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Evaluation of Relapse Rate and Survival Outcome of Patients with Diffuse Large B Cell Lymphoma after Consolidative Irradiation: Retrospective Study

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ABSTRACT

Background: Non-Hodgkin lymphomas are the most common lymphoid neoplasms of the lymphoid system in adults, accounting for anywhere from 4% to 10% of all malignancies worldwide. Diffuse large B-cell lymphoma (DLBCL) is the most dominant histological subtype.

Objective: This study aimed to assess the relapse rate and secondary endpoint, which was the survival outcome of DLBCL following consolidative irradiation.

Methods: This retrospective descriptive phase II study included 105 patients with DLBCL and received consolidation radiotherapy (RT) at Clinical Oncology Department, Tanta University Hospitals. The patients underwent chemotherapy and RT. The response was evaluated through computed tomography (CT)-scan or positron emission tomography/CT scan and bone marrow in those with involved bone marrow.

Results: The three-year overall survival (OS) was higher in patients with good performance status (ECOG0-1) compared to those with poor performance status (97% vs. 81% respectively). The difference was statistically significant ($p = 0.015$). The three-year OS was higher in patients without relapse compared to those with relapse (97% vs. 70% respectively). The difference was statistically significant ($p = 0.000$). The three-year OS was higher in patients with CR after consolidative RT compared to those with SD after consolidative RT (98% vs. 52% respectively). The difference was statistically significant ($p = 0.000$).

Conclusions: Consolidative RT remains a valuable component in the management of DLBCL, particularly for patients with bulky disease and adverse prognostic factors. Its selective use alongside immunochemotherapy may contribute to improved disease control and support individualized treatment strategies.

Keywords: Diffuse large B cell lymphoma, Relapse rate, Survival outcome, Consolidative irradiation.

INTRODUCTION

Non-Hodgkin lymphomas (NHL) are the most common lymphoid neoplasms of the lymphoid system in adults, accounting for approximately 4% to 10% of all malignancies worldwide. Its dominant histological subtype is the diffuse large B-cell lymphoma (DLBCL). A five-year survival rate of approximately 71% is achieved for all patients with NHL[(1)]. Aggressive (fast-growing) and indolent (slow-growing) are the two distinct clinical characteristics of mature B cell NHLs. Up to 50% of all NHL patients are comprised of the former [(2)]. The disease is staged in accordance with the Ann Arbor staging model. Stages I and II are classified as early stages, while substantial stages II, III, and IV are considered advanced stages. Combination chemotherapy is typically administered to early-stage diseases, which are subsequently treated with radiation to the afflicted sites. The results are generally favorable [(3)]. The utilization of ionizing radiation to eliminate malignant cells is known as radiotherapy (RT). It is frequently used to treat massive diseases, which are themselves an independent adverse prognostic factor. It is efficacious in the elimination of residual disease and the improvement of local control when RT is administered as consolidation therapy [(4)]. The poor prognosis that voluminous diseases confer has been demonstrated to be ameliorated by the addition of consolidation RT [(5)].

In early-stage aggressive NHL, consolidation RT has been investigated. Compared to a protracted course of chemotherapy alone, after abbreviated chemotherapy, the incorporation of consolidation RT has been demonstrated to yield a substantial five-year improvement in overall survival (OS) and progression-free survival (PFS) [(6)].

The objective of this study was to assess the relapse rate and assess the survival prognosis of diffuse large B cell lymphoma following consolidative irradiation.

PATIENTS AND METHODS

This retrospective descriptive phase II study was carried out on 105 patients with DLBCL and received consolidation RT at Clinical Oncology Department, Tanta University Hospitals throughout the period from September 2018 to September 2023.

Inclusion criteria: Patients with histopathological diagnosed DLBCL, who were administered chemotherapy with or without rituximab and who obtained a complete or partial response (PR), age ≥ 18 years, with world Health Organization performance status of ≤ 2 according to eastern cooperative oncology group (ECOG) [(7)], and patient with bulky (diameter ≥7.5 cm) disease or extra nodal disease.

All medical files were revised for careful history taking including personal history (age, sex, occupation, residence, marital status and personal habits), medical comorbidities including (diabetes mellitus, hypertension & cardiac disease), clinical examination including complete general examination and local examination. Laboratory investigations were conducted on all patients at the time of their initial presentation.

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These investigations included a complete blood count (CBC), serum blood chemistry, liver and renal function tests, fasting, and post-prandial blood sugar profiles, serum lactate dehydrogenase (LDH), and hepatitis (B & C). Additionally, all patients underwent CBC, hepatic, and renal function tests prior to the commencement of each preoperative computed tomography (CT) cycle.

Radiological examinations, such as computed tomography (CT) of the head, neck, thorax, abdomen, and pelvis with contrast, echocardiograms and positron emission tomography (PET_CT). Pathological findings including pathologically proven diffuse large B cell lymphoma by complete excision biopsy and CD20 +ve. All patients were evaluated according to Ann Arbor stage and international prognostic index (IPI). The number of cycles according to stage and dose of RT were collected from files. Chemotherapy including early stages received 4 cycles and advanced stages received 6 cycles.

RT was initiated approximately three to four weeks following the final chemotherapy dose. It was administered concurrently with rituximab without incident. Prophylactic anti-emetics were administered to patients who were undergoing radiation therapy to a significant portion of the abdomen. Simulation of the supine position, which includes the head and neck; arms by the side or on the chest; chin extended; thorax; arms above the head or by the sides; arms on the chest. The immobilisation and support of the head and neck were determined by the area of irradiation. Neck support, immobilisation mask, and shoulder retractors were employed, while the thorax was immobilised using a wing board and vacuum device. The pelvis was in an inclined position, and knee supports were employed. When irradiation of abdominal or pelvic sites was necessary, oral contrast/bolus was necessary. Bolus was employed when the target volume was in close proximity to the surface.

CT simulation including technique for RT for all patients was Intensity Modulated Radiation Therapy. By linear accelerator (unique), treatment planning was conducted using the Eclipse 13.7 treatment planning system from Varian. The Varian Trilogy linac, which consisted of a 120-leaf Millennium Multileaf Collimator, generated six MV photon beams. The dose calculations were conducted using the analytical anisotropic algorithm incorporated into the Eclipse treatment planning system (Varian Medical Systems). Depending on the tumor's location, each IMRT plan used 5 to 9 coplanar beams.

Initially, the treatment planning system was loaded with a set of initial optimization targets, and the beam angle optimization method was used to optimize the IMRT beam angles. The dosimetrists' expertise informed the adjustment of many beam angles. For each plan, an average of 40 segments were used based on 9 (whose angels were 0, 40, 80, 120, 160, 200, 240, 280, 320 degrees) coplanar beams with the angles depending on the tumor location.

Target volume involved site radiation therapy that was given. If separate nodal volumes were involved, they were potentially be encompassed in the same clinical target volume. If the involved nodes were more than 5 cm apart, they were treated with separate fields. Dose prescription according to radiation therapy oncology group (RTOG) guidelines, the dose prescription for consolidative RT after chemotherapy in DLBCL depended on disease response and initial tumor site. For CR (PET negative) after chemotherapy: 30-36 Gy, with beam energy (6-15 MV), (1.8 Gy/fraction), (5 fractions/week) was given. For PR (PET positive) after chemotherapy: 40-50 Gy, with beam energy (6-15 MV), (1.8 Gy/fraction), (5 fractions/week) was given. Target verification was done for all cases using bone weekly.

Toxicity was evaluated according to RTOG (acute or late). The response was evaluated through CT-scan or PET-CT scan and bone marrow (BM) in those with involved BM. Follow-up visits usually included a review of symptoms, physical examination, full blood count and biochemical profile including serum LDH and routine surveillance scanning in the form of CT or PET-CT.

Ethical approval: The investigation was directed with the approval of the Ethics Committee of the Faculty of Medicine at Tanta University Hospitals (approval code: 36264MS322/9/23). Informed written consent were obtained from all participants. The study followed The Helsinki Declaration through its execution.

Statistical analysis

This study used SPSS version 21.0, a statistical package for social science, to examine the data that had been collected, coded, and inputted into a computer. Quantitative data were shown as median, means, and standard deviation. Qualitative data were shown as frequency distribution with its percentage.

Quantitative data were compared using analysis of variance (ANOVA), whilst qualitative data were compared using Chi-square test and Fisher's t-test. From the time of diagnosis until the recorded date of death or last follow-up, OS was used as the definition. The time it took to go from starting treatment until the disease progressed or the patient died was called progression free survival. The many prognostic factors influencing the treatment were analyzed using Kaplan-Meier in a univariate fashion, and differences in survival curves were evaluated using the Log-rank test. The Cox regression model was used to calculate the multivariate analysis. The threshold for determining significance was a p-value less than 0.05.

To find out if there was a statistically significant relationship between two categories, we employed Fisher's exact test. Log-rank and Pearson's Chi-squared tests were employed.

RESULTS

Table (1) showed the clinicopathological characteristics of patients including (Patient characteristic, B symptoms, bulky (≥ 7.5.cm), extra-nodal and BM involvement). Regarding relapse, RT was administered to all patients, 79% were nodal and 21% were extra nodal sites. Seventy-nine percent of patients achieved chemotherapy response (CR) after consolidative RT. Relapse was experienced in 22.9% of patients. Most common site of relapse was combined.

Table (1): The clinicopathological characteristics of patients

Patient characteristic		**N=105 (%)**
Median age (years)	**< 58years**	48 (45.7%)
	≥58years	57 (54.3%)
Sex	**Male**	71 (67.6%)
	Female	34 (32.4%)
Ann arbor stage	**Stage I +II**	43 (41%)
	Stage III + IV	6 (259%)
B symptoms	**No**	49 (46.7%)
	Yes	56 (53.3%)
PS	**0-1**	70 (66.7%)
	2	35 (33.3%)
LDH (U/L)	**Normal**	38 (36.2%)
	Elevated	67 (63.8%)
Bulky (≥ 7.5.cm)		85 (79 %)
Presenting site at diagnosis	**Above diaphragm**	63 (60%)
	Below diaphragm	29 (27.6%)
	Both	13 (12.4%)
Extra-nodal	**No**	83 (79%)
	Yes	22 (21%)
Extra-nodal sites	**Stomach**	10 (45.5%)
	Brain	3 (13.6%)
	Testicular	3 (13.6%)
	Oropharyngeal	2 (9.1%)
	Liver	2 (9.1%)
	Kidneys & adrenal	2 (9.1%)
Bone marrow involvement	**No**	93 (88.6%)
	Yes	12 (11.4%)
IPI score	**0-1**	29 (27.6%)
	2-5	76 (72.4%)
Chemotherapy	**R-CHOP**	104 (99.04%)
	ICE	1 (0.95%)
Number of cycles of chemotherapy	**Stage I +II (4 cycles)**	43 (41%)
	Stage III + IV (6 cycles)	62 (59 %)
Post-chemotherapy response	**CR**	39 (37.1%)
	PR	66 (62.9%)
RT sites	**Bulky**	83 (79%)
	Extra-nodal	22 (21%)
Relapse		24 (22.9%)
Response after RT	**CR**	83 (79%)
	SD	22 (21%)
Site of relapse	**In-radiation site**	3 (12.5%)
	Distant recurrence	6 (25%)
	Combined	15 (62.5%)

Data are presented as frequency (%). PS: performance states, LDH: Lactate dehydrogenase, CR: Complete response, CT: Computed tomography, PR: Partial response, ICE: Ifosfamide, carboplatin, and etoposide.

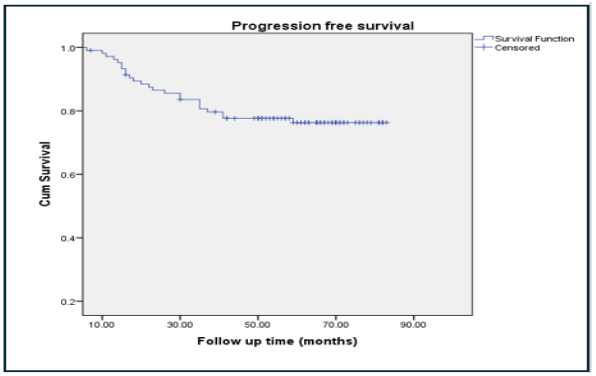
Acute toxicity related to RT was observed in 30.5% of patients, with the majority (69.5%) experiencing no toxicity. Among those affected, fatigue was the most frequently reported side effect (62.5%), followed by GIT toxicity (15.6%), CNS toxicity (9.4%), and both mucositis and skin toxicity (6.3% each). Most toxicities were mild to moderate in nature: 62.5% were grade G1, 34.4% were G2, and only 3.1% were G3. No cases of life-threatening (G4) or fatal (G5) toxicity were reported. 5 patients (4.8%) of them in our study developed chronic toxicity, with fatigue (G2) being the most common late effect (4 cases), and one patient presenting with chronic gastritis (G1) (Table 2).

Table (2): RT toxicity, grades of acute toxicity and late toxicity

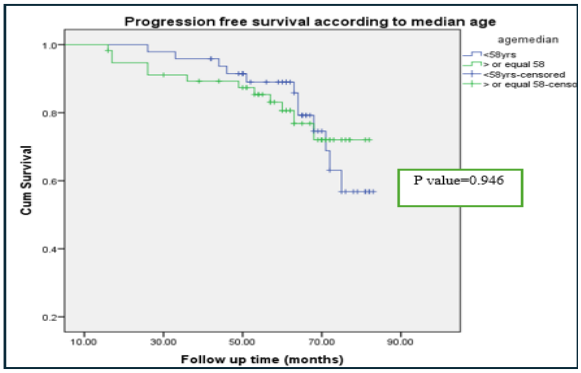
Characteristic				**N= 105**			
Toxicity of RT, n (%)				32 (30.5%)			
Type of toxicity, n (%) (From a total of 32)				**CNS toxicity**			3 (9.4%)
				Fatigue			20 (62.5%)
				GIT toxicity			5 (15.6%)
				Mucositis			2 (6.3%)
				Skin toxicity			2 (6.3%)
Grades of acute toxicity							
		Mild G1	**Moderate G2**	**Severe G3**	**Life threatening G4**	**Fatal G5**	**Total**
Type of toxicity	**CNS toxicity**	2 (66.7%)	1 (33.3%)	0 (0.0%)	0(0.0%)	0(0.0%)	3 (100.0%)
	Fatigue	13 (65.0%)	7 (35.0%)	0 (0.0%)	0(0.0%)	0(0.0%)	20(100.0%)
	GIT toxicity	4 (80.0%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	5 (100.0%)
	Mucositis	0 (0.0%)	(1 50.0%)	1 (50.0%)	0(0.0%)	0(0.0%)	2 (100.0%)
	Skin toxicity	1 (50.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)
	Total	20 (62.5%)	11 (34.4%)	1 (3.1%)	--	---	32 (100.0%)
Grades of late toxicity							
Type of toxicity	**Fatigue**	0 (0.0%)	4 (80%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (80%)
	GIT toxicity	1 (20%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20%)
	Total	1 (20%)	4 (80%)	0 (0.0%)	----	----	5 (100.0%)

Data are presented as frequency (%), CNS: central nervous system, GIT: gastrointestinal tract.

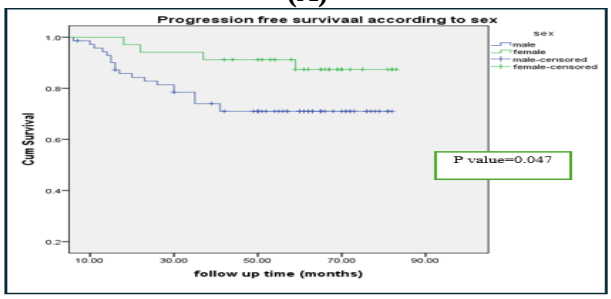
Figure 1A: PFS declines over time. The three-year progression free survival was 78%. **Figure 1B**: The three-year PFS was higher in patients < 58 years compared to those ≥ 58 years (79% vs. 77%, respectively); with no statistically significant difference between them. **Figure 1C**: The three-year PFS was higher in females compared to males (83% vs. 76% respectively) and the difference was statistically significant (p = 0.047). **Figure 1D**: The three-year PFS was significantly higher in early stages (I +II) compared to advanced stages (III + IV) (93% vs. 68% respectively) (p = 0.001). **Figure 1E**: The three-year PFS was significantly higher in patients with no B symptoms compared to with B symptoms (92% vs. 65% respectively) (p = 0.003). **Figure 1F**: The three-year PFS was non-significantly higher in patients with good performance status (ECOG 0-1) compared to those with poor performance status (81% vs. 71% respectively). **Figure 1G**: The three-year PFS was significantly higher in patients with normal level compared to those with elevated LDH (92% vs. 70% respectively) (p = 0.006). **Figure 1H**: The three-year PFS was non-significantly higher in patients with non-bulky disease compared to those with bulky (80% vs. 77% respectively). **Figure 1I**: The three-year PFS was significantly higher in patients with disease above diaphragm compared to those with blow diaphragm and both sides of diaphragm (89% vs. 69%vs.46% respectively) (p = 0.000). **Figure 1J**: The difference of three-year PFS was insignificant between groups however it was higher in patients with no extra-nodal disease compared to those with extra-nodal disease (82% vs. 77% respectively). **Figure 1K**: The three-year PFS was lower in patients with BM involvement compared to those with no BM involvement (67% vs. 79% respectively). The difference was not statistically significant. **Figure 1L**: The three-year PFS was non-significantly higher in patients with IPI score (0-1) compared to those with IPI score (2-5) (86% vs. 75% respectively). The difference was not statistically significant. **Figure 1M**: The three-year PFS was statistically significantly different between both group (p = 0.001) where it was higher in patients with CR compared to those with PR (95% vs. 68% respectively). The difference was statistically significant (p = 0.001). **Figure 1N**: The three-year PFS was non-significantly higher in patients with extra-nodal disease compared to those with bulky disease (82% vs. 77% respectively). The difference was not statistically significant **Figure 1O**: The three-year PFS was significantly higher in patients with CR after consolidative RT compared to those with stable disease (SD) after consolidative RT (95% vs. 14% respectively) (p = 0.000). **Figure 1 P**: The three-year PFS was non-significantly higher in patients with relapse in radiation field, distant relapse & combined (35% vs. 0% vs. 30% respectively). The difference was not statistically significant.


Progression free survival
Survival Function
Censored
Cum Survival
Follow up time (months)

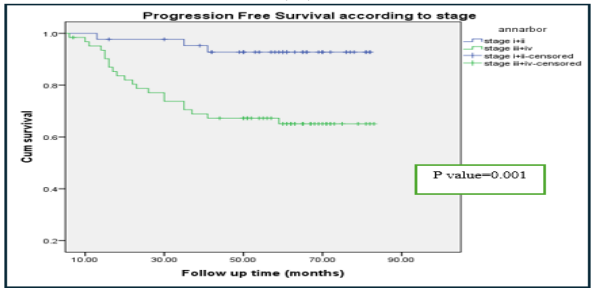
(A)


Progression free survival according to median age
agemedian
<58yrs
> or equal 58
<58yrs-censored
> or equal 58-censo
Cum Survival
P value=0.946
Follow up time (months)

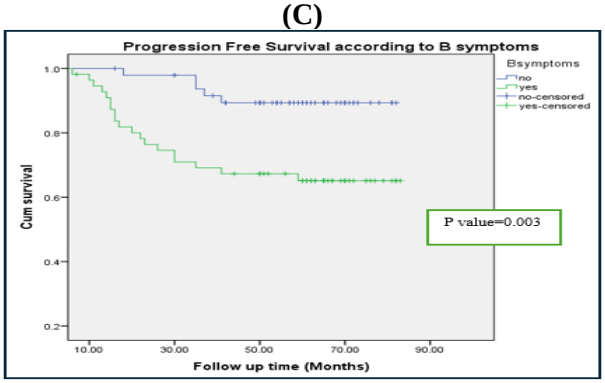
(B)


Progression free survivaal according to sex
sex
male
female
male-censored
female-censored
Cum Survival
P value=0.047
follow up time (months)

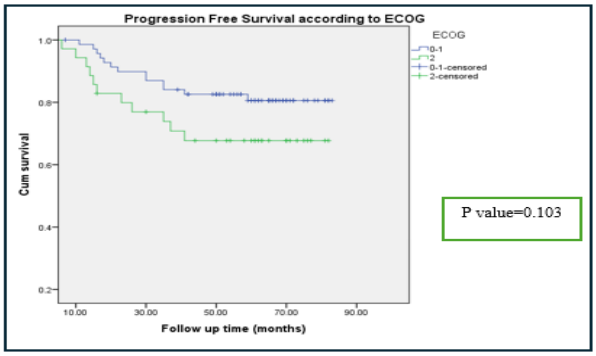
(C)


Progression Free Survival according to stage
annarbor
stage i+ii
stage iii+iv
stage i+ii-censored
stage iii+iv-censored
Cum survival
P value=0.001
Follow up time (months)

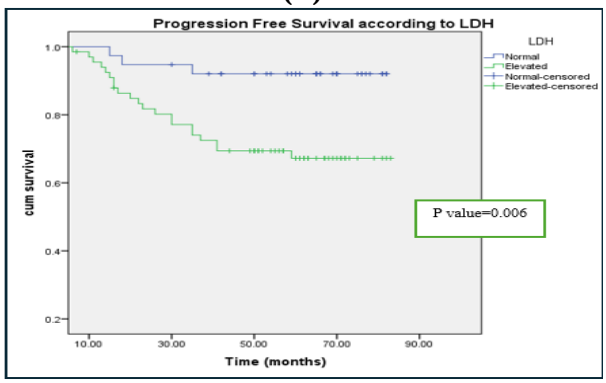
(D)


Progression Free Survival according to B symptoms
Bsymptoms
no
yes
no-censored
yes-censored
Cum survival
P value=0.003
Follow up time (Months)

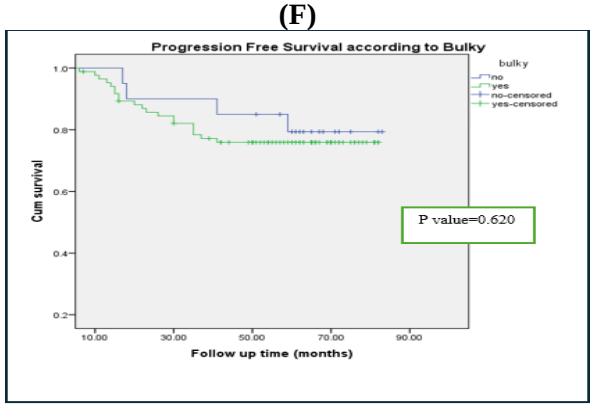
(E)


Progression Free Survival according to ECOG
ECOG
0-1
2
0-1-censored
2-censored
Cum survival
P value=0.103
Follow up time (months)

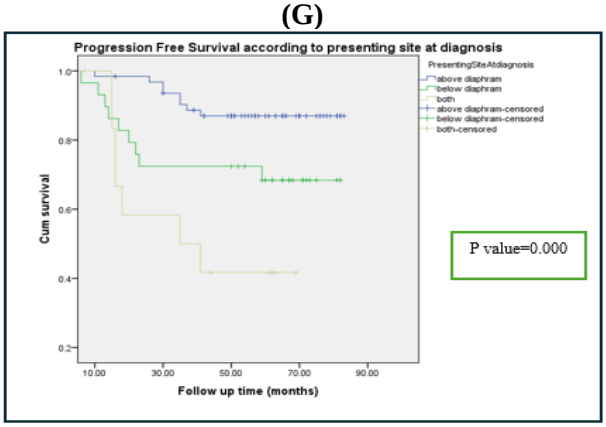
(F)


Progression Free Survival according to LDH
LDH
Normal
Elevated
Normal-censored
Elevated-censored
cum survival
P value=0.006
Time (months)

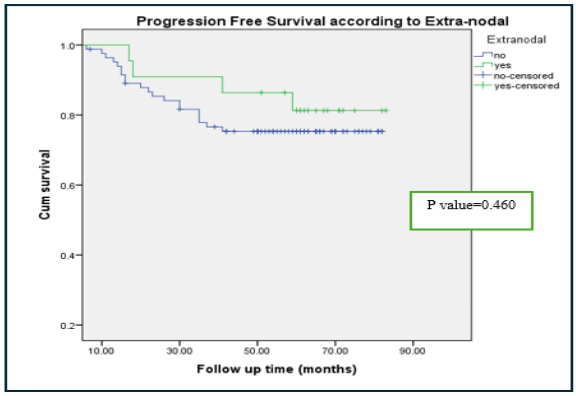
(G)


Progression Free Survival according to Bulky
bulky
no
yes
no-censored
yes-censored
Cum survival
P value=0.620
Follow up time (months)

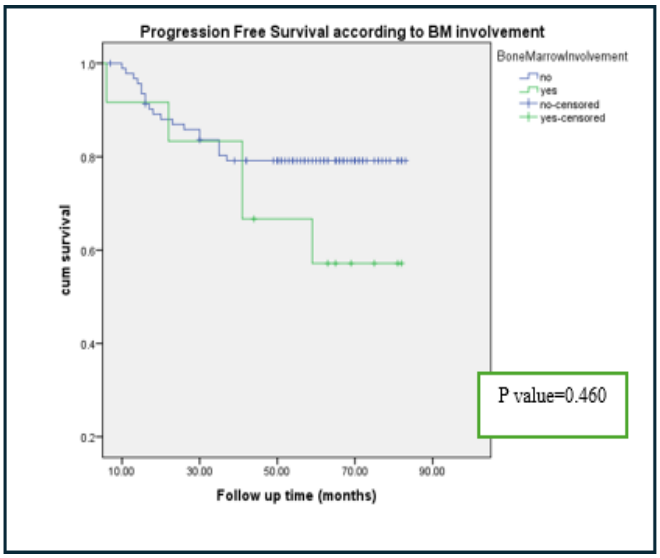
(H)


Progression Free Survival according to presenting site at diagnosis
PresentingSiteAtdiagnosis
above diaphram
below diaphram
both
above diaphram-censored
below diaphram-censored
both-censored
Cum survival
P value=0.000
Follow up time (months)

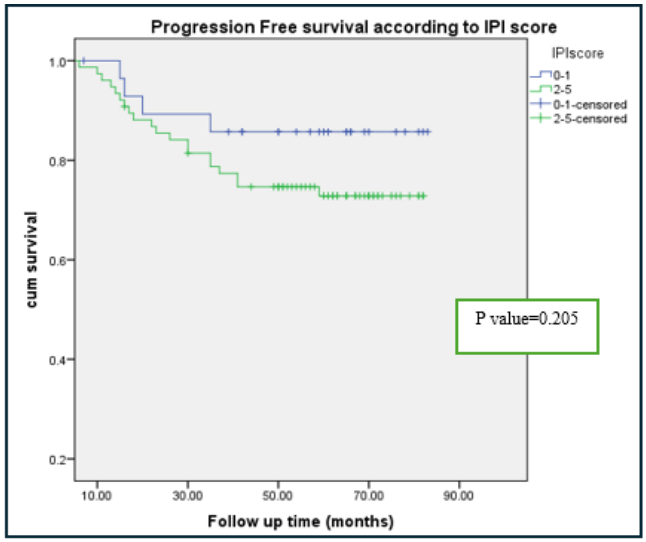
(I)


Progression Free Survival according to Extra-nodal
Extranodal
no
yes
no-censored
yes-censored
Cum survival
P value=0.460
Follow up time (months)

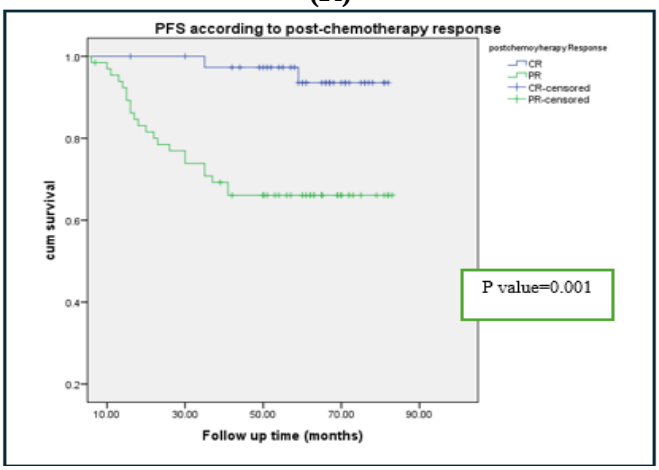
(J)



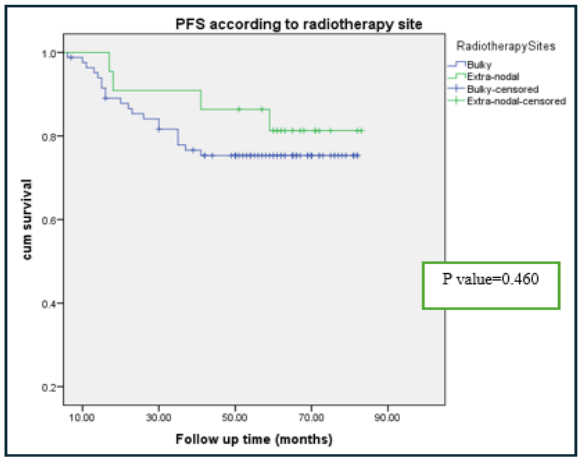
(K)



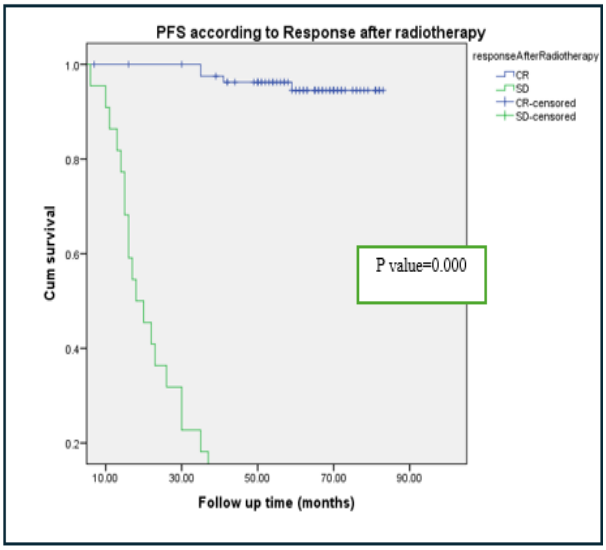
(L)



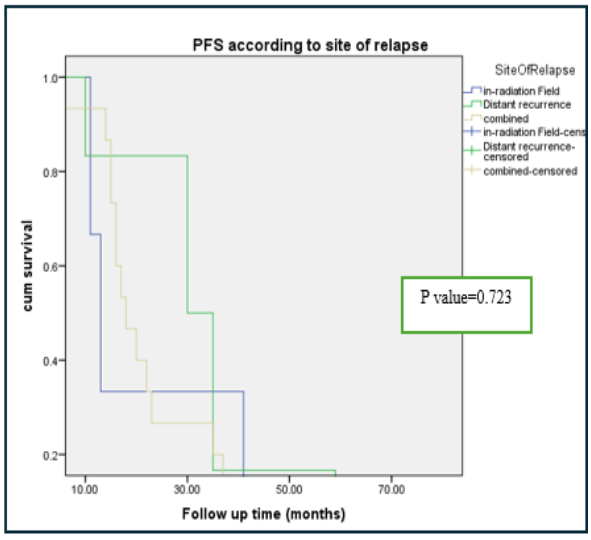
(M)



(N)



(O)



(P)

Figure 1: (A): Progression free survival, (B): PFS in relation to median age, (C): PFS in relation to sex, (D): PFS in relation to stage, (E): PFS in relation to B symptoms, (F): PFS in relation to performance status, (G): PFS in relation to LDH, (H): PFS in relation to bulky disease, (I): PFS in relation to presenting site at diagnosis, (J): PFS in relation to extra-nodal disease, (K): PFS in relation to bone marrow involvement, (L): PFS in relation to IPI score, (M): PFS in relation to post-chemotherapy response, (N): PFS in relation to RT site, (O): PFS according to response after consolidative RT, (P): PFS in relation to site of relapse. Figure 2A: The three-year OS was 92%. Figure 2B: The three-year OS was insignificantly different between groups however it was higher in patients aged >58 compared to those ≥ 58 years (94% vs. 89% respectively). Figure 2C: The three-year OS was higher in male compared to female (94% vs. 91% respectively). The difference was not statistically significant. Figure 2D: The three-year OS was higher in patients with no B symptoms compared to with B symptoms (96% vs. 87% respectively). The difference was not statistically

significant. Figure 2E: The three-year OS was in early stages (I +II) and advanced stages (III + IV) (93% vs. 91% respectively). The difference was not statistically significant. Figure 2F: The three-year OS was higher in patients with good performance status (ECOG0-1) compared to those with poor performance status (97% vs. 81%, respectively). The difference was statistically significant (p = 0.015). Figure 2G: The three-year OS was higher in patients with normal level compared to those with elevated LDH (97% vs. 89%, respectively) with no statistically significant difference between them. Figure 2H: The three-year OS was higher in patients with non-bulky disease compared to those with bulky (100% vs. 90%, respectively). The difference was not statistically significant. Figure 2I: The three-year OS was higher in patients with disease above diaphragm compared to those with blow diaphragm and both sides of diaphragm (95% vs. 90%vs.80% respectively) with no statistically significant difference between them. Figure 2J: The three-year OS was higher in patients with no extra-nodal disease compared to those with extra-nodal disease (90% vs. 100% respectively) but with no statistically significant difference between them. Figure 2K: The three-year OS was in patients with BM involvement compared to those with no BM involvement (92% vs. 88% respectively). The difference was not statistically significant. Figure 2L: The three-year OS was higher in patients with IPI score (0-1) compared to those with IPI score (2-5) (100% vs. 89% respectively). The difference was not statistically significant. Figure 2M: The three-year OS was higher in patients with CR compared to those with PR (95% vs. 90% respectively) however there was no statistically significant difference between them. Figure 2N: The three-year OS was higher in patients with extra-nodal disease compared to those with bulky disease (100% vs. 90% respectively) with no statistically significant difference between them. Figure 2O: The three-year OS was higher in patients without relapse compared to those with relapse (97% vs. 70% respectively). The difference was statistically significant (p = 0.000). Figure 2P: The three-year OS was higher in patients with CR after consolidative RT compared to those with SD after consolidative RT (98% vs. 52% respectively). The difference was statistically significant (p = 0.000). Figure 2Q: The three-year OS was in patients with relapse in radiation field, distant relapse & combined (55% vs.75% vs. 50% respectively) with no statistically significant difference between them.

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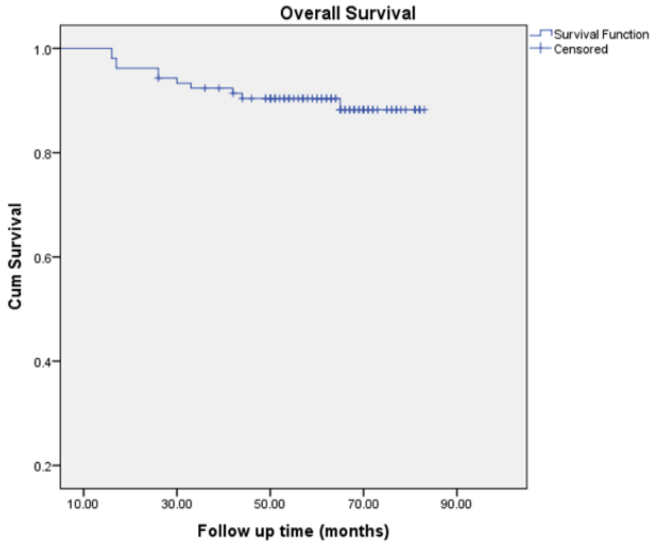

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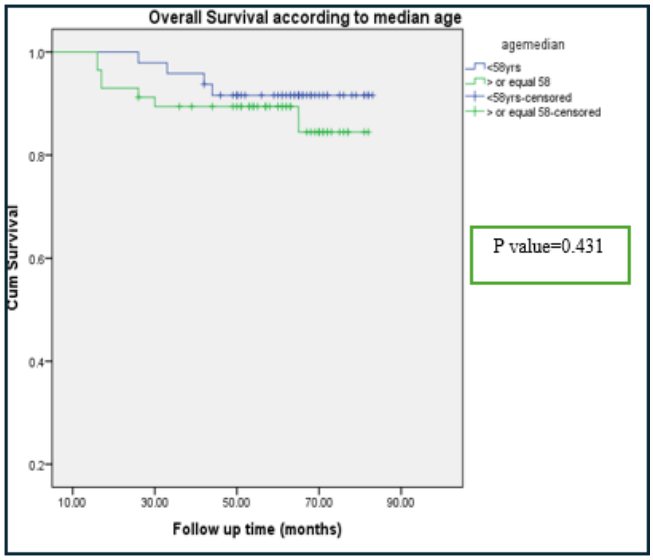

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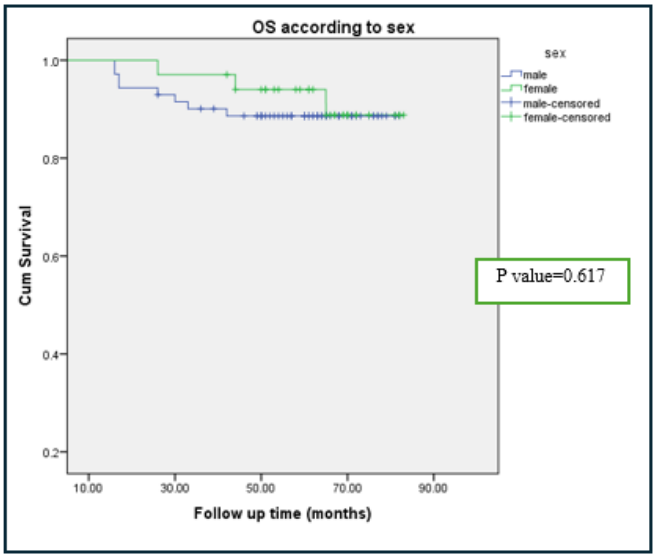

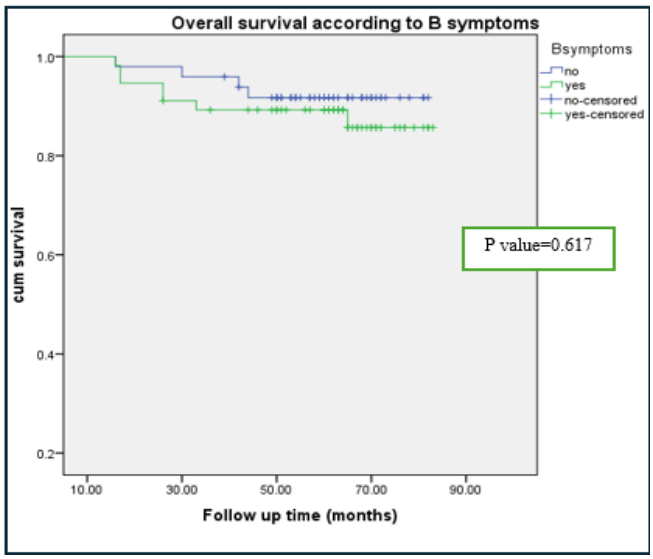

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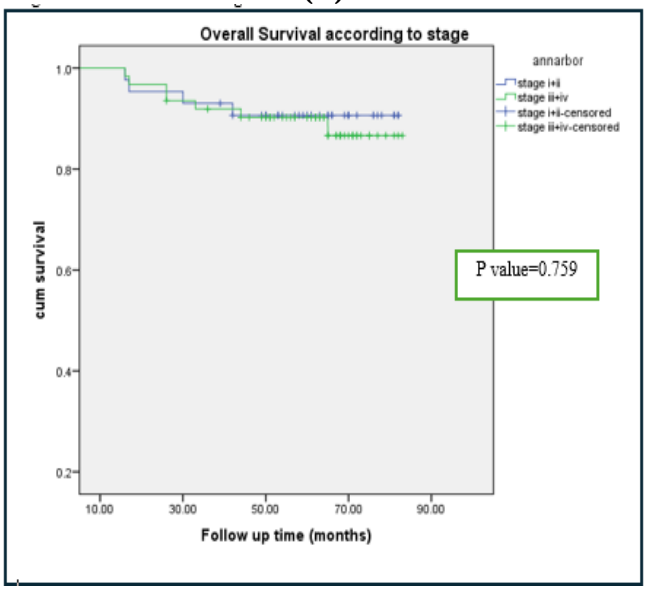
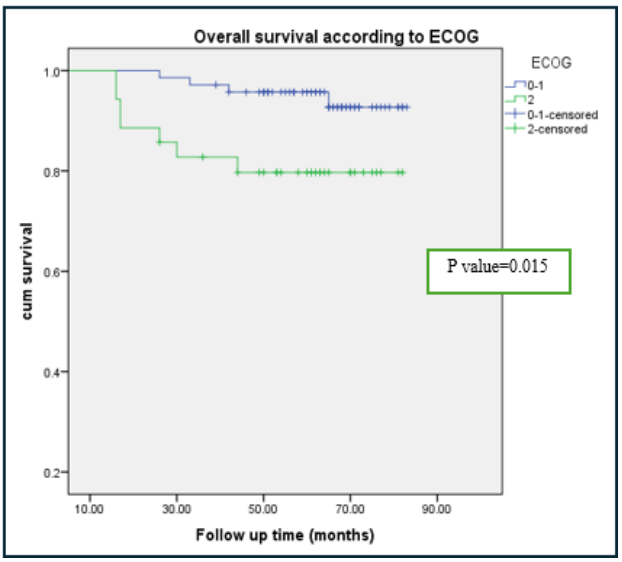
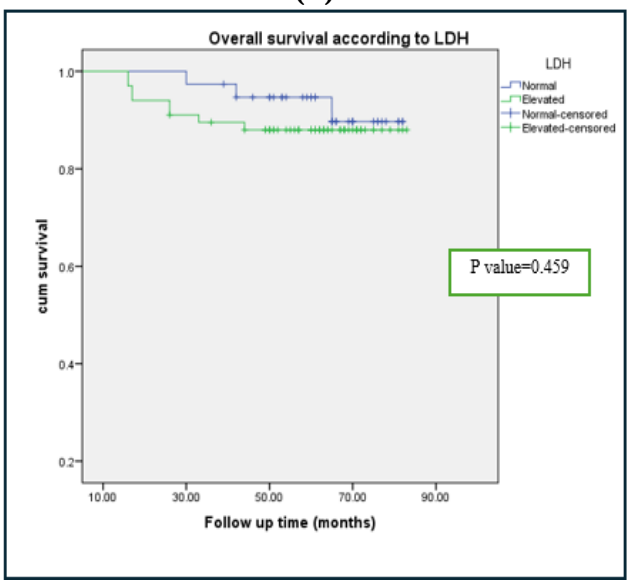
(C)


Overall Survival according to stage
annarbor
stage i+ii
stage iii+iv
stage i+ii-censored
stage iii+iv-censored
cum survival
Follow up time (months)
P value=0.759

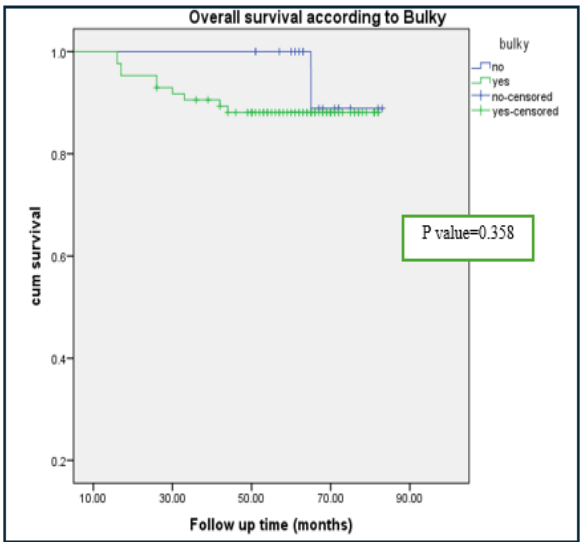
(D)


Overall survival according to ECOG
ECOG
0-1
2
0-1-censored
2-censored
cum survival
Follow up time (months)
P value=0.015

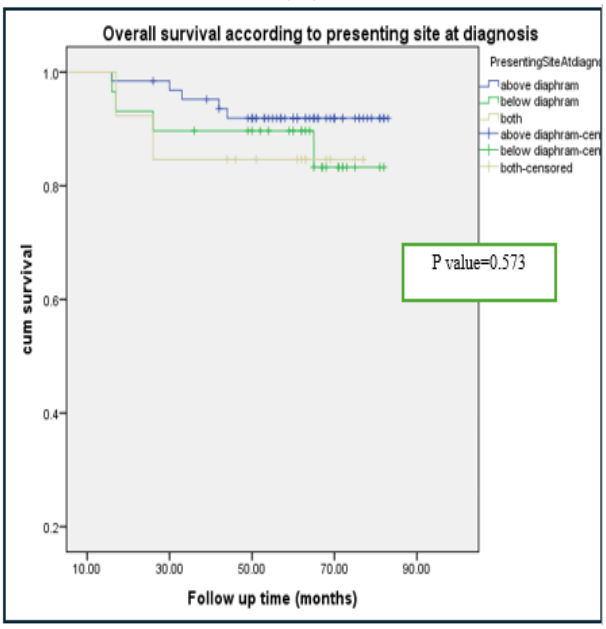
(E)


Overall survival according to LDH
LDH
Normal
Elevated
Normal-censored
Elevated-censored
cum survival
Follow up time (months)
P value=0.459

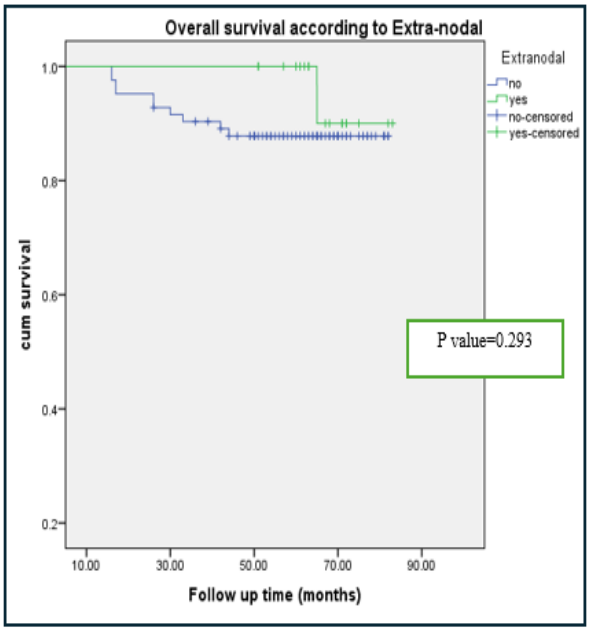
(F)


Overall survival according to Bulky
bulky
no
yes
no-censored
yes-censored
cum survival
Follow up time (months)
P value=0.358

(G)

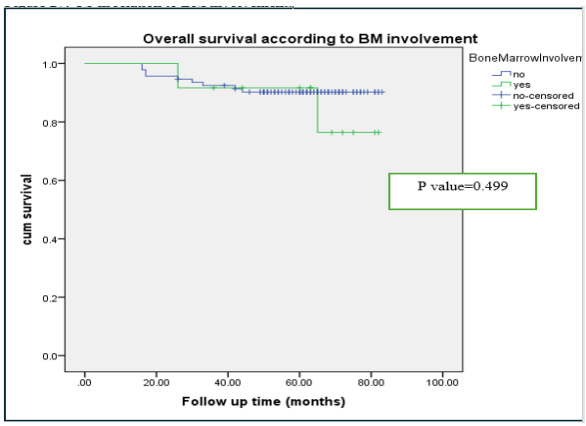

Overall survival according to presenting site at diagnosis
above diaphram
below diaphram
both
both-censored
cum survival
Follow up time (months)
P value=0.573

(H)


Overall survival according to Extra-nodal
Extranodal
no
yes
no-censored
yes-censored
cum survival
Follow up time (months)
P value=0.293

(I)

(J)



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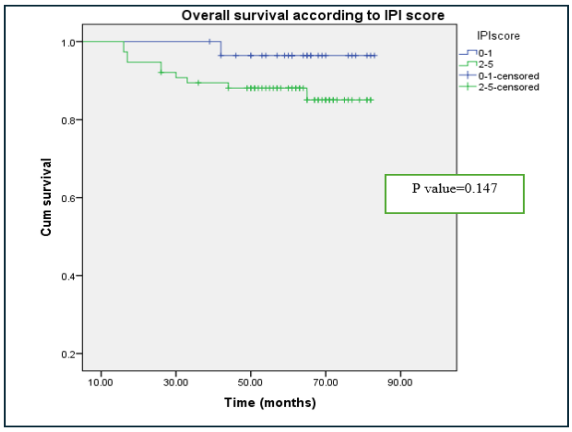

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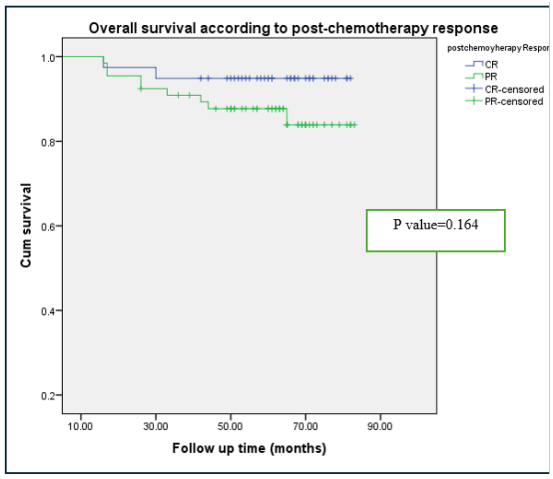

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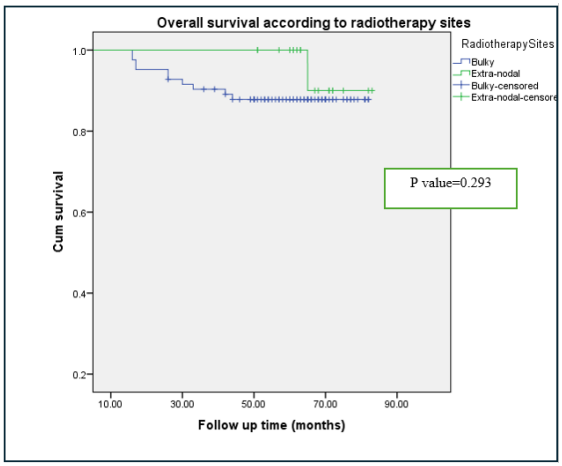
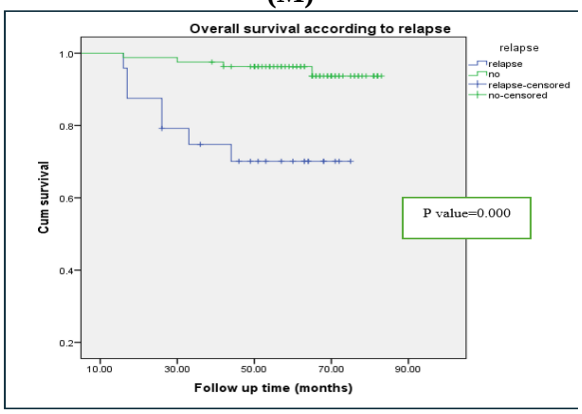
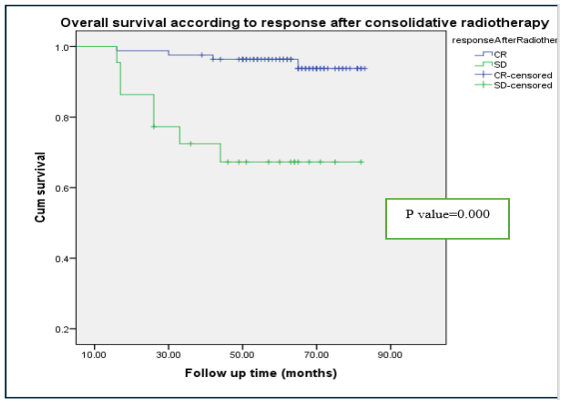


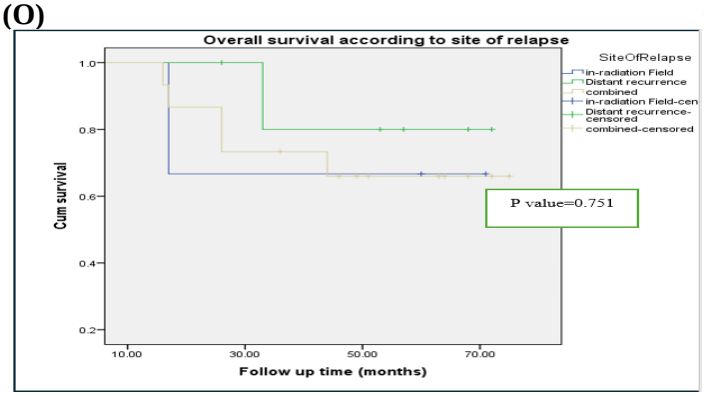
(N)



(O)



(P)



(Q)

Figure 2: (A): Overall survival, (B): OS in relation to median age, (C): OS in relation to sex, (D): OS in relation to B symptoms, (E): OS in relation to stage, (F): OS in relation to performance status, (G): OS in relation to LDH, (H): OS in relation to bulky disease, (I): OS in relation to presenting site at diagnosis, (J): OS in relation to extra-nodal, (K): OS in relation to BM involvement, (L): OS in relation to IPI score, (M): OS in relation to post-chemotherapy response, (N): OS in relation to RT sites, (O): OS in relation to relapse, (P): OS in relation to response after consolidative RT, (Q): OS in relation to site of relapse.

The univariate analysis showed that Ann arbor stage, B symptoms, LDH, presenting site at diagnosis, post-chemotherapy response and response after RT were statistically significant (p<.05), while in multi-variate analysis only RT response was statistically significant (p<.05). The univariate analysis showed that PS, relapse and response after consolidative RT were statistically significant with OS (p<.05), while in multi-variate analysis no factor was statistically significant with OS (p<.05) (**Table 3).**

Table (3): Uni-variate & multi-variate according to PFS and OS

Prognostic factor	Univariant	Multi-variants			
		Sig.	Exp(B)	95.0% CI for Exp(B)	
				Lower	Upper
PFS					
Ann arbor stage	**0.001***	0.992	1.009	0.195	5.230
B symptoms	**0.003***	0.728	1.252	0.354	4.432
LDH	**0.006***	0.887	.899	0.208	3.879
Presenting site at diagnosis	**0.001***	0.074	1.698	0.950	3.036
Post-chemotherapy response	**0.001***	0.818	.890	0.328	2.414
Response after RT	**0.001***	0.000	7.026	3.267	15.110
OS					
PS	**0.015***	0.059	3.361	0.955	11.825
Relapse	**0.001***	0.368	.367	0.041	3.256
Response after consolidative RT	**0.001***	0.299	1.778	0.601	5.260

Data are presented as numbers or frequency (%). PS: performance states, LDH: Lactate dehydrogenase. PFS: Progression-Free Survival, OS: overall survival.

Table (4) indicated that older patients (≥58 years) had slightly higher CR rates post-RT, without statistically significant value. Female patients had a higher CR rate compared to males, without statistically significant value. CR post-RT was higher in stage I & II, with statistically significant value (p<0.05). Significantly significant lower CR rates in patients with B symptoms (p<0.05). Better CR rates in patients with good performance status (0-1), without statistically significant value. Patients with normal LDH levels had higher CR rates, with statistically significant value (p<.05). Patients without bulky disease had higher CR rates, without statistically significant value. Patients with disease limited to above the diaphragm had higher CR rates compared to below and both sides of diaphragm, with statistically significant value (p<.05). CR was higher in extra-nodal, without statistically significant value. Patients with BM involvement had lower CR, without statistically significant value. Patients with lower IPI scores had better CR, without statistically significant value. CR was higher in extra-nodal disease than bulky disease, without statistically significant value. Patients who did not relapse had significantly better response rate, with statistically significant value (p<0.05). CR was higher in patients with combined relapse than in-radiation field and distant relapse, which was statistically insignificant.

Table (4): correlation of response after RT with age median age, sex, Ann arbor stage, B symptoms, performance status, LDH, Bulky disease, presenting site at diagnosis, Extra-nodal, BM involvement, IPI score, RT site, relapse and site of relapse

Response	Median age			
	<58	**≥ 58**	**Total**	**P value**
CR	36 (75%)	47 (82.5%)	83	0.350
SD	12 (25%)	10 (17.5%)	22	
Total	48100%	57 (100%)	105	
	Sex			
	Male	**Female**	**Total**	**P value**
CR	53 (74.6%)	30 (88.2%)	83	0.109
SD	18 (25.4%)	4 (11.8%)	22	
Total	71 (100%)	34 (100%)	105	
	Ann arbor stage			
	Stage I + II	**Stage III + IV**	**Total**	**P value**
41	41 (95.3%)	42 (67.7%)	83	**0.001***
2	2 (4.7%)	20 (32.3%)	22	
43	43 (100%)	62 (100%)	105	
	B symptoms			
	No	**Yes**	**Total**	**P value**

Response	Median age			
	<58	≥ 58	Total	P value
CR	46 (93.9%)	37 (66.1%)	83	0.000*
SD	3 (6.1%)	19 (33.9%)	22	
Total	49 (100%)	56 (100%)	105	
	PS			
	0-1	2	Total	P value
CR	59 (84.3%)	24 (68.6%)	83	0.062
SD	11 (15.7%)	11 (31.4%)	22	
Total	70 (100%)	35 (100%)	105	
	LDH			
	Normal	Elevated	Total	P value
CR	36 (94.7%)	47 (70.1%)	83	0.003*
SD	2 (5.3%	20 (29.9%)	22	
Total	38 (100%)	67 (100%)	105	
	Bulky			
	No	Yes	Total	P value
CR	17 (85%)	66 (77.6%)	83	0.467
SD	3 (15%)	19 (22.4%)	22	
Total	20 (100%)	85 (100%)	105	
	Presenting site at diagnosis			
	Above	below	Both	Total	P value
CR	56 (88.9%)	20 (69%)	7 (53.8%)	83	0.005*
SD	7 (11.1 %)	9 (31%)	6 (46.2%)	22	
Total	63 (100%)	29 (100%)	13 (100%)	105	
	Extra-nodal			
	No	Yes	Total	P value
CR	64 (77.1%)	19 (86.4%)	83	0.556
SD	19 (22.9%)	3 (13.6%)	22	
Total	83 (100%)	22 (100%)	105	
	BM involvement			
	No	Yes	Total	P value
CR	75 (90.4%)	8 (66.7%)	83	0.263
SD	18 (81.8%)	4 (33.3%)	22	
Total	93 (100%)	12 (100%)	105	
	IPI score			
	0-1	2-5	Total	P value
CR	26 (89.7%)	57 (75%)	83	0.099
SD	3 (10.3%)	19 (25%)	22	
Total	29 (100%)	76 (100%)	105	
	RT site			
	Bulky	Extra-nodal	Total	P value
CR	64 (77.1%)	19 (86.4%)	83	0.343
SD	19 (22.9%)	3 (13.6%)	22	
Total	83 (100%)	22 (100%)	105	
	Relapse			
	Yes	No	Total	P value
CR	4 (16.7%)	79 (97.5%)	83	0.000*
SD	20 (83.3%)	2 (2.5%)	22	
Total	24 (100%)	81 (100%)	105	
Site of relapse				
	In- radiation field	Distant recurrence	Combined	Total	P value
CR	0 (0%)	3 (50%)	2 (13.3%)	5	0.111
SD	3 (100%)	3 (50%)	13 (86.7%)	19	
Total	3 (100%)	6 (100%)	15 (100%)	24	

Data are presented as numbers. **PS:** performance states, **LDH:** Lactate dehydrogenase. **PFS:** Progression-Free Survival, **OS:** overall survival.

DISCUSSION

DLBCL is the most prevalent form of NHL and is regarded as an aggressive but potentially curable disease. R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) is the standard first-line treatment for DLBCL, which is immunochemotherapy [8]. While many patients respond well to chemotherapy, some may benefit from additional treatment such as consolidative RT, especially those with bulky disease or poor risk (PR) [9].

The present study revealed that among the 105 participants, 54.3% were aged ≥ 58 years, and males represented 67.6% of the sample. Most patients (59.0%) had advanced disease (Ann Arbor stage III–IV), with elevated LDH levels seen in 63.8%. Bulky disease was present in 81% of cases, and the most common site of presentation was above the diaphragm (60%). The gastrointestinal tract was the most frequent extranodal site (45.5%), while BM involvement was noted in 11.4% of patients. A high IPI score (2–5) was observed in 72.3% of cases. Nearly all patients (99.0%) received R-CHOP chemotherapy. Early-stage cases received 4 cycles, while advanced stages received 6 cycles. PR was observed in 62.9% of patients. PET-CT was the most commonly used imaging method post-chemotherapy (87.6%). All patients received RT, with 79% to nodal and 21% to extranodal sites. After RT, complete response (CR) was achieved in 79% of patients. Relapse occurred in 22.9% of cases, most commonly involving combined sites.

Our results is consistent with **Mauro *et al.*** [10] who reported that the mean age at diagnosis was 56.7 years, with 41.9% of patients aged ≥ 60 years. Males represented the majority of the cohort (61.3%). Most patients had good performance status (ECOG 0–1, 82.3%). Advanced-stage disease was common, with 66.1% of patients presenting at stage IV. According to the Revised International Prognostic Index, 61.3% of patients were classified as poor risk. Bulky disease and extranodal involvement were present in 77.4% and 83.9% of patients respectively. B symptoms were reported in 79.0% of cases. Most patients (90.3%) were HIV-negative, while 9.7% were HIV-positive. Most patients (80.6%) received R-CHOP as the first-line chemotherapy regimen, while 19.4% received other regimens. In terms of treatment response, 24.2% achieved CR, and 67.7% had poor response (PR) to first-line chemotherapy. Response was not identified in 8.1% of patients.

Our study showed that three-year PFS was generally favorable at 78%. Better PFS was associated with female gender, early-stage disease, absence of B symptoms, normal LDH levels, and CR to treatment or RT. These differences were statistically significant. Although some factors like age, performance status, bulky disease, and extranodal involvement showed trends toward lower PFS, they did not reach statistical significance. Our results is consistent with **Kwak *et al.*** [11] showed that in DLBCL treated with R-CHOP, women showed significantly longer PFS compared to men (median 90.6 vs. 55 months; HR 1.237, $p = 0.0262$). The 5-year RFS rate was 72%. Also, a study of primary mediastinal LBCL by **Shih *et al.*** [12] found that early-stage (I–II) disease was significantly associated with longer PFS (5-year PFS ~83% vs. ~61% in advanced stage; $p < 0.05$), In primary mediastinal DLBCL, adding RT after chemotherapy significantly increased PFS (5-year PFS ~87.7% with RT vs. ~64.5% without; $p = 0.013$). They showed that achieving complete remission is one of the strongest predictors of long-term PFS. Patients in CR have significantly prolonged PFS (5-year PFS ~96.5% vs. 0% if not).

Also, **Syed *et al.*** [13] showed that RT was significantly associated with improved PFS. Patients who received RT had a 77% reduction in the risk of disease progression (HR 0.23, 95% CI: 0.10–0.52, $p < 0.001$) and an 80% reduction in the risk of local failure (HR 0.20, 95% CI: 0.07–0.59, $p = 0.003$). Additionally, the benefit of RT was observed across tumor sizes, with significantly improved PFS for both tumors < 5 cm and those ≥ 5 cm in size (log-rank $p = 0.0454$ and 0.0003 respectively).

Acute toxicity from RT was seen in 30.5% of patients, while 69.5% had no side effects. The most common side effect was fatigue (62.5%), followed by gastrointestinal (15.6%) and central nervous system toxicity (9.4%). Mucositis and skin toxicity were less common (6.3% each). Most side effects were mild to moderate: 62.5% were grade 1, 34.4% grade 2, and only 3.1% were grade 3. No severe (grade 4) or fatal (grade 5) toxicities were reported. Chronic toxicity was reported in 5 patients (4.8%). The most frequent late effect was fatigue (grade 2) in 4 cases, and one patient had chronic gastritis (grade 1).

Our results is consistent with **Wang *et al.*** [14] who reported that 92% experienced acute toxicity following RT: Grade 1 or 2 toxicity was the vast majority. The most frequent side effects were fatigue (18%), skin toxicity (~30%), upper GI symptoms (15%), and mucositis/pharyngeal symptoms (10%). While, **Mauro *et al.*** [10] reported that regarding toxicity, 33.9% experienced grade 4 toxicity, while 66.1% had lower-grade toxicity (grades 0–3).

In our study, the three-year OS rate was high (92%). OS was better in patients with good performance status, CR after treatment, no relapse, and CR after RT. These differences were statistically significant. Other factors such as age, stage, B symptoms, LDH level, bulky disease, and extranodal involvement showed some differences in OS, but they were not statistically significant. This suggests that response to treatment and relapse status are strong predictors of survival. Our results is consistent with **Syed *et al.*** [13] showed that of DLBCL patients treated with R-CHOP, a 5-year OS of ~91% in low-risk patients who achieved CR after chemotherapy and consolidative RT. Similarly, a meta-

analysis of **Choi *et al.*** [15] included 813 advanced-stage patients treated with R-CHOP ± RT showed RT significantly improved OS (HR ~2.0, p = 0.002).

Univariate analysis showed that Ann Arbor stage, presence of B symptoms, LDH level, disease site at diagnosis, post-chemotherapy response, and response after RT were significantly associated with PFS. However, in multivariate analysis, only the response after RT remained statistically significant. For OS, univariate analysis showed that performance status, relapse, and response after RT were significantly associated. However, in multivariate analysis, no factor was independently associated with OS. Our findings are in agreement with **Zhang *et al.*** [16] who found that higher Ann Arbor stage (III/IV), presence of B symptoms, elevated LDH, and extranodal involvement were all significantly associated with lower three-year PFS (p-values: 0.004, 0.038, 0.045, and 0.006 respectively).

Also, our findings are in line with **Chen *et al.*** [17] who reported that relapse within one year of initial treatment was significantly associated with a worse overall survival in univariate analysis. In multivariate analysis, early relapse remained an independent predictor of decreased OS (HR 0.241, p = 0.002).

CR rates after RT were slightly higher in older patients (≥58 years) and in females, but with no statistically significant difference between them. CR was significantly higher in early-stage patients (stage I–II) and in those without B symptoms ($p < 0.05$). Patients with good performance status and without bulky disease had better CR rates, but these were not statistically significant. Patients with normal LDH levels and those with disease limited to above the diaphragm had significantly higher CR rates ($p < 0.05$). Higher CR rates were also observed in patients with extranodal disease, lower IPI scores, and no BM involvement, but these differences were not significant. Patients who did not relapse had significantly better CR rates ($p < 0.05$). Among those who relapsed, CR was highest in patients with combined relapse, though no statistically significant difference between them.

Also, our findings are in line with **Cassidy *et al.*** [18] who reported that those with normal LDH levels had significantly higher 5-year local control and improved PFS, and those who received consolidative RT all achieved 100% local control ($p = 0.047$). In the elderly DLBCL study, lack of relapse was strongly associated with better CR and disease control (100% local control, $p < 0.01$).

LIMITATIONS: The study's limitations included a comparatively small sample size, which inevitably reduced the statistical power of the analysis, a single-center study that rendered the results less generalizable, and a short-term follow-up.

CONCLUSIONS

Adding RT after chemotherapy in patients with DLBCL resulted in good outcomes. Most patients achieved CR, and both PFS (78%) and OS (92%) at three years that were high. RT was well tolerated with mostly mild side effects. Better outcomes were seen in patients with early-stage disease, no B symptoms, normal LDH levels, good performance status, and CR after treatment. These results suggest that RT is a valuable part of treatment in selected DLBCL patients.

Conflict of interest: Nil.
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