CHAPTER-4

RESULTS

A total of 161 patients were enrolled in the study, 73 in node-negative (N-) and 88 in node-positive (N+) cohorts. Table-4.1 and Figure-4.1 compare the baseline variables in the two groups; there was no significant difference in variables like gender, age, ECOG PS and co-morbidities. N+ cohort had higher proportion of patients with T3/4 stage (68.2% v/s 52%; p=0.000), tumor subsite oropharynx (30.7% v/s 13.7%; p=0.003) and poorly differentiated tumors (14.8% v/s 6.8%; p=0.018) as compared to N- cohort.

Table 4.1 Baseline data of patients (N=161).

Variable		0verall n/N(%)	Node negative (N=73)n/N(%)	Node positive (N=88)n/N(%)	p value
Gender	male	142/161(88.2)	64/73(87.7)	78/88(88.6)	
	female	19/161(11.8)	9/73(12.3)	10/88(11.4)	1.000*
Mean age (years±SD)		56.32±13.27	55.56±13.251	56.94±13.328	0.512**
Age (years)	<50	50/161(31)	26/73(35.6)	14/88(15.9)	0.877*
	≥50	111/161(69)	47/73(64.4)	74/88(84.1)	
Clinical T stage	T1	18/161(11.2)	16/73(21.9)	2/88(2.3)	
	T2	40/161(24.8)	19/73(26)	21/88(23.9)	
	T3	44/161(27.3)	21/73(28.8)	23/88(26.1)	**0.000***
	T4	54/161(33.5)	17/73(23.3)	37/88(42)	
	Tx	5/161(3.1)	0	5/88(5.7)	
Primary tumor subsite	Oral cavity	56/161(34.8)	31/73(42.5)	25/88(28.4)	
	Sinuses	7/161(4.3)	5/73(6.8)	2/88(2.3)	
	Oropharynx	37/161(23)	10/73(13.7)	27/88(30.7)	**0.003***
	Hypopharynx	19/161(11.8)	6/73(8.2)	13/88(14.8)	
	Larynx	37/161(23)	21/73(28.8)	16/88(18.2)	
	CUPS	5/161(3.1)	0	5/88(5.7)	
Primary site histopathology	Veruccous carcinoma	2/161(1.2)	1/73(1.4)	1/88(1.1)	
	WDSCC	17/161(10.6)	13/73(17.8)	4/88(4.5)	**0.018***
	MDSCC	120/161(74.5)	54/73(74)	66/88(75)	
	PDSCC	14/161(8.7)	4/73(5.5)	10/88(11.4)	
	PDC	4/161(2.5)	1/73(1.4)	3/88(3.4)	
	not applicable	4/161(2.5)	0	4/88(4.5)	
ECOGperformance ptatus	0	98/161(60.9)	50/73(68.5)	48/88(54.5)	
	1	26/161(16.1)	11/73(15.1)	15/88(17)	
	2	24/161(14.9)	9/73(12.3)	15/88(17)	0.290*
	3	12/161(7.5)	3/73(4.1)	9/88(10.2)	
	4	1/161(0.6)	0	1/88(1.1)	
Co-morbidities	DM	5/161(3.1)	1/73(1.4)	4/88(4.5)	
	Cardiac	7/161(4.3)	3/73(4.1)	4/88(4.5)	
	HT	16/161(9.9)	7/73(9.6)	9/88(10.2)	1.000*
	Pulmonary	2/161(1.2)	1/73(1.4)	1/88(1.1)	

*Pearson chi square test**Unpaired Student t test("SD-standard deviation, CUPS-carcinoma unknown primary site, WDSCC, MDSCC, PDSCC-well differentiated,moderately differentiated,poorlydifferentiated squamous cell carcinoma, PDC-poorly differentiated carcinoma, DM-diabetes mellitus, HT-hypertension")

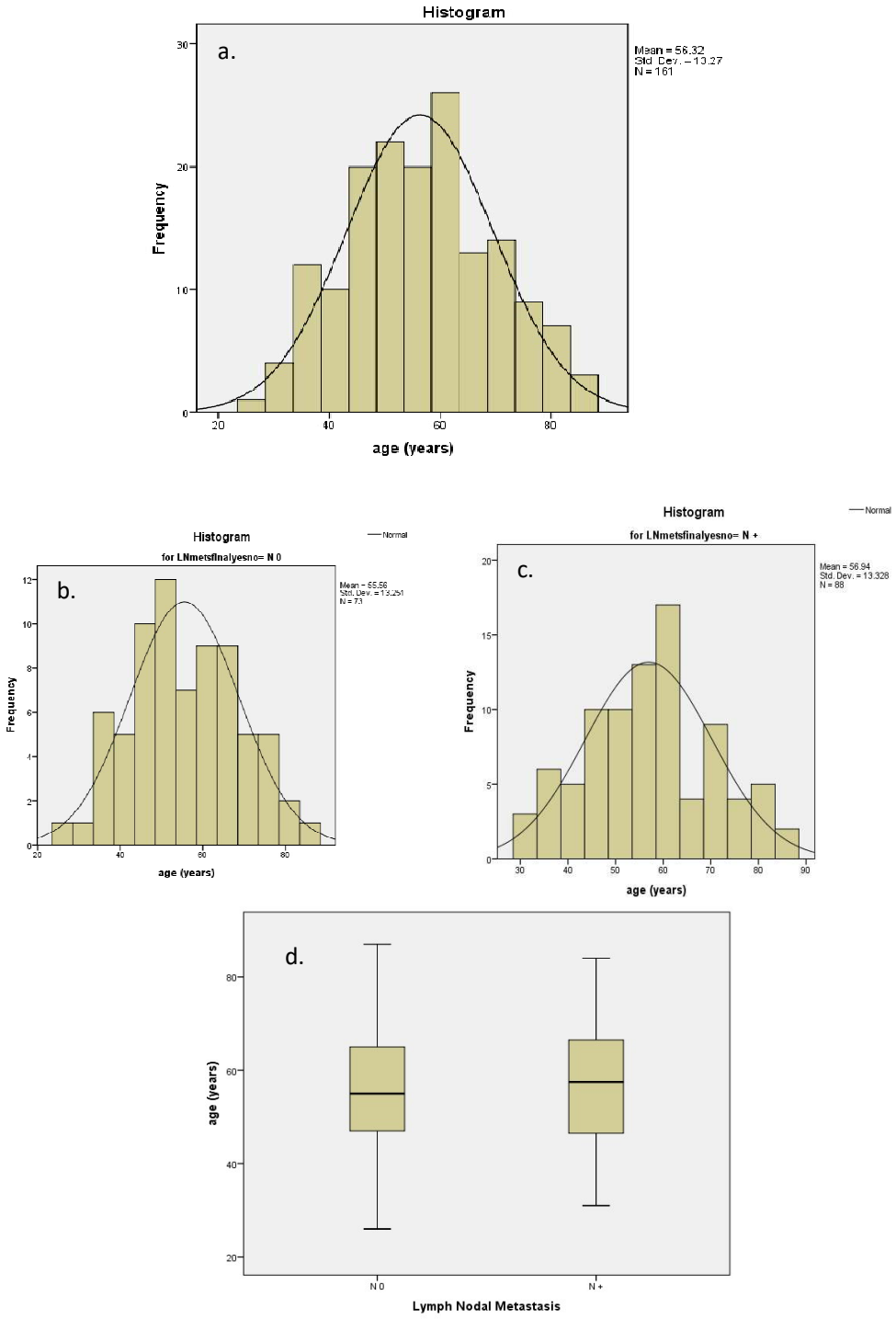

Figure 4.1 The age distribution of patients, with distribution normal curve (Kolmogorov-Smirnov p value=0.200). a. overall, b. node-negative group, c. node positive group, d. Box plot comparing the central measures of distribution for Age in the two groups.

4.1. Nutritional profile at baseline

As depicted in Table-4.2 and 4.3, mean weight, BMI and Hemoglobin (Hb) were similar in N- and N+ cohorts; however, median pre-treatment weight loss (6% v/s 0, p=0.004) and median SGA score (42 v/s 34, p=0.000) were significantly higher in N+ cohort; higher proportion of patients had ≥10%pre-treatment weight loss (28.4% v/s 13.7%, p=0.034), low MUAC (22.8% v/s 9.6%, p=0.036), ≥40 SGA score (58% v/s 34.2% ,p=0.015) and Bitot spots (18.2% v/s 4.1%, p= 0.006) in N+ cohort.

Table 4.2 Nutritional assessment before starting treatment compared in N- and N+ cohorts.

Variable		0verall	Node negative (N=73)	Node positive (N=88)	p value*
Weight (kg)	mean	57.750	59.121	56.614	0.179
	median	56	57	55	
	range	30-97	38-97	30-85	
	SD	11.7713	12.0118	11.5125	
BMI (kg/m^2)	mean	21.5822	22.2396	21.0368	0.070
	median	21	22	21.0368	
	range	12.84-37.02	14.86-34.0	12.84-37.02	
	SD	4.19650	4.36728	3.99239	
Percentage pre-treatment weight loss	mean	6.26	4.25	7.93	**0.004**
	median	4.00	0	6	
	range	0-36	0-32	0-36	
	SD	8.081	6.658	8.786	
Hemoglobin (g/dL)	mean	13.4213	13.3928	13.4445	0.854
	median	13.4100	13.4250	13.3400	
	range	7.0-18.0	7.0-18.0	9.0-17.50	
	SD	1.76753	1.87076	1.68890	
MUAC (cm)	mean	24.711	25.219	24.290	0.121
	median	25	25	24	
	range	16-49	20-34	16-49	
	SD	3.7793	2.9368	4.3283	
SGA score	mean	40.11	36.95	42.74	**0.000**
	median	39	34	42	
	range	26-65	26-59	27-65	
	SD	10.304	8.839	10.732	
*unpaired student t test ("BMI-body mass index, SGA-subjective global assessment, SD-standard deviation")					

Table 4.3 Cross-tabulation of nutritional assessment before starting treatment and node groups.

Variable		Number of patients n/N(%)			
		0verall	Node negative	Node positive	p value *
Weight (kg)	30-39	7/161(4.3)	2/73(2.7)	5/88(5.7)	0.612
	40-49	30/161(18.6)	11/73(15.1)	19/88(21.6)	
	50-59	57/161(35.4)	26/73(35.6)	31/88(35.2)	
	60-69	37/161(23)	19/73(26)	18/88(20.5)	
	70-79	21/161(13)	10/73(13.7)	11/88(12.5)	
	80-89	7/161(4.3)	3/73(4.1)	4/88(4.5)	
	90-99	2/161(1.2)	2/73(2.7)	0	
≥10% weight loss in the past 6months before starting treatment		35/161(21.7)	10/73(13.7)	25/88(28.4)	**0.034**
BMI (kg/m^2)	obese	8/161(4.9)	5/73(6.8)	3/88(3.4)	0.602
	over weight	24/161(14.9)	14/73(19.2)	10/88(11.3)	
	normal	90/161(55.9)	38/73(52)	52/88(59.1)	
	mild chronic energy deficiency	24/161(14.9)	11/73(15)	13/88(14.8)	
	moderate chronic energy deficiency	5/161(3.1)	2/73(2.7)	3/88(3.4)	
	severe chronic energy deficiency	7/161(4.3)	2/73(2.7)	5/88(5.7)	
	missing value	3/161(1.9)	1/73(1.3)	2/88(2.3)	
MUAC	normal	134/161(83.2)	66/73(90.4)	68/88(77.2)	**0.036**
	moderate malnutrition	23/161(14.3)	7/73(9.6)	16/88(18.2)	
	severe malnutrition	4/161(2.5)	0	4/88(4.5)	
SGA score	24-29	33/161(20.5)	18/73(24.6)	15/88(17)	**0.015**
	30-39	52/161(32.3)	30/73(41.1)	22/88(25)	
	40-49	44/161(27.3)	17/73(23.3)	27/88(30.7)	
	50-59	26/161(16.1)	8/73(10.9)	18/88(20.4)	
	60-71	6/161(3.7)	0	6/88(6.8)	
Pallor	present	10/161(6.2)	4/73(5.5)	6/88(6.8)	0.757
Bitot spots	present	19/161(11.8)	3/73(4.1)	16/88(18.2)	**0.006**
Hemoglobin	normal	110/161(68.3)	52/73(71.2)	58/88(65.9)	0.236
	mild anemia	39/161(24.2)	14/73(19.2)	25/88(28.4)	
	moderate anemia	8/161(5)	3/73(4.1)	5/88(5.7)	
	severe anemia	2/161(1.2)	2/73(2.7)	0	
	missing value	2/161(1.2)	2/73(2.7)	0	

* Pearson chi square test
("BMI-body mass index, MUAC-mid-upper arm circumference, SGA-subjective global assessment")

4.2. Systemic immunity at baseline

The TLC, absolute and % Neutrophil counts, absolute and % Lymphocyte counts and NLR are elaborated in Table 4.4. The mean NLR was 3.83±4.42 (SD). No differences were found in distribution of any of these variables in N- and N+ cohorts.

Table 4.4 Initial systemic immunity marker NLR compared in N- and N+ cohorts.

Variable		0verall	Node negative	Node positive	p value
Total Leukocyte Count	mean	8550.85	8457.40	8673.50	.445*
	median	8080.00	7750.00	8250.00	0.427**
	range	2630-16920	4100-16910	2630-15230	
	SD	2556.054	2515.731	2403.170	
Neutrophil %	mean	65.1236	64.8744	65.0341	0.506*
	median	65.0000	65.0000	65.0000	0.715**
	range	34-96	34-94	45.88-96.0	
	SD	11.04667	11.61695	10.05309	
Absolute Neutrophil count	mean	5688.06	5627.14	5716.25	0.571*
	median	5241.50	5220	5241.50	0.634**
	range	1940-14044	1940-13274	1958-12258	
	SD	2331.049	2393.758	2053.500	
Lymphocyte %	mean	23.9086	23.6211	24.2629	0.809*
	median	23.9050	23.6600	24.0000	0.874*
	range	3.0-51.99	4.0-47.0	3.0-44.0	
	SD	9.33334	9.82287	8.35289	
Absolute Lymphocyte count	mean	1973.86	1899.92	2070.45	0.373*
	median	1867.50	1798.00	2004.00	0.427**
	range	265-6701	432-4950	265-6701	
	SD	890.047	815.342	954.889	
Absolute Eosinophil count	mean	323.807	4.4659	3.7243	0.443*
	median	228.500	3	3.0000	0.873**
	range	0-1691	0.0-19.0	0.0-16.4	
	SD	299.3220	3.97447	3.24457	
Absolute Monocyte count	mean	560.95	6.6792	6.9267	0.127*
	median	548.50	7.0000	7.1650	0.427**
	range	0-1700	0-16.8	0.0-16.0	
	SD	273.684	3.12422	3.07461	
Absolute Basophil count	mean	24.71	25.70	24.04	0.598*
	median	23.00	24.00	19.50	0.459**
	range	0-131	0-131	0-87	
	SD	24.590	25.087	25.180	
NLR	mean	3.82982	3.93202	3.80243	0.992*
	median	3.00000	3.00000	2.95550	0.842**
	range	1.0-37.0	1.0-24.0	1.0-37.0	
	SD	4.424925	3.893264	5.155641	

* Independent sample T test, ** Independent-Samples Mann-Whitney U Test
(NLR- neutrophil/lymphocyte, SD-standard deviation)

4.3. Details of treatment, its complications and failure to complete planned treatment

Details of treatment are shown in Tables 4.5 and 4.6; 54.8% patients in N- cohort and 73.9% in N+ cohort were planned for multi-modality treatment, but only 50.7% in N- and 67% in N+ eventually received multi-modality treatment. Grade III complications occurred in 23.6% patients (same for both cohorts). Overall 13%, N- cohort 4.1%, and N+ cohort 20.5% patients failed to complete all planned treatment (p=0.002) (Table4.7).

Table 4.5 Details of treatment planned for patients at the time of enrollment into the study.

Variable		0verall n/N(%)	Node negative n/N(%)	Node positive n/N(%)	p value*
Single modality	Total	56/161(34.8)	33/73(45.2)	23/88(26.1)	**0.013**
	Surgery	15/161(9.3)	14/73(19.2)	1/88(1.1)	**0.000**
	Radiation therapy	40/161(24.8)	19/73(26)	21/88(23.9)	0.855
	Chemotherapy	1/161(0.6)	0	1/88(1.1)	1.000
Multi-modality	Total	105/161(65.2)	40/73(54.8)	65/88(73.9)	**0.013**
	Surgery+RT	29/161(18)	20/73(27.4)	9/73(10.2)	**0.007**
	Surgery+ChemoRT	32/161(19.9)	10/73(13.7)	22/88(25)	0.079
	ChemoRT	44/161(27.3)	10/73(13.7)	34/88(38.6)	**0.001**
* Pearson chi square test (RT-radiotherapy, ChemoRT- concurrent Chemotherapy and Radiotherapy)					

Table 4.6 Details of treatment received by the patients.

Variable		0verall n/N(%)	Node negative n/N(%)	Node positive n/N(%)	p value*
Single modality	Total	65/161(40.4)	36/73(49.3)	29/88(32.9)	**0.038**
	Surgery	19/161(11.8)	17/73(23.3)	2/88(2.3)	**0.000**
	Radiation therapy	43/161(26.7)	19/73(26)	24/88(27.3)	1.000
	Chemotherapy	3/161(1.9)	0	3/88(3.4)	0.252
Multi-modality	Total	96/161(59.6)	37/73(50.7)	59/88(67)	**0.038**
	Surgery+RT	26/161(16.1)	20/73(27.4)	6/88(6.8)	**0.000**
	Surgery+ChemoRT	30/161(18.6)	6/73(8.2)	24/88(27.3)	**0.002**
	ChemoRT	40/161(24.8)	11/73(15.1)	29/88(32.9)	**0.010**
* Pearson chi square test (RT-radiotherapy)					

Table 4.7 Tolerability of treatment compared in N- and N+ cohorts.

Variable		Number of patientsn/N(%)			
		0verall	Node negative (N=73)	Node positive (N=88)	p value*
Severe complications in surgery		10/132(7.6)	7/65(10.8)	3/67(4.5)	0.203
Radiation therapy/ Chemo + Radiotherapy	**Oral mucositis** Grade I	16/140(11.4)	7/57(12.3)	9/83(10.8)	0.083
	Grade II	91/140(65)	40/57(70.2)	51/83(61.4)	
	Grade III	24/140(14.9)	10/57(17.5)	14/83(16.9)	
	Skin reaction Grade I	22/140(15.7)	11/57(19.3)	11/83(13.3)	**0.015**
	Grade II	94/140(67.1)	41/57(71.9)	53/83(63.9)	
	Grade III	10/140(7.1)	4/57(7)	6/83(7.2)	
Total Grade III complications		38/161(23.6)	17/73(23.3)	21/88(23.9)	1.000
Delay in treatment		10/161(6.2)	7/73(9.6)	3/88(3.4)	0.187
Interruption of treatment		8/161(4.9)	4/73(5.5)	4/88(4.5)	1.000
Default of treatment		19/161(11.8)	3/73(4.1)	16/88(18.2)	**0.006**
Not completed all planned treatment		21/161(13.04)	3/73(4.1)	18/88(20.5)	**0.002**
* Pearson chi square test					

4.4. Nutritional status trend during treatment-

4.4.A. Overall group-

At the end of first, second modality, and completion of treatment-mean reduction in weight was 4.69%, 7.48% and 9.17%; mean reduction in BMI was 1.45, 2.71 and 2.09; proportion of patients with ≥10% weight loss from baseline was 27.2%, 38.1% and 45.3% respectively. Proportion of patients with low BMI before starting treatment and at completion of treatment increased from 22.8% to 43.4%, low MUAC from 16.8% to 30.8% and SGA score ≥40 from 47.2% to 87.4% respectively; median SGA score before starting treatment and at completion of treatment increased from 39 to 50 (Table 4.8).

4.4.B. Node-negative group-

At the end of first, second modality and completion of treatment, the mean reduction in weight was 6.2%, 6.7% and 8.9%; mean reduction in BMI was 1.52, 2.83 and 2.01; proportion of patients with ≥10% weight loss from baseline was 26.4%, 37% and 41.1% respectively. Proportion of patients with low BMI before starting treatment and at completion of treatment increased from 20.9% to 35.5%, low MUAC from 9.6% to 20.5%, and SGA

score ≥40 from 34.3% to 79.5% respectively; median SGA score before starting treatment and at completion of treatment increased from 34 to 48 (Table 4.9).

4.4.C. Node-positive group-

At the end of first, second modality and completion of treatment, the mean reduction in weight was 3.6%, 8% and 9.4%; mean reduction in BMI was 1.39, 2.62 and 2.16; proportion of patients with ≥10% weight loss from baseline was 27.9%, 38.9% and 48.8% respectively. Proportion of patients with low BMI before starting treatment and at completion of treatment increased from 24.4% to 50%, low MUAC from 22.7% to 39.5% and SGA score ≥40 from 58% to 94.2% respectively; median SGA score before starting treatment and at completion of treatment increased from 42 to 53 (Table 4.10).

Malnutrition (defined as low BMI or low MUAC or SGA score ≥40) was found in 47.2%, 34.3% and 58% patients overall, N- and N+ cohorts before starting treatment; this rate increased to 87.4%, 79.5% and 94.2% respectively at completion of treatment.

4.4.D. Single versus multi-modality treatment-

Comparison of nutritional parameters at treatment completion in patients having received *single modality versus multi-modality treatment* is shown in Table 4.11. PS and hemoglobin were not significantly different in any group. Although mean weight was significantly lower with single modality treatment in N+ cohort (47.85 v/s 52.44 kg), mean reduction in weight was significantly higher with multi-modality treatment in overall, N- and N+ cohorts (6.26% v/s 11.01%, 6.79% v/s 10.86% and 6.95% v/s 11.12% respectively). Proportion of patients with ≥10% weight loss was higher with multi-modality treatment in overall, N- and N+ cohorts (28.6% v/s 56.3%, 30.6% v/s 51.4% and 26% v/s 59.3% respectively). Although mean BMI and proportion of patients with low BMI was not significantly different, but mean reduction in BMI was higher with multi-modality treatment in overall, N- and N+ cohorts (1.29 v/s 2.57, 1.44 v/s 2.66 and 1.1 v/s 2.52 respectively); the same finding was noted for mean reduction in MUAC. Although median SGA scores were not significantly different, but median

increasein SGA score was higher with multi-modality treatment in overall, N- and N+ cohorts (6 v/s 13, 8 v/s 15 and 4 v/s 12 respectively) (Figure 4.2).

Table 4.8 Trend in nutritional status before, during and at completion of treatment.(N=161)

Variable		Baseline	End of first treatment	p value	End of second treatment	p value	At completion of treatment	p value
PS	Median	0	2		2		2	
Weight (kg) Mean(±SD)		57.83(11.8)	53.88(11.3)	**0.000***	53.07(8.72)	**0.000***	52.22(10.5)	**0.000***
<50	n/N (%)	37/161(23)	59/158(37.3)	**0.000****	22/64(34.4)		67/159(42)	**0.000****
<50		124/161(77)	99/158(62.7)		42/64(65.6)		92/159(58)	
Mean reduction in weight in kg from baseline (95%CI)			3.863 (3.19-4.53)	**0.000***	7.428 (6.04-8.82)	**0.000***	5.615 (4.82-6.41)	**0.000***
Mean reduction in % weight from baseline (±SD)			4.69(6.46)	**0.000***	7.48(6.99)	**0.032***	9.17(8.33)	**0.000***
Change in weight from baseline n/N(%)	≥10% loss		43/158(27.2)		24/63(38.1)	**0.016***	72/159(45.3)	**0.000****
	<10% loss		85/158(53.8)		31/63(49.2)		68/159(42.8)	
	no change		12/158(7.6)		5/63(7.9)		6/159(3.8)	
	<10% rise		17/158(10.8)		1/63(1.6)		12/159(7.5)	
	≥10% rise		1/158(0.6)		2/63(3.2)		1/159(0.6)	
BMI	Mean(± SD)	21.59(4.19)	20.14(4.03)	**0.000***	19.91(3.13)	**0.000***	19.54(3.79)	**0.000***
	Mean reduction from baseline(95%CI)		1.45(1.2-1.7)		2.7(2.2-3.2)		2.1(1.8-2.4)	
n/N (%)	obese	8/158(5.1)	4/158(2.5)	**0.000****	1/64(1.6)		4/159(2.5)	**0.000****
	over weight	24/158(15.2)	18/158(11.4)		2/64(3.1)		11/159(6.9)	
	normal	90/158(57)	76/158(48.1)		41/64(64.1)		75/159(47)	
	mild deficiency	24/158(15.2)	31/158(19.6)		14/64(21.9)		39/159(24)	
	moderate deficiency	5/158(3.2)	14/158(8.9)		0		10/159(6.3)	
	severe deficiency	7/158(4.4)	15/158(9.5)		6/64(9.4)		20/159(12)	

Variable		Baseline	End of first treatment	p value	End of second treatment	p value	At completion of treatment	p value
MUAC (cm) n/N (%)	Median (IQR)	25(22.5-26)	23(21-25)	0.000**	23(22-24)	0.000**	23(21-24)	0.000***
	normal	134/161 (83.2)	115/158(72.8)	0.000****	52/64(81.3)	0.003****	110/159(69)	0.000****
	moderate malnutrition	23/161(14.3)	37/158(23.4)		11/64(17.2)		42/159(26)	
	severe malnutrition	4/161(2.5)	6/158(3.8)		1/64(1.6)		7/159(4.4)	
SGA score	Mean (±SD)	40.11(10.3)	46.18(10.4)		49.63(8.6)		49.88(8.8)	
	Median (IQR)	39(31-48.5)	47(37-54)	0.000**	49.5(43-56.75)	0.000**	50(44-58)	0.000***
24-29	n/N (%)	33/161(20.5)	9/158(5.7)	0.000****	1/64(1.6)	0.000****	2/159(1.3)	0.000****
30-39		52/161(32.3)	39/158(24.7)		5/64(7.8)		18/159(11)	
40-49		44/161(27.3)	49/158(31)		26/64(40.6)		56/159(35)	
50-59		26/161(16.1)	41/158(25.5)		21/64(32.8)		55/159(34)	
60-71		6/161(3.7)	20/158(12.7)		11/64(17.2)		28/159(17)	
Hemoglobin (g/dL)	Mean (±SD)	13.5(1.8)	12.5(1.8)	0.000*	12.6(1.4)	0.000*	12.5(1.8)	0.000*
Normal	n/N (%)	110/159(69.2)	62/147(42.2)	0.000****	24/59(40.7)		59/148(40)	0.000****
Mild anemia		39/159(24.5)	61/147(41.5)		28/59(47.5)		64/148(43)	
Moderate anemia		8/159(5)	23/147(15.6)		7/59(11.9)		24/148(16)	
Severe anemia		2/159(1.3)	1/147(0.7)		0		1/148(0.7)	
Bitot spots present		19/161(11.8)	17/158(10.8)		3/64(4.7)		19/161(12)	

"*Paired-Sample t Test, **Related-Samples Wilcoxon Signed Rank Test, ***Related-samples Marginal Homogeneity Test"("SD-standard deviation, CI-confidence interval, IQR-inter-quartile range, PS-performance status, BMI-body mass index, MUAC-mid-upper arm circumference, SGA-subjective global assessment")

Table 4.9 Trend in nutritional status before, during and at completion of treatment in the Node negative group. (N=73)

Variable			Baseline	End of first treatment	p value	End of second treatment	p value	At completion of treatment	p value
PS		median	0	2		2		2	
Weight(kg)		Mean (SD)	58.94 (12.0)	54.91(11.6)	**0.000***	53.67(9.5)	**0.000***	53.66 (11.24)	**0.000***
<50		**n/N(%)**	13/73(18)	23/72(32)	**0.000*** **	9/27(33.3)		28/73(38.4)	**0.000*** **
≥50			60/73(82)	49/72(68)		18/27(66.7)		45/73(61.6)	
Mean reduction in weight from baseline (kg)(95%CI)				4.03 (3.05-5.01)	**0.000***	7.81 (5.71-9.92)	**0.000***	5.46 (4.27-6.65)	**0.000***
Mean %reduction in weight from baseline (SD)				6.21(5.84)	**0.000***	6.71(8.19)	0.821*	8.93(7.97)	**0.000***
Change in weight from baseline n/N(%)		≥10% loss		19/72(26.4)		10/27(37)		30/73(41.1)	**0.009*** **
		<10% loss		40/72(55.6)		13/27(48.1)		34/73(46.6)	
		no change		5/72(6.9)		2/27(7.4)		2/73(2.7)	
		<10% rise		8/72(11.1)		0		7/73(9.6)	
		≥10% rise		0		2/27(7.4)			
BMI		mean (SD)	22.17(4.35)	20.65(4.06)	**0.000***	20.33(2.92)	**0.000***	20.23(4.01)	**0.000***
		mean reduction from baseline (95%CI)		1.52 (1.15-1.88)	**0.000***	2.83 (2.01-3.65)	**0.005***	2.01 (1.55-2.46)	**0.000***
≥18.5		**n/N(%)**	57/72(79.2)	48/72(66.7)	**0.000*** **	21/27(77.8)		47/73(64.4)	**0.000*** **
<18.5			15/72(20.8)	24/72(33.3)		6/27(22.2)		26/73(35.6)	
MUAC n/N(%)	median (IQR) (cm)		25(23.8-26.8)	24(22-25.8)	**0.000****	23(22-24)	**0.000****	23(22-24)	**0.000***
	normal		66/73(90.4)	59/72(80.8)	**0.034*****	23/27(31.5)	0.157***	58/73(79.5)	**0.011*** **
	moderate malnutrition		7/73(9.6)	13/72(18.1)		4/27(14.5)		15/73(20.5)	
	severe malnutrition		0	0		0			
SGA	mean(SD)		37(8.84)	44.8(10.07)		48.8(8.64)		47.4(8.76)	
	Median(IQR)		34(30-43.5)	46.5(36-53)	**0.000****	48(42-54)	**0.000****	48(41-53.5)	**0.000***
24-29	**n/N(%)**		18/73(24.7)	5/72(6.9)		0		0	
30-39			30/73(41.1)	21/72(29.2)		3/27(11.1)		15/73(20.5)	
40-49			17/73(23.3)	22/72(30.6)		12/27(44.4)		29/73(39.7)	
50-59			8/73(11)	17/72(23.6)		8/27(29.6)		21/73(28.8)	
60-71			0	7/72(9.7)		4/27(5.5)		8/73(11)	
Hb (g/dL) n/N(%)	Mean(SD)		13.5(1.9)	12.86(1.81)	**0.001***	12.77(1.58)	0.117*	12.86(1.8)	**0.001***
	normal		52/71(73.2)	32/64(50)		13/25(52)		33/64(51.6)	
	mild anemia		14/71(19.7)	24/64(37.5)		8/25(32)		22/64(34.4)	
	moderate anemia		3/71(4.2)	8/64912.5)		4/25(16)		9/64(14.1)	
	severe anemia		2/71(2.8)	0		0		0	
Bitot	present		3/73(4.1)	3/72(4.2)		1/27(3.7)		4/73(5.5)	

"*Paired-Sample t Test, **Related-Samples Wilcoxon Signed Rank Test,***Related-samples Marginal Homogeneity Test"("SD-standard deviation, CI-confidence interval, IQR-inter-quartile range, PS-performance status, BMI-body mass index, MUAC-mid-upper arm circumference, SGA-subjective global assessment, Hb-hemoglobin")

Table 4.10 Trend in nutritional status before, during and at completion of treatment in the Node positive group. (N=88)

Variable			Baseline	End of first treatment	p value	End of second treatment	p value	At completion of treatment	p value
PS		median	0	2		3		3	
Weight (kg)		Mean (SD)	56.74(11.56)	53.02(11.04)	**0.000***	53.1(8.58)	**0.000***	51(9.75)	**0.000***
<50		**n/N(%)**	24/88(27)	36/86(42)	**0.000****	13/37(35)		39/86(45)	**0.000****
≥50			64/88(73)	50/86(58)		24/37(65)		47/86(55)	
Mean reduction in weight from baseline (kg)(95%CI)				3.72 (2.79-4.65)	**0.000***	7.15 (5.22-9.07)	**0.000***	5.74 (4.65-6.84)	**0.000***
Mean % reduction in weight from baseline (SD)				3.59(6.73)	**0.000***	8.04(6.03)	**0.005***	9.37(8.66)	**0.000***
Change in weight from baseline n/N(%)	≥10% loss			24/86(27.9)		14/36(38.9)		42/86(48.8)	**0.000****
	<10% loss			45/86(52.3)		18/36(50)		34/86(39.5)	
	no change			7/86(52.3)		3/36(8.3)		4/86(4.7)	
	<10% rise			9/86(10.5)		1/36(2.8)		5/86(5.8)	
	≤10% rise			1/86(1.2)		0		1/86(1.2)	
BMI	mean(SD)		21.11(4.01)	19.72(3.98)	**0.000***	19.59(3.28)	**0.000***	18.95(3.51)	**0.000***
	mean reduction from baseline (95%CI)			1.39 (1.04-1.74)	**0.000***	2.62 (1.9-3.33)	**0.000***	2.16 (1.74-2.57)	**0.000***
n/N(%)	≥18.5		65/86(76)	50/86(58)	**0.000****	23/37(62)		43/86(50)	**0.000****
	<18.5		11/86(24)	36/86(42)		14/37(38)		43/86(50)	
MUAC (cm)	median (IQR)		24(22-26)	23(20-25)	**0.000***	23(22-24.25)	**0.000***	22(20-24)	**0.000***
normal		n/N (%)	68/88(77.3)	56/86(65.1)	**0.001****	29/37(78.4)	**0.008****	52/86(60.5)	**0.000****
moderate malnutrition			16/88(18.2)	24/86(27.9)		7/37(18.9)		27/86(31.4)	
severe malnutrition			4/88(4.5)	6/86(7)		1/37(2.7)		7/86(8.1)	
SGA	mean(SD)		42.74(10.73)	47.3(10.58)		50.22(8.57)		51.97(8.42)	
	Median (IQR)		42 (32.25-50.75)	48 (38-57)	**0.000***	50 (44.5-58)	**0.000***	53 (47-59)	**0.000***
24-29		n/N (%)	15/88(17)	4/86(4.7)	**0.000****	1/37(2.7)	**0.000****	2/86(2.3)	**0.000****
30-39			22/88(25)	18/86(20.9)		2/37(5.4)		3/86(3.5)	
40-49			27/88(30.7)	27/86(31.4)		14/37(37.8)		27/86(31.4)	
50-59			18/88(20.5)	24/86(27.9)		13/37(35.1)		34/86(39.5)	
60-71			6/88(6.8)	13/86(15.1)		7/37(18.9)		20/86(23.3)	
Hemoglobin (g/dL)	mean(SD)		13.43(1.7)	12.17(1.81)	**0.000***	12.41(1.16)	**0.000***	12.13(1.67)	**0.000***
normal		n/N (%)	58/88(66)	30/83(36.1)		11/34(32.4)		26/84(31)	
mild anemia			25/88(28)	37/86(44.6)		20/34(58.8)		42/84(50)	
moderate anemia			5/88(5.7)	15/86(18.1)		3/34(8.8)		15/84(17.9)	
severe anemia			0	1/86(1.2)		0		1/84(1.2)	
Bitot spots present			16/88(18)	14/86(16.3)		2/37(5.4)		15/88(17)	

"*Paired-Sample T Test, **Related-Samples Wilcoxon Signed Rank Test, ***Related-samples Marginal Homogeneity Test"("SD-standard deviation, CI-confidence interval, IQR-inter-quartile range, PS-performance status, BMI-body mass index,MUAC-mid-upper arm circumference, SGA-subjective global assessment")

Table 4.11 Nutritional parameters at completion of treatment compared in patients having received single versus multi-modality treatment.

Variable			Overall			Node negative group			Node positive group		
At completion of treatment			Single modality	Multi-modality	p value	single modality	Multi-modality	p value	Single modality	Multi-modality	p value
PS n/N(%)		0-1	18/63 (28.57)	17/96 (17.7)	0.075*	13/36 (36.11)	10/37 (27.03)	0.166*	5/27 (18.52)	7/59 (11.86)	0.459*
		2- 4	45/63 (71.43)	79/96 (82.2)		23/36 (63.89)	27/37 (72.97)		22/27 (81.48)	52/59(88.14)	
Mean weight kg (SD)			51.25 (11.95)	52.85 (9.46)	0.349**	53.81 (13.21)	53.51 (9.1)	0.913**	47.85 (9.21)	52.44 (9.73)	**0.042****
Change in weight	mean reduction kg (SD)		3.64 (4.25)	6.89 (5.15)	**0.000****	4.07 (4.45)	6.78 (5.18)	**0.019****	3.07 (3.99)	5.56 (9.57)	**0.000****
	mean reduction % (SD)		6.26 (8.3)	11.01 (7.82)	**0.000****	6.79 (7.31)	10.86 (8.13)	**0.028****	6.95 (5.12)	11.12 (7.69)	**0.005****
≥10% loss		n/N(%)	18/63 (28.57)	54/96 (56.2)	**0.002***	11/36 (30.56)	19/37 (51.35)	**0.025***	7/27 (25.93)	35/59 (59.32)	**0.008***
<10% loss			33/63 (52.38)	35/96 (36.4)		18/36 (50)	16/37 (43.24)		16/27 (59.26)	19/59 (32.2)	
no change			5/63 (7.94)	1/96 (1.04)		2/36 (5.56)	0		3/27 (11.11)	1/59 (1.69)	
<10% rise			6/63 (9.52)	6/96 (6.25)		5/36 (13.89)	2/37 (5.41)		1/27 (3.7)	4/59 (6.78)	
≥10% rise			1/63 (1.59)	0		0	0		1/27 (3.7)	0	
BMI	mean (SD)		19.19 (4.33)	19.77 (3.39)	0.347**	20 (4.72)	20.46 (3.22)	0.628**	18.11 (3.56)	19.34 (3.46)	0.133**
	mean reduction (SD)		1.29 (1.62)	2.57 (1.87)	**0.000****	1.44 (1.64)	2.66 (1.98)	**0.006****	1.1 (1.61)	2.52 (1.81)	**0.001****
obese		n/N (%)	2/63 (3.17)	2/96 (2.08)	0.108*	2/36 (5.56)	0	0.099*	0	2/59 (3.39)	0.298*
overweight			6/63 (9.52)	5/96 (5.21)		5/36 (13.89)	5/37 (13.51)		1/27 (3.7)	0	
normal			25/63 (39.68)	50/96 (52.1)		14/36 (38.89)	21/37 (56.76)		11/27 (40.74)	29/59 (49.15)	
mild y deficiency			12/63 (19.05)	27/96) 28.13)		6/36 (16.67)	9/37 (24.32)		6/27 (22.22)	18/59 (30.51)	
moderate deficiency			6/63 (9.52)	4/96 (4.17)		2/36 (5.56)	0		4/27 (14.81)	4/59 (6.78)	
severe deficiency			12/63 (19.05)	8/96 (8.33)		7/36 (19.44)	2/37 (5.41)		5/27 (18.52)	6/59 (10.17)	
MUAC (cm)	Median (IQR)		23 (20-24)	23 (21-24)	0.466***	23.5 (22-24.75)	23 (22-24.25)	0.832***	21 (18-23)	23 (20.5-24)	0.067***
	median reduction (IQR)		1 (0-2)	2 (1-4)	**0.000*****	1 (0-2)	2 (0.88-4)	**0.009*****	2 (0-2)	3 (1-4)	**0.001*****
normal		n/N(%)	39/63 (61.9)	71/96 (73.9)	0.122*	26/36 (72.22)	32/37 (86.49)	0.157*	13/27 (48.15)	39/59 (66.1)	0.041*
moderate malnutrition			19/63 (30.16)	23/96 (23.96		10/36 (27.78)	5/37 (13.51)		9/27 (33.33)	18/59 (30.51)	
severe malnutrition			5/63 (7.93)	2/96 (2.08)		0	0		5/27 (18.52)	2/59 (3.39)	

Variable			Overall			Node negative group			Node positive group		
At completion of treatment			Single modality	Multi-modality	p value	Single modality	Multi-modality	p value	Single modality	Multi-modality	p value
Hb (g/dL)	mean (SD)		12.35 (2.04)	12.51 (1.58)	0.579**	12.82 (1.98)	12.89 (1.66)	0.879**	11.79 (2)	12.27 (1.5)	0.228**
	mean reduction (SD)		0.84 (1.27)	1.17 (1.43)	0.161**	0.49 (1.25)	0.86 (1.62)	0.320**	1.25 (1.19)	1.37 (1.27)	0.688**
normal		n/N (%)	20/53 (37.74)	39/95 (41.05)	0.403*	13/28 (46.43)	20/36 (55.56)	0.832*	7/25 (28)	19/59 (32.2)	0.160*
mild anemia			21/53 (39.62)	43/95 (45.26)		11/28 (39.29)	11/36 (30.56)		10/25 (40)	32/59 (54.24)	
moderate anemia			12/53 (22.64)	12/95 (12.63)		4/28 (14.29)	5/36 (13.89)		8/25 (32)	7/59 (11.86)	
severe anemia			0	1/95 (1.05)		0	0		0	1/59 (1.69)	
SGA Score	mean (SD)		48.9 (10.16)	50.52 (7.85)	0.261**	45.53 (9.48)	49.27 (7.68)	0.068**	53.41 (9.42)	51.31 (7.92)	0.285**
	mean increase (SD)		4.4 (12.86)	12.36 (8)	**0.000****	8.03 (6.19)	12.86 (7.69)	**0.004****	-0.1 (17.1)	12.05 (8.25)	**0.000****
	median (IQR)		49 (40-58)	50.5 (46-57)	0.380***	47 (37.25-50)	49 (44.5-54)	0.082***	55 (47-62)	51 (47-58)	0.168***
	median increase (IQR)		6(2-10)	13 (7-18)	**0.000****	8 (3.25-11.75)	15 (6.5-19)	**0.009****	4 (0-9)	12 (8-17)	**0.000****
24-29		n/N(%)	1/63 (1.59)	1/96 (1.04)	**0.020***	0	0	0.060*	1/27 (3.7)	1/59 (1.69)	0.553*
30-39			13/63 (20.63)	5/96 (5.21)		12/36 (33.33)	3/37 (8.11)		1/27 (3.7)	2/59 (3.39)	
40-49			18/63 (28.57)	38/96 (39.58)		12/36 (33.33)	17/37 (45.95)		6/27 (22.22)	21/59 (35.59)	
50-59			18/63 (28.57)	37/96 (38.54)		8/36 (22.22)	13/37 (35.14)		10/27 (37.04)	24/59 (40.68)	
60-71			13/63 (20.63)	15/96 (15.63)		4/36 (11.11)	4/37 (10.81)		9/27 (33.33)	11/59 (18.64)	
Bitot spots present			12/65 (18.46)	7/96 (7.29)	**0.045***	3/36 (8.33)	1/37 (2.7)	0.358*	9/29 (31.03)	6/59 (10.17)	**0.019***

"*Pearson Chi Square Test, **Unpaired Student T Test, ***Independent-Samples Mann-Whitney U Test"

("PS-performance status, SD-standard deviation, IQR-inter quartile range, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, Hb-hemoglobin")

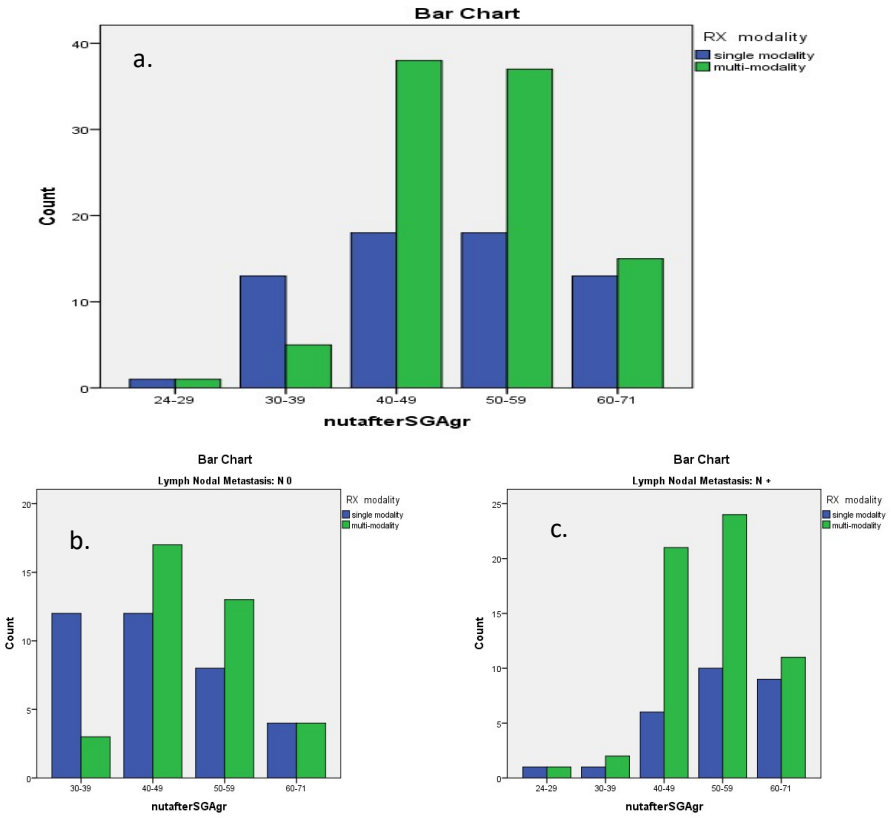

Figure 4.2 Distribution of SGA score at completion of treatment compared in patients having received single versus multi-modality treatment. a. overall, b. node negative group, c. node positive group.

4.5. Systemic immunity trend during treatment

4.5.A. Overall-

The mean TLC reduced from 8589 at baseline to 6746 at completion of treatment (p=0.000), mean change being 1823; mean %Neutrophil count increased from 65.2% to 71.5%; mean absolute Neutrophil count reduced from 5705 to 5015; mean %Lymphocyte count reduced from 23.9% to 15.3%; mean absolute Lymphocyte count reduced from 1987 to 999.8 respectively. The median NLR (IQR) was 3(2-4), 4(3-7), 5.86(4-9), and 5(3.8-8.4) at baseline, end of first, second modality, and completion of treatment (Table4.12).

4.5.B. Node-negative group-

The mean TLC reduced from 8576 at baseline to 7227 at completion of treatment (p=0.000), mean change being 1303; mean %Neutrophil count increased from 65.23% to 70.63%; mean absolute Neutrophil count reduced from 5753 to 5167; mean %Lymphocyte countreduced from 23.45% to 16.67%; mean absolute Lymphocyte count reduced from 1901 to 1180 respectively. The median NLR (IQR) was 3(2-4.13), 3.8(2.6-6), 5.52(3.81-9.63), and 4.5(3.02-8.23) at baseline, end of first, second modality, and completion of treatment (Table 4.13).

4.5.C. Node-positive group-

The mean TLC reduced from 8598 at baseline to 6368 at completion of treatment(p=0.000), mean change being 2231; mean %Neutrophil count increased from 65.15% to 72.12%; mean absolute Neutrophil count reduced from 5668 to 4896; mean %Lymphocyte countreduced from 24.17% to 14.22%; mean absolute Lymphocyte count reduced from 2053 to 858 respectively. The median NLR (IQR) was 3(2-4), 4.72(3.01-8), 6.3(3.91-7.64), and 6.08(4.8-7.8) at baseline, end of first, second modality, and completion of treatment (Table 4.14).

4.5.D. Single versus multi-modality treatment-

Comparison of systemic immunity marker at treatment completion between patients having received single versus multi-modality treatment is shown in Table 4.15. Mean TLC was significantly lower and median reductions in TLC significantly higher with multi-modality treatment in all groups. There was no difference in mean and mean change % neutrophil count in any group. But, mean absolute neutrophil count was significantly lower with multi-modality treatment in all groups, absolute neutrophil count was seen to increase with single modality and decrease with multi-modality treatment in all groups. There was no difference in mean and mean change %lymphocyte count in any group. But, mean absolute lymphocyte count was lower and median reduction in absolute lymphocyte count higher with

multi-modality treatment in all groups. Median NLR was not significantly different in N- cohort (4 v/s 5), but significantly higher with single modality treatment in N+ cohort (8 v/s 5.82). There was no significant difference noted in mean or median change in NLR with single versus multi-modality treatment in any group.

Table 4.12 Trends in systemic immunity marker before, during, and at completion of treatment. (N=161)

Variable		Baseline	End of first treatment	p value	End of second treatment	p value	At completion of treatment	p value
TLC	Mean (SD)	8588.83 (2520.57)	7734.99 (3406.9)	**0.005***	5761.5 (2475.78)	**0.000***	6745.83 (3437.55)	**0.000***
Mean change in TLC (95%CI)			853.84 (268.03-1439.64)		2760.05 (1917.53-3602.57)		1822.68 (1197.12-2448.24)	
Neutophil count	% mean (SD)	65.19 (10.79)	69.89 (10.71)	**0.000***	70.76 (10.84)	**0.001***	71.47 (10.51)	**0.000***
	mean change in % (95%CI)		4.70 (2.62-6.79)		6.35 (2.68-10.01)		6.33 (4.12-8.55)	
	absolute mean (SD)	5705.39 (2278.1)	5604.57 (2993.510	0.719*	4209.25 (2117.01)	**0.000***	5015.07 (2976.35)	**0.023***
	mean change in absolute (95%CI)		100.82 (450.96-652.6)		1419 (652.73-2185.28)		673.37 (92.37-1254.36)	
Lymphocyte count	% mean (SD)	23.86 (9.08)	17.69 (8.85)	**0.000***	14.75 (8.62)	**0.000***	15.3 (8.62)	**0.000***
	mean change in % (95%CI)		6.17 (4.44-7.89)		9.19 (6.39-12)		8.61 (6.87-10.35)	
	absolute mean (SD)	1986.62 (897.83)	1324.74 (7779.88)	**0.000***	816.18 (667.44)	**0.000***	999.75 (763.27)	**0.000***
	mean change in absolute (95%CI)		661.88 (528.18-795.58)		1167.38 (918.08-1416.69)		985.18 (837.71-1132.66)	
NLR	mean (SD)	3.87 (4.55)	5.58 (4.23)	**0.000***	6.98 (7.09)	**0.000***	6.71 (5.78)	**0.000***
	mean change in NLR (95%CI)		1.7 (0.8-2.61)		3.71 (1.79-5.63)		2.85 (1.72-3.98)	
	Median (IQR)	3 (2-4)	4 (3-7)	**0.000****	5.86 (3.97-8.96)	**0.000****	5 (3.77-8.38)	**0.000****
"*Paired-Sample t Test, **Related-Samples Wilcoxon Signed Rank Test"("TLC-total leukocyte count, SD-standard deviation, CI-confidence interval, IQR-inter quartile range, NLR-Neutrophil to Lymphocyte ratio")								

Table 4.13 Trends in systemic immunity marker before, during, and at completion of treatment in the node negative group. (N=73)

Variable		Baseline	End of first treatment	p value	End of second treatment	p value	At completion of treatment	p value
TLC	mean (SD)	8576.4 (2691.47)	7894.77 (2761.61)	0.094*	6820.38 (2854.49)	**0.024***	7227.12 (2791.07)	**0.009***
Mean change in TLC (95%CI)			681.63 (118.82-1482.08)		2118.69 (304.23-3933.16)		1303.27 (338.49-2268.05)	
Neutophil count	%mean mean (SD)	65.23 (11.67)	68.86 (10.12)	**0.026***	72.45 (9.51)	**0.035***	70.63 (9.7)	**0.001***
	mean change in % (95%CI)		3.63 (0.44-6.82)		6.34 (0.47-12.21)		5.52 (2.22-8.83)	
	absolute mean(SD)	5753.31 (2577.31)	5533.22 (2424.86)	0.560*	4986.73 (2444.18)	0.182*	5166.53 (2348.96)	0.214*
	mean change in absolute (95%CI)		220.09 (529.9-970.08)		1117.04 (556.91-2790.98)		547.52 (324.7-1419.73)	
Lymphocyte count	% mean (SD)	23.45 (9.77)	18.85 (8.37)	**0.001***	14.95 (9)	**0.002***	16.67 (8.47)	**0.000***
	mean change in % (95%CI)		4.6 (1.99-7.21)		7.4 (2.87-11.93)		6.9 (4.32-9.48)	
	absolute mean (SD)	1901.23 (802.68)	1436.05 (703.38)	**0.000***	1005.23 (890.52)	**0.001***	1180.14 (774.09)	**0.000***
	mean change in absolute (95%CI)		465.19 (269.36-661)		882.12 (417.3-1346.93)		718.55 (480.73-956.36)	
NLR	Mean (SD)	3.96 (3.85)	4.82 (3.19)	0.131*	8.26 (10.11)	0.054*	6.35 (6.94)	**0.015***
	mean change in NLR (95%CI)		0.86 (0.26-1.98)		4.25 (0.07-8.58)		2.41 (0.49-4.34)	
	Median (IQR)	3 (2-4.13)	3.8 (2.6-6)	**0.001****	5.52 (3.81-9.63)	**0.002****	4.5 (3.02-8.23)	**0.000****

"*Paired-Sample t Test, **Related-Samples Wilcoxon Signed Rank Test"
("TLC-total leukocyte count, SD-standard deviation, CI-confidence interval, IQR-inter quartile range, NLR-Neutrophil to Lymphocyte ratio")

Table 4.14 Trends in systemic immunity marker before, during, and at completion of treatment in the node positive group. (N=88)

Variable		Baseline	End of first treatment	p value	End of second treatment	p value	At completion of treatment	p value
TLC	Mean (SD)	8598.4 (2396)	7611.4 (3844.6)	**0.023***	4951.8 (1796.4)	**0.000***	6367.7 (3844.9)	**0.000***
Mean change in TLC (95%CI)			987.1 (139.4-1834.8)		3250.5 (2630.5-3870.5)		2230.8 (1403.2-3058.4)	
Neutophil count	% mean (SD)	65.15 (10.13)	70.68 (11.14)	**0.000***	69.47 (11.73)	**0.013***	72.12 (11.13)	**0.000***
	mean change in % (95%CI)		5.54 (2.74-8.33)		6.35 (1.41-11.29)		6.97 (3.94-10)	
	absolute mean(SD)	5668 (2032)	5650 (3382)	0.983*	3615 (1627)	**0.000***	4896 (3398)	0.057*
	mean change in absolute (95%CI)		852.4 (792.7-809.7)		1649.9 (1088.1-2211.7)		772.3 (22.1-1566.6)	
Lymphocyte count	% mean (SD)	24.17 (8.55)	16.79 (9.15)	**0.000***	14.59 (8.47)	**0.000***	14.22 (8.63)	**0.000***
	mean change in % (95%CI)		7.38(5.07-9.7)		10.56(6.89-14.24)		9.95(7.59-12.31)	
	absolute mean(SD)	2052.7 (964.6)	1238.6 (828.2)	**0.000***	671.6 (382.1)	**0.000***	858 (728.3)	**0.000***
	mean change in absolute (95%CI)		814.1 (635-993)		1385.5 (1127-1644)		1194.68 (1017-1372)	
NLR	mean(SD)	3.8(5)	6.16(4.82)	**0.001***	6(3.19)	**0.000***	7(4.7)	**0.000***
	mean change in NLR(95%CI)		2.36 (1-3.72)		3.29 (2.11-4.48)		3.19 (1.81-4.56)	
	Median (IQR)	3 (2-4)	4.72 (3.01-8)	**0.000****	6.3 (3.91-7.64)	**0.000****	6.08 (4-8.7.8)	**0.000****

"*Paired-Sample t Test, **Related-Samples Wilcoxon Signed Rank Test"
("TLC-total leukocyte count, SD-standard deviation, CI-confidence interval, IQR-inter quartile range, NLR-Neutrophil to Lymphocyte ratio")

Table 4.15 Systemic immunity marker at treatment completion compared in patients having received single versus multi-modality treatment.

Variable		Overall			Node negative group			Node positive group		
At completion of treatment		Single modality	Multi-modality	p value	Single modality	Multi-modality	p value	Single modality	Multi-modality	P value
TLC	mean (SD)	8622 (3865)	5680 (2659.2)	**0.000***	8318 (2650)	6371 (2625)	**0.004***	8975 (4955)	5262 (2612)	**0.000***
	mean change (SD)	112 (4103)	-2911 (3296)	**0.000***	295 (3253)	-2556 (3989)	**0.003***	-100 (4974	-3133 (2791)	**0.001***
	median change (IQR)	-50 (2377 to 2055)	-3024337 to -1452)	**0.000****	50 (-1925 to 5640)	-2570(-4605 to -930)	**0.000****	-420(-3280 to 1795)	-3140(-4300 to -2120)	**0.002****
NC	% mean (SD)	71.51(11.77)	71.44(9.8)	0.969	69.23(10.35)	71.73(9.15)	0.303	74.15(12.94)	71.26(10.26)	0.278
	mean change in % (SD)	5.11 (15.42)	7.02 (12.67)	0.415	4.85 (13.86)	6.05 (13.28)	0.721	5.4 (17.34)	7.63 (12.34)	0.511
	absolute mean (SD)	6388 (3543)	4242 (2284)	**0.000***	5890 (2379)	4600 (2193)	**0.026***	6967 (4525)	4019 (2329)	**0.000***
	mean change in absolute (SD)	609 (4287)	-1395 (2936)	**0.001***	535 (3228)	-1396 (3597)	**0.027***	695 (5332)	-1394 (2468)	**0.016***
	median change in absolute (IQR)	372 (-1445 to 2460)	-1522 (-2595 to -447)	**0.000****	359 (-1187 to 2100)	-1079(-3151 to -156)	**0.004****	385 (-2639 to 3288)	-1637(-2516 to -593)	**0.026****
LC	%mean (SD)	15.95(9.82)	14.93(7.9)	0.485*	18.2(7.9)	15.5(8.8)	0.192*	13.3(11)	14.7.3)	0.544*
	mean change in % (SD)	-7.13(11.84)	-9.47(10.17)	0.205*	-6.45(10.42)	-7.19(10.67)	0.778*	-7.92(13.48)	-10.93(9.66)	0.253*
	absolute mean (SD)	1257 (851)	856 (672)	**0.002***	1425(624)	989 (833)	**0.022***	1061 (1035)	772 (538)	0.096*
	mean change in absolute (SD)	-621 (755)	-1190 (935)	**0.000***	-414 (698)	-957 (1085)	**0.022***	-861 (760)	-1336 (803)	**0.014***
	median change in absolute	-604 (-1203 to -64)	-1883 (-1722 to-723)	**0.000****	-483(-908 to 88)	-1093 (-1650 to-399)	**0.003****	-850 (-1494 to-277)	-1240(-1823 to-836)	**0.027****

Variable		Overall			Node negative group			Node positive group		
At completion of treatment		Single modality	Multi-modality	p value	Single modality	Multi-modality	p value	Single modality	Multi-modality	P value
NLR	Mean(SD)	6.75(5.15)	6.68(6.13)	0.942*	4.94(3.32)	7.45(8.69)	0.147*	8.85(6.09)	6.2(3.76)	**0.017***
	median (IQR)	5(3.7-9.3)	5.31(3.9-8.2)	0.843**	4(2.8-5.7)	5(3.39-9.4)	0.116**	8 (4.13-11.41)	5.82(4-7.9)	**0.042****
	mean change (SD)	1.68(8)	3.48(6.35)	0.131*	0.77(5.41)	3.73(9.1)	0.125*	2.73(10.24)	3.21(3.84)	0.699*
	median change (IQR)	1.47(-0.05 to 4.98)	2.39(0.5 to 4.8)	0.311**	0.88(-0.09 to 2.94)	2.1(0.35 to 4.57)	0.146**	4.26(0.52 to 8.36)	2.45(0.74 to 4.88)	0.500**

"*Unpaired Student t Test, **Independent-Samples Mann-Whitney U Test"
("TLC-total leukocyte count, NC- neutrophil count, LC- lymphocyte count, SD-standard deviation, CI-confidence interval, IQR-inter quartile range, NLR-Neutrophil to Lymphocyte ratio")

4.6. Association between nutritional status and Neutrophil to Lymphocyte ratio

4.6.A. Median NLR at baseline and treatment completion-

The *differences in median NLR* between nutritional parameter groups are shown in Table 4.16 at baseline and Table 4.17 at completion of treatment. Median NLR was not different in patients with higher PS at baseline, but found to be significantly higher (6.34 v/s 4.67) in patients with PS >2 as compared to PS 0-2 at completion of treatment. Median NLR were same in all weight and BMI groups at baseline and at treatment completion, significantly higher (3.93 v/s 2.79) in N+ cohort in patients with ≥10% pre-treatment weight loss, same with ≥10% or <10% weight loss during treatment, higher in patients with low MUACin overall and N+ cohort(>21 cm- NLR 2.44, 17-21cm- NLR 3.21 and <17 cm-NLR 5.55) at baseline but same at treatment completion, higher with increasing SGA score at baseline.

4.6.B. NLR groups at baseline-

Cross-tabulation of N/R ratio groups (≤3, >3 and ≤6, >6) and nutritional parameters with relative risk (RR) before starting treatment is shown in Tables 4.18, 4.19 and 4.20 for overall, N- and N+ cohorts respectively. Percentage of patients with **NLR> 6** was significantly higher in patients with PS >2 v/s 0-2 in overall (30.77% v/s 8.9%; p=0.046; RR=2.171) and N- cohort (66.67% v/s 8.7%; p=0.031; RR=2.203) but not in N+ cohort; similar in weight ≤50 v/s >50kg and low v/s normal BMI in all groups; significantly higher in patients with pre-treatment weight loss ≥1;0% v/s <10% in overall (14.3% v/s 9.7%; p=0.057; RR=2.008) and N+ cohort (16% v/s 8%; p=0.015; RR=2.478) but not in N- cohort; higher in patients with MUAC ≤21 v/s>21cm in overall (25% v/s 9.1%; p=0.065; RR=-2.226), significantly higher in N+ cohort (14.3% v/s 9.1% p=0.006; RR=-3.253) and same in N- cohort; significantly higher in patients with hemoglobin <13 v/s ≥13g/dLin overall (22.45% v/s 4.7%; p=0.003; RR=-2.632), N- cohort (26.3% v/s 3.8%; p=0.014; RR=-2.569) and N+ cohort (20% v/s 5.3%; p=0.088; RR=-1.298); significantly higher in patients with SGA score ≥40 v/s <40 in overall group (17.33% v/s 4.76%; p=0.014; RR=2.806) and N+ cohort (16% v/s 2.7%; p=0.010; RR=2.935) but not in N- cohort.

4.6.C. NLR groups at treatment completion-

Cross-tabulation of N/R ratio groups (≤3, >3 and ≤6, >6) and nutritional parameters with relative risk (RR) at completion of treatment is shown in Tables 4.21, 4.22 and 4.23 for overall, N- and N+ cohorts respectively. Percentage of patients with **NLR> 6** was significantly higher in patients with PS >2 v/s 0-2 in overall (53.3% v/s 30.8%; p=0.013; RR=2.878) and N+ cohort (62% v/s 32.3%; p=0.014; RR=1.911) but not in N- cohort; significantly higher in patients with weight ≤50 v/s >50kg in only N- cohort(41.9% v/s 20.6%; p=0.018, RR= -2.689). No significant association was found with BMI, change in weight during treatment, MUAC, hemoglobin, SGA score or change in SGA score during treatment in any groups.

Table 4.16 Association between nutritional parameters and Neutrophil to Lymphocyte ratio at baseline before starting treatment.

Variable			NLR at baseline before starting treatment					
			Overall		Node negative		Node positive	
			median (IQR)	p value	media n (IQR)	p value	median (IQR)	p value
PS	0-2		3 (2)	0.078*	3 (2)	0.206*	3 (2)	0.175*
	>2		4 (4.2)		7 (2.5)		3.5 (2.3)	
Weight (kg)	30-39		3 (2.63)	0.239**	na	0.567**	3 (3.816)	0.234**
	40-49		3.32 (3)		4 (4)		3 (2.938)	
	50-59		3 (2.49)		3 (3)		3 (2.08)	
	60-69		3 (1.66)		3 (2)		3 (1.373)	
	70-79		2 (0.79)		2 (1.23)		2 (0.8)	
	80-89		2 (2)		2		2 (1.5)	
	90-99		4 (2)		4		na	
Weight loss in past 6m		<10%	3 (2)	0.135*	3 (2.25)	0.748*	2.79 (1.1)	**0.024***
		≥10%	3.4(2.6)		2 (2.2)		3.93(2.7)	
BMI	obese		2.0(1.8)	0.207**	3 (12.5)	0.886**	2	0.067**
	over weight		2 (2)		2 (2.58)		2.1 (1.25)	
	normal		3 (2)		3 (2)		3 (2)	
	mild deficiency		3 (3)		4 (6)		3 (2.35)	
	moderate deficiency		4 (16)		4		4	
	severe deficiency		4 (2)		3		4.63 (3.97)	
MUAC	normal		2.86 (2)	**0.010***	3 (2.1)	0.564**	2.44 (1.4)	**0.001***
	moderate malnutrition		3 (3)		2 (5)		3.21 (1.87)	
	severe malnutrition		5.5(3.6)		na		5.55 (3.58)	
Hemoglobin	normal		2.91 (2)	0.544**	2.89 (2)	0.695**	2.911 (2)	0.275**
	mild anemia		3 (3)		4 (6.45)		3 (2.316)	
	moderate anemia		3 (1.55)		2		3 (3)	
	severe anemia		4		4		na	
Bitot spots present		no	3 (2)	0.440*	3 (2.09)	0.750*	2.8 (2)	0.208*
		yes	3 (3.09)		2		3.5 (2.697)	
SGA score	24-29		2.43 (1)	0.069**	3 (1.5)	0.876**	2 (1)	**0.022***
	30-39		2.33 (2)		2.89 (3)		2.2 (1.03)	
	40-49		3 (2.2)		3 (2.3)		3 (2.3)	
	50-59		3 (3.7)		3 (5)		3 (3.7)	
	60-71		4.3(2.2)		na		4.3 (2.2)	

"*Independent-Samples Mann-Whitney U Test, **Independent-Samples Kruskal-Wallis Test"
("NLR-neutrophil to lymphocyte ratio, IQR-inter quartile range, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")

Table 4.17 Association between nutritional parameters and Neutrophil to Lymphocyte ratio at completion of treatment.

Variable			NLR at completion of treatment					
			Overall		Node negative		Node positive	
			median (IQR)	p value	median (IQR)	p value	median (IQR)	p value
PS	0-2		4.7(4)	**0.004***	4 (5)	0.072*	5 (4)	0.051*
	>2		6 (6)		5 (6)		6(7)	
Weight (kg)	30-39		7.6(8.5)	0.144**	3(2.5)	0.094**	6.7 (4.8)	0.811**
	40-49		5(4.5)		4.8(3.8)		5 (23)	
	50-59		6 (6.1)		5(8.5)		6(6.5)	
	60-69		6(4.5)		4 (7)		6.4(4)	
	70-79		3.8 (2)		3.7 (2.2)		na	
	80-89		5		4.5		na	
	90-99		na		na		na	
Weight loss during treatment	≥10% loss		5.5 (4.4)	0.066**	5 (4)	0.093**	6.4 (4.6)	0.276**
	<10% loss		5(4.3)		4 (3)		5.4 (5.1)	
	no change		4 (5.7		2.5		5.8(6.2)	
	<10% rise		8.6(5)		10 (8)		7.9 (10.9)	
	≥10% rise		na		na		na	
BMI	obese		4.9(1.5)	0.462**	4	0.871**	4.8	0.284**
	over weight		4.2(6.2)		4 (4)		na	
	normal		6(4.3)		5.1 (5.1)		6.3(4)	
	mild deficiency		4.3 (6)		4.2 (7)		5 (5.4)	
	moderate deficiency		6 (6.4)		4.7		7.4(6.7)	
	severe deficiency		6.7 (6.7)		5(7.6)		7.2 (6.5)	
MUAC (cm)	normal		5 (4.3)	0.283	4.2 (4.2)	0.124**	6.2 (5)	0.146**
	moderate malnutrition		5(5)		5.4 (6.7)		4 (4.6)	
	severe malnutrition		7.2 (12.7)		na		7.2(12.7)	
Hemoglobin (g/dL)	normal		4.8 (3.3)	0.224**	4.3 (3.2)	0.458**	5.9 (5.3)	0.315**
	mild anemia		6.1 (4.5)		4.7 (8)		6.3(4)	
	moderate anemia		5.8 (6.6)		5.8 (4.3)		6.6 (9.3)	
	severe anemia		na		na		na	
Bitot spots present		no	5(4.7)	0.939*	4.3 (5.7)	0.431*	6.3 (4.4)	0.394*
		yes	5.1 (5.7)		6.1		4.5 (7)	
SGA score		24-29	6	0.099**	na	0.111**	6	0.411**
		30-39	3.8 (2.3)		3.7 (1.8)		6.4	
		40-49	5.2 (4.5)		5.2 (6)		5.2 (3.2)	
		50-59	6.3(6)		4.8 (5.194)		7(6.2)	
		60-71	5(5.2)		5 (11.3)		5(4.2)	

"*Independent-Samples Mann-Whitney U Test, **Independent-Samples Kruskal-Wallis Test"("NLR-neutrophil to lymphocyte ratio, IQR-inter quartile range, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")

Table 4.18 Cross-tabulation and Risk Ratio between Nutritional parameters and Neutrophil to Lymphocyte ratio cutoff values at baseline before starting treatment.

Variable		NLR at baseline before starting treatment				
		Overall n/N (%)				
		≤3	>3 and ≤6	>6	p value*	RR**
PS	0-2	98/146 (67.1)	35/146 (24)	13/146 (8.9)	**0.046**	2.171
	>2	6/13 (46.15)	3/13 (23.08)	4/13 (30.77)		
Weight (kg)	≤50	24/45(53.33)	14/45(31.11)	7/45 (15.57)	0.123	-1.969
	>50	80/114(70.2)	24/114(21.1)	10/114 (8.8)		
Weight loss in past 6months	<10%	87/124(70.2)	25/124(20.1)	12/124 (9.7)	0.057	2.008
	≥10%	17/35(48.57)	13/35(37.14)	5/35 (14.29)		
BMI	<18.5	19/37(51.35)	12/37(32.43)	6/37 (16.22)	0.119	-1.964
	≥18.5	84/121(69.4)	26/121(21.5)	11/121 (9.1)		
MUAC (cm)	≤21	7/16 (43.75)	5/16 (31.25)	4/16 (25)	0.065	-2.226
	>21	97/143(67.8)	33/143(23.1)	13/143 (9.1)		
Hemoglobin (gm/gl)	<13	28/49(57.14)	10/49(20.41)	11/49(22.45)	**0.003**	-2.632
	≥13	76/109(69.7)	28/109(25.7)	5/109 (4.7)		
Bitot spots present	no	94/140(67.1)	31/140(22.1)	15/140(10.7)	0.416	0.86
	yes	10/19(52.63)	7/19 (36.84)	2/19 (10.53)		
SGA score	<40	62/84(73.81)	18/84(21.43)	4/84 (4.76)	**0.014**	2.806
	≥40	42/75(56)	20/75(26.67)	13/75(17.33)		

*Pearson Chi-Square Test **Cochran's and Mantel-Haenszel Statistic
("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")

T**able 4.19 Cross-tabulation and Risk Ratio between Nutritional parameters and Neutrophil to Lymphocyte ratio cutoff values at baseline before starting treatment in the node negative group.**

Variable		NLR at baseline before starting treatment				
		Node negative group n/N (%)				
		≤3	>3 and ≤6	>6	p value*	RR**
PS	0-2	45/69 (65.2)	18/69 (26.1)	6/69 (8.7)	**0.031**	2.203
	>2	1/3 (33.33)	0	2/3 (66.67)		
Weight (kg)	≤50	8/17 (47.1)	7/17 (41.2)	2/17 (11.8)	0.202	-1.193
	>50	38/55 (69.1)	11/55 (20)	6/55 (10.9)		
Weight loss in past 6months	<10%	40/62 (64.5)	15/62 (24.2)	7/62 (11.3)	1.000	0.137
	≥10%	6/10 (60)	3/10 (30)	1/10 (10)		
BMI	<18.5	8/16 (50)	5/16 (31.25)	3/16 (18.8)	0.364	-1.366
	≥18.5	37/55 (67.3)	13/55 (23.6)	5/55 (9.1)		
MUAC (cm)	≥21	3/3 (100)	0	0	0.688	1.208
	<21	43/69 (62.3)	18/69 (26.1)	8/69 (11.6)		
Hemoglobin (g/dL)	<13	9/19 (47.4)	5/19 (26.3)	5/19 (26.3)	**0.014**	-2.569
	≥13	37/52 (71.2)	13/52 (25)	2/52 (3.8)		
Bitot spots present	no	44/69 (63.8)	18/69 (26.1)	7/69 (10.1)	0.322	0.498
	yes	2/3 (66.67)	0	1/3 (33.33)		
SGA score	<40	31/47 (66)	13/47 (27.7)	3/47 (6.3)	0.205	1.144
	≥40	15/25 (60)	5/25 (20)	5/25 (20)		

*Pearson Chi-Square Test **Cochran's and Mantel-Haenszel Statistic
("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")

Table 4.20 Cross-tabulation and Risk Ratio between Nutritional parameters and Neutrophil to Lymphocyte ratio cutoff values at baseline before starting treatment in the node positive group.

		NLR at baseline before starting treatment				
At baseline		**Node positive group n/N (%)**				
Variable		**≤3**	**>3 and ≤6**	**>6**	**p value***	**RR****
PS	0-2	53/77 (68.8)	17/77 (22.1)	7/77(9.1)	0.436	1.307
	>2	5/10 (50)	3/10 (30)	2/10 (20)		
Weight (kg)	≤50	16/28 (57.1)	7/28(25)	5/28 (17.9)	0.237	-1.617
	>50	42/59 (71.2)	13/59 (22)	4/59 (6.7)		
Weight loss in past 6months	<10%	47/62 (75.8)	10/62 (16.1)	5/62(8.1)	**0.015**	2.478
	≥10%	11/25 (44)	10/25 (40)	4/25 (16)		
BMI	<18.5	11/21 (52.4)	7/21(33.3)	3/21 (14.3)	0.313	-1.417
	≥18.5	47/66 (71.2)	13/66(19.7)	6/66 (9.1)		
MUAC (cm)	≤21	4/13 (30.8)	5/13 (38.5)	4/13 (30.8)	**0.006**	-3.253
	>21	54/74 (73)	15/74 (20.3)	5/74 (6.8)		
Hemoglobin (g/dL)	<13	19/30 (63.3)	5/30 (16.7)	6/30(20)	0.088	-1.298
	≥13	39/57 (68.4)	15/57 (26.3)	3/57 (5.3)		
Bitot spots present	no	50-/71 (70.4)	13/71 (18.3)	8/71 (11.3)	0.092	0.822
	yes	8/16 (50)	7/16 (43.8)	1/16 (6.3)		
SGA score	<40	31/37 (83.8)	5/37 (13.5)	1/37(2.7)	**0.010**	2.935
	≥40	27/50 (54)	15/50 (30)	8/50 (16)		
*Pearson Chi-Square Test **Cochran's and Mantel-Haenszel Statistic ("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")						

Table 4.21 Cross-tabulation and Risk Ratio between Nutritional parameters and Neutrophil to Lymphocyte ratio cutoff values after completion of treatment.

Variable		NLR at completion of treatment				
		Overall				
		≤3	**>3 and ≤6**	**>6**	**p value***	**RR****
PS	0-2	18/78(23.1)	36/78 (46.1)	24/78 (30.8)	**0.013**	2.878
	>2	8/71 (11.3)	25/71 (35.2)	38/71 (53.5)		
Weight (kg)	≤50	9/79 (11.4)	33/79 (41.8)	37/79 (46.8)	0.098	-1.999
	>50	17/70 (24.3)	28/70(40)	25/70 (35.7)		
Weight change	no loss	4/18 (22.2)	3/18 (16.7)	11/18 (61.1)	0.141	0.071
	<10% loss	11/61 (18)	30/61 (49.2)	20/61 (32.8)		
	≥10% loss	11/70 (15.7)	28/70 (40)	31/70 (44.3)		
BMI	<18.5	8/64(12.5)	30/64 (46.9)	26/64 (40.6)	0.279	-0.574
	≥18.5	18/85 (21.1)	31/85 (36.5)	36/85 (42.4)		
MUAC (cm)	≤21	5/32(15.6)	11/32 (34.4)	16/32(50)	0.561	-0.891
	>21	21/117 (18)	50/117(42.7)	46/117(39.3)		
Hemoglobin (g/dL)	<13	15/89 (13.5)	31/89 (34.8)	43/89 (48.3)	0.128	-1.295
	≥13	10/58 (17.2)	29/58(50)	19/58 (32.8)		
Bitot spots present	no	23/133(17.3)	54/133(40.6)	56/133(42.1)	0.942	-0.313
	yes	3/16 (18.75)	7/16 (43.75)	6/16 (37.5)		
SGA score	<40	5/17 (29.41)	8/17 (47.06)	4/17 (23.53)	0.177	1.798
	≥40	21/132(15.9)	53/132(40.2)	58/132(43.9)		
SGA score change	no increase	1/166(0.25)	6/16 (37.5)	9/16 (56.25)	0.627	-1.295
	≤ 9 increase	10/60 (16.7)	26/60 (43.3)	24/60(40)		
	>9 increase	15/73 (20.5)	29/73 (39.7)	29/73 (39.7)		
*Pearson Chi-Square Test **Cochran's and Mantel-Haenszel Statistic ("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")						

Table 4.22 Cross-tabulation and Risk Ratio between Nutritional parameters and Neutrophil to Lymphocyte ratio cutoff values after completion of treatment in node negative group.

Variable		NLR at completion of treatment				
		Node negative group				
		≤3	>3 and ≤6	>6	p value*	RR**
PS	0-2	14/44 (31.8)	17/44(38.6)	13/44 (29.6)	0.149	1.316
	>2	2/21 (9.5)	12/21(57.1)	7/21 (33.3)		
Weight (kg)	≤50	3/31 (9.7)	15/31(48.4)	13/31 (41.9)	**0.018**	-2.689
	>50	13/34 (38.2)	14/34(41.2)	7/34 (20.6)		
Weight change	no loss	3/8 (37.5)	0	5/8 (62.5)	0.081	-0.071
	<10% loss	7/28(25)	15/28 (60)	6/28 (21.4)		
	≥10% loss	6/29 (23.1)	14/29(48.3)	9/29 (31)		
BMI	<18.5	3/23 (13)	13/23(56.5)	7/23 (30.4)	0.216	-0.897
	≥18.5	13/42 (31)	16/42(38.1)	13/42 (31)		
MUAC (cm)	≤21	1/8 (12.5)	3/8 (37.5)	4/8 (50)	0.399	-1.267
	>21	15/57 (26.3)	26/57(45.6)	16/57 (28.1)		
Hemoglobin (g/dL)	<13	7/31 (22.6)	12/31(38.7)	12/31 (38.7)	0.500	-0.857
	≥13	8/32(25)	16/32 (50)	8/32(25)		
Bitot spots present	no	16/63(25.4)	28/63(44.4)	19/63 (30.2)	1.000	0.843
	yes	0	1/2 (50)	1/2 (50)		
SGA score	<40	5/12 (41.67)	6/12 (50)	1/12 (8.33)	0.129	2.027
	≥40	11/53 (20.8)	23/53(43.4)	19/53 (35.9)		
SGA score change	no increase	0	1/2 (50)	1/2 (50)	0.798	0.009
	≤ 9 increase	9/29 (31)	11/29(37.9)	9/29 (31)		
	>9 increase	7/34 (20.6)	17/34 (50)	10/34 (29.4)		

*Pearson Chi-Square Test **Cochran's and Mantel-Haenszel Statistic("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")

Table 4.23 Cross-tabulation and Risk Ratio between Nutritional parameters and Neutrophil to Lymphocyte ratio cutoff values after completion of treatment in the node positive group.

Variable		NLR at completion of treatment				
		Node positive group				
		≤3	>3 and ≤6	>6	p value*	RR**
PS	0-2	4/34 (11.8)	19/34(55.9)	11/34(32.3)	**0.014**	1.911
	>2	6/50 (12)	13/50 (26)	31/50 (62)		
Weight (kg)	≤50	6/48(12.5)	18/48(37.5)	24/48(50)	1.000	0.091
	>50	4/36 (11.1)	14/36(38.9)	18/36(50)		
Weight change	no loss	1/10 (10)	3/10 (30)	6/10 (60)	0.840	0.044
	<10% loss	4/33 (12.1)	15/33(45.5)	14/33(42.4)		
	≥10% loss	5/41(12.2)	14/41(34.1)	22/41(53.7)		
BMI	<18.5	5/41(12.2)	17/41(41.5)	19/41(46.3)	0.864	0.510
	≥18.5	5/43 (11.6)	15/43(34.9)	23/43(53.5)		
MUAC (cm)	≤21	4/24 (16.7)	8/24 (33.3)	12/24(50)	0.701	0.399
	>21	6/60 (10)	24/60 (40)	30/60 (50)		
Hemoglobin (g/dL)	<13	8/58 (13.8)	19/58(32.8)	31/58(53.5)	0.306	-0.308
	≥13	2/26 (7.7)	13/26(50)	11/26(42.3)		
Bitot spots present	no	7/70(10)	26/70(37.1)	37/70(52.9)	0.389	-1.409
	yes	3/14 (21.4)	6/14 (42.9)	5/14 (35.7)		
SGA score	<40	0	2/5 (40)	3/5 (60)	0.862	-0.729
	≥40	10/79(12.7)	30/79 (38)	39/79(49.4)		
SGA score change	no increase	1/14(7.1)	5/14 (35.7)	8/14 (57.2)	0.180	-1.182
	≤ 9 increase	1/31(3.2)	15/31(48.4)	15/31(48.4)		
	>9 increase	8/39 (20.5)	12/39(30.8)	19/39(48.7)		

*Pearson Chi-Square Test **Cochran's and Mantel-Haenszel Statistic("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")

4.7. Correlation between nutritional status and Neutrophil to Lymphocyte ratio

Linear correlation coefficients were calculated for nutrition parameters and NLR before treatment and after treatment completion. At baseline statistically significant moderate positive correlation was found for SGA score and pre-treatment % weight loss; moderate negative correlation for weight and BMI; mild negative correlation for PS and hemoglobin in the overall group. Similar findings were noted for the N+ cohort, there was no significant correlation in the N- cohort (Table4.24).

At treatment completion in overall and N+ cohort there was statistically significant mild positive correlation for PS only. In N- cohort significant negative mild correlation was found for weight, MUAC and positive mild correlation for SGA score (Table4.25).

Table 4.24 Parametric and Non-parametric linear correlation between nutrition parameters and Neutrophil to Lymphocyte ratio at baseline before starting treatment.

At baseline	NLR at baseline before starting treatment											
	Overall				Node negative group				Node positive group			
Variable	R*	p value	Rho **	p value	R*	p value	Rho **	Pvalue	R*	p value	Rho **	p value
PS	na		-0.20	**0.011**	na		0.09	0.433	na		0.26	**0.017**
Weight (kg)	-0.45	**0.000**	-0.17	**0.033**	-0.07	0.579	-0.11	0.343	-0.22	**0.037**	-0.23	**0.033**
Weight loss in 6months	0.42	**0.000**	0.21	**0.007**	0.00	0.987	0.15	0.222	0.10	0.370	0.31	**0.003**
BMI	-0.37	**0.000**	-0.1	**0.047**	-0.12	0.333	-0.05	0.688	-0.23	**0.038**	-0.26	**0.016**
MUAC	-0.44	**0.000**	-0.171	**0.030**	-0.06	0.642	-0.00	0.976	-0.20	**0.069**	-0.35	**0.001**
Hb	-0.24	**0.002**	-0.17	**0.028**	-0.17	0.154	-0.25	**0.038**	-0.17	0.120	-0.10	0.381
SGA score	0.59	**0.000**	0.24	**0.002**	0.04	0.74	0.13	0.292	0.26	**0.017**	0.38	**0.000**
* Pearson's coefficient, ** Spearman's coefficient ("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, Hb-hemoglobin, SGA-subjective global assessment")												

Table 4.25 Parametric and Non-parametric linear correlation between nutrition parameters and Neutrophil to Lymphocyte ratio at baseline at completion of treatment.

At treatment completion	NLR at completion of treatment											
	Overall				Node negative group				Node positive group			
Variable	R*	p value	Rho **	P value	R*	p value	Rho **	p value	R*	p value	Rho **	p value
PS	na		0.24	**0.004**	na		0.20	0.102	na		0.22	**0.047**
Weight	-0.14	0.087	-0.10	0.245	-0.30	**0.015**	-0.31	**0.010**	0.09	0.418	0.07	0.510
Weight change (kg)	0.02	0.782	-0.01	0.924	0.08	0.549	-0.01	0.929	-0.04	0.741	-0.01	0.960
Weight change (%)	-0.02	0.837	-0.03	0.731	0.00	0.972	-0.08	0.504	-0.04	0.713	0.02	0.892
BMI	-0.12	0.134	-0.08	0.731	-0.21	0.091	-0.16	0.188	0.10	0.935	-0.01	0.965
BMI change	0.02	0.792	-0.01	0.902	0.06	0.654	-0.03	0.795	-0.00	0.844	0.00	0.998
MUAC	-0.16	**0.047**	-0.10	0.248	-0.31	**0.010**	-0.23	0.062	-0.05	0.662	0.03	0.804
Hb	-0.17	**0.042**	-0.20	**0.015**	-0.21	0.098	-0.24	0.051	-0.10	0.345	-0.14	0.192
SGA score	0.19	**0.017**	0.20	**0.016**	0.31	**0.013**	0.32	**0.010**	0.05	0.639	0.07	0.549
SGA score change	0.05	0.553	-0.00	0.989	0.19	0.135	0.15	0.245	-0.07	0.539	-0.06	0.589

* Pearson's coefficient, ** Spearman's coefficient
("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, Hb-hemoglobin, SGA-subjective global assessment")

4.8. Variables associated with failure to complete treatment (*FailureTxCompletion*)-

The baseline variable like age, gender, primary tumor subsite, cT stage and tumor grade were not found to be associated with *FailureTxCompletion* (Table 4.26). Proportion of patients with *FailureTxCompletion* was significantly higher with single versus multi-modality treatment in overall (20% v/s 4%; p=0.035; RR=2.75) and N+ cohort (34.5% v/s 13.46%; p=0.028; RR=3.35), but not in N- cohort. In N+ patients single modality treatment was given with palliative intent. PS was not associated with *FailureTxCompletion* (Table 4.27 a&b).

Nutrition parameters were found to be significantly associated with *FailureTxCompletion* in N+ cohort and systemic immunity in N- cohort.

In N+ cohort patients with *FailureTxCompletion* had significantly lower mean weight and BMI; significantly higher median pre-treatment % weight loss and SGA scores (Table 4.27 a&b). Proportion of patients who had *FailureTxCompletion* was significantly higher with low BMI (40.9% v/s 13%; p=0.002; RR=4.385), ≥10% pre-treatment weight loss (44% v/s 11.1%; p=0.001; RR=6.25) and low MUAC (46% v/s 16%; p=0.002; RR=4.5).

In N- cohort patients with *FailureTxCompletion* had significantly higher mean TLC, mean absolute and % neutrophil count and median NLR; significantly lower mean % neutrophil count (Table 4.27a&b). Proportion of patients who had *FailureTxCompletion* significantly increased with rising NLR ≤3, >3 ≥6, and >6 (0%, 1.92% and 25%; p=0.035).

Table 4.26 Comparing baseline variables with outcome measure- Completion of planned treatment.

Variable		Failed to complete all planned treatment							
		Overall			Node negative group		Node positive group		
		n/N (%)	p value	RR ***	n/N (%)	p value	n/N (%)	p value	RR ***
Age (years)	≤50	6/58 (10.3)	0.479**		1/31(3.2)	1.000**	5/27(18.52)	0.787**	
	>50	15/103 (14.6)			2/42(4.8)		13/61(12.3)		
Gender	male	18/142 (12.7)	0.717**		3/64(4.7)	1.000**	15/78(19.2)	0.680**	
	female	3/19 (15.8)			0		3/10(30)		
Primary tumor subsite	oral cavity	7/56 (12.5)	0.769**		2/31(6.5)	1.000**	5/25(20)	0.965**	
	sinuses	0			0		0		
	oropharynx	7/37 (18.9)			0		7/27(25.9)		
	hypopharynx	2/19 (10.5)			0		2/13(15.4)		
	larynx	4/37 (10.8)			1/21(4.8)		3/16(18.8)		
	CUPS	1/5(20)			na		1/5(20)		
cT stage	T1	1/18(5.6)	0.370**		0	0.549**	1/2(50)	0.474**	
	T2	3/40(7.5)			0		3/21(14.3)		
	T3	9/44 (20.5)			2/21(9.5)		7/23(30.4)		
	T4	7/54(13)			1/17(5.9)		6/37(16.2)		
	Tx	1/5(20)			na		1/5(20)		
Histo-pathology	Veruccous carcinoma	0	0.828**		0	0.302**	0	0.881**	
	WDSCC	1/17(5.9)			0		1/4(25)		
	MDSCC	17/120 (14.2)			2/54(3.7)		15/66(22.7)		
	PDSCC	2/14 (14.29)			1/4(25)		1/10(10)		
	PDC	0			0		0		
	CUPS	1/5(20)			na		1/5(20)		
Modality of treatment	single	13/65(20)	**0.035****	2.75	3/36(8.3)	0.115**	10/29(34.5)	**0.028****	3.35
	multiple	8/96 (4)			0		8/59 (13.56)		

"*Independent-Samples Student T Test **Pearson Chi-Square Test ***Cochran's and Mantel-Haenszel Statistic"

("RR-relative risk, SD-standard deviation, CUPS-carcinoma unknown primary with neck secondary, cT-clinical T, WDSCC-well differentiated squamous cell carcinoma, MDSCC- moderatly differentiated squamous cell carcinoma, PDSCC- poorly differentiated squamous cell carcinoma, PDC- poorly differentiated carcinoma")

Table 4.27a. Comparing nutrition and systemic immunity variables with outcome measure-Completion of planned treatment.

		Completed all planned treatment								
		Overall			Node-negative			Node-positive		
Variable		no	yes	p value	no	yes	p value	no	yes	p value
Weight kg	mean (SD)	51.8 (12.5)	58.7(11.3)	**0.012****	55.7(4.5)	59.3(12.2)	0.614**	51.1(13.4)	58(10.6)	**0.002****
BMI	mean (SD)	19.4 (4.3)	21.9(4.1)	**0.009****	18.8 (2)	22.4 (4.4)	0.159**	19.5(4.6)	21.4(3.8)	**0.006****
% pre-treatment weight loss	mean (SD)	11.5 (10.5)	5.5 (7.4)	**0.001****	4 (4.6)	4.3 (6.8)	0.948**	12.8(10.7)	6.7 (7.8)	**0.008****
	median (IQR)	11 (21)	3 (8)	**0.010****	3	0(5)	0.723**	12.5 (22)	5.5 (9)	**0.032****
MUAC (cm)	mean (SD)	23.9 (7.2)	24.8 (3)	0.268**	25 (1)	25.2 (3)	0.896**	23.7 (7.7)	24.5 (3)	0.497**
Hb (g/dL)	mean (SD)	13.4 (1.7)	13.4 (1.8)	0.975**	13.7 (3.8)	13.4 (1.8)	0.786**	13.4 (1.3)	13.5 (1.8)	0.823**
SGA score	mean (SD)	40.1 (12.4)	38.9 (9.4)	**0.000****	40.7 (5)	36.8 (9)	0.46**	49.3 (13)	41.1 (9.5)	**0.003****
	median (IQR)	49 (21)	38 (16)	**0.002***	43	33 (14)	0.300*	52.5 (22)	41 (17)	**0.001***
TLC count	mean (SD)	9221 (3043)	8449.6 (2471)	0.198**	11227 (424)	8255.7 (2666)	**0.000****	8886.7 (3169)	8640.7 (2265)	0.707**
NC	absolute mean (SD)	6227.2 (2461)	5606.6 (2309)	0.257**	8895(1029)	5427.5 (2519)	**0.021****	5782.6 (2353)	5783.1 (2084)	0.999**
	% mean (SD)	67.13 (11.6)	64.82 (10.97)	0.374**	79.61 (11.7)	63.82 (11.7)	**0.024****	65.05 (10.5)	65.81 (10.3)	0.781**
LC	absolute mean (SD)	2032.8 (1399)	1964.9 (792.6)	0.746**	1404(1125)	1926.1(790)	0.274**	2137.6 (1440)	2003.3 (798.9)	0.598**
	% mean (SD)	21.74 (10.4)	24.24 (9.16)	0.255**	12.42 (9.2)	24.61 (10)	0.042**	23.29 (9.95)	23.86 (8.32)	0.804**
NLR	mean (SD)	4.187 (3.44)	3.78 (4.56)	0.701**	9.67 (6.5)	3.58 (3.4)	**0.005****	3.22 (1.45)	3.98 (5.48)	0.577**
	median (IQR)	3.21 (2.54)	3 (2)	0.171*	10	3 (2)	**0.045***	3 (2.39)	2.96 (2)	0.493*

"**Unpaired-Sample Student T Test, ***Cochran's and Mantel-Haenszel Statistic, *Independent-Samples Mann-Whitney U Test"("BMI-body mass index, MUAC-mid-upper arm circumference, Hb-hemoglobin, SGA-subjective global assessment, TLC-total leukocyte count, NC-neutrophil count, LC-lymphocyte count, NLR-neutrophil/lymphocyte ratio")

Table 4.27b Comparing nutrition and systemic immunity variables with outcome measure-Completion of planned treatment.

At baseline		Failed to complete all planned treatment								
		Overall			Node-negative			Node-positive		
Variable		n/N (%)	p value	RR**	n/N (%)	p value	RR**	n/N (%)	p value	RR**
PS	0 to 2	18/148(12.2)	0.380*	0.462	3/70(4.3)	1.000*		15/78(19.2)	0.680*	0.556
	>2	313 (23.1)			0			3/10 (30)		
Weight (kg)	≤50	9/45 (20)	0.120*	2.167	0	0.579*		9/28 (32.1)	0.089*	2.684
	>50	12/116(10.3)			3/56(5.4)			9/60 (15)		
BMI	<18.5	11/ 38 (28)	**0.002***	4.563	2/16(12.5)	0.122*	7.857	9/ 22 (40.9)	**0.012***	4.385
	≥18.5	10/ 122 (8.2)			1/ 56 (1.8)			9/ 66 (13.6)		
Pre-treatment %weight loss	<10	10/126 (7.9)	**0.001***	5.32	3/ 63 (4.8)	1.000*		7/ 63 (11.1)	**0.001***	6.25
	≥10	11/ 35 (31.4)			0			11/ 25 (44)		
MUAC (cm)	≤21	6/ 16 (37.5)	**0.008***	5.2	0	1.000*		6/ 13 (46.2)	**0.022***	4.5
	>21	15/145(10.3)			3/70 (4.3)			12/75 (16)		
Hb (g/dL)	<13	9/49 (18.4)	0.212*	1.838	2/ 9 (10.5)	0.173*	6	7/ 30 (23.3)	0.781*	1.3
	≥13	12/110(10.9)			1/52 (1.9)			11/58 (19)		
SGA score	<40	6/85 (7.1)	**0.020***	2.56	1/48(2.01)	0.547*	0.245	5/37(13.5)	0.192*	2.19
	≥40	15/76 (19.7)			2/ 25 (8)			13/51(25.5)		
NLR	≤3	3/ 24 (12.5)	0.861*		0	**0.035***		3/ 12 (25)	0.730*	
	>3 and ≤6	14/118(11.9)			1/52 (1.9)			13/66(19.7)		
	>6	3/ 17 (17.7)			2/ 8 (25)			1/9 (11.1)		

*Pearson Chi-Square Test,**Cochran's and Mantel-Haenszel Statistic

("RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, Hb-hemoglobin, SGA-subjective global assessment, NLR-neutrophil to lymphocyte ratio")

4.9. Variables associated with Grade III complications

The baseline variables like age, gender, tumor grade, and treatment modality were not associated with Grade III complications. In N- cohort only primary tumor subsite and cT stage were significantly associated with GradeIII complications, but this was not seen in N+ cohort (Table 4.28). PS, nutrition parameters and systemic immunity were not found to be associated with Grade III complications in any group (Table 4.29).

Table 4.28 Comparing baseline variables with Grade III complications.

Variable		Grade III complicationsn/N (%)								
		Overall			Node negative group			Node positive group		
		no	p value	RR***	no	p value	RR***	no	p value	RR***
Age (yrs)	≤50	46/58(79.3)	0.556**	1.29	26/31(83.9)	0.269**	2.08	20/27(74.1)	0.790**	
	>50	77/103(74.7)			30/42(71.4)			47/61(77.1)		
Gender	male	108/142(76)	1.000**		49/64(76.6)	1.000**		59/78(75.6)	1.000**	
	female	15/19(78.95)			7/9 (77.8)			8/10(80)		
Primary tumor subsite	oral cavity	45/56(80.4)	0.231**		27/31(87.1)	**0.010****		18/25(72)	0.564**	
	sinuses	3/7 (42.86)			2/5 (40)			1/2 (50)		
	oropharynx	30/37(81.1)			7/10(70)			23/27(85.2)		
	hypopharynx	13/19(68.4)			2/6(33.3)			11/13(84.6)		
	larynx	29/37(78.4)			18/21(85.7)			11/16(68.8)		
	CUPS	3/5 (60)			na			3/5 (60)		
cT stage	T1	16/18(88.9)	0.066**		14/16(87.5)	**0.015****		2/2(100)	0.249**	
	T2	31/40(77.5)			12/19(63.2)			19/21(90.5)		
	T3	38/44(86.4)			20/21(95.2)			18/23(78.3)		
	T4	35/54(64.8)			10/17(58.8)			25/37(67.6)		
	Tx	3/5 (60)			na			3/5 (60)		
Histo-pathology	Verrucous carcinoma	1/2 (50)	0.689**		1/1 (100)	1.000**		0	0.191**	
	WDSCC	14/17(82.4)			10/13(76.9)			4/4(100)		
	MDSCC	91/120(75.8)			41/54(75.9)			50/66(75.8)		
	PDSCC	12/14(85.7)			3/4(75)			9/10(90)		
	PDC	3/4(75)			1/1(100)			2/3(66.67)		
	CUPS	2/4(50)			na			2/4(50)		
Modality of treatment	single	51/65(78.5)	0.706**	1.21	29/36(80.6)	0.581**	1.53	22/29(75.9)	1.000**	0.97
	multiple	72/96(75)			27/37(73)			45/59(76.3)		

"*Independent-Samples Student t Test **Pearson Chi-Square Test ***Cochran's and Mantel-Haenszel Statistic"

("RR-relative risk, SD-standard deviation, CUPS-carcinoma unknown primary with neck secondary, cT-clinical T, WDSCC-well differentiated squamous cell carcinoma, MDSCC- moderatly differentiated squamous cell carcinoma, PDSCC- poorly differentiated squamous cell carcinoma, PDC- poorly

differentiated carcinoma")

Table 4.29 Comparing nutrition and systemic immunity variables with Grade III complications.

Variable At Baseline		Overall			Node negative group			Node positive group		
		no	yes	p	no	yes	p	no	yes	p
PS n/N(%)	0-2	114/148 (77.0)	34/148 (23)	0.735*	54/70 (77.1)	16/70 (22.9)	1.000*	60/78 (76.9)	18/78 (23.1)	0.697*
	>2	9/13 (69.23)	4/13 (30.77)		2/3 (66.67)	1/3 (33.33)		7/10 (70)	3/10 (30)	
Weight (kg)	mean (SD)	57.74 (11.61)	57.79 (12.45)	0.981**	58.93 (12.13)	59.77 (11.97)	0.497**	56.75 (11.15)	56.19 (12.89)	0.848**
n/N(%)	≤50	33/45 (73.33)	12/45 (26.67)	0.353*	13/17 (76.47)	4/17 (23.53)	1.000*	20/28 (71.43)	8/28(28.57)	0.592*
	>50	90/116 (77.59)	26/116 (22.41)		43/56 (76.79)	13/56 (23.21)		47/60 (78.33)	13/60 (21.67)	
BMI	mean (SD)	21.46 (3.96)	21.99 (4.93)	0.499**	21.99 (4.36)	23.07 (4.43)	0.373**	21.01 (3.66)	21.11 (5.23)	0.927**
n/N(%)	<18.5	29/38 (76.31)	9/38(23.68)	1.000*	13/16 (81.25)	3/16 (18.75)	0.746*	16/22 (72.73)	6/22(27.27)	0.774*
	≥18.5	93/122 (76.23)	29/122 (23.77)		41/56 (73.21)	14/56 (26.79)		51/66 (77.27)	15/66 (22.73)	
% weight loss in past 6 months	mean (SD)	6 (7.43)	7.1(10)	0.463*	4.1 (6)	4.8(8.7)	0.686**	7.6(8.1)	9(10.8)	0.5545**
	median (IQR)	4 (9)	4 (12)	0.985	1 (8)	1 (5)	0.883	6 (12)	6 (14)	0.905
n/N(%)	<10	98/126 (7.78)	28/126 (22.22)	0.500**	49/63 (77.78)	14/63 (22.22)	0.689*	49/63 (77.78)	14/63 (22.22)	0.587*
	≥10	25/35 (71.43)	10/35 (28.57)		7/10 (70)	3/10 (30)		18/25 (72)	7/25 (28)	
MUAC (cm)	mean (SD)	24.63 (3.76)	24.97 (3.89)	0.63**	25.07 (2.76)	25.71 (3.5)	0.44**	24.26 (4.41)	24.38 (4.18)	0.91**
n/N(%)	≤21	12/16 (75)	4/16 (25)	1.000*	2/3 (66.67)	1/3 (33.33)	1.000*	10/13 (76.92)	3/13 (23.08)	1.000*
	>21	111/145 (76.55)	34/145 (23.45)		54/70 (77.14)	16/70 (22.86)		57/75 (76)	18/75 (24)	
Hemoglobin (g/dL)	mean (SD)	13.5 (1.71)	13.15 (1.94)	0.28**	13.46 (1.83)	13.16 (2.05)	0.58**	13.54 (1.62)	13.14 (1.89)	0.34**
	<13	36/49	13/49	0.5	16/19	3/19	0.5	20/30	10/30	0.1

n/N(%)		(73.47)	(26.53)	45*	(84.21)	(15.79)	31*	(66.67)	(33.33)	8*
	≥13	86/110 (78.18)	24/110 (21.82)		39/52(75)	13/52 (25)		47/58 (81.03)	11/58 (18.97)	
Variable At Baseline		**Overall**			**Node negative group**			**Node positive group**		
		no	**yes**	**p value**	**no**	**yes**	**p value**	**no**	**yes**	**p value**
Bitot spots present	n/N(%)	13/19 (68.42)	6/19(31.58)	0.395*	2/3(66.7)	1/3 (33.3)	1.000*	11/16 (68.75)	5/16(31.3)	0.519*
SGA score	mean (SD)	40.11 (10.26)	40.13 (10.6)	0.99**	37.11(8. 67)	36.41(9.63)	0.78**	42.61 (10.86)	43.14 (10.6)	0.85**
	median (IQR)	39 (17)	39 (20)	0.978$	34.5 (15)	35.5 (11)	0.642$	42 (17)	41 (20)	0.773
n/N(%)	<40	63/85 (74.12)	22/85 (25.9)	0.58*	35/48 (72.92)	13/48 (27.1)	0.386*	28/37 (75.67)	9/37 (24.3)	1.000*
	≥40	60/76 (78.95)	16/76 (21.1)		21/25 (84)	4/25 (16)		39/51 (76.47)	12/51 (23.5)	
TLC count	mean (SD)	8334.5 (2441.3)	9270 (2882)	0.051**	8565.71 (2689.3)	7728 (2617)	0.273**	8141.24 (2215)	10445 (2419)	**0.000***
Neutrophil count	mean of absolute (SD)	5555.64 (2260.3)	6128 (2535)	0.19**	5745.11 (2580)	4966 (2508)	0.28**	5397.3 (1959)	7013 (2223)	**0.002***
	mean of % (SD)	65.19 (10.78)	64.9 (12.1)	0.88**	65 (11.5)	62.67 (13.7)	0.49**	65.35 (10.21)	66.6 (10.6)	0.63**
Lymphocyte count	mean of absolute (SD)	1913.89 (7773.5)	2173(1190)	0.12**	1899.84 (737.3)	1920(1028)	0.93**	1925.64 (807.8)	2366(1291)	0.06**
	meano f%(SD)	23.86 (9)	24.08 (10.5)	0.90**	23.65 (9.63)	25.7 (12.2)	0.48**	24.03 (8.51)	22.84 (9.11)	0.58**
NLR	mean (SD)	3.77 (4.27)	4.02 (4.97)	0.77**	3.99 (4.08)	3.3 (2)	0.52**	3.59 (4.45)	4.57 (6.38)	0.43**
	median (IQR)	3 (2)	3 (2)	0.827$	2.89 (2.13)	3 (2.82)	0.995$	3 (2)	3 (2)	0.845$
n/N(%)	≤3	78/104 (75)	26/104 (25)	0.71*	35/46 (76.09)	11/46 (23.91	0.841*	43/58 (74.14)	15/58 (25.8)	0.461*
	>3 and ≤6	31/38 (81.58)	7/38 (18.4)		14/18 (77.78)	4/18 (22.2)		17/20 (85)	3/20 (15)	
	>6	13/17 (76.47)	4/17 (23.5)		7/8 (87.5)	1/8 (12.5)		6/9 (66.67)	3/9 (33.3)	

"*Pearson Chi-Square Test, ** Unpaired-Sample Student t Test, ***Cochran's and Mantel-Haenszel Statistic, $Independent-Samples Mann-Whitney U Test"("NLR-neutrophil to lymphocyte ratio, RR-risk ratio, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment")

4.10. Overall and progression free survival at 6months after completion of treatment

The overall median follow up was 182 days range being (0 to 640 days); 4.3% patients were lost to follow up. Disease progression at 6 months was seen in 36.02%, 23.3%, and 46.6% patients; death at 6 months in 14.9%, 8.2%, and 20.5% patients overall, N- and N+ cohorts respectively (Table4.30). Six months overall survival (OS) and progression free survival (PFS) is shown in Table4.31; median OS was 121days in N- and 91days in N+ cohort, but this difference was not statistically significant; median PFS was 91 days in both the groups. Table 4.32 shows the temporal profile of disease progression at primary, secondary, and distant sites. Disease progression at primary site during the first 6 weeks occurred in 2.8% and 13.25%, 6 weeks to 3 months in 9.72% and 25.33%, 3 to 6 months in 14.71% and 27.27% patients in N- and N+ cohorts respectively (all differences statistically significant). Disease progression at secondary site (neck nodes) during the first 6 weeks occurred in 4.17% and 10.84%, 6 weeks to 3 months in 8.33% and 21.33%, 3 to 6 months in 5.88% and 22.73% patients in N- and N+ cohorts respectively (all differences statistically significant).Disease progression at distant sites during the first 6 weeks occurred in 0 and 1.21%, 6 weeks to 3 months in 1.39% and 1.33%, 3 to 6 months in 1.47% and 3.03% patients in N- and N+ cohorts respectively (all differences statistically significant).

Table 4.30 Disease outcome at 6 months follow up.

	Overall (N=161)	Node negative (N=73)	Node positive (N=88)
Median follow up (days)	182	182	182
Follow up range (days)	0 to 640	3 to 640	0 to 640
Loss to follow up n/N (%)	7/161 (4.3)	1/73 (1.38)	6/88 (6.8)
Disease progression at 6 months n/N (%)	58/161 (36.02)	17/73 (23.3)	41/88 (46.6)
Death due to cancer at 6 months n/N (%)	24/161 (14.9)	6/73 (8.2)	18/88 (20.5)
Death due to other cause at 6 months	0	0	0

Total deaths on follow up n/N (%)	28/161 (17.4)	7/73 (9.6)	21/88 (23.9)

Table 4.31 Overall and progression free survival compared in node negative and node positive groups.

		Overall (N=161)	Node negative (N=73)	Node positive (N=88)	p value*
OS (days)	Median(IQR)	99(43.5-144.2)	121(13-171)	91(49- 121)	0.604*
6 month OS		85.1%	91.8%	79.5%	**0.009****
PFS(days)	median (IQR)	91(45-137)	91(45-182)	91(47.25-123)	0.615*
6 month PFS		63.98%	76.7%	53.4%	**0.000****
"*Independent-Samples Mann-Whitney U Test **Pearson Chi Square Test" (OS-overall survival, PFS-progression free survival)					

Table 4.32 Disease progression compared in node negative and node positive groups.

		Disease progression present n/N (%)			
Duration since completion of treatment		**Overall**	**Node negative**	**Node positive**	**p value***
0 to 6 weeks	primary site	13/155 (8.39)	2/72 (2.78)	11/83 (13.25)	**0.000**
	secondary site	12/155 (7.74)	3/72 (4.17)	9/83 (10.84)	**0.000**
	distant metastasis	1/155 (0.65)	0	1/83 (1.2)	0.073
6 weeks to 3 months	primary site	26/147(17.7)	7/72 (9.72)	19/75 (25.33)	**0.001**
	secondary site	22/147(15)	6/72(8.33)	16/75 (21.33)	**0.000**
	distant metastasis	2/147 (1.36)	1/72 (1.39)	1/75 (1.33)	**0.005**
3 to 6 months	primary site	28/134 (20.9)	10/68 (14.71)	18/66 (27.27)	**0.003**
	secondary site	19/134(14.2)	4/68(5.88)	15/66 (22.73)	**0.000**
	distant metastasis	3/134 (2.24)	1/68 (1.47)	2/66(3.03)	**0.005**
*Pearson Chi-Square Test					

4.11. Factors associated with disease progression at 6months after completion of treatment

As depicted in Tables 4.33 and 4.34, baseline variables like age, gender, primary tumor subsite and tumor grade were not associated with disease progression. Higher proportion of patients had disease progression with cT3/4 stage v/s cT1/2 stage (34.2% v/s 11.43%; p=0.02; RR=4.03) in N- cohort but not in N+ cohort; single v/s multi-modality treatment

(84.62% v/s 32.76%; p=0000; RR=11.1) in N+ cohort but not in N- cohort; *FailureTxCompletion* v/s completed treatment (75% v/s 42.65%; p=0.026; RR=4) in N+ cohort but not in N- cohort.

In overall group, PS >2 at baseline and treatment completion; low weight, BMI, MUAC at baseline and treatment completion; high SGA score at baseline and treatment completion; high TLC, absolute and % neutrophil counts at treatment completion, low % lymphocyte count at treatment completion and high NLR at treatment completion were significantly associated with disease progression (Tables4.35 and 4.38).

In N- cohort, no nutrition or systemic immunity variables at baseline were associated with disease progression. Low weight and BMI at treatment completion; high SGA score, % neutrophil count and NLR at treatment completion were significantly associated with disease progression (Tables4.36 and 4.39).

In N+ cohort, PS >2 at baseline; ≥10% pre-treatment weight loss; low weight, MUAC and % lymphocyte count at baseline and treatment completion; high SGA score, TLC, absolute neutrophil count and NLR at baseline and treatment completion were significantly associated with disease progression (Tables4.37 and 4.40).

Table 4.33 Comparing mean age in patients with or without disease progression or death at 6 months after completion of treatment.

		Age in years		
Disease progression at 6months		**mean age**	**SD**	**p value***
overall	no	56.46	13.33	0.708
	yes	55.64	13.35	
node negative group	no	56.45	13.26	0.304
	yes	52.65	13.18	
node positive group	no	56.49	13.59	0.895
	yes	56.88	13.84	
Death at 6months				
overall	no	56.11	13.28	0.918
	yes	56.42	13.69	
node negative group	no	56.1	13	0.245
	yes	49.5	15.81	
node positive group	no	56.12	13.67	0.469
	yes	58.72	12.56	
* Independent-Samples Student t Test				

Table 4.34 Cross-tabulation of percentage disease progression at 6 months from completion of treatment with baseline and treatment parameters.

		Progression at 6 months from completion of treatmentn/N (%)					
		OverallN=157		Node negative N=73		Node positive N=84	
Variable		**yes**	**p value**	**yes**	**p value**	**yes**	**p value**
Age (years)	≤50	19/58 (32.76)	0.494*	8/31 (25.81)	0.781*	11/27 (40.74)	0.356*
	>50	39/99 (39.4)		9/42 (21.43)		30/57 (52.63)	
Gender	male	51/138 (36.96)	1.000*	16/64 (25)	0.448*	35/74 (47.3)	0.515*
	female	7/19 (36.84)		1/9 (11.11)		6/10 (60)	
Primary tumor subsite	oral cavity	19/56 (33.93)	0.090*	6/31 (19.35)	0.080*	13/25 (52)	0.727*
	sinuses	4/7 (57.14)		3/5 (60)		1/2 (50)	
	oropharynx	19/36 (52.78)		4/10 (40)		15/26 (57.69)	
	hypopharynx	7/17 (41.18)		2/6 (33.33)		5/11 (45.45)	
	larynx	8/36 (22.22)		2/21 (9.52)		6/15 (40)	
	CUPS	1/5 (20)		na		1/5 (20)	
cT stage	T1/ T2	12/56 (21.43)	**0.004***	4/35 (11.43)	**0.028* RR=4.03**	8/21 (38.1)	0.167*
	T3/ T4	45/96 (46.88)		13/38 (34.2)		32/58 (55.17)	
	Tx	1/5 (20)		na		1/5 (20)	
Histopathology	veruccous carcinoma	0	0.479*	0	0.763*	0	0.648*
	WDSCC	4/17 (23.53)		3/13 (23.08)		1/4 (25)	
	MDSCC	45/117 (38.46)		12/54 (22.22)		33/63 (52.38)	
	PDSCC	7/13 (53.85)		2/4 (50)		5/9 (55.56)	
	PDC	1/4 (25)		0		1/3 (33.33)	
	CUPS	1/4 (25)		na		1/4 (25)	
Modality of treatment	single	29/62 (46.77)	**0.044*, RR=5.9**	7/36 (19.44)	0.581*	22/26 (84.62)	**0.000*, RR=11.1**
	multiple	29/95 (30.53)		10/37 (27.03)		19/58 (32.76)	
Completed all planned treatment	no	14/19 (73.68)	**0.001*, RR=2**	2/3 (66.67)	0.133*	12/16 (75)	**0.026*, RR=4**
	yes	44/138 (31.88)		15/70 (21.43)		29/68 (42.65)	
*Pearson Chi-Square Test							

Table 4.35 Comparing nutrition status and systemic immunity parameters at baseline with disease progression at 6 months of completion of treatment in the overall group. (N=157)

At baseline		Progression at 6months from completion of treatment				
Variable		**no**	**yes**	**p value**	**RR**	**p value$**
PS n/N(%)	0-2	95/144 (66)	49/144 (34)	**0.016***	4.36	**0.019**
	>2	4/13 (30.77)	9/13 (69.23)			
Weight (kg)	mean (SD)	58.3 (12)	55 (10.7)	0.201**		
	median (IQR)	60 (18.3)	55 (13.3)	**0.002*****		
n/N(%)	≤50	23/44 (52.3)	21/44 (47.7)	0.098*	0.53	0.083
	>50	76/113 (67)	37/113 (33)			
BMI	mean (SD)	21.74 (4.08)	21.04 (4.82)	0.456**		
	median (IQR)	21.38 (5.71)	20.15 (4.36)	**0.007*****		
n/N(%)	<18.5	16/35 (45.7)	19/35 (54.3)	**0.028***	0.401	**0.019**
	≥18.5	82/121 (68)	39/121 (32)			
% weight loss in past 6 months	mean (SD)	5.68 (7.68)	8.96 (9.92)	0.068**		
	median (IQR)	2 (8)	5 (13)	0.064***		
n/N(%)	<10	82/123 (67)	41/123 (33)	0.107*	2	0.078
	≥10	17/34 (50)	17/34 (50)			
MUAC (cm)	mean (SD)	24.96 (3.72)	23.63 (4.15)	0.114**		
	median (IQR)	25 (3.6)	24 (5)	**0.007*****		
n/N(%)	≤21	3/16 (18.7)	13/16 (81.3)	**0.000***	0.108	**0.001**
	>21	96/141 (68)	45/141 (32)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	13.13 (2.23)	13.49 (1.65)	0.350		
	<13	27/48 (56.3)	21/48 (43.8)	0.287*	0.680	0.276
	≥13	70/107 (65)	37/107 (35)			
Bitot spots presentn/N(%)	no	92/139 (66)	47/139 (34)	**0.036***	3.08	**0.029**
	yes	7/18 (38.89)	11/18 (61.1)			
SGA score	mean (SD)	38.95 (9.78)	45.2 (11.72)	**0.006****		
	median (IQR)	36 (16)	44.5 (20)	**0.000*****		
n/N(%)	<40	61/84(72.62)	23/84(27.38)	**0.009***	2.44	**0.008**
	≥40	38/73 (52)	35/73 (48)			
TLC count	mean (SD)	8337 (2425)	9336 (2937)	0.074**		
	median (IQR)	77720(2720)	8280 (3860)	0.132		
Neutrophil count	mean of absolute (SD)	5498(2202)	6516 (2906)	**0.050****		
	median of absolute (IQR)	5039 (2136)	5830 (3292)	0.064***		
	mean of % (SD)	64.56 (9.91)	68 (15.3)	0.150		
	median of %(IQR)	64.1 (13.2)	69.3 (16.5)	**0.035*****		
Lymphocyte count	mean of absolute (SD)	1965.4 (743)	1828 (1071)	0.441**		
	median of absolute (IQR)	1981.5 (917)	1706 (1087)	0.081***		
	mean of % (SD)	24.5 (8.6)	20.5(11.3)	**0.049****		
	median of % (IQR)	25.8 (10.1)	20.3 (10.9)	**0.003*****		
NLR	mean (SD)	3.35 (2.74)	6.68 (9.02)	**0.001****		
	median (IQR)	2.63 (1.05)	3.66 (3.2)	**0.005*****		
n/N(%)	≤3	74/102(72.5)	28/102(27.5)	**0.001***		
	>3 and ≤6	18/37(48.6)	19/37 (51.4)			
	>6	6/17 (35.3)	11/17 (64.7)			

"*Pearson Chi-Square Test **Independent-Samples Student T Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.36 Comparing nutrition status and systemic immunity parameters at baseline with disease progression at 6 months of completion of treatment in the node negative group.(N=73)

At baseline		Progression at 6months from completion of treatment				
Variable		no	yes	p value	RR	p value$
PS n/N(%)	0-2	54/70 77.14)	16/70(22.86)	1.000*	1.69	0.677
	>2	2/3 (66.67)	1/3 (33.33)			
Weight (kg)	mean (SD)	60.6 (12.77)	54.47 (8.26)	0.068**		
	median (IQR)	60 (18)	55 (11.5)	0.108***		
n/N(%)	≤50	11/17 (64.7)	6/17 (35.29)	0.202*	0.448	0.187
	>50	45/56 80.36)	11/56 19.64)			
BMI	mean (SD)	22.64 (4.53)	20.53 (3.16)	0.065**		
	median (IQR)	22 (5.47)	21 (5.63)	0.103***		
n/N(%)	<18.5	10/16 (62.5)	6/16 (37.5)	0.183*	0.407	0.145
	≥18.5	45/56 80.36)	11/56(19.64)			
% weight loss in past 6 months	mean (SD)	4.56 (7.2)	3.47 (4.7)	0.587**		
	median (IQR)	0 (8)	2 (4.7)	0.806***		
n/N(%)	<10	47/63 (74.6)	16/63 (25.4)	0.435*	0.326	0.306
	≥10	9/10 (90)	1/10 (10)			
MUAC (cm)	mean (SD)	25.59 (3.08)	24.47 (2.43)	0.233**		
	median (IQR)	25 (3)	25 (3.5)	0.511***		
n/N(%)	≤21	1/3 (33.33)	2/3 (66.67)	0.133*	0.136	0.113
	>21	55/70 78.57)	15/70 21.43)			
Hemoglobin (g/dL)	mean (SD)	13.45 (1.73)	13.22 (2.33)	0.663**		
n/N(%)	<13	14/19 73.68)	5/19 (26.32)	1.000*	0.840	0.777
	≥13	40/52 76.92)	12/52 23.08)			
Bitot spots presentn/N(%)	no	54/70 77.14)	16/70 22.86)	1.000*	1.69	0.677
	yes	2/3 (66.67)	1/3 (33.33)			
SGA score	mean (SD)	36.15 (8.42)	40 (9.8)	0.104**		
	median (IQR)	33 (13)	39 (19)	0.112***		
n/N(%)	<40	38/48 79.17)	10/48 20.83)	0.564*	1.48	0.493
	≥40	18/25 (72)	7/25 (28)			
TLC count	mean (SD)	8322(2481)	8565 (3317)	0.746**		
	median (IQR)	7730 (2930)	6940 (5905)	0.755***		
Neutrophil count	mean of absolute (SD)	5456 (2403)	5946 (3095)	0.496**		
	median of absolute (IQR)	5150 (2398)	4926 (5071)	0.776***		
	meanof%(SD)	63.75 11.09)	66.83 14.61)	0.359**		
	median of %(IQR)	64 (15.63)	67 (19.8)	0.196***		
Lymphocyte count	mean of absolute (SD)	1967 (782)	1701 (860)	0.234**		
	median of absolute (IQR)	1855 (877)	1508 (1269)	0.178***		
	meanof% (SD)	24.94 (9.63)	21.4 (11.76)	0.213**		
	median of %(IQR)	24.57 (11.5)	18 (13.68)	0.096***		
NLR	mean (SD)	3.58 (3.73)	4.67 (3.66)	0.293**		
	median (IQR)	2.78 (2)	4 (4)	0.118***		
n/N(%)	≤3	38/46 82.61)	8/46 (17.39)	0.312*		
	>3 and ≤6	12/18 66.67)	6/18 (33.33)			
	>6	5/8 (62.5)	3/8 (37.5)			

"*Pearson Chi-Square Test **Independent-Samples Student t Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.37 Comparing nutrition status and systemic immunity parameters at baseline with disease progression at 6 months of completion of treatment in the node positive group.

At baseline		Progression at 6months from completion of treatment				
		Node positive group N=84				
Variable		no	yes	p value	RR	p value$
PS	0-2	41/74 (55.41)	33/74 (44.59)	**0.046***	4.97	0.052
n/N(%)	>2	2/10 (20)	8/10 (80)			
Weight (kg)	mean (SD)	59.81 (11.85)	53.32 (10.33)	**0.009****		
	median (IQR)	60 (19)	55 (14.5)	**0.015*****		
	≤50	12/27 (44.44)	15/27 (55.56)	0.485*	0.671	0.396
n/N(%)	>50	31/57 (54.39)	26/57 (45.61)			
BMI	mean (SD)	21.81 (3.7)	20.37 (4.2)	0.099**		
	median (IQR)	21.08 (4.87)	20 (4.09)	0.063***		
	<18.5	6/19 (31.58)	13/19 (68.42)	0.069*	0.349	0.057
n/N(%)	≥18.5	37/65 (56.92)	28/65 (43.08)			
% weight loss in past 6 months	mean (SD)	6.33 (8.03)	9.46 (9.56)	0.107**		
	median (IQR)	5 (9)	7 (15)	0.134***		
	<10	35/60 (58.33)	25/60 (41.67)	**0.033***	2.8	**0.042**
n/N(%)	≥10	8/24 (33.33)	16/24 (66.67)			
MUAC (cm)	mean (SD)	25.5 (4.69)	23.25 (3.75)	**0.013****		
	median (IQR)	25 (4)	23 (6)	**0.017*****		
n/N(%)	≤21	2/13 (15.38)	11/13 (84.61)	**0.006***	0.113	**0.012**
	>21	41/71 (57.75)	30/71 (42.25)			
Hemoglobin (g/dL)	mean (SD)	13.58 (1.81)	13.36 (1.48)	0.553**		
	<13	13/29 (44.83)	16/29 (55.17)	0.491*	0.677	0.398
n/N(%)	≥13	30/55 (54.55)	25/55 (45.45)			
Bitot spots presentn/N(%)	no	38/69 (55.07)	31/69 (44.93)	0.160*	2.45	0.134
	yes	5/15 (33.33)	10/15 (66.67)			
SGA score	mean (SD)	38.84 (9.46)	46.29 (10.99)	**0.001****		
	median (IQR)	37 (16)	47 (18)	**0.002*****		
n/N(%)	<40	23/36 (63.89)	13/36 (36.11)	**0.050***	2.48	**0.046**
	≥40	20/48 (41.67)	28/48 (58.33)			
TLC count	mean (SD)	8107(2226.9)	9087 (2501)	0.061**		
	median (IQR)	7620 (2450)	8460 (2855)	0.058***		
Neutrophil count	mean of absolute (SD)	5230.37 (1706.9)	6245.32 (2438.43)			
	median of absolute (IQR)	4896 (1698)	5855 (2607)	**0.050*****		
	meanof % (SD)	63.82 (7.78)	67.51 (11.73)	0.092**		
	median of % (IQR)	64.74 (8.48)	69.68 (17.3)	0.095***		
Lymphocyte count	mean of absolute (SD)	2081.79 (709.28)	1870.27 (881.3)	0.228**		
	median of absolute (IQR)	2072 (942)	1827 (1109)	0.119***		
	meanof % (SD)	25.87 (6.51)	21.28 (9.2)	**0.010****		
	median of %(IQR)	26 (9.11)	20.65 (10.33)	**0.008*****		
NLR	mean (SD)	2.68 (1.12)	5.15 (6.93)	**0.024****		
	median (IQR)	2.44 (1)	3.4 (2.56)	**0.013*****		
	≤3	36/56 (64.29)	20/56 (35.71)	**0.001***		
n/N(%)	>3 and ≤6	6/19 (31.58)	13/19 (68.42)			
	>6	1/9 (11.11)	8/9 (88.89)			

"*Pearson Chi-Square Test **Independent-Samples Student T Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.38 Comparing nutrition status and systemic immunity parameters at completion of treatment with disease progression at 6 months of completion of treatment in overall group. (N=157)

At completion of treatment		Progression at 6months from completion of treatment				
Variable		**no**	**yes**	**p**	**RR**	**p$**
PS n/N(%)	0-2	60/85 (70.59)	25/85 (29.41)	**0.047***	1.97	**0.044**
	>2	39/71 (54.93)	32/71 (45.07)			
Weight (kg)	mean (SD)	54.59 (11.47)	49.11 (8.13)	**0.001****		
	median (IQR)	53 (16)	50 (12)	**0.006*****		
n/N(%)	≤50	48/84 (57.14)	36/84 (42.86)	0.096*	0.549	0.078
	>50	51/72 (70.83)	21/72 (29.17)			
BMI	mean (SD)	20.2 (3.92)	18.7 (3.34)	**0.007****		
	median (IQR)	20 (5)	18.5 (5)	**0.011*****		
n/N(%)	<18.5	37/67 (55.22)	30/67 (44.78)	0.068*	0.537	0.065
	≥18.5	62/89 (69.66)	27/89 (30.34)			
Change in weight (kg)	mean (SD)	-6.14 (5.19)	-5.14 (5.01)	0.683**		
	median (IQR)	-5 (8)	-4 (6.25)	0.495***		
	no decrease	10/19 (52.63)	9/19 (47.37)	0.507*	na	
	<10% decrease	44/66 (66.67)	22/66 (33.33)			
n/N(%)	≥10% decrease	45/71 (63.38)	26/71 (36.62)			
MUAC (cm)	mean (SD)	23.6 (4)	21.73 (3.02)	**0.001****		
	median (IQR)	23 (3.5)	22 (4)	**0.006*****		
n/N(%)	≤21	15/34 (44.12)	19/34 (55.88)	**0.010***	0.357	**0.009**
	>21	84/122(68.85)	38/122 (31.15)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	12.65 (1.74)	12.14 (1.73)	0.084**		
	<13	51/87 (58.62)	36/87 (41.38)	0.224*	0.638	0.208
	≥13	40/58 (69)	18/58 (31)			
Bitot present n/N(%)	no	90/139 (64.7)	49/139 (35.25)	0.299*	1.84	0.227
	yes	9/18 (50)	9/18 (50)			
SGA score	mean (SD)	48.06 (8.6)	53.33 (7.92)	**0.000****		
	median (IQR)	49 (12)	53 (14)	**0.000*****		
n/N(%)	<40	19/20 (95)	1/20 (5)	**0.002***	13.3	**0.013**
	≥40	80/136 58.82)	56/136 (41.18)			
Change in SGA score n/N(%)	no increase	10/18 (55.56)	8/18 (44.44)	0.593*	na	
	≤9 point increase	38/62 (61.29)	24/62 (38.71)			
	>9 point increase	51/76 (67.1)	25/76 (32.89)			
TLC count	mean (SD)	6001 (2502)	7873 (4313)	**0.001****		
	median (IQR)	5850 (3025)	6925 (5090)	**0.010*****		
Neutrophil count	meanofabsolute(SD)	4357 (2052)	6098 (3917)	**0.001****		
	median of absolute (IQR)	4045 (2402)	4951 (4413)	**0.004*****		
	mean of % (SD)	70.14 (9.75)	73.94 (10.73)	**0.030****		
	median of % (IQR)	70.39 (9.94)	75.02 (11.8)	**0.014*****		
Lymphocyte count	meanofabsolute(SD)	1007.5 (630)	919.9 (746)	0.449**		
	median of absolute (IQR)	808 (672)	734 (542)	0.239***		
	mean of % (SD)	16.44 (7.62)	13.13 (9.5)	**0.002****		
	median of % (IQR)	15.94 (8.26)	11 (7.29)	**0.000*****		
NLR	mean (SD)	5.51 (4.33)	8.73 (8.19)	**0.001****		
	median (IQR)	4.33 (3.5)	6.73 (6.44)	**0.001*****		
	≤3	18/25 (72)	7/25 (28)	**0.039***	na	
n/N(%)	>3 and ≤6	43/60 (71.67)	17/60 (28.33)			
	>6	31/61 (50.82)	30/61 (49.18)			

"*Pearson Chi-Square Test **Independent-Samples Student T Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.39 Comparing nutrition status and systemic immunity parameters at completion of treatment with disease progression at 6 months of completion of treatment in the node negative group. (n=73)

At completion of treatment		Progression at 6months from completion of treatment				
Variable		**no**	**yes**	**p value**	**RR**	**p value$**
PS n/N(%)	0-2	41/51 (80.39)	10/51 (19.61)	0.365*	1.91	0.261
	>2	15/22 (68.18)	7/22 (31.82)			
Weight (kg)	mean (SD)	55.82 (12.36)	49.56 (6.5)	**0.045****		
	median (IQR)	53.5 (17)	50 (8)	0.086***		
n/N(%)	≤50	26/36 (72.22)	10/36 (27.78)	0.417*	0.607	0.373
	>50	30/37 (81.08)	7/37 (18.92)			
BMI	mean (SD)	20.9 (4.25)	18.69 (2.6)	**0.031****		
	median (IQR)	20 (6)	19 (5)	0.056***		
n/N(%)	<18.5	18/26 (69.23)	8/26 (30.77)	0.386*	0.533	0.264
	≥18.5	38/47 (80.85)	9/47 (19.15)			
Change in weight (kg) n/N(%)	mean (SD)	-5.72 (4.9)	-5.96 (5.84)	0.604**		
	median (IQR)	-5 (8.25)	-5 (9.25)	0.891***		
	no decrease	5/9 (55.56)	4/9 (44.44)	0.138*	na	
	<10% decrease	29/34 (85.29)	5/34 (14.71)			
	≥10% decrease	22/30 (73.33)	8/30 (26.67)			
MUAC (cm)	mean (SD)	23.8 (3.12)	22.75 (2.08)	0.158**		
	median (IQR)	23 (3)	23 (2.8)	0.413***		
n/N(%)	≤21	6/10 (60)	4/10 (40)	0.228*	0.390	0.189
	>21	50/63 (79.36)	13/63 (20.63)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	12.97 (1.79)	12.52 (1.82)	0.380**		
	<13	21/31 (67.74)	10/31 (32.26)	0.252*	0.467	0.199
	≥13	27/33 (81.82)	6/33 (18.18)			
Bitot n/N(%)	no	53/69 (76.81)	16/69 (23.19)	1.000*	1.1	0.934
	yes	3/4 (75)	1/4 (25)			
SGA score	mean (SD)	46.46 (8.7)	51.81 (6.88)	**0.005****		
	median (IQR)	47.5 (14)	50.5 (12)	**0.011*****		
n/N(%)	<40	15/15 (100)	0	**0.035***	na	
	≥40	41/58 (70.69)	17/58 (29.31)			
Change in SGA score n/N(%)	No increase	2/3 (66.67)	1/3 (33.33)			
	≤9 point increase	28/33 (84.85)	5/33 (15.15)	0.329*	na	
	>9 point increase	26/37 (70.27)	11/37 (29.73)			
TLC count	mean (SD)	6931.8 (2344)	8150 (3822.2)	0.130**		
	median (IQR)	6905 (2468)	7210 (5288)	0.390***		
Neutrophil count	mean of absolute(SD)	4849(1952)	6158 (3174)	0.052**		
	median of absolute (IQR)	4420 (1921)	5546.5 (3835)	0.139***		
	mean of % (SD)	69.38 (9.16)	74.54 (10.58)	0.063**		
	median of % (IQR)	70 (9.38)	75.86 (11.4)	**0.043*****		
Lymphocyte count	meanof absolute (SD)	1183(620)	1170 (1157)	0.952**		
	median of absolute (IQR)	1064 (805)	788.5 (824)	0.185***		
	mean of % (SD)	17.33 (7.93)	14.6 (9.98)	0.266**		
	median of % (IQR)	16.09 (7.98)	11 (13.62)	0.094***		
NLR	mean (SD)	5.32 (3.56)	9.55 (12.35)	**0.033****		
	median (IQR)	4.23 (2.98)	6.68 (7.59)	0.094***		
n/N(%)	≤3	12/16 (75)	4/16 (25)	**0.020***		
	>3 and ≤6	26/29 (89.66)	3/29 (10.34)			
	>6	11/20 (55)	9/20 (45)			

"*Pearson Chi-Square Test **Independent-Samples Student T Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.40 Comparing nutrition status and systemic immunity parameters at completion of treatment with disease progression at 6 months of completion of treatment in the node positive group. (N=83)

At completion of treatment		Progression at 6months from completion of treatment				
Variable		**no**	**yes**	**p value**	**RR**	**p value$**
PS n/N(%)	0-2	19/34 (55.88)	15/34 (44.12)	0.656*	1.32	0.536
	>2	24/49 (48.98)	25/49 (51.02)			
Weight (kg)	mean (SD)	53.16 (10.31)	48.92 (8.8)	**0.037****		
	median (IQR)	50 (15)	49.5 (14)	0.053***		
n/N(%)	≤50	22/48 (45.83)	26/48 (54.17)	0.267*	0.564	0.204
	>50	21/35 (60)	14/35 (40)			
BMI	mean (SD)	19.4 (3.38)	18.71 (3.64)	0.266**		
	median (IQR)	20 (4)	18 (5)	0.207***		
n/N(%)	<18.5	19/41 (46.34)	22/41 (53.66)	0.383*	0.648	0.326
	≥18.5	24/42 (57.14)	18/42 (42.86)			
Change in weight (kg)	mean (SD)	-6.64 (5.54)	-4.79 (6)	0.301**		
	median (IQR)	-5.5 (7)	-4 (6)	0.167***		
	No decrease	5/10 (50)	5/10 (50)	0.783*	na	
	<10%decrease	15/32 (46.88)	17/32 (53.12)			
n/N(%)	≥10%decrease	23/41 (56.1)	18/41 (43.9)			
MUAC (cm)	mean (SD)	23.36 (4.8)	21.3 (3.27)	**0.019****		
	median (IQR)	23 (4)	22 (4.4)	**0.029*****		
n/N(%)	≤21	9/24 (37.5)	15/24 (62.5)	0.145*	0.441	0.100
	>21	34/59 (57.63)	25/59 (42.37)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	12.28 (1.61)	12 (1.69)	0.411**		
	<13	30/56 (53.57)	26/56 (46.43)	1.000*	1.065	0.896
	≥13	13/25 (52)	12/25 (48)			
Bitot spots presentn/N(%)	no	37/70 (52.86)	33/70 (47.14)	0.566*	1.5	0.496
	yes	6/14 (42.86)	8/14 (57.14)			
SGA score	mean (SD)	49.93 (8.24)	53.97 (8.32)	**0.036****		
	median (IQR)	50 (9)	55 (14)	**0.036*****		
n/N(%)	<40	4/5 (80)	1/5 (20)	0.361*	4	0.224
	≥40	39/78 (50)	39/78 (50)			
Change in SGA score n/N(%)	no increase	8/15 (53.33)	7/15 (46.67)	0.056*	na	
	≤9point increase	10/29 (34.48)	19/29 (65.52)			
	>9point increase	25/39 (64.1)	14/39 (35.9)			
TLC count	mean (SD)	4918.2(2252)	7756(4547.1)	**0.001****		
	median (IQR)	4460 (3010)	6720 (5113)	**0.000*****		
Neutrophil count	meanof absolute (SD)	3783.9(2038)	6073.8(4229)	**0.002****		
	median of absolute(IQR)	3373 (2048)	4947 (4808)	**0.002*****		
	mean of % (SD)	71.02 (10.44)	73.69 (10.92)	0.266**		
	median of % (IQR)	74 (10.41)	75.02 (12.55)	0.208***		
Lymphocyte count	mean of absolute(SD)	803 (583)	815 (465)	0.922**		
	median of absolute(IQR)	642 (542)	721.5 (541)	0.369***		
	mean of % (SD)	15.42 (7.2)	12.51 (9.36)	0.119**		
	median of % (IQR)	15 (8)	11 (6.5)	**0.007*****		
NLR	mean (SD)	5.73 (2.85)	8.39 (5.81)	**0.009****		
	median (IQR)	5 (4.1)	6.73 (6.59)	**0.019*****		
n/N(%)	≤3	6/9 (66.67)	3/9 (33.33)	0.626*	na	
	>3 and ≤6	17/31 (54.84)	14/31 (45.16)			
	>6	20/41 (48.78)	21/41 (51.22)			

"*Pearson Chi-Square Test **Independent-Samples Student T Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

4.12. Factors associated with overall survival (OS) at 6months after completion of treatment

The baseline variables like age, gender, primary tumor subsite, tumor grade were not significantly associated with OS. OS was higher with cT1/2 stage in overall and N- cohort but not in N+ cohort; multi-modality treatment in overall and N+ cohort but not in N- cohort; no *FailureTxCompletion*in overall, N- and N+ cohorts (Table4.41).

In overall group, worse OS was associated with PS >2 at baseline and treatment completion; ≥10% pre-treatment weight loss; low MUAC and hemoglobin at baseline; low % lymphocyte count at baseline and treatment completion; high SGA score, absolute neutrophil count and NLR at baseline and treatment completion; high TLC, %neutrophil count at treatment completion (Tables4.42 and 4.45).

In N- cohort, no nutrition or systemic immunity variables at baseline were associated with OS. OS was worse with greater reduction in weight, greater increase in SGA score; high SGA score, TLC, absolute neutrophil count and NLR at treatment completion (Tables 4.43 and 4.46).

In N+ cohort, worse OS was associated with PS >2 at baseline; ≥10% pre-treatment weight loss; high SGA at baseline; high NLR at baseline and treatment completion, high TLC, absolute and % neutrophil count at treatment completion; low % lymphocyte count at baseline and treatment completion (Tables4.44 and 4.47).

Table 4.41 Cross-tabulation of percentage death at 6 months from completion of treatment with baseline and treatment parameters.

		Death at 6 months from completion of treatment n/N (%)					
		Overall N=157		Node negative group N=73		Node positive group N=84	
Variable		yes	p value	yes	p value	yes	p value
Age (years)	≤50	5/58 (8.62)	0.107*	2/31 (6.45)	0.697*	3/27 (11.11)	0.157*
	>50	19/99 (19.19)		4/42 (9.52)		15/57 (26.32)	
Gender	male	21/138(15.2)	1.000*	6/64 (9.38)	0.597*	15/74 (20.27)	0.682*
	female	3/19 (15.77)		0		3/10 (30)	
Primary tumor subsite	oral cavity	9/56 (16.07)	0.375*	4/31 (12.9)	0.023*	5/25 (20)	0.584*
	sinuses	3/7 (42.86)		2/5 (40)		1/2 (50)	
	oropharynx	5/36 (13.89)		0		5/26 (19.23)	
	hypopharynx	2/17 (11.76)		0		2/11 (18.18)	
	larynx	5/36 (13.89)		0		5/15 (33.33)	
	CUPS	0		na		0	
cT stage	T1/T2	2/56 (3.57)	**0.005***	0	**0.026***	2/21 (9.52)	0.139*
	T3/T4	22/96 (22.92)		6/38 (15.79)		16/58 (27.59)	
	Tx	0		na		0	
Histopathology	veruccous carcinoma	0	0.809*	0	0.614*	0	0.479*
	WDSCC	2/17 (11.76)		1/13 (7.69)		1/4 (25)	
	MDSCC	20/117 (17.09)		4/54 (7.41)		16/63 (25.4)	
	PDSCC	1/13 (7.69)		1/4 (25)		0	
	PDC	1/4 (25)		0		1/3 (33.33)	
	CUPS	0		na		0	
Modality of treatment	single	14/62 (22.58)	**0.045* RR=2.48**	2/36 (5.56)	0.674*	12/26 (46.15)	**0.000* RR=7.41**
	multiple	10/95 (10.53)		4/37 (10.81)		6/58 (10.34)	
Completed at planned treatment	no	9/19 (47.37)	**0.000* RR=7.35**	2/3 (66.67)	**0.016* RR=33.33**	7/16 (43.75)	**0.023* RR=4.03**
	yes	15/138(10.9)		4/70 (5.71)		11/68 (16.18)	
*Pearson Chi-Square Test							

Table 4.42 Comparing nutrition status and systemic immunity parameters at baseline with death at 6 months of completion of treatment in the overall group. (N=157)

At baseline		Death at 6months from completion of treatment				
Variable		**no**	**yes**	**p value**	**RR**	**p value$**
PS n/N(%)	0-2	126/144 (87.5)	18/144 (12.5)	**0.006***	6	**0.003**
	>2	7/13 (53.85)	6/13 (46.15)			
Weight (kg)	mean (SD)	58.31 (11.94)	54.96 (10.68)	0.201**		
	median (IQR)	56 (15.8)	56.5 (16)	0.234***		
n/N(%)	≤50	36/44 (81.82)	8/44 (18.18)	0.622*	0.742	0.530
	>50	97/113(85.8)	16/113(14.2)			
BMI	mean (SD)	21.74 (4.08)	21.04 (4.82)	0.456**		
	median (IQR)	21 (5)	21 (5)	0.442***		
n/N(%)	<18.5	28/35 (80)	7/35 (20)	0.427*	0.654	0.393
	≥18.5	104/121 (85.9)	17/121(14.1)			
% weight loss in past 6 months	mean (SD)	5.68 (7.68)	8.96 (9.92)	0.068**		
	median (IQR)	3 (9)	8 (14)	0.160***		
n/N(%)	<10	108/123(/88)	15/123(12)	**0.042***	2.59	**0.046**
	≥10	25/34 (73.53)	9/34 (26.47)			
MUAC (cm)	mean (SD)	24.96 (3.72)	23.63 (4.14)	0.114**		
	median (IQR)	25 93.5)	23.5 (5.8)	0.145***		
n/N(%)	≤21	10/16 (62.5)	6/16 (37.5)	**0.019***	0.244	**0.014**
	>21	123/141(87.2)	18/141(12.8)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	13.49 (1.65)	13.13 (2.23)	0.350**		
	<13	36/48 (75)	12/48 (25)	**0.034***	0.379	**0.032**
	≥13	95/107(88.8)	12/107(11.2)			
Bitot spots present n/N(%)	no	120/139(86.3)	19/139(13.7)	0.157*	2.43	0.127
	yes	13/18 (72.22)	5/18 (27.78)			
SGA score	mean (SD)	38.95 (9.78)	45.17 (11.72)	**0.006****		
	median (IQR)	38 (16)	46 (22)	**0.012*****		
n/N(%)	<40	74/84 (88.1)	10/84 (11.9)	0.267*	1.76	0.210
	≥40	59/73 (80.82)	14/73 (19.18)			
TLC count	mean (SD)	8337(2426)	9336(2937)	0.074**		
	median (IQR)	7740 (2948)	8565 (3958)	0.080***		
Neutrophil count	mean of absolute(SD)	5498 (2202)	6516 (2906)	**0.050****		
	median of absolute(IQR)	5075 (2554)	6188 (3467)	0.086***		
	mean of % (SD)	64.56 (9.91)	68.06 (15.37)	0.150**		
	median of % (IQR)	64.87 (13)	69 (22.42)	0.198***		
Lymphocyte count	mean of absolute(SD)	1965 (743)	1828 1071)	0.441**		
	median of absolute (IQR)	1873 (883)	1538.5 (1460)	0.283***		
	mean of % (SD)	24.46 (8.63)	20.46 (11.28)	**0.049****		
	median of % (IQR)	24 (10.98)	18.5 (13.52)	**0.043*****		
NLR	mean (SD)	3.35 (1.74)	6.68 (9.02)	**0.001****		
	median (IQR)	3 (2)	4 (4.12)	**0.047*****		
n/N(%)	≤3	92/102 (95.1)	10/102 (4.9)	**0.014***		
	>3 and ≤6	29/37 (78.38)	8/37 (21.62)			
	>6	11/17 (64.71)	6/17 (35.29)			

"*Pearson Chi-Square Test **Independent-Samples Student t Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.43 Comparing nutrition status and systemic immunity parameters at baseline with death at 6 months of completion of treatment in the node negative group.

At baseline		Death at 6months from completion of treatment				
		Node negative group N=73				
Variable		no	yes	p value	RR	p value$
PS n/N(%)	0-2	64/70 (91.43)	6/70 (8.57)	1.000*	na	
	>2	3/3 (100)	0			
Weight (kg)	mean (SD)	59.18 (12.36)	58.8 (9.56)	0.952**		
	median (IQR)	56.5 (14.8)	60 (13.8)	0.680***		
n/N(%)	≤50	16/17 (94.12)	1/17(5.88)	1.000*	1.57	0.691
	>50	51/56 (91.07)	5/56 (8.93)			
BMI	mean (SD)	22.21 (4.41)	21.48 (3.44)	0.658**		
	median (IQR)	22 (6.09)	21.93 (7.25)	0.825***		
n/N(%)	<18.5	14/16 (87.5)	2/16 (12.5)	0.609*	0.538	0.500
	≥18.5	52/56 (92.86)	4/56 (7.14)			
% weight loss in past 6 months	mean (SD)	4.47 (6.91)	2.5 (3.21)	0.506**		
	median (IQR)	1 (7)	1.5 (5)	0.755***		
n/N(%)	<10	57/63 (90.48)	6/63 (9.52)	0.587*	na	
	≥10	10/10 (100)	0			
MUAC (cm)	mean (SD)	25.48 (2.99)	25 (2.68)	0.850**		
	median (IQR)	25 (3.3)	25.5 (2.8)	0.824***		
n/N(%)	≤21	2/3 (66.67)	1/3 (33.33)	0.230*	0.154	0.153
	>21	65/70 (92.86)	5/70 (7.14)			
Hemoglobin (g/dL)	mean (SD)	13.46 (1.65)	2.61 (3.65)	0.290**		
n/N(%)	<13	16/19 (84.21)	3/19 (15.79)	0.332*	0.327	0.196
	≥13	49/52 (63.87)	3/52 (36.13)			
Bitot spots present n/N(%)	no	64/70 (91.43)	6/70 (8.57)	1.000*	na	
	yes	3/3 (100)	0			
SGA score	mean (SD)	36.92 (9)	38.5 (7.4)	0.656**		
	median (IQR)	33.5 (15)	37 (14)	0.387***		
n/N(%)	<40	44/48 (91.67)	4/48 (8.33)	1.000*	0.957	0.961
	≥40	23/25 (92)	2/25 (8)			
TLC count	mean (SD)	8288.94(2673.09)	9376.42(2765.85)	0.345**		
	median (IQR)	7615 (3108)	9995 (5534)	0.289***		
Neutrophil count	mean of absolute (SD)	5501.55 (2555)	6347.17 (2824.59)	0.444**		
	median of absolute (IQR)	5050.5 (2523)	7079.5 (4699)	0.289***		
	mean of % (SD)	64.39 (11.26)	65.49 (19.63)	0.831**		
	median of % (IQR)	64.13 (16.19)	66 (32.8)	0.706***		
Lymphocyte count	mean of absolute (SD)	1705.05 (770.67)	2012.5 (1191)	0.733**		
	median of absolute (IQR)	1793.5 (835)	1938 (1911)	0.935***		
	mean of % (SD)	24.22 (9.87)	22.84 (14.42)	0.754**		
	median of % (IQR)	24 (13.68)	20.5 (23.05)	0.618***		
NLR	mean (SD)	3.7 (3.54)	5.31 (5.52)	0.312**		
	median (IQR)	3 (2.04)	3.5 (6.84)	0.643***		
n/N(%)	≤3	43/46 (93.48)	3/46 (6.52)	0.850*		
	>3 and ≤6	16/18 (88.89)	2/18 (11.11)			
	>6	7/8 (87.5)	1/8 (12.5)			

"*Pearson Chi-Square Test **Independent-Samples Student t Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.44 Comparing nutrition status and systemic immunity parameters at baseline with death at 6 months of completion of treatment in the node positive group.(N=84)

At baseline		Death at 6months from completion of treatment				
Variable		**no**	**yes**	**p**	**RR**	**p$**
PS n/N(%)	0-2	62/74 (83.78)	12/74 (16.22)	**0.005***	7.75	**0.004**
	>2	4/10 (40)	6/10 (60)			
Weight (kg)	mean (SD)	57.46 (11.64)	53.67 (10.97)	0.219**		
	median (IQR)	55.5 (16.3)	54 (14.3)	0.154***		
n/N(%)	≤50	20/27 (74.07)	7/27 (25.93)	0.572*	0.683	0.491
	>50	46/57 (80.7)	11/57 (19.3)			
BMI	mean (SD)	21.16 (3.61)	20.9 (5.28)	0.806**		
	median (IQR)	21 (4.3)	20.9 (5.04)	0.601***		
n/N(%)	<18.5	14/19 (73.68)	5/19 (26.32)	0.751*	0.7	0.556
	≥18.5	52/65 (80)	13/65 (20)			
% weight loss in past 6 months	mean (SD)	6.97 (8.28)	11.11 (10.51)	0.080**		
	median (IQR)	5 (9)	10.5 (20)	0.129***		
n/N(%)	<10	51/60 (85)	9/60 (15)	**0.038***	3.4	**0.028**
	≥10	15/24 (62.5)	9/24 (37.5)			
MUAC (cm)	mean (SD)	24.67 (4.35)	23.17 (4.5)	0.200**		
	median (IQR)	24 (3.9)	23 (6)	0.132***		
n/N(%)	≤21	8/13 (61.54)	5/13 (38.46)	0.140*	0.359	0.113
	>21	58/71 (81.69)	13/71 (18.31)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	13.52 (1.66)	13.3 (1.63)	0.617**		
	<13	20/29 (68.97)	9/29 (31.03)	0.163*	0.435	0.124
	≥13	46/55 (83.64)	9/55 (16.36)			
Bitot present n/N(%)	no	56/69 (81.16)	13/69 (18.84)	0.296*	2.15	0.222
	yes	10/15 (66.67)	5/15 (33.33)			
SGA score	mean (SD)	41.14 (10.13)	47.39 (12.21)	**0.029****		
	median (IQR)	41 (17)	49 (22)	**0.041*****		
n/N(%)	<40	30/36 (83.33)	6/36 (16.67)	0.428*	1.67	0.360
	≥40	36/48 (75)	12/48 (25)			
TLC count	mean (SD)	8384(2169)	9323(3068)	0.143**		
	median (IQR)	8000 (2928)	8280 (3753)	0.226***		
Neutrophil count	mean of absolute(SD)	5494 (1802)	6573 (3011)	0.058**		
	median of absolute (IQR)	5122.5 (2378)	5946.5 (3765)	0.243***		
	mean of % (SD)	64.73 (8.43)	68.91 (14.26)	0.117**		
	median of % (IQR)	65 (10.33)	10.89 (21.15)	0.206***		
Lymphocyte count	mean of absolute(SD)	2036 (714)	1767 (1057)	0.207**		
	median of absolute (IQR)	2033.5 (986)	1538.5 (1334)	0.243***		
	mean of % (SD)	24.71 (7.25)	19.67 (10.4)	**0.020****		
	median of % (IQR)	23.97 (10.33)	17.81 (13.38)	**0.027*****		
NLR	mean (SD)	3 (1.54)	7.13 (10.02)	**0.002****		
	median (IQR)	2.96 (1.4)	4 (4.37)	**0.036*****		
n/N(%)	≤3	49/56 (87.5)	7/56 (12.5)	**0.007***		
	>3 and ≤6	13/19 (68.42)	6/19 (31.58)			
	>6	4/9 (44.44)	5/9 (55.56)			

"*Pearson Chi-Square Test **Independent-Samples Student t Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.45 Comparing nutrition status and systemic immunity parameters at completion of treatment with death at 6 months of completion of treatment in overall group.(N=157)

At completion of treatment		Death at 6months from completion of treatment				
Variable		**no**	**yes**	**p**	**RR**	**p$**
PS n/N(%)	0-2	80/85 (94.12)	5/85 (5.88)	**0.001***	5.43	**0.002**
	>2	53/71 (74.65)	18/71 (25.35)			
Weight (kg)	mean (SD)	53.05 (10.73)	49.76 (10.16)	0.147**		
	median (IQR)	50 (14)	50 (18)	0.181***		
n/N(%)	≤50	71/84 (84.52)	13/84 (15.48)	0.824*	0.881	0.781
	>50	62/72 (86.11)	10/72 (13.89)			
BMI	mean (SD)	19.75 (3.69)	19.1 (4.35)	0.262**		
	median (IQR)	20 (5)	18 (5)	0.218***		
n/N(%)	<18.5	54/67 (80.6)	13/67 (19.4)	0.176*	0.526	0.159
	≥18.5	79/89 (88.76)	10/89 (11.24)			
Change in weight (kg)	mean (SD)	-5.71 (5.23)	-6.14 (4.63)	0.272**		
	median (IQR)	-5 (8)	-5 (5.5)	0.480***		
n/N(%)	no decrease	17/19 (89.47)	2/19 (10.53)	0.299*	na	
	<10%decrease	59/66 (89.39)	7/66 (10.67)			
	≥10%decrease	57/71 (80.28)	14/71 (19.72)			
MUAC (cm)	mean (SD)	23.11 (3.69)	21.71 (3.94)	0.055**		
	median (IQR)	23 (3)	22 (6.5)	0.148***		
n/N(%)	≤21	26/34 (76.47)	8/34 923.53)	0.168*	0.456	0.108
	>21	107/122(88)	15/122 (12)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	12.53 (1.74)	12.07 (1.79)	0.271**		
	<13	72/87 (82.76)	15/87 (17.24)	0.337*	0.554	0.252
	≥13	52/58 (89.66)	6/58 (10.34)			
Bitot spots present n/N(%)	no	119/139(86)	20/139 (14)	0.483*	1.7	0.389
	yes	14/18 (77.78)	4/18 (22.22)			
SGA score	mean (SD)	49.36 (8.75)	53.86 (7.64)	**0.024****		
	median (IQR)	50 (12)	54 (15)	**0.028*****		
n/N(%)	<40	20/20 (100)	0	**0.046***	na	
	≥40	113/136(83)	23/136 (17)			
Change in SGA score n/N(%)	no increase	14/18 (77.78)	4/18 (22.22)	0.687*	na	
	≤9 point increase	53/62 (85.48)	9/62 (14.52)			
	>9 point increase	66/76 (86.84)	10/76 (13.16)			
TLC count	mean (SD)	6299(3207)	9024(3622)	**0.001****		
	median (IQR)	5835 (2948)	8840 (4670)	**0.000*****		
Neutrophil count	mean of absolute(SD)	4642(2787)	7123 (3333)	**0.000****		
	median of absolute (IQR)	4070 (2450)	6311(4393)	**0.000*****		
	mean of % (SD)	70.72 (9.86)	76.41 (11.41)	**0.018****		
	median of % (IQR)	71.39 (9.32)	79.09 (15.59)	**0.011*****		
Lymphocyte count	mean of absolute (SD)	988.5 (766.05)	896.57 (663)	0.564**		
	median of absolute (IQR)	771 (660)	732 (694)	0.533***		
	mean of % (SD)	15.96 (8.48)	10.82 (7.2)	**0.010****		
	median of % (IQR)	15 (9)	9.65 (5.5)	**0.001*****		
NLR	mean (SD)	5.9 (3.69)	11.43 (11.44)	**0.000*****		
	median (IQR)	5 (4.27)	8.2 (7)	**0.002*****		
n/N(%)	≤3	23/25 (92)	2/25 (8)	**0.012***	na	
	>3 and ≤6	56/60 (93.33)	4/60 (6.67)			
	>6	46/61 (75.41)	15/61 (24.59)			
"*Pearson Chi-Square Test **Independent-Samples Student t Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"						

Table 4.46 Comparing nutrition status and systemic immunity parameters at completion of treatment with death at 6 months of completion of treatment in node negative group. (N=73)

At completion of treatment		Death at 6months from completion of treatment				
Variable		no	yes	p	RR	p$
PS n/N(%)	0-2	49/51 (96.08)	2/51 (3.92)	0.063*	5.44	0.062
	>2	18/22 (81.82)	4/22 (18.18)			
Weight (kg)	mean (SD)	54.82 (11.58)	49.17 (9.99)	0.310**		
	median (IQR)	51.5 (13)	49 (21)	0.355***		
n/N(%)	≤50	33/36 (91.67)	3/36 (8.33)	1.000*	0.971	0.972
	>50	34/37 (91.89)	3/37 (8.11)			
BMI	mean (SD)	20.62 (4)	17.83 (3.49)	0.127**		
	median (IQR)	20 (4)	16.5 (7)	0.136***		
n/N(%)	<18.5	22/26 (84.62)	4/26 (15.38)	0.178*	0.244	0.119
	≥18.5	45/47 (95.74)	2/47 (4.26)			
Change in weight (kg)	mean (SD)	-5.38 (4.92)	-9.67 (5.65)	**0.012****		
	median (IQR)	-5 (9)	-8.5 (8.25)	**0.043*****		
n/N(%)	no decrease	9/9 (100)	0	0.085*	na	
	<10% decrease	33/34 (97.06)	1/34 (2.94)			
	≥10% decrease	25/30 (83.33)	5/30 (16.67)			
MUAC (cm)	mean (SD)	23.67 (2.9)	22.33 (3.14)	0.349**		
	median (IQR)	23 (2)	22.5 (5.8)	0.562***		
n/N(%)	≤21	8/10 (80)	2/10 (20)	0.188*	0.271	0.167
	>21	59/63 (93.65)	4/63 (6.35)			
Hemoglobin (g/dL) n/N(%)	mean (SD)	12.87 (1.71)	12.73 (2.68)	0.853**		
	<13	27/31 (87.1)	4/31 (12.9)	0.419*	0.435	0.358
	≥13	31/33 (93.94)	2/33 (6.06)			
Bitot spots present n/N(%)	no	63/69 (91.3)	6/69 (8.7)	1.000*	na	
	yes	4/4 (100)	0			
SGA score	mean (SD)	47.05 (8.28)	54.83 (8.82)	**0.030****		
	median (IQR)	48 (13)	57 (16)	**0.044*****		
n/N(%)	<40	15/15 (100)	0	0.335*	na	
	≥40	52/58 (89.66)	6/58 (10.34)			
Change in SGA score n/N(%)	no increase	3/3 (100)	0	**0.049***	na	
	≤9 point increase	33/33 (100)	0			
	>9 point increase	31/37 (83.78)	6/37 (16.22)			
TLC count	mean (SD)	7009 (2420.6)	9410 (5083.44)	**0.044****		
	median (IQR)	6905 (2918)	8940 (10195)	0.231***		
Neutrophil count	mean of absolute (SD)	4956.6 (1962)	7265.8 (4525)	**0.020****		
	median of absolute (IQR)	4420 (2078)	6924 (7443)	0.167***		
	mean of % (SD)	70.32 (9.2)	73.72 (14.54)	0.418**		
	median of % (IQR)	70.2 (10.8)	73.86 (24.43)	0.465***		
Lymphocyte count	mean of absolute (SD)	1181.42 (744.51)	1167.33 (1117.52)	0.966**		
	median of absolute (IQR)	1003 (810)	785.5 (1470)	0.520***		
	mean of % (SD)	16.86 (8.16)	14.71 (11.97)	0.557**		
	median of % (IQR)	15.87 (9.71)	10.68 (18.84)	0.425***		
NLR	mean (SD)	5.6 (3.59)	13.84 (19.98)	**0.005****		
	median (IQR)	4.33 (3.88)	6.97 (18.83)	0.506***		
n/N(%)	≤3	14/16 (87.5)	2/16 (12.5)	0.466*	na	
	>3 and ≤6	28/29 (96.55)	1/29 (3.45)			
	>6	17/20 (85)	3/20 (15)			

"*Pearson Chi-Square Test **Independent-Samples Student t Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

Table 4.47 Comparing nutrition status and systemic immunity parameters at completion of treatment with death at 6 months of completion of treatment in node positive group.(N=83)

At completion of treatment		Death at 6months from completion of treatment				
Variable		**no**	**yes**	**p**	**RR**	**p$**
PS n/N(%)	0-2	31/34 (66)	3/34 (34)	0.051*	4.13	**0.038**
	>2	35/49 (71.43)	14/49(28.57)			
Weight (kg)	mean (SD)	51.44 (9.69)	50 (10.57)	0.436**		
	median (IQR)	50 (15)	50 (15)	0.429***		
n/N(%)	≤50	38/48 (79.17)	10/4 (20.83)	1.000*	0.95	0.926
	>50	28/35 (80)	7/35 (20)			
BMI	mean (SD)	18.95 (3.21)	19.6 (4.66)	0.915**		
	median (IQR)	19 (4)	19 (5)	0.887***		
n/N(%)	<18.5	32/41 (78.05)	9/41 (21.95)	0.791*	0.837	0.743
	≥18.5	34/42 (80.95)	8/42 (19.05)			
Change in weight (kg)	mean (SD)	-6.01 (5.51)	-4.73(3.43)	0.801**		
	median (IQR)	-5 (7)	-4 (6)	0.483***		
	no decrease	8/10 (80)	2/10 (20)	0.929*	na	
n/N(%)	<10% decrease	26/32 (81.25)	6/32 (18.75)			
	≥10% decrease	32/41 (78.05)	9/41 (21.95)			
MUAC (cm)	mean (SD)	22.61 (4.25)	21.47 (4.29)	0.205**		
	median (IQR)	22 (4)	22 (6)	0.315***		
n/N(%)	≤21	18/24 (75)	6/24 (25)	0.555*	0.688	0.517
	>21	48/59 (81.36)	11/59(18.64)			
Hemoglobin (g/dL)	mean (SD)	12.21 (1.71)	11.81 (1.33)	0.397**		
n/N(%)	<13	45/56 (80.36)	11/56(19.64)	0.768*	0.779	0.697
	≥13	21/25 (84)	4/25 (16)			
Bitot present n/N(%)	no	56/70 (80)	14/70 (20)	0.724*	1.6	0.478
	yes	10/14 (71.43)	4/14 (28.57)			
SGA score	mean (SD)	51.45 (8.7)	53.47(7.42)	0.460**		
	median (IQR)	51(12)	54 (12)	0.520***		
n/N(%)	<40	5/5 (100)	0	0.364*	na	
	≥40	61/78 (78.21)	17/78(21.79)			
Change in SGA score n/N(%)	no increase	11/15 (73.33)	4/15 (26.67)	0.105*	na	
	≤9 point increase	20/29 (69)	9/29 (31)			
	>9 point increase	35/39 (89.74)	4/39 (10.26)			
TLC count	mean (SD)	5654 (3173)	8870 (3070)	**0.002****		
	median (IQR)	4625 (3173)	8840 (3190)	**0.000*****		
Neutrophil count	mean of absolute (SD)	4356.23 (3357.82)	7066.67 (2923)	**0.005****		
	median of absolute (IQR)	3509.5 (2563)	6311 (3382)	**0.000*****		
	mean of % (SD)	71.09 (10.49)	77.49 (10.3)	**0.035****		
	median of % (IQR)	72.92 (9.64)	79.42(15.19)	**0.014*****		
Lymphocyte count	mean of absolute (SD)	813.12 (559.3)	788.2 (371)	0.870**		
	median of absolute (IQR)	647 (523)	732 9539)	0.508***		
	mean of % (SD)	15.14 (8.74)	9.27 (3.72)	**0.013****		
	median of % (IQR)	13 (8)	9.65 (4.2)	**0.001*****		
NLR	mean (SD)	6.18 (3.78)	10.47 (6.41)	**0.001****		
	median (IQR)	5.24 (4.03)	8.2 (5.57)	**0.003*****		
n/N(%)	≤3	9/9 (100)	0	**0.034***	na	
	>3 and ≤6	28/31 (90.32)	3/31 (9.68)			
	>6	29/41 (70.73)	12/41(29.27)			

"*Pearson Chi-Square Test **Independent-Samples Student t Test ***Independent-Samples Mann-Whitney U Test $Mantel-Haenszel Estimate"

("RR-relative risk, PS-performance status, BMI-body mass index, MUAC-mid upper arm circumference, SGA-subjective global assessment, TLC-total leucocyte count, NLR-neutrophil to lymphocyte ratio")

4.13. Multivariate analysis for factors associated with OS and PFS at 6months after completion of treatment

Mutivariate analysis revealed, in N- cohort only post-treatment NLR and in N+ cohort cT 3/4 stage, single modality treatment, failure to complete planned treatment and high pre-treatment NLR were significantly associated with poor 6month PFS (Table 4.48). In the overall group high pre-treatment SGA score was associated poor PFS but this did not reach statistical significance (p=0.057). The multivariate analysis was performed to take care of confounding factors like single modality treatment in N+ patients, proving it is an independently significant factor.

No variables were found to be significantly associated with 6 months OS in N- cohort. In N+ cohort cT 3/4 stage, baseline PS >2, single modality treatment, failure to complete planned treatment, high pre-treatment SGA score and NLR and high post-treatment NLR were significantly associated with poor 6 month OS (Table 4.49).

Table 4.48 Result of multivariate analysis for disease progression at 6 months.

Disease progression at 6 months			
Variables	**0verall p value***	**Node negative group p value***	**Node positive group p value***
c T 3/4 stage	0.044	NS	0.009
Single modality treatment	0.031	NS	0.005
Not completed all planned treatment	0.006	NS	0.015
Baseline NLR	0.039	NS	0.015
Post-treatment SGA score	0.057	NS	NS
Post-treatment NLR	0.016	0.017	NS
* Multivariate analysis- Multi-nominal Logistic Regression model (NLR-neutrophil/lymphocyte ratio, SGA-subjective global assessment)			

Table 4.49 Result of multivariate analysis for death at 6 months.

Death at 6 months			
Variable	**0verall p value***	**Node negative group p value***	**Node positive group p value***
c T 3/4 stage	0.000	NS	0.000
Baseline PS 3 or more	NS	NS	0.029
Single modality treatment	0.007	NS	0.044
Not completed all planned treatment	0.016	NS	0.057
Baseline SGA score	0.043	NS	0.033
Baseline NLR	NS	NS	0.024
Post-treatment NLR	0.045	NS	0.028
* Multivariate analysis- Multi-nominal Logistic Regression model (NLR-neutrophil/lymphocyte ratio, SGA-subjective global assessment)			

4.14. ROCs for variables to predict failure to complete all planned treatment

Figure 4.3 depicts the ROCs for variables- *pre-treatment weight, MUAC and BMI*. Area under the curve (AUC) and 95%Confidence Interval (95%CI) for pre-treatment *weight* in overall, N- and N+ cohorts were 0.699 (0.537-0.802), 0.564 (0.373-0.755) and 0.684 (0.53-0.838) respectively (Table 4.50); for *MUAC*in overall, N- and N+ AUC (95%CI) were0.637 (0.485-0.789), 0.507 (0.327-0.688) and 0.645 (0.471-0.819) respectively(Table4.51); and *BMI* in overall, N- and N+ AUC (95%CI) were 0.694 (0.568-0.821),0.767 (0.589-0.945), and 0.667 (0.514-0.819) respectively (Table4.52). In N+ cohort, **Specificity** to predict *FailureTxCompletion* was as follows- weight cut-offs ≤45kg- 91.4%, 39.5kg-97.1%, 32.5kg-100%; MUAC cut-offs ≤20.5cm-90%, 19.5cm-97.1%, 16.5 cm-100%; BMI cut-offs ≤17kg/m^2-92.9% , 15.5kg/m^2-97.1%, 13.9kg/m^2-100%. As noted previously these variables were not associated with *FailureTxCompletion* in N- cohort.

Figure 4.4 depicts the ROC for *pre-treatment %weight loss*. The AUC (95%CI) for overall, N- and N+ cohorts was 0.667(0.526-0.808), 0.564 (0.266-0.863) and 0.661 (0.499-0.823) respectively (Table4.53). In N+ cohort, **Specificity** to predict *FailureTxCompletion* for pre-treatment %weight loss was- cut-offs ≥10.5-80%, 18-91.4%, 20-94.3%, 23.5-97.1, 37-100%. As noted previously this variable was not associated with *FailureTxCompletion* in N- cohort.

Figure 4.5 depicts the ROCs for *pre-treatment SGA and NLR*. The AUC (95%CI) for pre-treatment SGA scores in overall, N- and N+ cohorts was 0.702(0.561-0.844), 0.683(0.529-0.838), and 0.695(0.53-0.861) respectively (Table 4.54). In N+ cohort, **Specificity** to predict *FailureTxCompletion* for pre-treatment SGA score was- cut-offs ≥50.3-81.4%, 53-87.1%, 57.5-97.1%, 63.5-100%. As noted previously this variable was not associated with *FailureTxCompletion* in N- cohort.The AUC (95%CI) for pre-treatment NLR in overall, N- and N+ cohorts was 0.594(0.46-0.728), 0.841(0.616-1) and 0.553(0.396-0.711) respectively (Table4.55). In N- cohort, **Specificity** to predict *FailureTxCompletion* for pre-treatment NLR

was- cut-offs ≥ 5.99-87%, 6.5-91.3%, 7.5-94.2%, 9-97.1%, 25-100%. As noted previously this variable was not associated with *FailureTxCompletion* in N+ cohort.

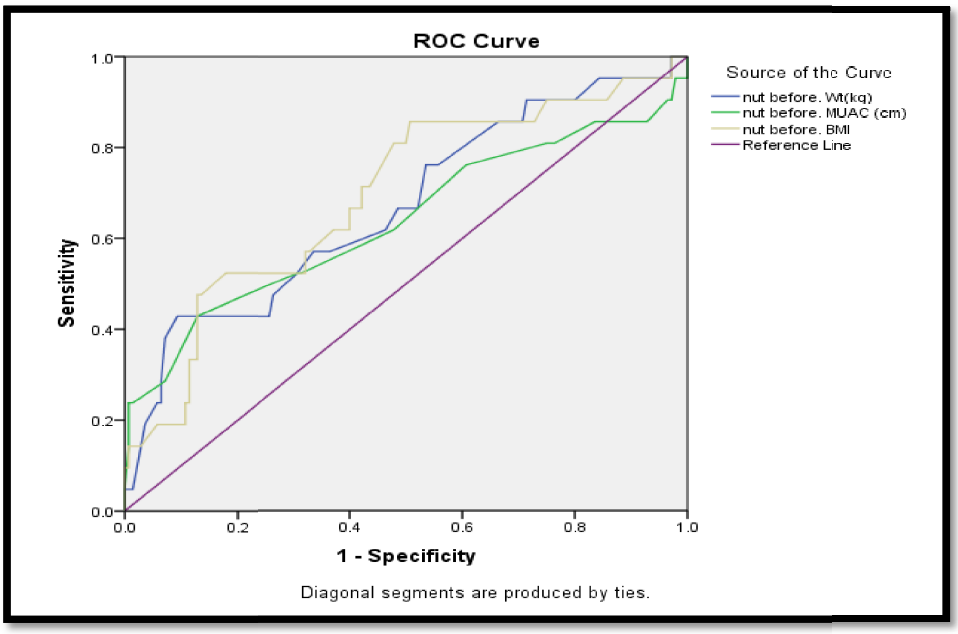

Figure 4.3 ROC curves for pre-treatment weight, MUAC and BMI to predict failure to complete planned treatment.

Table 4.50 Sensitivity and specificity cut-off points for pre-treatment weight to predict failure to complete all planned treatment.

Failure to complete all planned treatment								
Pre-treatmentweight (kg)								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.699	0.067	0.537-0.802	0.564	0.097	0.373-0.755	0.684	0.079	0.53-0.838
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
						29	0	100
32.5	4.8	100				**32.5**	5.6	100
36	4.8	99.3	**37**	0	100			
			38.5	0	98.6			
41	19	96.4	**40.5**	0	97.1	**39.5**	16.7	97.1
			43.9	0	92.9	**43.5**	33.3	94.3
45.5	42.9	90.7	**45.5**	0	90	**45.5**	50	91.4
			48.5	0	82.9	**47.5**	50	82.9
50.5	42.9	74.3	**50.5**	0	75.7	**49.5**	50	78.6
						52.5	55.6	70
55.5	61.9	53.6	**55.5**	33.3	54.3	**54.5**	61.1	61.4
			59.5	66.7	47.1	**59.5**	77.8	41.4
60.5	85.7	33.6	**60.5**	100	34.3			
65.5	90.5	25.7				**63**	83.3	30
70.5	95.2	15.7				**69.5**	88.9	18.6
						83.5	94.4	0
86	100	2.9				**86**	100	0

("AUC- area under the curve, Std. error- standard error, CI- confidence interval")

Table 4.51 Sensitivity and specificity cut-off points for pre-treatment MUAC to predict failure to complete all planned treatment.

Failure to complete all planned treatment								
Baseline Mid-Upper Arm Circumference(cm)								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.637	0.078	0.485-0.789	0.507	0.092	0.327-0.688	0.645	0.089	0.471-0.819
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
						15	0	100
16.5	4.8	100				**16.5**	5.6	100
17.5	14.5	99.3				**17.5**	16.7	98.6
18.5	23.8	99.3						
19.5	23.8	98.6	**19**	0	100	**19.5**	27.8	97.1
20.5	28.6	91.5	**20.5**	0	95.7	**20.5**	33.3	90
21.5	42.9	87.1	**21.5**	0	90	**21.5**	50	84.3
22.5	47.6	78.6	**22.5**	0	80	**22.5**	55.6	77.1
			23.3	0	75.7	**23.5**	61.1	62.9
			24.5	33.3	57.1			
			25.5	66.7	44.3	**25.5**	77.8	34.3
26.2	81	25	**26.8**	100	27.1			
27.5	85.7	16.4				**27.5**	83.3	14.3
30.5	90.5	3.6				**30.5**	88.9	2.9
32.5	95.2	2.1				**32.5**	94.4	1.4
50	100	0				**50**	100	0
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

Table 4.52 Sensitivity and specificity cut-off points for pre-treatment BMI to predict failure to complete all planned treatment.

Failure to complete all planned treatment								
Baseline BMI								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.694	0.065	0.568-0.821	0.767	0.091	0.589-0.945	0.667	0.078	0.514-0.819
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
						11.8	0	100
13.9	9.5	100	**13.9**	0	100	**13.9**	11.1	100
						14.2	11.1	98.6
14.9	14.3	98.6	**15.2**	0	98.6			
15.8	14.3	97.1	**15.8**	0	97.1	**15.5**	16.7	97.1
			16.5	0	94.3	**16.5**	22.2	94.3
16.9	19	93.6	**17**	0	91.4	**17**	22.2	92.9
17.6	33.3	88.6	**17.4**	33.3	88.6	**17.6**	33.3	88.6
18	52.4	82.1	**18**	33.3	85.7	**18**	50	87.1
18.5	52.4	80.7	**18.5**	66.7	80	**18.4**	50	81.4
						18.9	50	80
			19.3	66.7	74.3	**19.3**	50	70
20	61.9	62.9	**20.1**	66.7	65.7	**20.3**	61.1	57.1
						20.7	66.7	55.7
22	85.7	42.9	**21.3**	100	55.7	**21.3**	77.8	44.3
24	90.5	25				**23.8**	83.3	22.9

						25.7	88.9	11.4
26.5	95.2	11.4						
32.2	100	2.9				**31**	94.4	1.4
						34.5	100	1.4
("AUC- area under the curve,Std. error- standard error,CI- confidence interval, BMI- body mass index")								

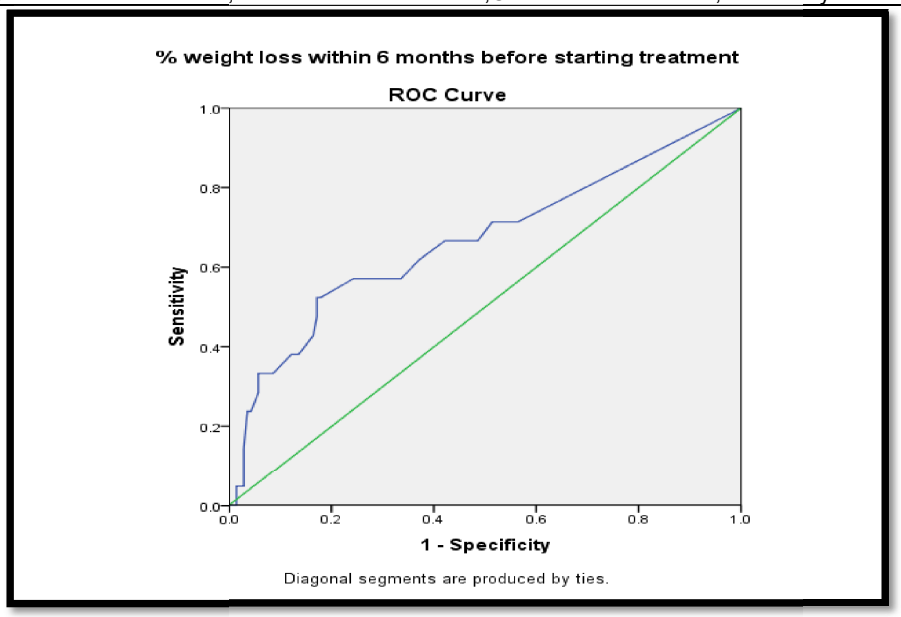

Figure 4.4 ROC curve for pre-treatment %weight loss to predict failure to complete all planned treatment.

Table 4.53 Sensitivity and specificity cut-off points for pre-treatment %weight loss to predict failure to complete all planned treatment.

Failure to complete all planned treatment								
%weight loss within 6 months before treatment								
Overall			**Node Negative group**			**Node Positive group**		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.667	0.072	0.526-0.808	0.564	0.152	0.266-0.863	0.661	0.083	0.499-0.823
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
37	0	100				**37**	0	100
			33	0	100	**34**	0	97.1
32.5	4.8	98.6						
23.5	14.3	97.1	**24**	0	97.1	**23.5**	16.7	97.1
20.5	23.8	95.7				**20.5**	27.8	94.3
18.5	33.3	94.3	**17**	0	95.7	**18**	38.9	91.4
15.5	33.3	91.4	**15.5**	0	94.3	**15.5**	38.9	88.6
14.5	38.1	87.9	**14.5**	0	90	**14.5**	44.4	85.7
12.5	42.9	83.6	**13.5**	0	88.6	**13.5**	44.4	84.3
10.5	52.4	82.9	**11**	0	85.7	**10.5**	61.1	80
8.5	57.1	75.7	**8.5**	33.3	81.4	**8.5**	61.1	70
6.5	57.1	66.4	**7**	33.3	77.1	**6.5**	61.1	55.7
3.5	66.7	51.4	**5.5**	33.3	75.7	**3.5**	72.2	41.4
2.5	71.4	48.6	**2.5**	66.7	58.6	**2.5**	72.2	38.6
-1	100	0	**-1**	100	0	**-1**	100	0
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

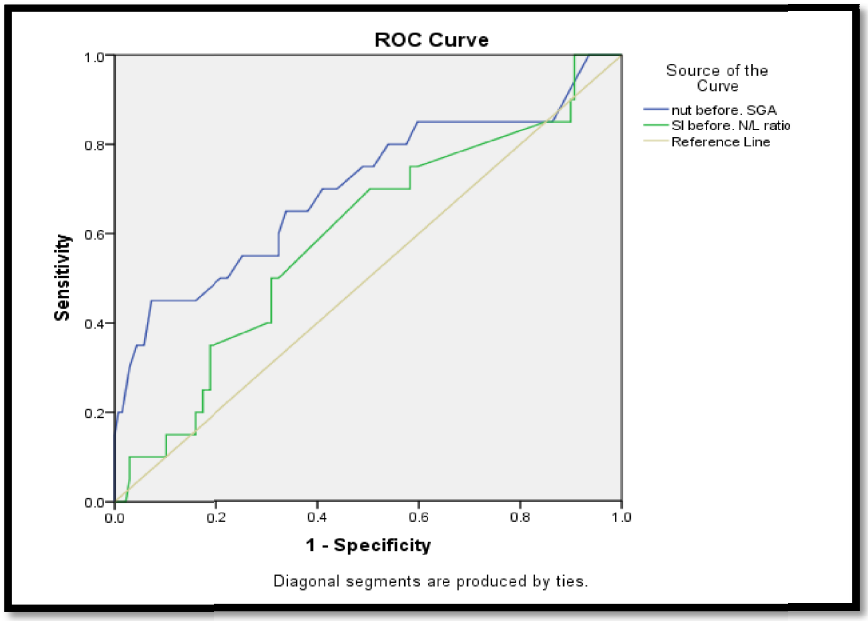

Figure 4.5 ROC curves for pre-treatment SGA score and NLR to predictf to complete planned treatment.

Table 4.54 Sensitivity and specificity cut-off points for pre-treatment SGA score to predict failure to complete all planned treatment.

Failure to complete all planned treatment								
Pre-treatment SGA score								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.702	0.072	0.561-0.844	0.683	0.079	0.529-0.838	0.695	0.084	0.53-0.861
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
63.5	15	100				**63.5**	16.7	100
			60	0	100	**61.5**	22.2	98.6
57.5	30	97.1	**57.5**	0	97.1	**57.5**	33.3	97.1
55.5	35	94.2				**56.5**	38.9	95.7
53	45	90.6	**54**	0	94.3	**53**	50	87.1
50	45	87.1	**51**	0	92.9	**50.5**	50	81.4
48.5	50	79.1	**48.5**	0	85.7	**48.5**	61.1	72.9
47.5	50	77.7				**46**	66.7	65.7
45.5	55	73.4	**45.5**	0	81.4			
42.5	65	66.2	**41.5**	66.7	71.4			
40	70	59				**40.5**	72.2	48.6
			38.5	66.7	60			
36.5	80	46				**36.5**	83.3	38.6
34.5	85	40.3	**34.5**	100	52.9			
28.5	85	13.7				**28.5**	83.3	5.7
27.5	100	6.5				**27.5**	100	4.3
("AUC- area under the curve, Std. error- standard error, CI- confidence interval, SGA- subjective global assessment")								

Table 4.55 Sensitivity and specificity cut-off points for pre-treatment NLR to predict failure to complete all planned treatment.

Failure to complete all planned treatment								
Pre-treatmentNLR								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.594	0.069	0.46-0.728	0.841	0.114	0.616-1	0.553	0.080	0.396-0.711
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
38	0	100				**38**	0	100
			25	0	100			
			20	0	98.6	**20**	0	97.1
13	5	97.1						
9.5	10	97.1	**9**	66.7	97.1			
8.5	10	96.4				**8.5**	0	95.7
7.5	10	93.5	**7.5**	66.7	94.2	**7.5**	0	92.9
7	10	90.6	**7**	66.7	92.8			
6.5	10	89.9	**6.5**	66.7	91.3	**6.6**	0	88.6
6	15	89.9	**5.99**	66.7	87			
5.5	15	87.1						
5	15	87.1	**4.8**	66.7	81.2	**5**	5.9	87.1
4.5	25	81.3	**4.6**	66.7	79.7	**4.6**	11.8	85.7
4	35	80.6	**4.1**	66.7	76.8	**4**	35.3	71.4
3.4	50	69.1	**3.6**	66.7	66.7	**3.4**	47.1	71.4
3	70	49.6	**3.1**	66.7	65.2	**3**	64.7	50
			2.89	100	49.3			
2.5	70	43.9						
2	75	40.3				**2.2**	70.6	38.6
1.94	85	15.1				**1.9**	82.4	12.9
1.34	90	9.4				**1.3**	88.2	7.1
1.14	95	9.4						
1.12	100	9.4				**1.1**	94.1	7.1
						1.07	100	7.1
("AUC- area under the curve, Std. error- standard error, CI- confidence interval, NLR- neutrophil to lymphocyte ratio")								

4.15. ROCs for various variables to predict disease progression at 6months

As previously noted, in multivariate analysis pre-treatment NLR and post-treatment SGA score and NLR were found to be significantly associated with 6month PFS. Figure4.6 depicts the ROCs for pre-treatment NLR. The AUC (95%CI) for pre-treatment NLR in overall, N- and N+ cohorts was 0.634(0.54-0.729), 0.625(0.459-0.79) and 0.655(0.535-0.776) respectively (Table 4.56). In N+ cohort, **Specificity** to predict disease progression at 6months for pre-treatment NLR was- cut-offs ≥ 3.68-86%, 4.16-93%, 4.81-95.3%, 5.58-97.7%, 7.5-100%. As noted previously this variable was not associated with 6month PFS in N- cohort.

Figure 4.7 depicts the ROCs for post-treatment NLR. The AUC (95%CI) for post-treatment NLR in overall, N- and N+ cohorts was 0.662(0.568-0.756), 0.640(0.467-0.813) and 0.651 (0.531-0.772) respectively (Table 4.57). In N- cohort, **Specificity** to predict disease progression at 6 months for post-treatment NLR was- cut-offs ≥ 7.5-80%, 8.47-82%, 9.15-84%, 10.02-92%, 11.04-94%, 15.2-96%, 15.98-98%, 35.3-100%. As noted previously this variable was not associated with 6month PFS in N+ cohort.

Figure 4.8 depicts the ROCs for post-treatment SGA score. The AUC (95%CI) for post-treatment SGA score in overall, N- and N+ cohorts was 0.662(0.568-0.756), 0.640(0.467-0.813) and 0.651 (0.531-0.772) respectively (Table 4.58). Overall, **Specificity** to predict disease progression at 6months for post-treatment SGA score was- cut-offs ≥ 51.5-69.7%, 55.5-79.8%, 57.5-84.8%, 59.5-91.9%, 60.5-93.9%, 62.5-93.9% 65-100%.

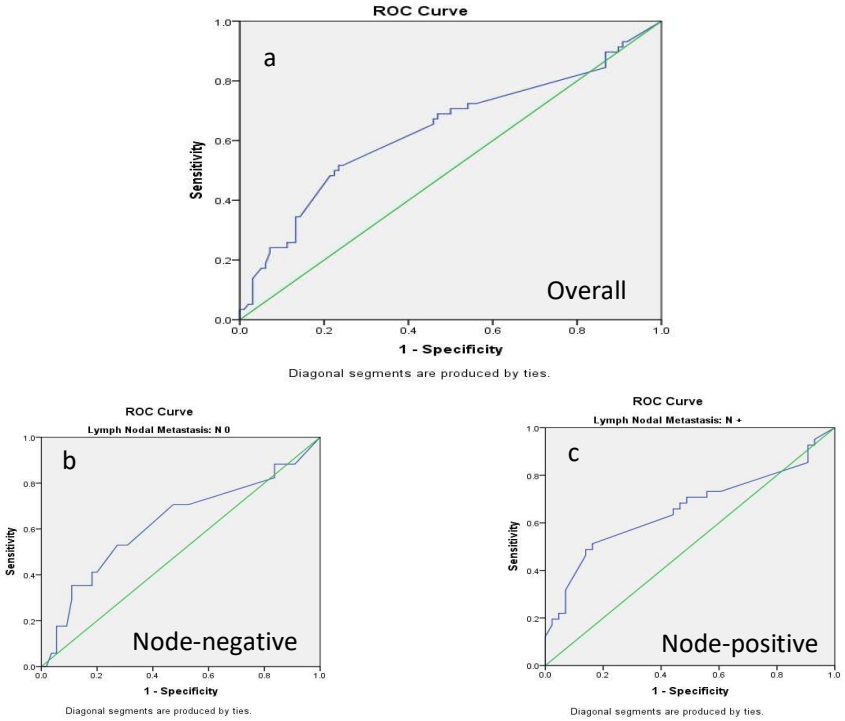

Figure 4.6 ROC curves for pre-treatment NLR to predict disease progression at 6months.

(a. overall, b. node-negative group, b. node-positive group)

Table 4.56 Sensitivity and specificity cut-off points for pre-treatment NLR score to predict disease progression at 6 months.

Disease progression at 6 months								
Pre-treatmentNeutrophil/ Lymphocyte ratio								
Overall			Node Negative group			Node Positive group		
AUC	Std. Error	95% CI	AUC	Std. Error	95% CI	AUC	Std. Error	95% CI
0.634	0.048	0.54-0.729	0.625	0.084	0.459-0.79	0.655	0.062	0.535-0.776
cut-off	Sensitivity (%)	Specificity (%)	cut-off	Sensitivity (%)	Specificity (%)	cut-off	Sensitivity (%)	Specificity (%)
27.50	3.4	100	**25.00**	0	100			
			20.00	0	98.2	**20.0**	4.9	100
13.00	5.2	98	**13.00**	5.9	92.8			
7.500	13.8	96.9	**7.500**	17.6	94.5	**7.50**	12.2	100
6.081	19	93.9	**6.96**	17.6	92.7			
			6.46	17.6	90.9			
5.485	24.1	92.9	**5.49**	35.3	89.1	**5.58**	19.5	97.7
4.812	25.9	88.8	**4.83**	35.3	83.6	**4.81**	22	95.3
4.246	34.5	86.7	**4.33**	41.2	81.8			
4.085	34.5	85.7	**4.09**	41.2	80	**4.16**	31.7	93
3.999	48.3	78.6	**3.999**	52.9	72.7			
3.676	50	77.6	**3.603**	52.9	70.9	**3.67**	48.8	86
3.303	51.7	76.5						
3.105	51.7	75.5	**3.105**	52.9	69.1	**3.19**	51.2	83.7
2.956	65.5	54.1				**2.95**	63.4	55.8
			2.891	70.6	52.7	**2.856**	65.9	55.8
2.669	69	50	**2.654**	70.6	49.1	**2.669**	68.3	51.2
2.205	70.7	45.9	**2.264**	70.6	47.3	**2.20**	70.7	44.2
2.041	72.4	45.9				**2.04**	73.2	39.5
			1.938	82.4	16.4	**1.93**	85.4	9.3
1.876	86.2	13.3				**1.85**	87.9	9.3
						1.61	90.2	9.3
1.396	89.7	10.2						
1.222	91.4	9.2				**1.221**	92.7	7
1.056	93.1	8.2	**1.056**	88.1	9.1	**1.07**	95.1	7
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

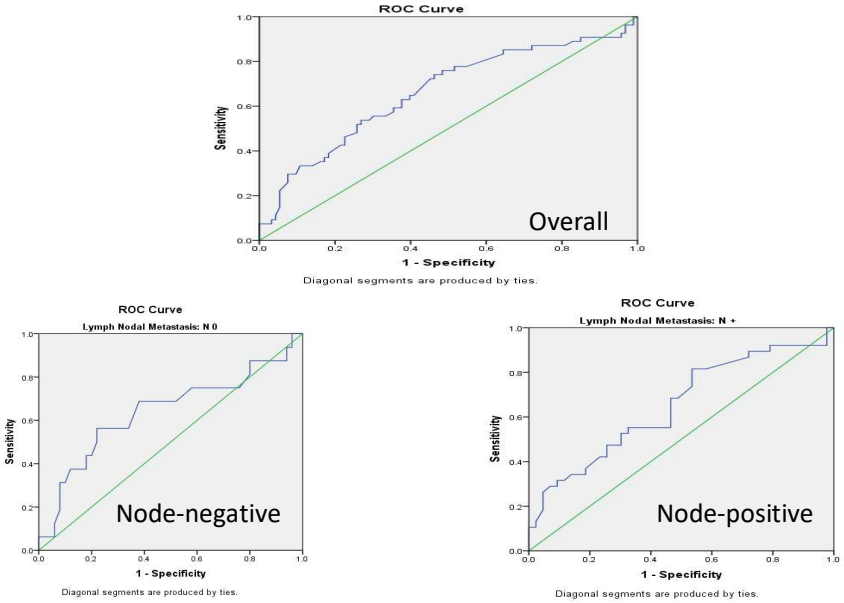

Figure 4.7 ROC curves for post-treatment NLR to predict disease progression at 6months.

Table 4.57 Sensitivity and specificity cut-off points for post-treatment NLR score to predict disease progression at 6 months.

Disease progression at 6 monthspost-treatmentNeutrophil/ Lymphocyte ratio								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.662	0.048	0.568-0.756	0.640	0.008	0.467-0.813	0.651	0.062	0.531-0.772
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
20.2	7.4	100	**35.3**	6.3	100			
15.9	7.4	98.9	**15.9**	6.3	98			
15.0	7.4	96.8	**15.2**	6.3	96	**14.2**	10.5	100
12.8	9.3	95.7				**12.1**	13.2	97.7
11.8	14.8	94.6	**11.0**	12.5	94	**11.1**	26.3	95.3
10.9	25.9	92.5	**10.3**	31.3	92	**10.6**	28.9	93
10.1	29.6	90.3	**10.1**	31.3	92	**9.57**	31.6	90.7
9.22	33.3	87.1	**9.15**	37.5	84	**9.07**	31.6	88.4
8.95	53.2	82.8	**8.47**	43.8	82	**8.98**	34.2	84
7.95	42.6	78.5	**7.5**	43.8	80	**7.94**	42.1	76.7
6.88	48.1	74.2				**6.66**	52.6	69.8
6.35	55.6	69.9	**6.18**	56.3	78	**6.35**	55.3	61.5
5.62	61.1	62.4	**5.62**	56.3	70	**5.61**	63.2	54.5
5.03	64.8	60.2	**5.11**	56.3	66	**5.00**	68.4	51.2
4.73	74.1	53.8	**4.75**	68.8	60	**4.71**	76.3	46.5
4.49	75.9	51.6				**4.46**	78.9	46.5
4	83.3	35.5	**4.07**	68.8	48	**4.03**	81.6	42.9
3.64	87	28				**3.72**	89.5	21.9
2.96	88.9	17.2	**3.01**	75	24			
2.62	90.7	15.1	**1.87**	87.5	6			
1.5	92.6	3.2	**1.5**	93.8	4	**1.73**	92.1	2.3
0.82	98.1	1.1				**0.82**	97.4	2.3
0.61	100	1.1				**0.61**	100	2.3
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

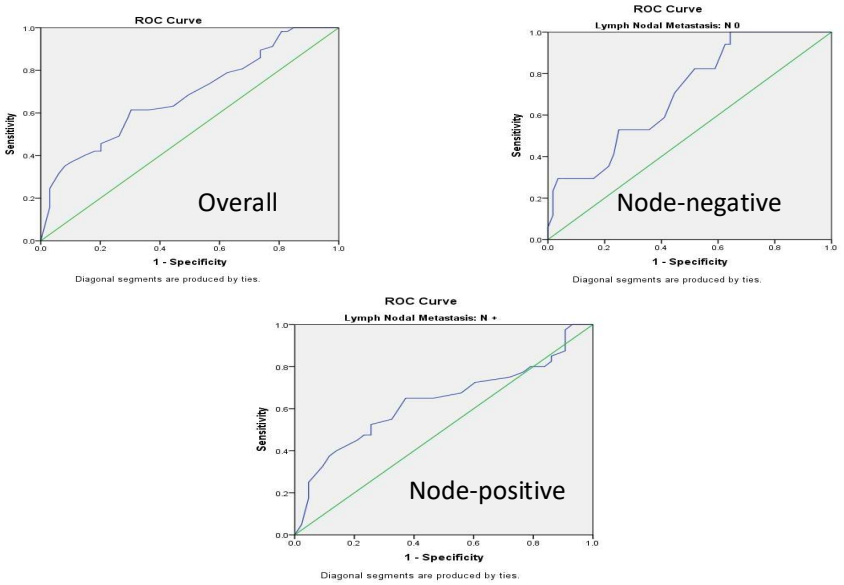

Figure 4.8 ROC curves for post-treatment SGA score to predict disease progression at 6months.

Table 4.58 Sensitivity and specificity cut-off points for post-treatment SGA score to predict disease progression at 6 months.

Disease progression at 6 months								
Post-treatment Subjective Global Assessment score								
Overall			**Node Negative group**			**Node Positive group**		
AUC	Std. Error	95% CI	AUC	Std. Error	95% CI	AUC	Std. Error	95% CI
0.681	0.045	0.593-0.768	0.702	0.067	0.573-0.835	0.634	0.063	0.511-0.757
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
65	0	100				**65**	0	100
			63.5	5.9	100	**63.5**	5	97.7
62.5	15.8	97	**62.5**	11.8	98.2	**62.5**	17.5	95.3
60.5	31.6	93.9	**60.5**	23.5	96.4	**60.5**	32.5	90.7
59.5	35.1	91.9				**59.5**	37.5	88.4
58.5	36.8	89.9	**58.5**	29.4	92.9	**58.5**	40	86
57.5	40.4	84.8	**57.5**	29.4	89.3	**57.5**	45	79.1
55.5	42.1	79.8	**55**	29.4	83.9	**55.5**	47.5	74.4
51.5	61.4	69.7	**51.5**	52.9	75	**50.5**	65	53.5
49.5	63.2	55.6	**49.5**	52.9	71.4			
47.5	73.7	43.4	**47.5**	70.6	55.4	**47.5**	75	27.9
45.5	80.7	32.3	**45.5**	82.4	41.1	**45.5**	80	20.9
			44.5	88.2	39.3			
42.5	86	26.3	**43.5**	94.1	37.5	**42.5**	82.5	14
40.5	91.2	22.2	**41.5**	100	35.7	**40.5**	87.5	9.3
39.5	98.2	19.2				**39**	97.5	9.3
37.5	100	15.2				**36.5**	100	7
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

4.16. ROCs for various variables to predict overall survival at 6months

Figure4.9 depicts the ROCs for pre-treatment SGA score. The AUC (95%CI) for pre-treatment SGA score in overall, N- and N+ cohorts was 0.66(0.54-0.781), 0.607(0.433-0.781) and 0.657(0.504-0.811) respectively (Table4.59). In N+ cohort, **Specificity** to predict overall survival at 6months for pre-treatment SGA s was- cut-offs ≥ 50.5-80.3%, 53-84.8%, 55.5-90.9%, 57.5-93.6%, 59.5-95.5%, 63.5-98.5%,66-100%. As noted previously this variable was not associated with 6month OS in N- cohort.

Figure 4.10 depicts the ROCs for pre-treatment NLR. The AUC (95%CI) for pre-treatment NLR in overall, N- and N+ cohorts was 0.627(0.487-0.766), 0.557(0.27-0.844) and 0.660(0.492-0.828) respectively (Table 4.60). In N+ cohort, **Specificity** to predict overall survival at 6months for pre-treatment NLR was- cut-offs ≥ 3.68-77.3%, 4.17-87.9%, 4.97-92.4%, 5.56- 93.9%, 7.5-97%, 8.5-98.5%, 20-100%. As noted previously this variable was not associated with 6month OS in N- cohort.

Figure 4.11 depicts the ROCs for post-treatment NLR. The AUC (95%CI) for post-treatment NLR in overall, N- and N+ cohorts was 0.709(0.581-0.837), 0.585(0.297-0.873) and 0.743(0.605-0.880) respectively (Table4.61). In N+ cohort, **Specificity** to predict overall survival at 6months for post-treatment NLR was- cut-offs ≥ 8.09-78.8%, 9.07-84.8%, 10.09-87.9%, 12.08-93.9%, 14.25-97%, 19,42-98.5%, 24.1-100%. As noted previously this variable was not associated with 6month OS in N- cohort.

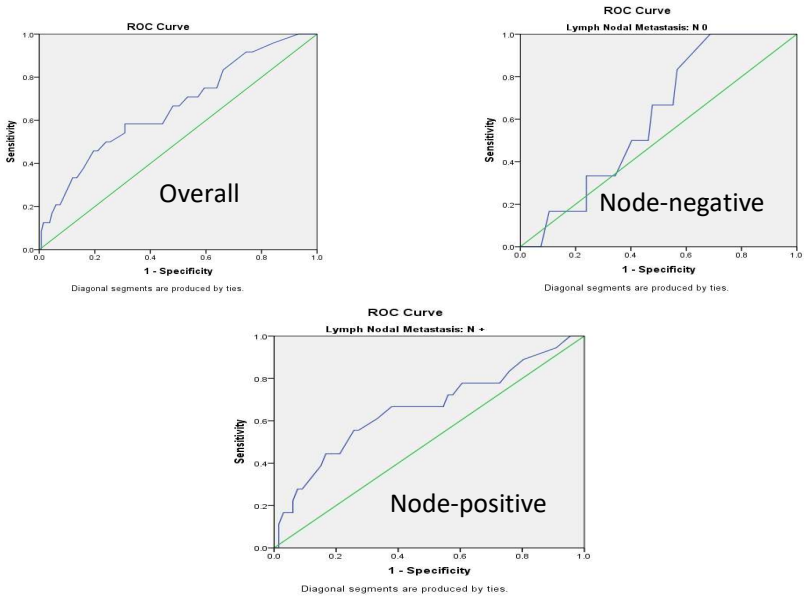

Figure 4.9 ROC curves for pre-treatment SGA score to predict overall survival at 6months.

Table 4.59 Sensitivity and specificity cut-off points for pre-treatment SGA score to predict overall survival at 6months.

Death at 6 months								
Pre-treatmentSubjective Global Assessment score								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.66	0.062	0.54-0.781	0.607	0.089	0.433-0.781	0.657	0.078	0.504-0.811
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
66	0	100				**66**	0	100
63.5	8.3	92				**63.5**	11.1	98.5
59.5	12.5	97.7	**60**	0	100	**59.5**	16.7	95.5
57.5	16.7	95.5	**57.5**	0	97	**57.5**	22.2	93.6
55.5	20.8	92.5	**56.5**	0	95.5	**55.5**	27.8	90.9
53	29.2	89.5	**54**	0	94	**53**	38.9	84.8
50	33.3	86.5	**49.5**	16.7	89.6	**50.5**	44.4	80.3
48.5	45.8	80.5	**48.5**	16.7	86.6	**48.5**	55.6	74.2
45.5	50	74.4	**45.5**	16.7	82.1	**46**	61.1	66.7
42.5	58.3	66.9	**42.5**	33.3	74.6	**42.5**	66.7	59.1
40.5	58.3	58.6	**40.5**	33.3	68.7	**40.5**	66.7	48.5
37.5	66.7	49.6	**37.5**	50	56.7	**37.5**	72.2	42.2
35.5	70.8	42.9	**34.5**	66.7	52.2	**35.5**	77.8	31.8
32.5	75	36.1	**32.5**	66.7	44.8	**32.5**	83.3	59.1
31.5	83.3	33.8	**31.5**	83.3	43.3	**31.5**	83.3	24.2
29.5	91.7	23.3	**30.5**	100	31.3	**30**	88.9	19.7
27.5	100	6.8				**27.5**	100	4.5
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

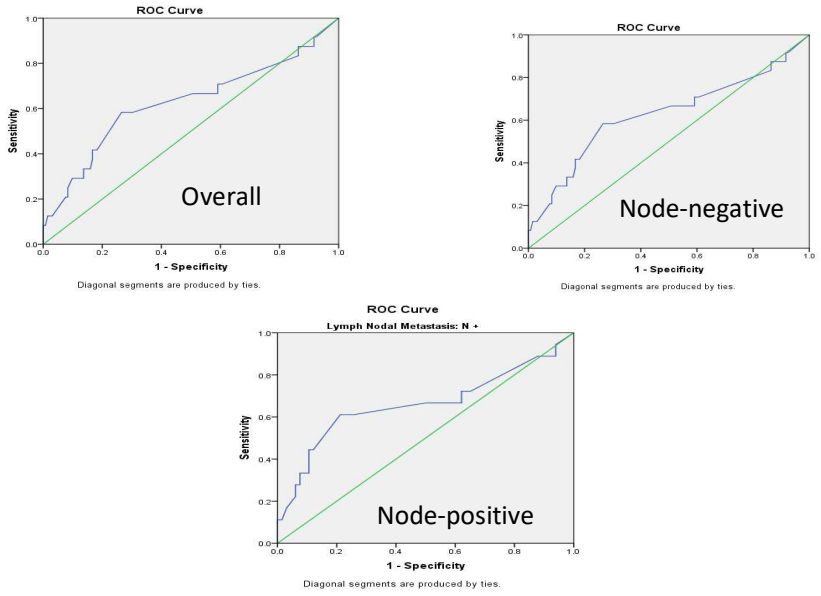

Figure4.10 ROC curves for pre-treatment NLR predict overall survival at 6months.

Table 4.60 Sensitivity and specificity cut-off points for pre-treatment NLR to predict death at 6 months.

Death at 6 months								
Pre-treatmentNeutrophil/ Lymphocyte ratio								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.627	0.071	0.487-0.766	0.557	0.146	0.27-0.844	0.660	0.086	0.492-0.828
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
27.5	8.3	100	**25**	0	100			
20	8.3	99.2	**20**	0	98.5	**20**	11.1	100
13	12.5	98.5	**13**	16.7	97			
9.5	12.5	97.7	**9**	16.7	95.5			
7.5	16.7	94.7	**7.5**	16.7	92.4	**7.5**	16.7	97
6.96	20.8	92.4	**6.96**	16.7	90.9			
6.54	20.8	91.7	**6.46**	16.7	89.4	**6.58**	22.2	93.9
6.08	25	91.7	**5.99**	33.3	86.4			
5.49	29.2	89.4	**5.49**	33.3	84.8	**5.58**	27.8	93.9
4.97	29.2	86.4	**4.83**	33.3	80.3	**4.97**	27.8	92.4
4.56	33.3	84.1	**4.58**	33.3	78.8	**4.56**	33.3	90.9
4.39	41.7	83.3	**4.33**	33.3	77.3	**4.39**	44.4	90.9
4.08	41.7	81.8	**4.08**	33.3	75.8	**4.17**	44.4	87.9
3.68	58.3	72	**3.6**	50	66.7	**3.68**	61.1	77.3
2.96	66.7	49.2	**3.1**	50	65.2	**3.2**	61.1	74.2
2.56	66.7	43.9	**2.65**	66.7	45.5	**2.51**	66.7	42.4
2.16	70.8	40.9	**2.26**	66.7	43.9	**2.16**	72.2	37.9
1.94	83.3	13.6	**1.94**	66.6	15.2	**1.94**	88.9	12.1
1.87	87.5	13.6	**1.74**	83.3	15.2	**1.62**	88.9	19.7
1.13	91.7	8.3	**1.06**	83.3	9.6	**1.07**	94.4	6.1
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

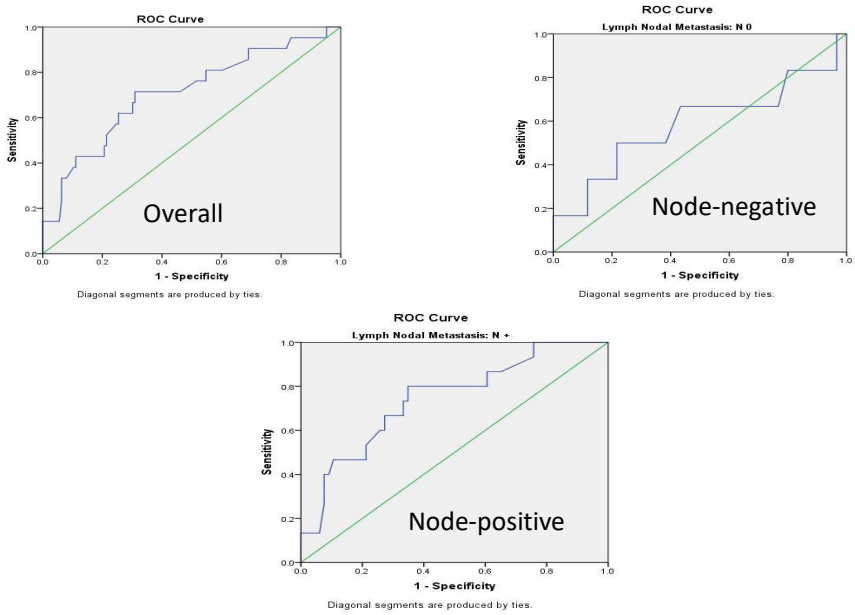

Figure 4.11 ROC curves for post-treatment NLR predict overall survival at 6months

Table 4.61 Sensitivity and specificity cut-off points for post-treatment NLR to predict death at 6 months.

Death at 6 months								
Post-treatmentNeutrophil/ Lymphocyte ratio								
Overall			Node Negative group			Node Positive group		
AUC	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**	**AUC**	**Std. Error**	**95% CI**
0.709	0.065	0.581-0.837	0.585	0.147	0.297-0.873	0.743	0.070	0.605-0.880
cut-off	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**	**cut-off**	**Sensitivity (%)**	**Specificity (%)**
24.09	14.6	100	**35.33**	16.7	100	**24.1**	13.3	100
20.25	14.3	98.2				**19.42**	13.3	98.5
15.03	14.3	96.8	**15.1**	16.7	96.7	**14.25**	13.3	97
12.08	14.3	94.4				**12.08**	13.3	93.9
11.04	33.3	92.1	**11.04**	16.7	93.3	**11.13**	40	91.9
10.04	42.9	88.3	**10.04**	33.3	86.7	**10.09**	46.7	87.9
9.07	42.7	83.5	**8.97**	33.3	78.3	**9.07**	46.7	84.8
8.09	52.4	79.6	**8.47**	50	78.7	**8.09**	53.3	78.8
7.28	61.9	74.8	**7.5**	50	76.7	**7.28**	66.7	71.2
						6.66	73.3	66.7
6.08	71.4	64.5	**6.18**	50	71.7	**6.08**	80	56.1
5.00	71.4	54	**5.11**	50	61.7	**5.00**	80	47
4.67	76.2	45.2	**4.68**	66.7	54.3	**4.03**	86.7	34.8
4.03	81	39.7	**4.07**	66.7	45	**3.94**	100	24.2
3.02	90.5	18.3	**3.02**	66.7	23.3			
1.5	95.2	4.8	**1.5**	83.3	3.3			
0.61	100	0.8	**1.42**	100	3.3			
("AUC- area under the curve, Std. error- standard error, CI- confidence interval")								

4.17. Survival Analysis for 6months PFS

Survival analysis was performed for variables statistically significantly associated with the outcome. Kaplan-Meier curves were generated and Cox-Regression model was used for Hazard Ratio (HR)

4.17.A. Overall group-

Poor 6month PFS was noted with cT3/4 stage (HR 4.06), single modality treatment (HR 2.67), failure to complete all planned treatment (HR 2.88), pre-treatment SGA score ≥40 (HR 1.83), post-treatment NLR>6 (HR 2.54) (Table4.62). The Kaplan-Meier curves are depicted in Figure 4.12.

Table 4.62 Hazard ratios for variables significantly associated with 6months PFS.

Hazard Ratio for 6month Progression Free Survival overall group					
Variable		**PFS (%)**	**HR***	**95% CI***	**p value***
Clinical T stage	T1/2	78.6	4.06	0.53-21.22	**0.021**
	T3/4	53.1			
	Tx	80			
Modality of treatment	single	52.2	2.67	1.46-4.97	**0.001**
	multiple	69.5			
Completed all planned treatment	no	26.3	2.88	1.32-6.29	**0.008**
	yes	68.1			
Pre-treatment SGA score	≥40	52.1	1.83	1.08-3.09	**0.025**
	<40	72.6			
Pre-treatment NLR	≤3	72.6	1.28	0.55-2.97	0.559
	>3 ≤6	48.7			
	>6	35.3			
Post-treatment NLR	≤3	72	2.54	1.3-4.92	**0.006**
	>3 ≤6	71.7			
	>6	50.8			
* Cox-Regression model (SGA-subjective global assessment, NLR-neutrophil/lymphocyte ratio, CI-confidence interval)					

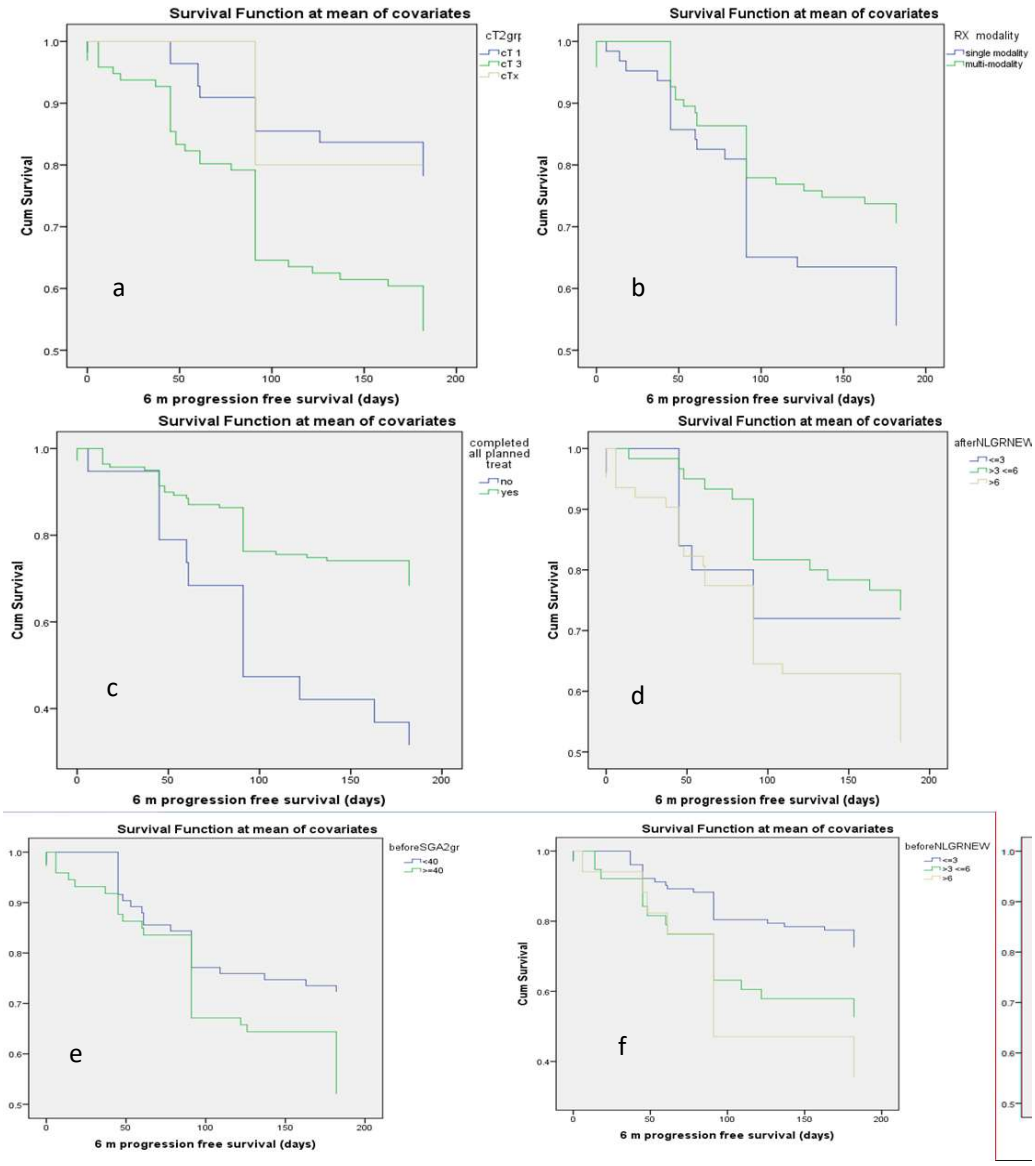

Figure 4.12 Kaplan-Meier survival curves for 6months Progression Free Survival in overall group. a. clinical T stage, b. treatment modality, c. failure to complete planned treatment, d. pre-treatment SGA score, e. pre-treatment NLR, f. post-treatment NLR.

4.17.B. Node negative group-

Poor 6months PFS was noted with cT3/4 stage (HR 3.24) and post-treatment NLR>6 (HR 4.76) (Table4.63, Figure4.13).

Table 4.63 Hazard ratios for variables significantly associated with 6months PFS node-negative group.

Hazard Ratio for 6monthProgression Free Survival Node-negative group					
Variable		**PFS (%)**	**HR**	**95% CI**	**p value**
Clinical T stage	T1/2	88	3.24	1.05-9.9	**0.040**
	T3/4	65.75			
Post-treatment NLR	≤3	75	4.76	1.29-17.5	**0.019**
	>3 ≤6	89.7			
	>6	55			
* Cox-Regression model (SGA-subjective global assessment, NLR-neutrophil/lymphocyte ratio, CI-confidence interval)					

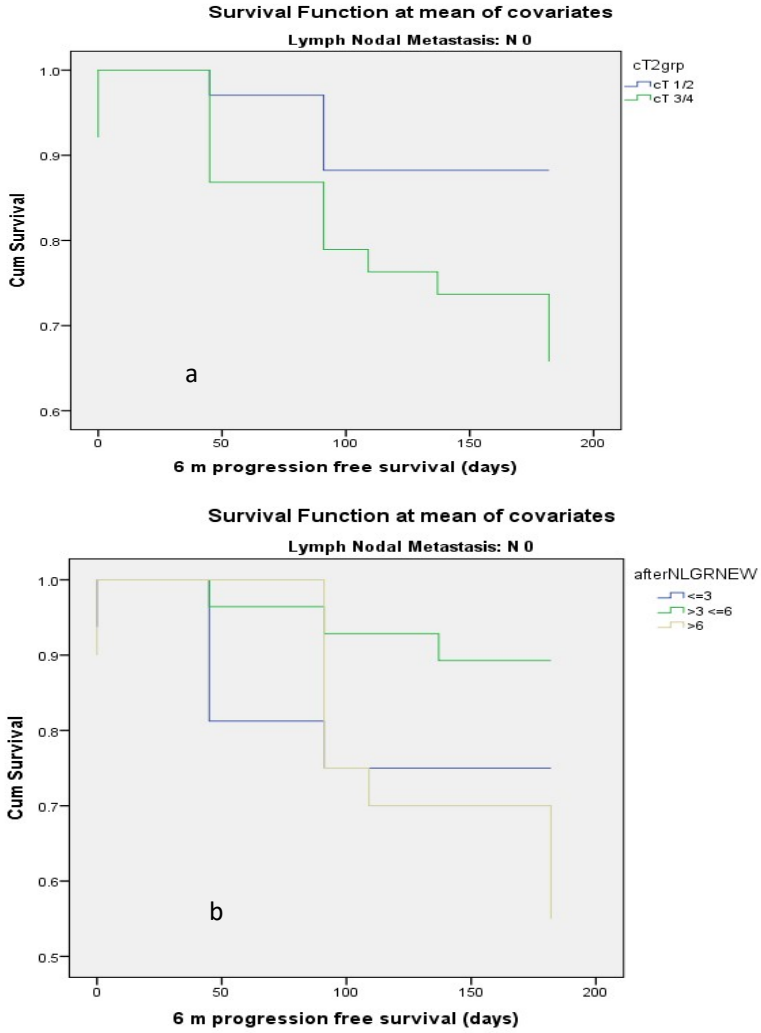

Figure 4.13 Kaplan-Meier Survival Curves for 6months Progression Free Survival in node-negative group. a. clinical T stage, b. post-treatment NLR.

4.17.C. Node positive group-

Poor 6months PFS with was noted with cT3/4 stage (HR 2.2), single modality treatment (HR 3.53), failure to complete all planned treatment (HR 2.1) and pre-treatment NLR>3 (HR 1.28) only (Table4.64, Figure 4.14). Pre-treatment SGA score and post-treatment NLR did not have significant p values on Cox-Regression analysis.

Table 4.64 Hazard ratios for variables significantly associated with 6months PFS node-negative group.

Hazard Ratio for 6month Progression Free Survival Node-positive group					
Variable		**PFS (%)**	**HR**	**95% CI**	**p value**
Clinical T stage	T1/2	61.9	2.2	1.04-4.65	**0.039**
	T3/4	44.8			
	Tx	80			
Modality of treatment	single	15.4	3.53	1.8-6.85	**0.000**
	multiple	67.2			
Completed all planned treatment	no	26.3	2.1	0.97-4.52	**0.008**
	yes	68.1			
Pre-treatment NLR	≤3	72.6	1.28	0.55-2.97	**0.036**
	>3 ≤6	48.7			
	>6	35.3			
* Cox-Regression model (SGA-subjective global assessment, NLR-neutrophil/lymphocyte ratio, CI-confidence interval)					

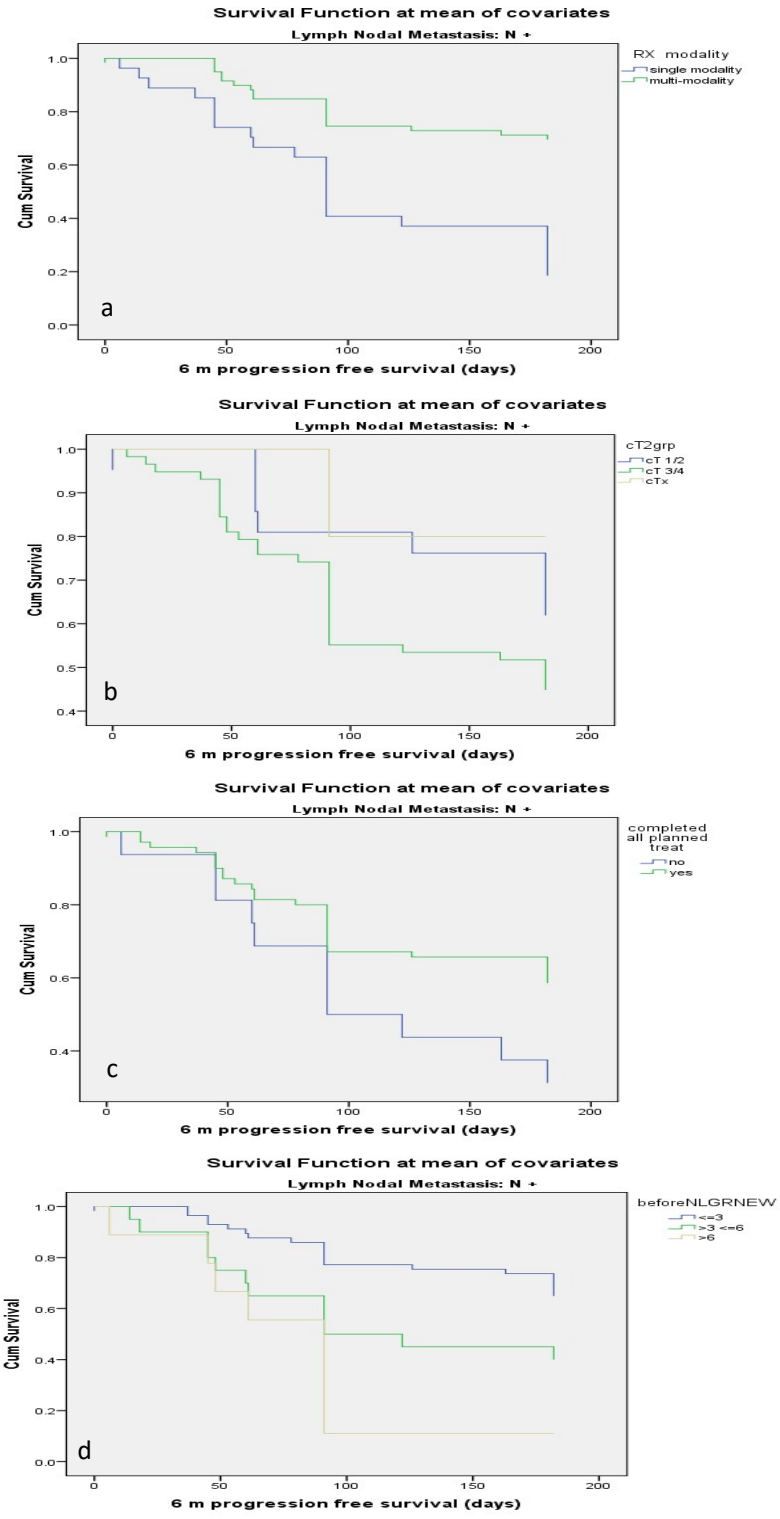

Figure 4.14 Kaplan-Meier survival curves for 6months Progression Free Survivalin node-positive group. a. clinical T stage, b. treatment modality, c. failure to complete planned treatment, d. pre-treatment NLR.

4.18. Survival Analysis for 6months OS

4.18.A. Overall group-

Poor 6months OS was noted with cT3/4 stage (HR 2.47), single modality of treatment (HR 5.56), failure to complete planned treatment (HR 7.31), post-treatment NLR>6 (HR 7.94) (Table 4.65, Figure 4.15).

Table 4.65 Hazard ratios for variables significantly associated with 6months OS overall group.

Hazard Ratio for 6month Overall Survival overall group					
Variable		**PFS (%)**	**HR**	**95% CI**	**p value**
Clinical T stage	T1/2	96.4	2.47	1.16-5.23	**0.018**
	T3/4	77.1			
	Tx	100			
Modality of treatment	single	77.4	5.56	1.75-17.69	**0.004**
	multiple	89.5			
Completed all planned treatment	no	52.6	7.31	2.13-25.11	**0.002**
	yes	89.1			
Pre-treatment SGA score	≥40	80.8	2.97	0.92-9.57	0.068
	<40	88.1			
Post-treatment NLR	≤3	92	7.94	2.83-27.8	**0.001**
	>3 ≤6	93			
	>6	75			
* Cox-Regression model (SGA-subjective global assessment, NLR-neutrophil/lymphocyte ratio, CI-confidence interval)					

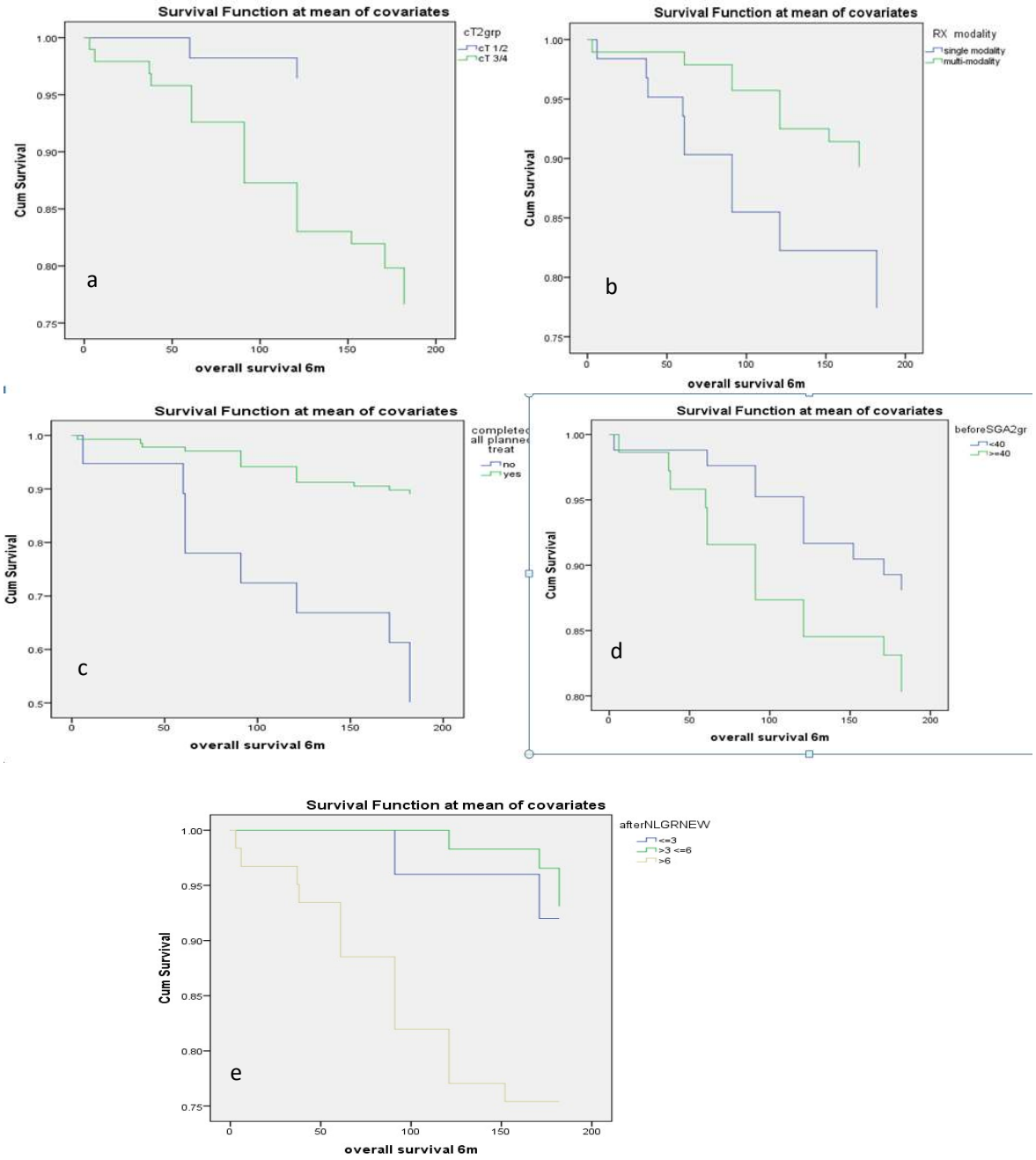

Figure 4.15 Kaplan-Meier survival curves for 6months Overall Survival in overall group. a. clinical T stage, b. treatment modality c. failure to complete planned treatment, d. pre-treatment SGA score, e. post-treatment NLR.

4.18.B. Node-negative group-

Poor 6month OS was noted with failure to complete all planned treatment (HR 43.94) only (Table 4.66, Figure 4.16).

Table 4.66 Hazard Ratios for variables significantly associated with 6months OS node-negative group.

Hazard Ratio for 6month Overall Survival Node-negative group					
Variable		**PFS (%)**	**HR**	**95% CI**	**p value**
Completed all planned treatment	no	33.3	43.94	2.45-797.7	**0.010**
	yes	82.8			
Post-treatment NLR	≤3	87.5	0.047	0.002-1.016	0.051
	>3 ≤6	96.6			
	>6	85			
* Cox-Regression model (NLR-neutrophil/lymphocyte ratio, CI-confidence interval)					

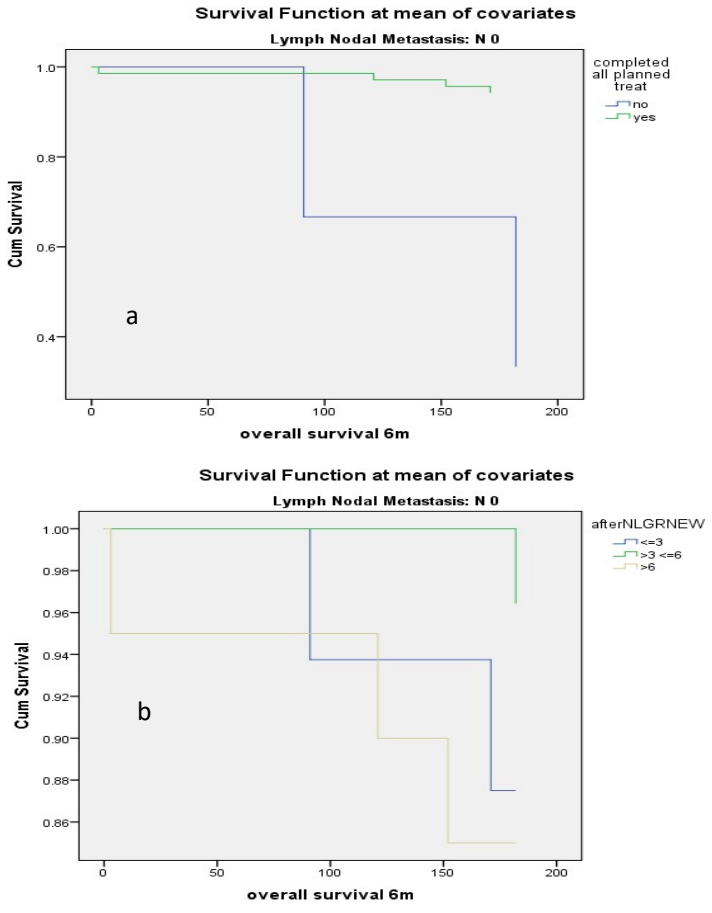

Figure 4.16 Kaplan-Meier Survival Curves for 6months Overall Survival in Node-negative group.
a. failure to complete planned treatment, b. post-treatment NLR.

4.18.C. Node-positive group-

Poor 6months OS was noted with single modality treatment (HR 17.47), failure to complete all planned treatment (HR 6.16), pre-treatment SGA score ≥40 (HR 15.8), pre-treatment NLR>3 (HR 5.15) and post-treatment NLR>6 (HR 10.99) (Table 4.67, Figure 4.17).

Table 4.67 Hazard ratios for variables significantly associated with 6months OS node-positive group.

Variable		PFS (%)	HR	95% CI	p value
Clinical T stage	T1/2	90			0.224
	T3/4	72.4			
	Tx	100			
Pre-treatment PS	0-2	84.8	1.87	0.408-8.55	0.420
	>2	40			
Modality of treatment	single	53.9	17.47	2.63-116.03	**0.003**
	multiple	89.7			
Completed all planned treatment	no	56.3	6.16	1.14-33.4	**0.035**
	yes	83.8			
Pre-treatment SGA score	≥40	40.8	15.8	1.88-132.84	**0.011**
	<40	83.3			
Pre-treatment NLR	≤3	87.5	5.15	1-27	**0.050**
	>3 ≤6	68.4			
	>6	44.4			
Post-treatment NLR	≤3	100	10.99	2.17-55.6	**0.004**
	>3 ≤6	90.3			
	>6	70.7			
* Cox-Regression model (SGA-subjective global assessment, NLR-neutrophil/lymphocyte ratio, CI-confidence interval)					

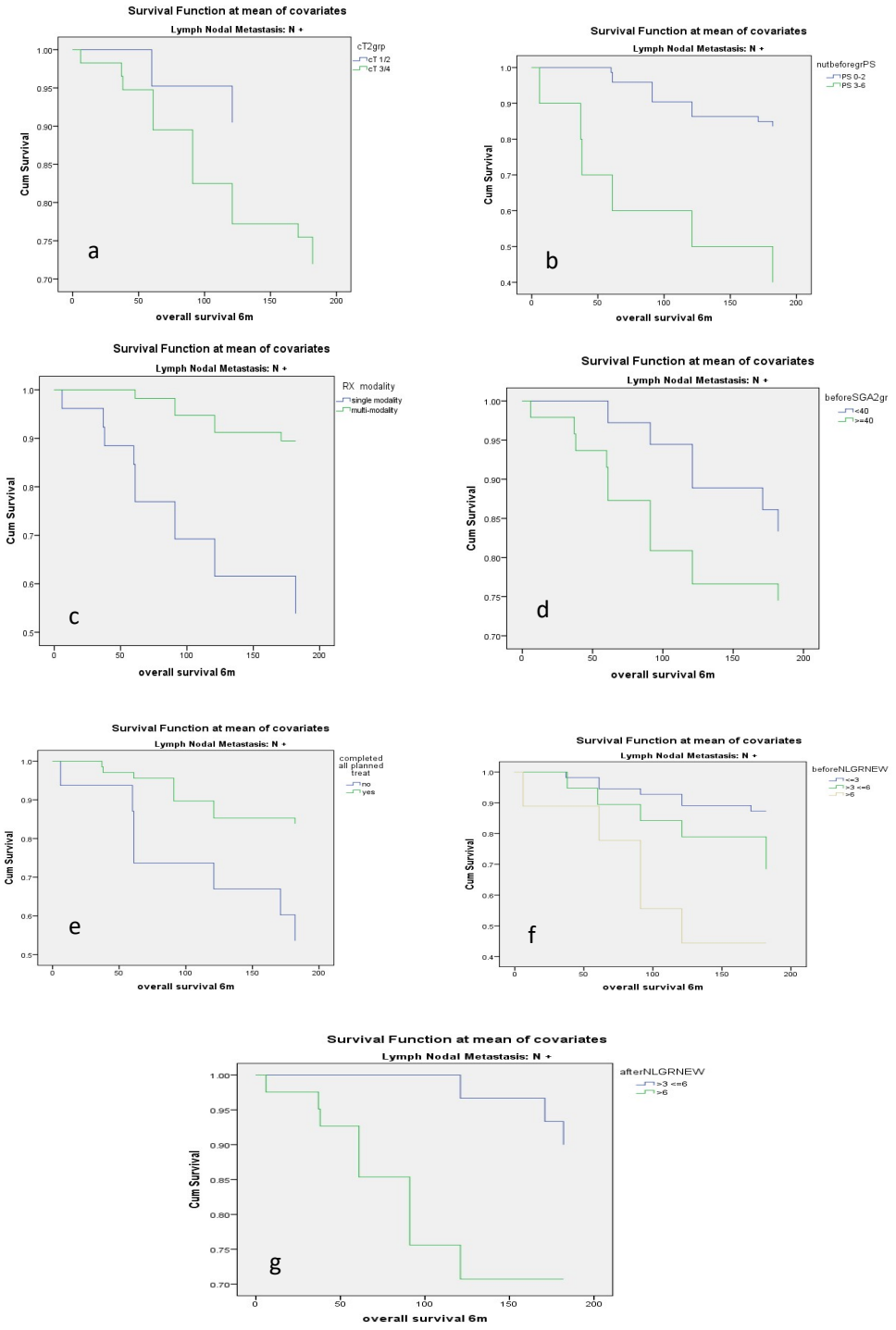

Figure 4.17 Kaplan-Meier survival curves for 6months Overall Survival in node-positive group. a. clinical T stage, b. pre-treatment performance status, c. pre-treatment SGA score, d. treatment modality, e. failure to complete planned treatment, f. pre-treatment NLR, g. post-treatment NLR

4.19. Risk stratification model for failure to complete all planned treatment

To construct risk stratification model for failure to complete planned treatment, variables found to be significantly associated with it were identified. The mean with SD or median with IQR, strength of association in the form of RR and cut-off points for high specificity from ROCs were used to assign points for various values of these variables. This novel model is detailed in Table4.68. Score could range from 0 to 17, risk stratification was assigned as follows- low score 0-4, moderate score 5-10 and high score 11-17. This model was then applied on the current data set to test for internal validation.

In overall group, 75%, 18% and 6.8% patients were stratified as low, medium and high risk for *FailureTxCompletion* respectively; 6.6% patients in low, 27.6% in medium and 45.5% in high risk group had *FailureTxCompletion* (p=0.000).In N- cohort, 83.6%, 12.3% and 0% patients were stratified as low, medium and high risk for *FailureTxCompletion*respectively; 3.3% patients in low and 22.1% in medium risk groups had *FailureTxCompletion* (p=0.421). In N+ cohort, 68.2%, 22.7% and 9.1% patients were stratified as low, medium and high risk for *FailureTxCompletion* respectively; 10% patients in low, 35% in medium and 62.5% in high risk group had *FailureTxCompletion* (p=0.001) (Table 4.69).

Table 4.68 Risk stratification model to predict failure to complete planned treatment.

Variable pre-treatment	Points				category	score
	0	1	2	3		
Weight (kg)	>50	45-50	40-44.9	<40	low risk	0 - 4
BMI	≥18.5	18 - 18.5	16 - 17.9	<16		
% weight loss in past 6 months	<10	10 - 15	15.1 - 20	>20		
Mid Upper Arm Circumference (cm)	≥21		<21		medium risk	5 - 10
Bitot spots	absent	present				
Subjective Global Assessment score	≤40	41-50	51-57	>57	high risk	11- 17
Treatment modality	multi		single			

Table 4.69 Cross-tabulation of risk stratification model for failure to complete planned treatment with study data.

Number of patients who failed to complete planned treatmentn/N (%)						
RISK GROUP	**Overall N=161**	**p***	**Node negative N=73**	**p***	**Node positive N=88**	**p***
Low	8/121 (6.61)	**0.000**	2/61 (3.28)	0.421	6/60 (10)	**0.001**
Medium	8/29 (27.59)		1/9 (11.11)		7/20 (35)	
High	5/11 (45.45)		0		5/8 (62.5)	
* Chi-square test						

4.20. Risk Stratification model for disease progression at 6months

Similar methodology was followed to develop risk stratification to predict disease progression at 6months (Table 4.70). The following variables were assigned points- clinical T stage, modality of treatment, failure to complete all planned treatment, pre and post-treatment NLR and post-treatment SGA scores. The total score could range from 0 to 16, risk stratification was assigned as follows- low score 0-5, moderate score 6-10 and high score 11-16. This model was then applied on the current data set to test for internal validation.

In overall group, 45.2%, 45.9% and 8.9% patients were stratified as low, medium and high risk for disease progressionrespectively; 16.9% patients in low, 47.2% in medium and 85.7% in high risk group had disease progression (p=0.000). In N- cohort, 52.1%, 41.1% and 6.9% patients were stratified as low, medium and high risk for disease progression respectively; 10.5% patients in low, 33.3% in medium and 60% in high risk group had disease progression (p=0.014). In N+ cohort,39.3%, 50% and 10.7% patients were stratified as low, medium and high risk for disease progression respectively; 24.2% patients in low, 57.1% in medium and 100% in high risk group had disease progression(p=0.000) (Table 4.71).

Table 4.70 Risk stratification model to predict disease progression at 6months after completion of treatment.

Variable	Points				category	score
	0	1	2	3		
Clinical T stage	cT1/T2		cT3/T4		low risk	0-5
Treatment modality	multiple			single		
Completed all planned treatment	yes		no		medium risk	6-10
Neutrophil/Lymphocyte ratio (pre treatment)	≤3	3.1-6	6.1-7.4	≥7.5		
Subjective Global Assessment score (post treatment)	≤40	41-50	51-57	≥58	high risk	11-16
Neutrophil/Lymphocyte ratio (post treatment)	≤3	3.1-6	6.1-7.4	≥7.5		

Table 4.71 Cross-tabulation of risk stratification model to predict disease progression at 6months with study data.

Number of patients with Disease Progression at 6 months n/N (%)						
RISK GROUP	**Overall group N=157**	**p value ***	**Node negative group N=73**	**p value ***	**Node positive group N=84**	**p value ***
Low risk (0 to 5)	12/71 (16.9)		4/38 (10.53)		8/33 (24.24)	
Medium risk (6 to 10)	34/72 (47.22)	**0.000**	10/30 (33.33)	**0.014**	24/42 (57.14)	**0.000**
High risk (11 to 16)	12/14 (85.71)		3/5 (60)		9/9 (100)	
* Chi-square test						

4.21. Risk stratification model for death due to disease at 6 months

Similar methodology was followed to develop risk stratification to predict death due to disease at 6 months (Table 4.72). The following variables were assigned points- clinical T stage, modality of treatment, failure to complete all planned treatment, pre-treatment ECOG PS, pre and post-treatment NLR and pre-treatment SGA scores. The total score could range from 0 to 20, risk stratification was assigned as follows- low score 0-5, moderate score 6-10 and high score 11-20. This model was then applied on the current data set to test for internal validation.

In overall group, 57.3%, 30.6% and 12.1% patients were stratified as low, medium and high risk for death due to disease respectively; 4.4% patients in low, 18.8% in medium and 57.9% in high risk group had death due to disease (p=0.000). In N- cohort, 68.5%, 26% and 5.5% patients were stratified as low, medium and high risk for death due to disease respectively; 4% patients in low, 15.8% in medium and 25% in high risk group had death due to disease (p=0.093). In N+ cohort, 47.6%, 34.5% and 17.9% patients were stratified as low, medium and high risk for death due to disease respectively; 5% patients in low, 20.7% in medium and 66.7% in high risk group had death due to disease (p=0.000) (Table 4.73).

Table 4.72 Risk stratification model to predict death due to disease at 6months after completion of treatment.

Variable	Points				category	score
	0	1	2	3		
Clinical T stage	cT1/T2		cT3/T4		low risk	0-5
Treatment modality	multiple			single		
Completed all planned treatment	yes			no	medium risk	6-10
ECOG Performance Status (Pre treatment)	0 to 2			3 or more		
Subjective Global Assessment score (pre treatment)	≤40	41-50	51-60	≥61	high risk	11-20
Neutrophil/Lymphocyte ratio (pre treatment)	≤3	3.1-6	6.1-7.4	≥7.5		
Neutrophil/Lymphocyte ratio (post treatment)	≤3	3.1-6	6.1-7.4	≥7.5		

Table 4.73 Cross-tabulation of risk stratification model to predict death due to disease at 6months after completion of treatment with the study data.

Number of patients with Death due to disease at 6 months n/N (%)						
RISK GROUP	Overall N=157	p*	Node negative N=73	p*	Node positive N=84	p*
Low risk(0-5)	4/90 (4.44)	0.000	2/50 (4)	0.093	2/40 (5)	0.000
Mediumrisk(6-10)	9/48 (18.75)		3/19 (15.79)		6/29 (20.69)	
High risk (11-20)	11/19(57.89)		1/4 (25)		10/15 (66.67)	
* Chi-square test						