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# Prognostic Value of Neutrophil-Lymphocyte Ratio in Patients with Locally Advanced Oropharyngeal Carcinoma Undergoing Definitive Chemoradiation

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**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

## Abstract

**Aim**: To evaluate the prognostic value of the neutrophil-lymphocyte ratio for predicting treatment response in patients with locally advanced oropharyngeal cancer receiving definitive Radiotherapy and Chemotherapy.

**Material and Methods:**

**Study Design:** Single-institution, retrospective cohort study.

**Study Population:** 100 patients with locally advanced oropharyngeal carcinoma (stages II-IVA), aged 18-70 years. Patients who had previously received chemotherapy or radiotherapy were excluded.

**Study Period:** The study included 100 patients treated from 2022 to 2023. These patients received curative radiotherapy of 70 Gy over 35 fractions, along with concurrent weekly chemotherapy with platinum-based drugs.

**Outcome Measurement**: Treatment response was evaluated using CECT scan reports three months post-chemoradiation.

**Results and Conclusion:** Out of 51 patients having high NLR, 25 had relapsed. While out of 49 patients having normal NLR, 12 had relapsed within 18 months.

The p-value = 0.0085 indicates that the difference between the two groups is statistically significant ($p < 0.05$).

A high NLR is associated with a higher relapse rate, making it a potential prognostic marker for patient outcomes.

Clinically, this suggests that monitoring NLR levels in patients might help predict relapse risks, and those with high NLR may require closer follow-up or more aggressive treatment strategies.

**Keywords:** Chemotherapy, Neutrophil-Lymphocyte Ratio, Radiotherapy, Relapse free survival

## Introduction

The incidence of oropharyngeal cancer is on the rise in the developed countries.[1] Neutrophil-to-lymphocyte ratio (NLR) is a simple biomarker of systemic inflammation and has been demonstrated to be a prognostic marker in several solid cancers, including prostate, renal, gastric, brain and hypopharyngeal cancers [3][4]. Here we evaluated the effect of pre-treatment NLR on outcomes in patients with oropharyngeal carcinoma who received definitive chemoradiation.

NLR= Absolute Lymphocyte Count (ALC)

Absolute Neutrophil Count (ANC)

- **Absolute Neutrophil Count (ANC)** = Total White Blood Cell (WBC) count × Percentage of Neutrophils ÷ 100
- **Absolute Lymphocyte Count (ALC)** = Total WBC count × Percentage of Lymphocytes ÷ 100

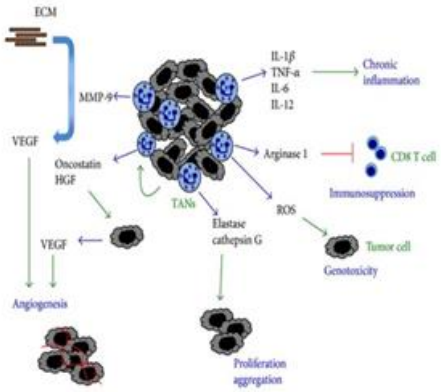



Figure 1:[5]

- Tumour associated neutrophils (TANs)are associated with anti-tumour or pro-tumour activities. They secrete metrix metalloproteinase-9(MMP-9) which release VEGF and stimulate new blood vessel formation.
- These neutrophils also secrete IL-1β, TNF-α, IL-6, IL-12 leading to inflammation.
- They are associated with creating immunosuppressive state by releasing Arginase-1, inhibiting CD8 cells.
- Produce ROS (reactive oxygen species, leads DNA damage and mutation in tumour cells.
- Serine proteases (elastase, cathepsin G) stimulate tumour growth.
- Oncostatin is IL-6 like cytokine, induced by breast cancer cells, it leads to promote angiogenesis by secreting VEGF.
- HGF which increases tumour invasiveness, secreted by HCC cells.

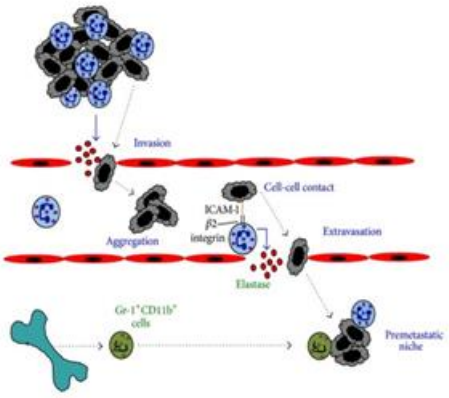



Figure 2:[5]

### Tumour cell metastasis

- Tumour associated neutrophils secrete elastase breaking down basement membrane. It promotes tumour cell invasion.
- Tumour cell aggregation is promoted, leading to increasing their survival in bloodstream.
- Tumour cell adhesion with neutrophils by ICAM-1 and β2-integrin interaction, leading to extravasation of tumour cells.

### Study Hypothesis

Whether the prognosis and local control and relapse free survival is better or poor in patients receiving definitive chemoradiation in patients with normal neutrophil-

lymphocyte ratio is comparable with high neutrophil-lymphocyte ratio.

**Aims and Objectives**

To evaluate the prognostic value of the neutrophil-lymphocyte ratio for predicting treatment response in patients with locally advanced oropharyngeal cancer receiving definitive chemoradiation.

**Study Design: -** Single-institution, retrospective cohort study.

**Study type:** Retrospective Cohort Study.

**Study site:** Department of Radiation Oncology, SSG Hospital, Baroda.

**Study duration:** July 2022 to July 2023.

**Sample size:** 100.

**Inclusion criteria**

- Patients with age between 18 to 70 years.
- Patients with locally advanced oropharyngeal squamous cell carcinoma who have not received any form of chemotherapy or radiotherapy or undergone surgery previously.
- Patients in stage II-IVA, any N and $M_0$ according to TNM classification of head and neck cancer.
- Patients in ECOG 0,1,2.
- Patients who give consent to receive definitive chemoradiation.

**Exclusion criteria**

- Patients with age of less than 18 and more than 70.
- Patients with locally advanced head and neck cancer who have received any form of chemotherapy or radiotherapy or surgery previously.
- Patients having any histological type other than squamous cell carcinoma.
- Patients who received curative standard fractionated radiotherapy previously.
- Patients in ECOG 3.
- Patients who do not give consent to receive curative chemoradiation.

**Material and Methods**

This single-institution, retrospective cohort study included 100 patients aged 18-70 with stage II-IVA locally advanced oropharyngeal carcinoma, conducted over 2022-2023.

Exclusion criteria included prior chemotherapy or radiotherapy and presence of distant metastasis.

Patients underwent a pre-treatment assessment with a complete blood count within 10 days before treatment, and were divided into two groups based on their Neutrophil Lymphocyte Ratio (NLR):

Group 1 with normal neutrophil-lymphocyte ratio (0.7-2.5).

Group 2 with elevated neutrophil-lymphocyte ratio (>2.5).

The treatment protocol consisted of 70 Gy of radiotherapy over 35 fractions with concurrent weekly platinum-based chemotherapy. Treatment outcomes were evaluated three months post-treatment using a CECT scan, with weekly toxicity assessments conducted throughout the treatment period.

| Parameters | Population (%) |
|---|---|
| Age | 18-70 years |
| Sex | |
| Male | 87 |
| Female | 13 |
| Smoking Status | |
| Never | 43 |
| <10 Pack Years | 12 |
| >10 Pack Years | 26 |
| Current | 19 |

| Stage | No. of Patients |
|---|---|
| II | 36 |
| III | 27 |
| IV | 37 |

**Study Design**

- A single institutional, Retrospective Cohort Study.

**Study Area**

- This study was conducted in Department of Radiation Oncology, SSG Hospital, Baroda.

**Subject selection**

- Locally advanced cases of squamous cell carcinoma of oropharynx who have not received any treatment previously and are not fit for surgery.

**Study end point**

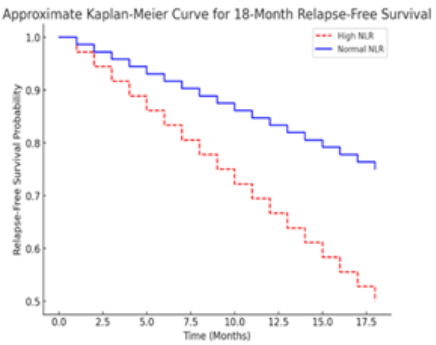
- Treatment response was evaluated using CECT scan reports three months post-chemoradiation.

**Results**

**18-Month Relapse-Free Survival (RFS)**

| Group | No Relapse (n, %) | Relapsed (n, %) | Total (n) |
|---|---|---|---|
| High NLR (n=51) | 26 (50%) | 25 (50%) | 51 |
| Normal NLR (n=49) | 37 (75%) | 12 (25%) | 49 |
| Total (n=100) | 63 (63%) | 37 (37%) | 100 |

p-value = 0.0085




**1. What the Graph Represents**

This Kaplan-Meier survival curve estimates the probability of remaining relapse-free over an 18-month period for two groups:

- High NLR (Red, Dashed Line) – Patients with a high Neutrophil-to-Lymphocyte Ratio (NLR).
- Normal NLR (Blue, Solid Line) – Patients with a normal NLR.

The y-axis represents the probability of being relapse-free, starting from 100% at time zero and decreasing over time as more patients experience relapse. The x-axis represents time in months (0 to 18 months).

**2. Interpretation of the Survival Curves**

- High NLR Group
  - The survival probability decreases more rapidly, reaching 50% at 18 months (meaning half of the patients in this group have relapsed).
  - This suggests that a high NLR is associated with poorer relapse-free survival.
- Normal NLR Group
  - The decline in survival probability is slower, reaching 75% at 18 months (only 25% of patients relapsed).
  - This suggests that patients with a normal NLR have better relapse-free survival compared to those with high NLR.

**Conclusion and Clinical Implications**

- The p-value = 0.0085 indicates that the difference between the two groups is statistically significant ($p < 0.05$).
- A high NLR is associated with a higher relapse rate, making it a potential prognostic marker for patient outcomes.
- Clinically, this suggests that monitoring NLR levels in patients might help predict relapse risks, and those

with high NLR may require closer follow-up or more aggressive treatment strategies.

As this study is continued further, we will publish data for 5-year overall survival later after the study will be completed.

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