Relapse-free survival was calculated using the Kaplan-Meier method[16], starting from the time of diagnosis. SPSS software Package version 21.0 was used for statistical analysis. The log-rank test was used to test the differences in relapse-free survival (RFS) probability for both 3D-CRT and VMAT. Pearson chi-square test was used to compare the two treatment plans in terms of acute toxicity incidence. The Student`s T-test for independent samples for normally distributed parametric data was used to compare the means between 3D-CRT and VMAT. Values were expressed as means± standard deviation according to data distribution. All P-values reported are two-sided and $P < 0.05$ is considered significant.

3. Results

The clinical characteristics for the 34 patients are described in table 2. The clinical features of both groups are comparable including age, sex, sites involved and their number, stage and pathological subtypes. The median follow up period for the whole group of patients was 30 months. For the 3D-CRT group of patients the median follow up was 32 months (18-50months) and for VMAT group was 27months (18-38months). The PFS and OS in both groups were 100%. Acute radiation toxicities were summarized in table 3. Oropharengeal mucositis was the commonest toxicity in both groups, with grade I mucositis occurring in 6 patients (31.6%) and 3 patients (20%) for 3D-CRT and VMAT techniques respectively. Grade II mucositis occurred in only 1 patient (6.7%) treated by VMAT and in 3 patients (15.8%) treated with 3D-CRT. Two patients in 3D-CRT group developed grade II skin reaction and two patients in the same group developed grade I radiation pneumonitis. There was no statistically significant deference between the acute radiation toxicities in both groups. The dosimetric data for both groups including the PTVs and organs at risk were expressed as mean values in Gy± Standard Deviation (SD) and the volume (V) as percentage of the received prescribed dose, as seen in Table 4.

3.1. Target volume coverage

Figures 1 and 2 show the dose distribution for two patient treated by VMAT and 3D-CRT, respectively. For the PTV the mean doses in both 3D-CRT and VMAT were similar at, 29.5% and 30.5% respectively, with no statistically significant deference. Also, the dose coverage for the PTV in both techniques was optimal as indicated by V90%, V95% and V107% values. The V<95% for 3D-CRT was 2.4 ± 2.3% and for the VMAT was 3.0 ± 2.6%. For V>107% the VMAT showed higher value of (3.3%) compared with 3D-CRT (2.9%) but not statistically significant ($P = 0.67$).

3.2. Lung

The D_{mean} value for lung was higher in 3D-CRT than VMAT (12.0 ± 6.1 Gy vs. 9.9 ± 8.6 Gy). However, for the low doses (V_5 & V_{10}) lung volumes were increased in VMAT (46.6% & 35.8%) more than in 3D-CRT (39.8% and 31.3%) respectively. For the lung volumes receiving higher dose (V_{20}) the mean lung volumes for both techniques were similar at, 21.4% and 21.7% for 3D-CRT and VMAT respectively.

Table 2: Patient's criteria.

Characteristics	Number	3D-CRT No. (%)	RA No. (%)	*P*-Value
Number of patients	34	19 (55.9%)	15 (44.1%)	
Age				
Rang	15-71	15-57	18-71	0.30
Mean	29.8	27.3	32.9	
Sex				
Male	17	11 (64.7%)	6 (35.3)	0.49
Female	17	8 (47.1%)	9 (52.9%)	
Stage				
IA	4 (11.8%)	1 (5.3%)	3 (20.0%)	0.27
IB	2 (9.5%)	1 (5.3%)	1 (6.7%)	
IIA	25 (73.5%)	14 (73.7%)	11 (73.3%)	
IIB	3 (8.8%)	3 (15.8%)	0 (0%)	
Number of involved sites				
< 4 sites	10 (29.4%)	6 (31.6%)	4 (26.7%)	0.53
> 4 sites	24 (70.6%)	13 (68.4%)	11(73.3%)	
Involved sites				
Mediastinum	1 (2.9%)	1 (5.3%)	0 (0.0%)	0.28
Bilateral cervical	11 (32.4%)	5 (26.3%)	6 (40.0%)	
Bilateral cervical/axilla	2 (5.9%)	0 (0.0%)	2 (13.3%)	
Cervical/Mediastinum	12 (35.3%)	7 (36.8%)	5 (33.3%)	
Cervical/Mediastinum/axilla	3 (8.8%)	3 (15.8%)	0 (0.0%)	
Unilateral Cervical	5 (14.7%)	3 (15.8%)	2 (13.3%)	
Pathologic subtype				
Lymphocytic depletion	2 (5.9%)	2 (10.5%)	0 (0.0%)	0.08
Lymphocytic predominance	7 (20.6%)	3 (15.8%)	4 (26.7%)	
Mixed cellularity	10 (29.4%)	3 (15.8%)	7 (46.7%)	
Nodular Sclerosis	15 (44.1%)	11 (57.9%)	4 (26.7%)	
Chemotherapy regimen				
2 cycles ABVD	3 (8.8%)	1 (5.3%)	2 (13.3%)	0.19
3 cycles ABVD	2 (5.9%)	2 (10.5%)	0 (0.0%)	
4 cycles ABVD	12 (35.3%)	4 (21.1%)	8 (53.3%)	

Table 3: Acute Radiation toxicities during treatment with 3D-CRT & RA techniques.

Toxicity grades	3D-CRT	RA	P-value
Skin reaction			
Grade I	4 (21.1%)	2 (13.3%)	0.19
Grade II	2 (10.5%)	0 (0.0%)	
Mucositis			
Grade I	6 (31.6%)	3 (20.0%)	0.45
Grade II	3 (15.8%)	1 (6.7%)	
Neutropenia			
Grade I	10 (52.6%)	3 (20.0%)	0.15
Grade II	1 (5.3%)	1 (6.7%)	
Pneumonitis			
Grade I	2 (10.5%)	1 (6.7%)	0.59
Grade II	-	-	

Table 4: Comparison of doses to treatment volumes and organs at risk.

Variable	Parameter	3D-CRT Mean	RA Mean	P-value
PTV	D_{mean} (Gy)	29.5±2.8	30.5±0.2	0.18
	V<90%	0.4±0.3	0.61±0.5	0.10
	V<95%	2.4±2.3	3.0±2.6	0.42
	V>107%	2.9±1.8	3.3±3.1	0.67
Lung	D_{mean} (Gy)	12.0±6.1	9.9±8.6	0.45
	V5 Gy	39.8±13.3	46.6±32.7	0.46
	V10 Gy	31.3±11.7	35.8±30.9	0.61
	V20 Gy	21.4±9.8	21.7±29.3	0.97
Breast	V5 Gy	7.6±3.8	6.6±5.6	0.71
	V10 Gy	4.3±2.61	3.4±3.3	0.60
Heart	D_{mean} (Gy)	13.6±8.2	15.7±8.7	0.56
	V5Gy	40.0±25.9	51.9±28.9	0.32
	V10 Gy	30.7±22.5	41.0±24.6	0.32
Parotid	D_{mean} (Gy)	18.9±2.8	12.0±4.1	0.00
Larynx	D_{mean} (Gy)	15.8±9.2	19.4±2.8	0.20
Thyroid	D_{mean} (Gy)	26.8±4.1	21.8±7.7	0.06
	D_{Max} (Gy)	31.9±1.5	29.0±3.6	0.01
	V30 Gy	53.4±31.3	24.4±17.2	0.03
Esophagus	D_{mean} (Gy)	20.9±5.8	15.4±6.4	0.02
	D_{Max} (Gy)	28.0±8.2	31.0±1.8	0.19

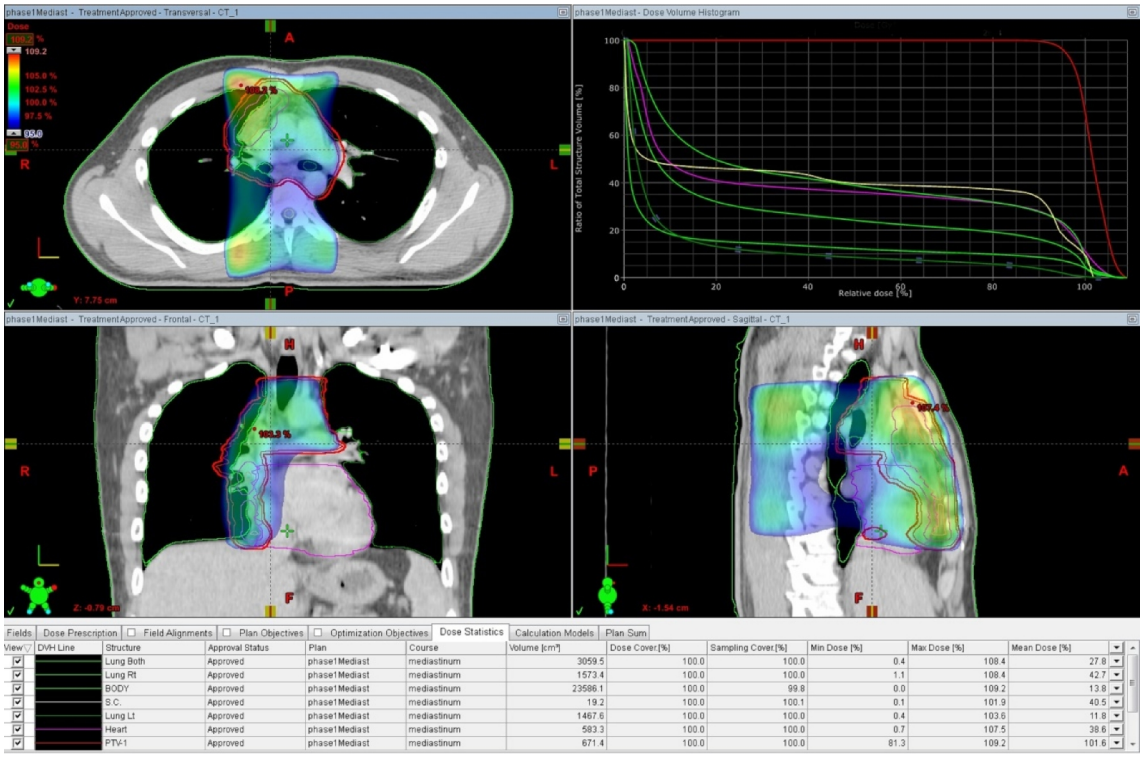

Figure 1: Dose distribution for a three-dimensional radiotherapy (3D-RT) plan in the transversal, sagittal, and coronal plane for a patient with typical planning target volume (PTV) involving the superior mediastinal lymph nodes. Dose volume histogram data is included.

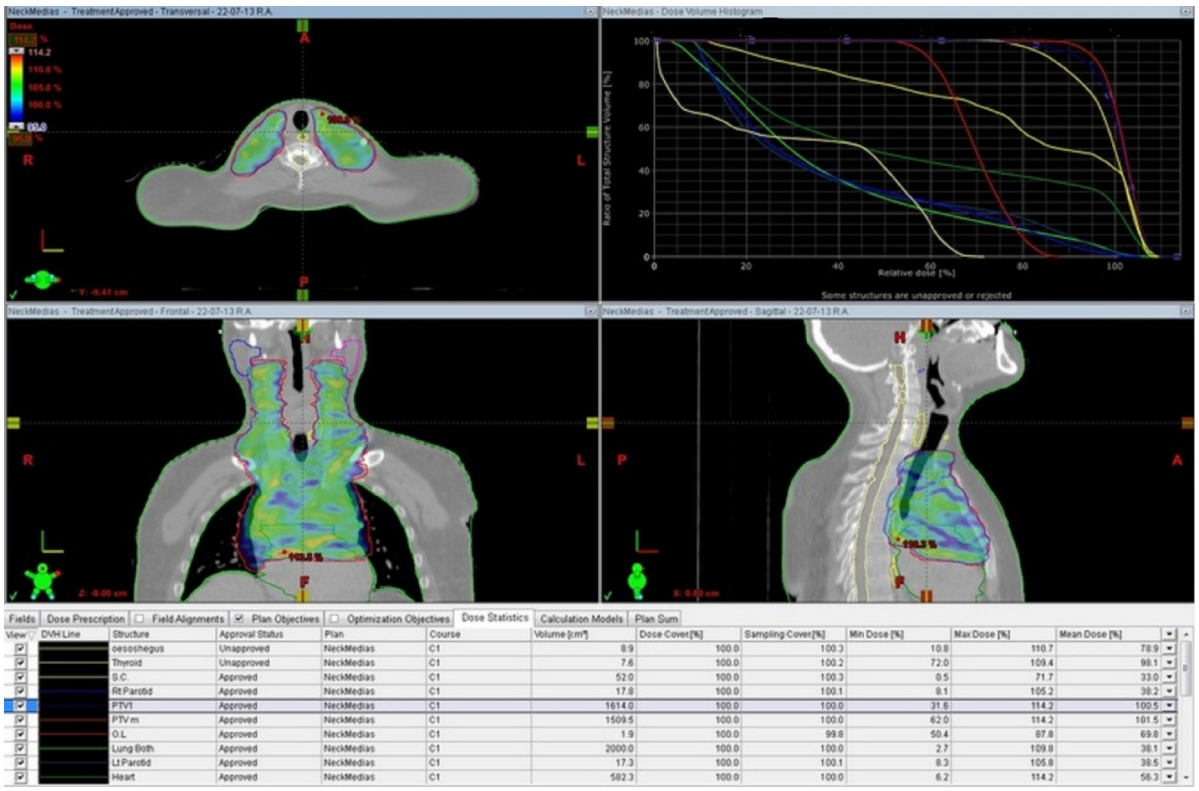

Figure 2: Dose distribution for a volumetric modulated arc therapy (VMAT) plan in the transversal, sagittal, and coronal plane for a patient with planning target volume involving cervical and mediastinal lymph nodes. Dose volume histogram is illustrated.

3.3. Breast

For the breasts volume, the V_5 was slightly higher for 3D-CRT compared with VMAT at, 7.6% and 6.5% respectively. Also, the V_{10} for 3D-CRT was higher compared with VMAT, at 4.3% and 3.4% respectively, but no statistically significant differences.

3.4. Heart

For the heart, the mean dose received was similar in 3D-CRT and VMAT (13.6% and 15.7%) respectively. V_5 and V_{10} values were higher for the VMAT than for 3D-CRT accounting for (51.9 ± 28.9% and 41.0 ± 24.6%) versus (40.0 ± 25.9% and 30.7 ± 22.5%) respectively but not statistically significant (P = 0.32).

3.5. Parotids

For the parotids the mean doses were statistically significant lower for VMAT (12.0 ± 4.1 Gy) than 3D-CRT (18.9 ± 2.8 Gy), (P = 0.00).

3.5. Larynx

The mean dose for the larynx was higher for VMAT (19.4 ± 2.8 Gy) compared with 3D-CRT (15.8 ± 9.2 Gy).

3.5. Thyroid

Thyroid gland mean dose was lower for VMAT (21.8 ± 7.7 Gy) than for 3D-CRT (26.8 ± 4.1 Gy) but did not reach statistically significant value (P = 0.06).However, The D_{max} to thyroid gland in VMAT (29.0 ± 3.6 Gy) was significantly lower than that for 3D-CRT (31.9 ± 1.5 Gy), (P=0.01). Also, the V30 value was statistically significant lower for VMAT (24.4%) than for 3D-CRT (53.4%), (P = 0.03).

3.5. Esophagus

For the esophagus D_{mean} was significantly lower in RA (15.4 Gy) versus (20.9 Gy) in 3D-CRT (P=0.02). However, D_{max} were similar in both techniques with 28.0 Gy in 3D-CRT and 31.0Gy in VMAT.

4. Discussion

Patients with early-stage HL have about 95% cure rate with the combined chemo-radiation therapy, therefore the current and future studies are concerned with reduction of late complications while simultaneously maintaining high cure rates. This can be achieved through reducing total radiation dose, radiation volume, and/or improvement of radiation techniques.

Highly conformal irradiation modalities, utilizing different IMRT approaches, may improve PTV coverage and/or critical organs sparing by improving conformity, resulting theoretically in potentially clinical significant consequences in patients with Hodgkin's lymphoma.[10, 17-18] In the present study, we aimed to provide dosimetric findings and clinical data for the use of rapid Arc in comparison to 3D-CRT in limited stage HL

patients treated by involved-site. Our study shows that reduction of target volume to IS-PTV most effectively improves OAR sparing, regardless of the radiation technique used. Like in our study, the reduction in RT volumes from the conventional involved-field RT to involved-nodal was previously investigated in retrospective studies, without any influence on the relapse pattern in early stage HL. Lu *et al*. retrospectively analyzed a cohort of 52 patients affected with mediastinal stage I-II HL treated with a combination of 4 to 6 cycles ABVD followed by 30 to 40 Gy involved field IMRT (step-and-shoot technique).[19] The patients were heterogeneous group with different response to chemotherapy and different total dose (30-40 Gy). The median mean lung dose and V20 to the lungs were 13.8 Gy and 25.9%, respectively. The median follow-up time was 36.3 months. Three-year local control, overall and progression-free survival rates were 97.9%, 100%, and 96%, respectively. Two patients experienced grade 3 toxicity (mucositis and leukopenia) and 5 patients grade 2 mucositis. The second most frequent toxicity was skin reactions (46.2% grade 1 and 5.8% grade 2). No patients developed ≥grade 2 pneumonitis. Filippi *et al*.[20] analyzed the clinical data of 90 patients with stage IIA HL treated with either involved-site 3D-CRT (54.4%) or IG-IMRT (45.6%) for total dose of 30 Gy after complete response following 3-4 cycles of ABVD. After a median follow up time of 54.2 months and 24.1 months for 3D-CRT group and IG-IMRT group respectively, there were no differences in RFS between the two groups. The incidence of grade 2 mucositis was significantly lower in IG-IMRT than in 3D-CRT (P = 0.43).In our study, the pattern of acute toxicity was similar to the previous two studies with mucositis being the commonest recorded toxicity and grade 1 mucositis less common in RA group (20.0%). No patients developed grade 2 radiation pneumonitis. Furthermore, no significant difference in the toxicity profile between the two groups.

From the dosimetric point; cardiac sparing was similar in both 3D-CRT and VMAT the same finding was reported by Koeck *et al*.[21] in a comparative planning study for 20 patients with early unfavorable mediastinal HL. Also, He compared IF-PTV and IN-PTV for both conventional 3D-CRT and IMRT and observed OAR dose reduction of 20% to 50%, with maximal reduction of high doses to the heart and within low doses to the right breast. The same finding was supported previously in a planning study by Weber *et al*.[10] comparing target field reduction from IF-PTV to IN-PTV for IMRT and VMAT for 10 female patients with mediastinal HL, and showed a significant reduction of dose to OAR when using IN-PTV instead of IF-PTV. As already shown by other authors, in similar planning comparison studies, different IMRT solutions were better in terms of lowering mean doses to certain OAR (thyroid gland, lung, heart and coronary Ostia).[12, 13, 22] In this study, the mean doses to the lungs, thyroid, parotids and esophagus were lower in VMAT technique than in 3D-CRT. Better sparing of the thyroid gland could reduce the risk of late toxicity as hypothyroidism and second cancer. In addition, no patients developed grade 2 radiation pneumonitis in our study. In contrast, Girinsky *et al*.[23] demonstrated lung toxicity of › grade 2 in 10% of patients receiving mean lung dose of 12.8 Gy and 5% lung toxicity with V20 of 25% in patients treated for mediastinal HL. There is also an important open issue regarding the potential increase in the risk of second malignancies with IMRT and VMAT, secondary to the increased volume of normal tissues receiving lower doses. The currently available data for the risk of radiation-induced secondary tumors are only theoretical and somehow controversial, with studies showing no differences between 3D-CRT and dedicated IMRT techniques[24] and others indicating a potential increased risk [25, 26], especially for breast and lung cancer. However, long-term toxicity of low doses to a large volume of normal tissues in young patients with highly curable disease is also a significant concern. The limitations of this study include, the small number of patients, short follow up period and the late toxicity were not assessed.

Accordingly, every patient should be assessed individually and the choice of treatment plans and technique selected based on clinical needs and priorities. In certain situations, 3D-CRT still represents the standard choice because of the smaller volume of irradiated normal tissues. In other patients, IMRT or VMAT may be the preferred technique that, offers a significantly better sparing of organs at risk, in spite of the larger volumes of normal tissues receiving low doses. Future clinical and dosimetric studies are needed to recommend different IMRT solutions for different disease presentations of HL at diagnosis, with second cancer risk modeling in the planning process.

5. Conclusion

In early-stage Supradiaphragmatic HL patients, involved-site VMAT technique is safe and effective in term of providing excellent Local control up to 100%, equivalent to the local control achieved with 3D-CRT.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Acknowledgement

The authors would like to acknowledge the contribution of the technologists and staff members of Radiation Oncology Department, King Abdullah Medical City, Jeddah.

 ISSN 2330-4049

References

1. Specht L, Yahalom J, Illidge T, *et al*. Modern radiation therapy for Hodgkin lymphoma: field and dose guidelines from the international lymphoma radiation oncology group (ILROG). Int J Radiat Oncol Biol Phys. 2014;89(4):854-62.
2. Aleman BM, van den Belt-Dusebout AW, Klokman WJ, *et al*. Long-term cause-specific mortality of patients treated for Hodgkin's disease. J Clin Oncol. 2003;21:3431-9.
3. Dores GM, Metayer C, Curtis RE, *et al*. Second malignant neoplasms among long-term survivors of Hodgkin's disease: a population-based evaluation over 25 years. J Clin Oncol. 2002;20:3484-94.
4. Shahidi M, Kamangari N, Ashley S, *et al*. Site of relapse after chemotherapy alone for stage I and II Hodgkin's disease. Radiother Oncol. 2006;78:1-5.
5. Campbell BA, Voss N, Pickles T, *et al*. Involved-nodal radiation therapy as a component of combination therapy for limited-stage Hodgkin's lymphoma: a question of field size. J Clin Oncol. 2008; 26:5170-4.
6. Girinsky T, van der Maazen R, Specht L, *et al*. Involved-node radiotherapy (INRT) in patients with early Hodgkin lymphoma: concepts and guidelines. Radiother Oncol. 2006;79:270-7.
7. Campbell BA, Hornby C, Cunninghame J, *et al*. Minimizing critical organ irradiation in limited stage Hodgkin lymphoma: a dosimetric study of the benefit of involved node radiotherapy. Ann Oncol. 2012: 23:1259-66.
8. Daoud MA, Saleh YM, Habash AS. Simultaneous integrated boost by RapidArc therapy plus temozolomide for treatment of patients with glioblastoma multiform: A single institution experience. Int J Cancer Ther Oncol. 2015;3(3):3314.
9. Teoh M, Clark CH, Wood K, *et al*. Volumetric modulated arc therapy: a review of current literature and clinical use in practice. Br J Radiol. 2011;84(1007):967-96.
10. Weber DC, Peguret N, Dipasquale G, Cozzi L. Involved-node and involved-field volumetric modulated arc vs. fixed beam intensity-modulated radiotherapy for female patients with early-stage supra-diaphragmatic Hodgkin lymphoma: A comparative planning study. Int J Radiat Oncol Biol Phys. 2009;75:1578-86.
11. Fogarty GB, Ng D, Liu G, *et al*. Volumetric modulated arc therapy is superior to conventional intensity modulated radiotherapy - a comparison among prostate cancer patients treated in an Australian center. Radiat Oncol. 2011;6:108.
12. Lee YK, Bedford JL, Taj M, Saran FH. Use of volumetric-modulated arc therapy for treatment of Hodgkin lymphoma. Med Dosim. 2013;38(4):372-5.
13. Girinsky T, Specht L, Ghalibafian M, *et al*. The conundrum of Hodgkin lymphoma nodes: to be or not to be included in the involved node radiation fields. The EORTC-GELA lymphoma group guidelines. Radiother Oncol. 2008;88(2):202–10.
14. Girinsky T, Ghalibafian M, Bonniaud G, *et al*. Is FDG-PET scan in patients with early stage Hodgkin lymphoma of any value in the implementation of the involved-node radiotherapy. Radiother Oncol. 2007;85(2):178-87.
15. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phy. 1995;31(1):1341–6.
16. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc. 1958;53:457–81.
17. Ghalibafian M, Beaudre A, Girinsky T. Heart and coronary artery protection in patients with mediastinal Hodgkin lymphoma treated with intensity modulated radiotherapy: Dose constraints to virtual volumes or to organs at risk? Radiother Oncol. 2008;87(1):82–8.
18. Cella L, Liuzzi R, Conson M, *et al*. Dosimetric predictors of asymptomatic heart valvular dysfunction following mediastinal irradiation for Hodgkin's lymphoma. Radiat Oncol. 2011;101:316–21.
19. Lu NN, Li YX, Wu RY, *et al*. Dosimetric and clinical outcomes of involved-field intensity modulated radiotherapy after chemotherapy for early stage Hodgkin's lymphoma with mediastinal involvement. Int J Radiat Oncol Biol Phys. 2012;84:210-6.
20. Filippi AA, Ciammella P, Piva C, *et al*. Involved-site image-guided intensity modulated versus 3d conformal radiation therapy in early stage supradiaphragmatic Hodgkin Lymphoma. Int J Radiat Oncol Biol Phys. 2014;89:370-5.
21. Koeck J, Abo-Madyan Y, Lohr F, *et al*. Radiotherapy for early mediastinal Hodgkin

 ISSN 2330-4049

Lymphoma according to the German Hodgkin Study Group (GHSG): The roles of intensity-modulated radiotherapy and involved-node radiotherapy. Int J Radiat Oncol Biol Phys. 2012;83:268–76.
22. Findra C, Filippi AR, Catuzzo P, *et al*. Different IMRT solutions vs. 3D-conformal radiotherapy in early stage Hodgkin's lymphoma: Dosimetric comparison and clinical considerations. Radiat Oncol. 2012;7:186.
23. Girinsky T, Pichenot C, Beaudre A, *et al*. Is intensity-modulated radiotherapy better than conventional radiation treatment and three-dimensional conformal radiotherapy for mediastinal masses in patients with Hodgkin's disease, and is there a role for beam orientation optimization and dose constraints assigned to virtual volumes? Int J Radiat Oncol Biol Phys. 2006;64:218–26.
24. Filippi AR, Ragona R, Fusella M, *et al*. Changes in breast cancer risk associated with different volumes, doses and techniques in female Hodgkin's lymphoma patients treated with supra-diaphragmatic radiotherapy. Pract Radiat Oncol. 2013;3:216-22.
25. Maraldo MV, Brodin NP, Aznar MC, *et al*. Estimated risk of cardiovascular disease and secondary cancers with modern highly conformal radiotherapy for early stage mediastinal Hodgkin's lymphoma. Ann Oncol. 2013;24:2113-8.
26. Cella L, Conson M, Pressello MC, *et al*. Hodgkin's lymphoma emerging radiation treatment techniques: trade-offs between late radio-induced toxicities and secondary malignant neoplasms. Radiat Oncol. 2013;8:22.

 ISSN 2330-4049