Original Article

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Reviewing of radical radiotherapy to the mediastinum in patients with lymphoma

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ABSTRACT

Background: Historically and clinically, lymphomas are categorized into two major groups: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Over the years, radiotherapy techniques have advanced from extended-field to involved-field and more recently to involved-site/involved node radiation therapy (RT) (ISRT/INRT). **Aim**: This study aimed to evaluate the efficacy of mediastinal radiotherapy in lymphoma patients in Iraq. **Methods**: A prospective study was conducted to assess clinical and dosimetric changes in various radiotherapy planes and dosimetry between January 2023 and December 2023. The data collected included The data collected included patient demographics, medical history, treatment details, lymphoma characteristics, staging, radiotherapy plans, dose/fraction, and organ doses. **Results**: The study included 30 lymphoma patients (19 HL and 11 NHL cases) with a mean age of 31.3 ± 9.11 years. The non-coplanar group demonstrated superior mean PTV coverage compared to the coplanar volumetric modulated arc therapy (VMAT) group (P = 0.005). Additionally, the mean heart dose in the coplanar plans was greater than that in the non-coplanar arm ($p < 0.0001$). The coplanar plans also showed higher mean doses to the left lung at V20 in comparison to the non-coplanar plans ($p = 0.007$). Furthermore, the mean dose to the spinal cord in the coplanar VMAT group was greater than that in the non-coplanar group ($p = 0.003$). The median survival times were 11 months for HL and 12 months for NHL. Patients treated with coplanar plans had a median survival of 10.36 months, while those treated with non-coplanar plans had a median survival of 8.13 months. The recurrence rate was 23.3%, with a 3.3% risk of cardiac toxicity. **Conclusions**: The mean PTV coverage in the non-coplanar group surpassed that of the coplanar VMAT group. The median survival for HL patients was less than that for NHL patients within the same follow-up period. The survival rate of patients under coplanar plans exceeded that of patients under non-coplanar plans.

Keywords: lymphoma, diffuse large B-cell lymphoma, median survival, non-Hodgkin lymphoma

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INTRODUCTION

The term lymphoma refers to a heterogeneous group of neoplasms originating from lymphoid cells, primarily mature B cells, with fewer cases arising from the T-cell lineage. Historically and clinically, lymphomas have been categorized into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). HL is characterized by the

presence of Reed–Sternberg cells and has an incidence of 2.3/100,000 individuals in Western countries,[1,2] with young adults aged 20 to 40 years being most commonly affected. Histologically, classical HL accounts for 95% of all HL cases.[1] Additionally, classical lymphomas are classified as nodular sclerosis, a common subtype accounting for 60 to 65% of cases, followed by mixed cellularity (15–30%), lymphocyte-rich (5%), and lymphocyte-depleted (1%).[1]

NHLs are neoplastic transformations of mature B, T, and/or natural killer cells,[1] with diffuse large B-cell lymphoma (DLBCL), Burkitt's lymphoma, and lymphoblastic lymphoma being the most common subtypes.[2,3] DLBCL is the predominant histological subtype in adults,[3] with incidence increasing with age. Risk factors for NHL include family history, autoimmune disease, human immunodeficiency virus (HIV) infection, hepatitis C virus (HCV) infection, and high body mass index (BMI).[3] Combined modality therapies have shown cure rates of over 90% for lymphomas. In recent years, radiation therapy (RT) fields have evolved from extended-field to involved-field and mostly to involved-site/involved node RT (ISRT/INRT).[4,5] Retrospective studies have revealed that ISRT/INRT has not resulted in any marginal misses and has yielded progression free survival (PFS) rates exceeding 90%.[6,7]

First described by British physician Thomas Hodgkin in 1832, HL has seen significant improvements in outcomes since the introduction of combination chemotherapy. This advancement has led to effective management, particularly in patients with unfavorable prognostic features or advanced-stage disease.[8]

Recent improvements in RT techniques have further enhanced treatment options for HL, including more uniform and targeted dose delivery, advances in radiographic imaging technology, less toxic multi-agent chemotherapy protocols, the development of more effective agents, and the refinement of prognostic factors. These developments have allowed for better tailoring of management, making HL one of the most curable forms of cancers.[8,9]

According to the Iraqi Cancer Registry (ICR) reports in 2022, there was an estimated 726 (2.03%) cases of HL and 1433 (4%) cases of NHL in Iraq.[10]

Globally, NHL accounted for 544,352 cases, with 304,151 males and 240,201 females, resulting in 259,793 deaths. HL accounted for 83,087 cases (48,981 males and 34,106 females), with 23,376 deaths recorded.[11,12] NHL ranked 11th among all cancer types, while HL ranked 26th.[13]

Although surgery is used for diagnosis and management in selected cases, primary treatment modalities include chemotherapy and RT. In the past, surgical resection was the only potentially curative treatment for NHL in extranodal sites, such as the stomach or head and neck, when the disease was localized. However, surgery is now primarily used for biopsy to establish a diagnosis. This may involve major surgical operations, such as exploratory laparotomy or laparoscopic techniques, for the diagnosis of stomach, intestinal, retroperitoneal, or mesenteric lymphoma.[8]

In HL, 60% of cases are diagnosed in the early stages, making extended-field RT the primary treatment modality, often combined with chemotherapy such as adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD). The utilization of combination modalities have substantially increased the cure rate to over 90%.[6,7]

For NHL, the aim of RT is to deliver an adequate radiation dose to the target volume to achieve a high rate of local control. Careful consideration of dose fractionation parameters is imperative to balance local control with acceptable acute and long-term toxicity. RT is typically initiated four to six weeks after the completion of chemotherapy to allow for recovery of blood counts and minimize the drug-radiation sensitization effect.[8]

Various chemotherapy regimens are employed for NHL, including single agents used for indolent lymphoma, anthracycline-containing regimens potentially curative for DLCBL (e.g., CHOP-rituximab) or T-cell lymphomas, and regimens used for patients with recurrent disease. For high-grade lymphoblastic and Burkitt lymphomas, dose-intensive protocols are used with concurrent intrathecal chemotherapy for central nervous system (CNS) prophylaxis.[8]

While extended-field radiation therapy (EFRT) remains the standard treatment for HL, several randomized trials have explored the use of involved-field radiation therapy (IFRT) as an alternative.[14]

Cross-sectional imaging for radiation planning, accurate dosimetry, multileaf collimation, and intensity-modulated beam delivery have made it possible to better define and further decrease radiation fields in cases of lymphomas. Guidelines for involved node radiation therapy (INRT) and involved-site radiation therapy (ISRT) based on the best available evidence and consensus on expert opinions were recently published by the International Lymphoma Radiation Oncology Group (ILROG).[15]

This study aims to estimate dosimetric data for coplanar and non-coplanar RT in lymphoma treatment and investigate the radiation dose delivered to organs at risk, including the heart, lung, spinal cord, breast, and esophagus.

MATERIALS AND METHODS

Study Design and Setting

A prospective study was conducted to observe clinical and dosimetric changes in different radiotherapy planes and dosimetry at the Baghdad Radiotherapy and Nuclear Medicine Center complex between January 2023 and December 2023.

Data Collection

Thirty patients with mediastinal lymphoma were managed with chemotherapy and RT. Patient files, planning reports, dose-volume histogram (DVH) data, and medical physics records were collected. Data included age, sex, residence (rural and urban), comorbid conditions, chemotherapy history, radiotherapy history, site of lymphoma, symptoms (b-symptoms and other), lymphoma types and subtypes, staging, RT plans (coplanar and non-coplanar), dose/fraction (30/15, 36/18, 20/10, and 40/20), RT field, PTV95%, mean dose to the heart, lung mean dose at V20 and V5, Spinal cord Dmax, esophagus Dmax, and breast mean dose.

Follow-Up

The follow-up period was extended to 12 months in this study. Progression events in lymphoma status, such as recurrence or relapse, any cardiac toxicity signs assessed by history, electrocardiogram (ECG), echo study, and any death due to or related to treatment were monitored.

Inclusion Criteria

1. Histologically proven mediastinal lymphomas
2. Age ≥ 18 and ≤ 70 years
3. ECOG performance status 0–2
4. Post chemotherapy
5. Non-metastatic cases

Exclusion Criteria

1. ECOG performance 3–4
2. Loss of follow-up
3. Extra nodal cases

Treatment Protocols

The gross target volume (GTV) represents the lymph nodes (LN) involved in lymphoma, clinically identified or radiologically recognized by computed tomography (CT), positron emission tomography (PET), and ultrasound (US) (pre-chemotherapy or biopsy GTV, which represents the part of LN involved in clinical or radiologic assessment before therapy, and a post-therapy GTV).

The clinical target volume (CTV) encompasses macroscopic lymphoma sites evident at the time of CT scan simulation and potential locations of microscopic lymphoma tissues. When adjacent tissues/structures have been involved, some or all of the invaded structure/organ may be included in the CTV. However, the first echelon nodes of uncertain status close to the primary organ are included, and part of a nodal chain is included in the CTV as part of the volume delineation.

Fields

Various radiation therapy techniques were utilized to meet the planning requirements, including EFRT, IFRT, and INRT. ISRT was used for HL and nodal NHL. The ISRT guidelines follow field design principles and volume definitions defined by the International Commission on Radiation Units and Measurements (ICRU).

Tools

1. CT pore scanner (85 cm) (Philips ® 16 series).\
2. Linear Accelerator [InfinityTM and Synergy®]; 2013 (core-beam CT). Elekta Synergy system.
3. Monaco® Electa HP version 5.
4. XiO® Electa system version 5

Ethical Consideration

Ethical approval for this study was granted by the Iraqi Board of Health Specialization. Written informed consent was obtained from all the patients or their parents prior to enrollment in this study.

Statistical Analysis

Electronic data was collected and processed using view capture tools (Monaco® Electa HP version 5) and statistical analysis was performed using SPSS v24 (IBM Inc., Chicago, IL, USA). Descriptive statistics, including numbers and percentages, were measured, along with mean, median, range, min, max, and standard deviation (SD) for categorical data. The (unpaired t-test), and Pearson correlation were utilized for data analysis, with statistically significance set at a two-sided P value of less than 0.05.

RESULTS

Baseline Demographic and Clinical Characteristics

Thirty patients with lymphoma (19 HL cases and 11 NHL cases) revealed a mean age of 31.3 ± 9.11 years and a median age of 30.5 years. Females comprised 60% of the patient population, while males made up 40%. Most patients lived in urban regions (63.3%) and received ABVD (doxorubicin, bleomycin, vinblastine and

dacarbazine) (63.3%) and R-CHOP (cyclophosphamide, doxorubicin hydrochloride (hydroxydaunomycin), and vincristine sulfate (Oncovin), Rituximab, and prednisone) (36.7%) treatment. In terms of lymphoma stages, stage I accounted for 60% (18 cases: 10 HL and 8 NHL), stage II accounted for 36.7% (11 cases: 9 HL and 2 NHL), and stage III accounted for 3.3% (only 1 NHL case). Most patients presented with B-symptoms (17, accounting for 56.7%), while others complained of dyspnea (8, making up 26.7%) and weight loss (5, comprising 16%). The HL subclasses were classical mixed cellularity (MC) and nodular sclerosis (NS) (n = 9, 47.4%), while the NHL subclasses were DLBCL (n = 8, 72.7%) and follicular lymphoma (n = 3, 27.3%).

The distribution of lymphomas was predominantly in the mediastinum (70%) and mediastinum + cervical (30%). All cases treated using the VMAT technique were coplanar or non-coplanar. The RT doses (Gy/fx) were divided into 30/15 (26.7%), 36/18 (53.3%), 36/20 (10%) and 45/25 (10%). The RT techniques were INRT in 10% and ISRT in 90% of the patients (Table 1).

Organ at risk (OAR) Dosimetry

Table 2 details the mean dose delivered to the PTV for both techniques used in this study. The mean PTV coverage in the non-coplanar group was significantly better than that of the coplanar VMAT group (97.42% > 96.9%), with a statistically significant difference (p = 0.005).

Analysis of the dose delivered to the heart revealed that the mean dose in the non-coplanar plans was significantly greater than that of the coplanar arm (233.019 > 214.68 cG), with a highly significant difference (p < 0.0001) (Table 3).

Table 4 shows the dose delivered to the right lung at V20 and V5 for both techniques. The mean dose at V20 in the coplanar plans was nearly the same as that in the noncoplanar plans, with no significant difference (p = 0.606). The mean dose at V5 in the coplanar plans was greater than that in the noncoplanar plans with no significant difference (p = 0.118).

Table 5 reveals the dose delivered to the left lung at V20 and V5 for both techniques. The mean dose at V20 in the coplanar plans was significantly higher than that in the noncoplanar plans (p = 0.007). The mean dose at V5 in the coplanar plans was similar to that in the noncoplanar plans, with no significant difference (p = 0.264).

Table 1. The baseline demographic and clinical characteristics of patients.

Variables		No. / mean ± SD	%
Age (years)		31.3±9.11	-
Sex	Male	12	40.0
	Female	18	60.0
Residency	Rural	11	36.7
	Urban	19	63.3
Regimen of chemotherapy	R-CHOP	11	36.7
	ABVD	19	63.3
Stage	I	18	60.0
	II	11	36.7
	III	1	3.3
Symptoms	B-symptoms	17	56.7
	Dyspnea	8	26.7
	Weight loss	5	16.6
HL	Classical MC	9	47.4
	Classical NS	9	47.4
	Other	1	5.2
NHL	DLBCL	8	72.7
	Follicular	3	27.3
Site	Mediastinum	21	70.0
	Mediastinum + cervical	9	30.0
Dose of radiotherapy (Gy/fx)	30/15	8	26.7
	36/18	16	53.3
	36/20	3	10.0
	45/25	3	10.0
RT protocol	INRT	3	10.0
	ISRT	27	90.0

Table 2. Dosimetric parameters for VMAT plans (Coplanar and non-coplanar) for PTV.

Parameter	Coplanar	Non-coplanar
Mean %	96.9 ± 1.44	97.42 ± 1.47
Median %	96.22	97.28
Minimum %	95.07	95.09
Maximum%	99.96	99.97
95% CI	-0.87-—-0.17-	
t-test	-3.06-	
P value	0.005	

Table 3. Dosimetric parameters for VMAT plans for heart.		
Parameter	Coplanar	Non-coplanar
Mean cGy	233.019 ± 122.95	214.68 ± 115.07
Median cGy	258.9	244.5
Minimum cGy	17.7	21.5
Maximum cGy	468.8	450.1
95% CI	11.27–25.75	
t-test	5.23	
P value	< 0.0001	

Table 4. Dosimetric parameters for VMAT plans for right lung at V20 and V5.				
Parameter	Right lung V20		Right lung V5	
	Coplanar	Non-coplanar	Coplanar	Non-coplanar
Mean %	14.92 ± 7.88	14.84 ± 7.82	49.12 ± 22.82	46.47 ± 19.64
Median %	15.77	14.67	40.52	44.64
Minimum %	2.96	2.54	6.6	6.7
Maximum %	29.65	29.45	83.6	80.2
95% CI	-0.24–0.41		-0.71–6.01	
t-test	0.522		1.61	
P value	0.606		0.118	

Table 5. Dosimetric parameters for VMAT plans for left lung at V20 and V5.				
Parameter	Left lung V20		Left lung V5	
	Coplanar	Non-coplanar	Coplanar	Non-coplanar
Mean %	16.18 ± 8.45	15.21 ± 7.41	44.91 ± 18.84	43.99 ± 18.89
Median %	17.27	17.56	43.69	44.21
Minimum %	0	0	3.32	3.82
Maximum %	26.3	23.7	76.45	74
95% CI	0.28–1.64		-0.72–2.56	
t-test	2.895		1.139	
P value	0.007		0.264	

Table 6 presents the mean doses delivered to the spinal cord using both techniques. The mean dose in the coplanar VMAT group was greater in comparison to the non-coplanar group (1982.36 ± 479.82 > 1888.7 ± 502.78 cG), with a highly significant difference (p = 0.003).

Table 7 shows the mean doses delivered to the esophagus in both techniques. The mean dose in the coplanar group was greater than that in the non-coplanar plans (1866.92 ± 809.99 > 1641.09 ± 646.62 cG), but the difference was not significant (p = 0.054).

Table 8 lists the doses delivered to both breasts using both techniques. In both sides, the coplanar arm had greater dose than the non-coplanar group, with no significant difference (p = 0.7 and 0.172), respectively.

Table 6. Dosimetric parameters for VMAT plans for spinal cord.		
Parameter	Coplanar	Non-coplanar
Mean cGy	1982.36 ± 479.82	1888.7 ± 502.78
Median cGy	2005.5	1849.5
Minimum cGy	863.5	863.0
Maximum cGy	3016.8	2999.3
95% CI	34.74–152.57	
t-test	3.251	
P value	0.003	

Table 7. Dosimetric parameters for VMAT plans for esophagus.		
Parameter	Coplanar	Non-coplanar
Mean cGy	1866.92 ± 809.99	1641.09 ± 646.62
Median cGy	1684.25	1465.45
Minimum cGy	873.8	855.6
Maximum cGy	3731.0	3731.0
95% CI	(-4.45) - (- 456.11)	
t-test	2.029	
P value	0.054	

Table 8. Dosimetric parameters for VMAT plans for right and left breasts.				
Parameter	Right breast		Left breast	
	Coplanar	Non-coplanar	Coplanar	Non-coplanar
Mean cGy	341.44 ± 159.47	295.78 ± 110.5	411.8 ± 286.15	392.87 ± 253.95
Median cGy	299.9	316.0	323.1	334.5
Minimum cGy	185.4	124.0	140.6	117.4
Maximum cGy	606.8	428.2	894.4	809.4
95% CI	-4.42 – 95.74		-9.48 – 47.32	
t-test	1.986		1.451	
P value	0.07		0.172	

DISCUSSION

In the present study, 30 patients with lymphoma (19 HL cases and 11 NHL cases) participated, with a mean age of 31.3 ± 9.11 years. Females made up the majority (60%) of the participants, most of whom resided in urban areas (63.3%). Stage I lymphomas accounted for 60% of the cases, whereas stage II and stage III lymphomas accounted for 36.7% and 3.3%, respectively. The majority of patients presented with B symptoms (56.7%). The HL subclasses included classical MC and NS (47.4%), while NHL subclasses were DLBCL (72.7%) and follicular lymphoma (27.3%). The most common sites of lymphomas were the mediastinum (70%) and mediastinum + cervical (30%). All cases treated using the VMAT technique were either coplanar or non-coplanar. The RT doses (Gy/fx) were divided into 30/15 (26.7%), 36/18 (53.3%), 36/20 (10%) and 45/25 (10%). The RT techniques used were INRT in 10% and ISRT in 90% of the patients. In comparison to Alhilfi et al.,[16] who studied 80 cases aged (mean ± SD) 36±12.8 years, our study had different demographics. Most of our participants (67.5%) lived in rural areas and the male-to-female ratio was 1.5:1 (48 males and 32 females). NHL was three times more prevalent than HL, mostly at stage IV. However, our findings align with theirs regarding classical subtypes of lymphomas.

The most frequent histological subtype of HL was mixed cellularity, which deviates from earlier reports from the north of Iraq[17,18] but is consistent with earlier reports from other countries, such as Jordan,[19] Oman,[20] Saudi,[21,22] Bahrain,[23] UAE,[24] Kuwait,[25], and India.[26]

Jalili et al.[27] studied 659 cases of lymphoma diagnosed between 2018 and 2021, revealing that approximately 59% of the patients were men. The participants' mean age was 50.5 ± 19.8 years. Most cases (61.6%) were mature B-cells, 8.8% were mature T-cells, and 27.5% were HL. DLBCL stands out as the most prevalent NHL subtype worldwide.

In Iran, other studies have reported higher rates of HL frequency compared to other countries, ranging from 10% to 40%.[28] This could be attributed to Iran having one of the highest HL proportions in the world due to geographical variations. Similarly, other countries in the Middle East and North Africa, such as Jordan, Bahrain, and Lebanon, have also reported high percentages of HL (24–39%).[29]

In Western countries, HL exhibits a bimodal age distribution with a peak incidence in the 3rd and 6th decades of life.[29,30]

Studies in Middle East and North Africa (MENA) countries[31] reported similar data on NHL distribution. However, a greater number of cases have been reported in most East Asian countries, such as South Korea (72.5%),[32] China (64.4%),[33] Sri Lanka (65.1%),[34] and Thailand (78.3%).[35] B-cell lymphoma (BCL) constitutes a large proportion of NHL in the USA (83.5%)[36] and Europe (79.9%).[37]

Laurent et al.[38] examined 938 lymphoma cases and found that the most frequent sites were cervical (36.8%), inguinal (16.4%), axillary (11.9%), and supraclavicular (11%), which is inconsistent with the results of the current study.

In this study, the mean PTV coverage in the non-coplanar group was significantly better than that in the coplanar VMAT (97.42 > 96.9), with a statistically significant difference ($p = 0.005$). Regarding the dose delivered to the heart, the mean of coplanar plans was greater than non-coplanar arm (233.019 > 214.68 cG) with a high significant difference ($p < 0.0001$). The mean dose to the right lung at V20 in the coplanar plans was nearly identical to that in the non-coplanar plans, with no significant difference. However, the mean dose at V5 in the coplanar plans was greater than that in the noncoplanar plans, with no significant difference. Furthermore, the mean dose to the left lung at V20 in the coplanar plans was significantly higher than that in the non-coplanar plans ($p = 0.007$). The mean dose at V5 in the coplanar plans was similar to that in the noncoplanar plans, with no significant difference. The mean dose of the spinal cord in coplanar VMAT was greater than non-coplanar group with a highly significant difference ($p = 0.003$). The mean dose to the esophagus in the coplanar group was greater than that in the non-coplanar plans, with no significant difference. On both sides of the breast, the coplanar arm had a greater dose than the non-coplanar arm, with no significant difference. Similarly, Oertel et al.[39] reported dosimetric data on the plans of 139 patients with mediastinal lymphomas. The mean dose to the PTV was 5.3 to 34.2 Gy (median: 30.0 Gy). RT techniques were predominantly three-dimensional conformal radiation therapy (3DCRT) (54.0%) in comparison to advanced approaches such as VMAT (46.0%). There was no significant difference in PTV size between the two techniques. The mean doses to the heart and right and left lungs were 13.3 Gy, 10.1, and 10.8 Gy. There was a significant correlation between PTV volume and the mean lung dose ($p < 0.001$) and mean heart dose ($p < 0.001$). There was no significant

correlation between PTV size and the mean dose to the right (p = 0.601) or left breast (p = 0.654).

RT to the mediastinum may lead to a spectrum of illnesses, such as cardiomyopathy, coronary heart disease (CHD), conduction disorders, valvular dysfunction, pericardial effusion, or inflammatory diseases.[40] The cardiac substructures reveal a different response to radiation exposure in CHD because of the linear correlation with the mean dose of the heart.[41] In the lungs, RT induces damage to the alveolar epithelium, such as cell senescence, DNA damage, (sub-)acute pneumonitis, and chronic consecutive lung fibrosis.[40]

In the study by Oertel et al.,[39] when comparing IFRT- and INRT-groups, most OAR parameters did not show significant differences except for V25 in both lungs, which disagreed with the left lung and agreed with the right lung. The maximum dose to the spinal cord was significantly different (p < 0.001), which aligns with our findings. The mean dose to the esophagus was similar (p = 0.044).

The ILROG recommends reducing the mean heart, breast, and lung doses below 5, 4, and 10 Gy, respectively.[42]

Interestingly, bulky disease and extranodal spreading significantly impacted low-dose lung exposure, which may be associated with an increase in secondary lung cancers.[43] The ILROG recommends keeping the respective doses below 55%, with precautions established to ensure that V5 is never over 60%.[42,44]

Oertel et al.[39] documented significant differences in V5 to the left lung and mean heart dose but with different distributions in each subgroup, which is similar to the data of this study. Additionally, they[45] analyzed a larger patient collective in HD17 and found a reduction in V20–V30 to the lungs with a concomitant raise in V5–V10 with modern Intensity-modulated radiation therapy (IMRT).

The German Hodgkin Study Group (GHSG) has a long-standing tradition of quality assessment and analysis of treatment protocols.[45] This showed a decline in relapse-free survival (72% with relevant protocol violations vs. 84% without).[39]

Jones et al.[46] and Liu et al.[47] concluded that the use of deep inspiration breath-hold (DIBH) resulted in lower estimated doses to the lungs, breasts, and heart than free breathing (FB), which may reduce the probability of pulmonary, breast, and cardiac radiation toxicities.

Similarly, Campbell et al[48] demonstrated the benefits of reducing the RT field size from IFRT to INRT and decreasing the proportion of tissues receiving higher radiation doses. In the IFRT plans, the mean V95% was 2625.9 cm3 (1010–4286). In the conventional INRT plans, the mean V95% was 1474.6 cm3 (range, 800–2946). Thus, reducing the field size from IFRT to INRT decreased the volume of tissue that received over 95% of the prescribed dose. In addition, they reduced the field sizes from IFRT to INRT, which was associated with relative reductions in the mean doses received by the lungs, breasts, and heart by 0.29, 0.33, and 0.35, respectively. VMAT has also been shown to reduce the volumes of OAR receiving high-dose radiation, leading to relative reductions in the mean lung V20 by 0.56, breast by 0.95, and heart by 0.85.

The rationale behind implementing INRT is to minimize RT-induced morbidity while maintaining the excellent disease control achieved by IFRT. Cardiac toxicity and secondary malignancy are the most concerning among these radiation-induced late morbidities, constituting the most common causes of non-lymphoma death in long-term HL survivors. The dosimetric advantages of reducing the RT field sizes to INRT are twofold: reducing the volumes of the OARs exposed and reducing the total doses of radiation received by the OARs.[49]

In this study, the median survival for HL was 11 months), while it was 12 months for NHL. Additionally, patients under coplanar plans had a survival rate of 10.36 months, whereas those under non-coplanar plans had a survival rate of 8.13 months. The recurrence rate in this study was 23.3%, and the risk of cardiac toxicity was 3.3%. Many clinical studies have demonstrated that reducing RT field sizes from EFRT to IFRT decreases the incidence of secondary malignancies.[50] Campbell et al.[48] concluded that dropping the field size from IFRT to INRT reduces radiation exposure to the lungs, breasts, and heart in HL. These improvements are likely to translate into lower rates of radiotherapy-induced toxicity, including the risk of second malignancy. VMAT for INRT may play a useful role in individualizing INRT for patients at high risk of radiotherapy-induced morbidity.

Murray et al.[51] calculated dosimetric parameters and found that IFRT resulted in significantly elevated doses to normal tissue. Compared to ISRT, both INRT and residual techniques resulted in significantly lower normal tissue doses, except for breast V5 and breast V20. Although INRT led to significantly lower doses than ISRT, the differences were less pronounced than those between ISRT and residual techniques.

Maraldo et al.[52] reported no marginal failures in a retrospective study of 97 HL patients treated with

chemotherapy and INRT. The interim analysis of the Raemaekers et al. study, which used INRT in the control arm of patients with HL, showed rates of disease progression similar to previous data with IFRT.[53] In a retrospective analysis of 258 NHL cases treated with the INRT technique, only one case failed in a region that would have been enrolled in the radiation fields if treated with IFRT.[54]

Murray et al.[51] demonstrated similar findings as the present study, indicating a reduction in doses to the lung, heart, and esophagus when comparing ISRT and INRT techniques with IFRT; only small differences were observed regarding breast doses. This finding is supported by Koeck et al.[55] and Reymen et al.[56]

ISRT leads to a significant reduction in relative cancer risks based on the organ equivalent dose (OED) compared to IFRT for lung, thyroid, and breast OARs. INRT OEDs were significantly lower than ISRT OEDs for the thyroid, lung, and breast. The median values were consistently lowest for the residual technique and highest for IFRT in terms of thyroid, lung, and breast cancers. The risk of esophageal cancer was similar for all four techniques.[51]

Meyer et al.[57] reported an overall survival (OS) rate of 87% in patients who received RT and disease free survival (DFS) rate of 92% after 12 years of follow-up. However, 10 patients died from HL-related treatment complications, whereas no deaths were recorded in the present study. The OS rate was 97% and DFS rate was 93% when combined therapy was used, according to Huang et al.[58]

Murray et al.[51] concluded that decreasing the treatment volumes from IFRT to ISRT and INRT reduces radiation exposure to OAR. Second malignancy modelling suggests that this reduction in treatment volume will lead to a reduction in absolute excess second malignancies.

CONCLUSIONS

The mean PTV coverage in the non-coplanar group was better than that in the coplanar VMAT group. Additionally, the heart received a greater mean dose in the coplanar plans than in the non-coplanar group, while the lungs received a greater mean dose in the coplanar plans than in the non-coplanar plans. Furthermore, the spinal cord received a greater mean dose in the coplanar plans than in the non-coplanar plans. Low recurrence rates and cardiac toxicity hazards were observed in patients with lymphoma who completed chemotherapy and radiotherapy. Another study investigated the role of radiotherapy in the treatment of extranodal lymphomas. A comprehensive clinical, medical physics, and dosimetric study of pediatric lymphomas is currently underway. It is imperative to conduct a longer follow-up on a large cohort study on mediastinal lymphoma to gather more conclusive data.

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