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ROLE OF PROGNOSTIC NUTRITIONAL INDEX IN HEAD AND NECK CANCER – A MNJ REGIONAL CANCER CENTRE EXPERIENCE

Dr. Rashmi. C. Shekar	MD Radiotherapy, Senior Resident, Department of Radiation Oncology, Mehdi Nawaz Jung Institute of Oncology & Regional Cancer Centre, Hyderabad.
Dr M. Vishnupriya	MD Radiotherapy, Associate Professor, Department of Radiation Oncology, Mehdi Nawaz Jung Institute of Oncology & Regional Cancer Centre, Hyderabad.
Dr. Iqra Tajammul	MD Radiotherapy, Senior Resident, Department of Radiation Oncology, Kakatiya Medical College, Warangal.
Dr G. Joseph Benjamin	MD Radiotherapy, Professor, Department of Radiation Oncology, Mehdi Nawaz Jung Institute of Oncology & Regional Cancer Centre, Hyderabad.

ABSTRACT **Introduction:** Locally advanced head and neck cancer (LAHNC), one of the most common cancers in the country is a heterogenous disease with a huge disease burden for which predictive and prognostic factors other than the TNM staging that hold a vital impact on the survival are needed. **Methods:** Study includes retrospective analysis of 50 patients with LAHNC treated with induction-chemotherapy followed by concurrent-chemoradiotherapy at our hospital. Entire clinical data, including Prognostic Nutritional Index (PNI), neutrophil-to-lymphocyte ratio(NLR) and derived-neutrophil-to-lymphocyte ratio(dNLR) were analysed. Receiver operating characteristic curve analysis was used to establish optimal cut-off. Univariate and multivariate analyses of prognostic factors for overall survival (OS) were performed. **Results:** The independent prognostic factors in univariate analysis of OS were identified as PNI(cut-off45) (p=0.042), NLR (NLR≥2.6) (p=0.05),dNLR(dNLR≥1.7) (p=0.02)were statistically significant. In the multivariate analysis only PNI (HR 2.84, 95% CI 1.04 to 7.78, p=0.042) and dNLR (HR 3.53, 95% CI 1.13 to 11.03, p=0.03) retained their independent prognostic power.

KEYWORDS :

INTRODUCTION:

Head and neck squamous cell carcinoma (HNSCC) includes a heterogeneous group of tumors that originate in the upper aerodigestive tract with being one of the common cancers in the country. Inflammation plays a vital role in the carcinogenesis of HNSCC by the chronic action of chemical carcinogens or chronic infection of oncogenic viruses. 42%- 77% of patients with LAHNSCC present a high risk of malnutrition at diagnosis owing to multifactorial origin. Definitive radiotherapy in association with induction or concurrent chemotherapy represents a non-surgical treatment of choice for these patients where nutritional status plays a pivotal role in response to the treatment. The Prognostic Nutritional Index (PNI), is a marker of both inflammation and nutritional status. Neutrophils have a role in tumor promotion, inflammation and immunosuppression associated with tumors based on this, hematological biomarkers linked with inflammation, like the neutrophil to lymphocyte ratio (NLR) and the derived neutrophil to lymphocyte ratio (dNLR), have been developed and have shown their prognostic value in several solid tumors. However, data in HNSCC is scarce. Henceforth our study aimed at predicting the prognostic value of different hematological inflammation-based prognostic scoring systems such as the PNI and the NLR and their correlation with overall survival (OS) in patients with LAHNSCC.

MATERIAL AND METHODS:

Patients:

The present retrospective study includes 50 LAHNC patients treated with induction chemotherapy followed by concurrent chemoradiotherapy at our institution between January 2017 to December 2022. Information of all the patients is retrieved through the medical records and confidentiality was maintained. This study included patients with(a) Age>18 years(b)Histopathologically confirmed LAHNSCC(c)AJCC stage T3-T4, N2-3(d)Baseline investigations available: age, sex, performance score, complete blood count (including absolute neutrophil and lymphocyte counts) and blood biochemistry (including albumin), HPV/P16 status. Patients with history of inflammatory disease, an active concomitant infection, distant metastases at diagnosis, history of malignancy in the past 5 years, baseline blood test results unavailable, radical radiotherapy alone or with concurrent chemoradiotherapy without induction chemotherapy were excluded.

Study Design:

All the patients were staged according to the AJCC 8th edition and were evaluated for treatment indication by a multidisciplinary tumor board. Patients were treated with induction chemotherapy of 3cycles with cisplatin(75mg/m2), docetaxel(75mg/m2) on day 1 along with 5fluorouracil(750mg/m2) on day 1-5 of a 21day cycle followed by external beam radiotherapy along with concurrent chemotherapy with cisplatin 40 mg/m^2 weekly. Baseline characteristics of age, gender, performance score, lymphocyte count, serum albumin, site of disease and stage were evaluated. Pre-treatment **PNI** was calculated using Ondera's formula of 10 × baseline serum albumin (g/dL) + 0.005 × baseline absolute lymphocyte count (cells/mm^3), **NLR** was calculated by dividing the baseline absolute peripheral neutrophil count (cells/mm^3) by the absolute peripheral lymphocyte count (cells/mm^3),**dNLR** was defined as the quotient of the baseline absolute peripheral neutrophil count (cells/mm^3) by the difference between the absolute baseline peripheral leucocyte count (cells/mm^3) less the absolute baseline peripheral neutrophil count (cells/mm^3).post treatment follow-up was done according to NCCN guidelines and overall survival was assessed.

Statistical Analysis:

Overall survival was calculated from time of cancer to death. Receiver operator characteristic curve was used to determine similarities between NLR, dNLR and PNI and to establish optimal threshold for the overall survival which were set accordingly as PNI [45], NLR [2.6], dNLR [1.6]. Association between the variables was established by student t-test. Kaplan-Meier statistics, log-rank test, and cox regression model were used to assess the impact of the different clinical factors associated with OS on univariate and multivariate analysis. For all statistical analyses<0.05 was considered statistically significant.

RESULTS:

Baseline characteristics: Most of the patients had performance score of 1, with majority of them being men in fifth decade of life with history of tobacco use. Most of them had large primary tumors[T4] with advanced lymph nodal metastasis[N2b-N3] belonging to stage IV A as per AJCC.

Table 1: Baseline Characteristics Of 50 Patients

Characteristics	Number (%)
Age(years), mean(range)	55(41-59)
ECOG Performance score 0 1	 2(4) 48(96)

Sex	
Male	42(84)
Female	8(16)
Primary tumor	
Oral cavity	15(30)
Oropharynx	12(24)
Larynx	12(24)
Hypopharynx	7(14)
other	4(8)
TNM stage	
T1-T3	20(40)
T4	30(60)
N0-N2a	22(44)
N2b-N3	28(56)
AJCC cancer staging	
Stage III	8(16)
Stage IV A	41(82)
Stage IV B	1(2)
NLR	
<2.6	23(46)
>=2.6	27(54)
dNLR	24(48)
<1.7	26(52)
>=1.7	
PNI	
PNI-High	40(80)
PNI-Low	10(20)

On analysis, 23 patients had died with a median follow up of 20 months with median OS being 20 months according to Kaplan-Meier plot for OS.

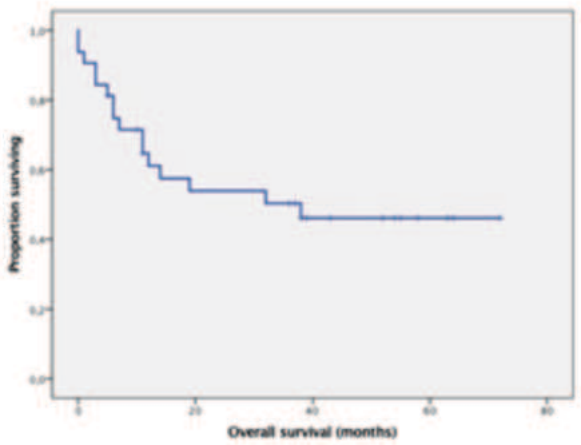

Figure 1: Kaplan-Meier plot for overall survival of 50 patients

The crude median PNI value was 42 and using ROC analysis,45 was selected as optimal cutoff to divide PNI into two values, PNI-high and PNI-low thus representing adequate and deficient nutritional state and low risk versus high risk of mortality. Similar ROC analysis was used to divide and link NLR and dNLR to OS and optimal threshold were set to NLR>=2.6 and dNLR>=1.7.

Table 2: Univariate Analysis For Overall Survival Using Cox Regression Model

Variable	HR	95%CI	P value
NLR >=2.6 VS <2.6	2.849	0.91 to 8.80	0.073
dNLR >=1.7 vs <1.7	3.360	1.13 to 11.03	0.030
PNI <45 vs >=45	2.754	1.04 to 7.783	0.042

On multivariate analysis, only PNI and d NLR were statistically significant prognostic indicators. NLR did not retain its prognostic value on multivariate analysis.

Table 3: Multivariate Analysis For Overall Survival

Variable	HR	95%CI	P value
ECOG PS 1vs0	1.320	0.605 to 6.012	0.345
T4 vs T1-3	1.823	0.616 to 5.945	0.262
N2b-N3 vs N0-N2a	1.186	0.373 to 3.648	0.792
NLR >=2.6 VS <2.6	2.849	0.9 to 8.80	0.05
dNLR >=1.7 vs <1.7	3.359	1.129 to 11.038	0.03
PNI <45 vs >=45	2.754	1.04 to 7.783	0.042

DISCUSSION

This study highlights the importance of baseline serum inflammatory indices for the prediction of OS in LAHNSCC with inflammation being one of the root causes for its development. Inflammation-based biomarkers reflect the underlying immune status and host inflammatory responses which can be easily calculated with routine blood tests. Integrating PNI into the management of LAHNSCC provides insight on the response to treatment, the need to aggressive management by predicting the overall survival and helps in further management of the nutritional status of these patients. PNI as a prognostic marker has been established in upper gastrointestinal tract cancers and to know the pretreatment nutritional status however, its role as a prognostic marker has not yet been established in LAHNSCC. According to our study PNI is stage independent prognostic marker of overall survival with is value retained in both univariate and multivariate analysis.

CONCLUSION:

Prognostic value of PNI in patients with LAHNSCC can be easily calculated using : albumin and lymphocyte count-readily accessible. PNI is a robust biomarker, with validity and less variability based on external factors, reproducible, inexpensive, providing reliable information on nutrition status. PNI could be useful in our daily clinical practice to improve on prognostic assessment and to guide clinical decision making.

Limitations:

This study is a retrospective analysis with limited sample size in comparison to the population data.

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