Prognostic significance of pre-treatment neutrophil-to-lymphocyte ratio in patients with oropharyngeal cancer treated with radiotherapy

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Purpose

Neutrophil-to-lymphocyte ratio (NLR) is a marker of systemic inflammation and has been demonstrated to be a prognostic marker in several cancers including hypopharyngeal and prostate cancers\textsuperscript{1-2}. The impact of systemic inflammation in patients with oropharyngeal cancer, particularly those with human papillomavirus (HPV)-related disease remain unknown. Here, we evaluated the effect of pre-treatment NLR on outcomes in patients with oropharyngeal cancer.
Methods and materials

A retrospective analysis of patients who completed definitive radiotherapy (RT) for oropharyngeal cancer at The University of Texas MD Anderson Cancer Center and had pre-treatment blood counts taken before RT from 2002 to 2013 were included. Patient, tumor and treatment characteristics, clinical outcomes, and total neutrophil (TNC) and lymphocyte counts (TLC) pre-radiotherapy were recorded. Neutrophil-to-lymphocyte ratio (NLR) prior to radiotherapy and was calculated as TNC/ TLC. Survival rates were estimated using the Kaplan-Meier method and compared with log-rank tests. Univariate and multivariate analyses were conducted with linear and Cox regression methods. NLR was analyzed posteriori and dichotomized on the discovered median (rounded to nearest whole number).
Results

849 patients were eligible for analysis (Figure 1). The median age was 57 years and 87% were males. The primary sites were mainly base of tongue (55%) and tonsil (43%). Six hundred three (71%) had p16/HPV-positive disease and 43% were never smokers. Seven hundred forty-seven (88%) received concurrent chemotherapy. The median pre-treatment NLR was 3.

Patients who had NLR of < 3 had significantly improved overall survival (OS) than those with NLR # 3 (5-year OS 85% vs 74%, p <0.0001) (Figure 2), and the OS difference was significant when stratified according to HPV status (HPV positive - 5-year OS 85% vs 78%, p=0.011; HPV negative - 5-year OS 88% vs 61%, p=0.003) (Figure 3). Freedom from recurrence (FFR), freedom from locoregional failure (FLF), and freedom of distant recurrence (FDR) were better in those with NLR < 3 (5-year FFR 86% vs 77%, p=0.0009; 5-year FLF 92% vs 85%, p=0.003; 5-year FDR 91% vs 86%, p=0.038) (Figure 2). When stratified according to HPV status, those with NLR < 3 had better 5-year FFR than those with higher NLR (HPV positive - 86% vs 80%, p=0.04; HPV negative - 84% vs 69%, p=0.051). No significant differences were detected in terms of FLF and FDR when stratified according to HPV status.

The negative impact of elevated pre-RT NLR on OS (RR = 1.5, 95% CI 1.13 - 2.08, p=0.005), FFR (RR = 1.5, 95% 1.07 - 2.13, p=0.018), and FLF (RR = 1.6, 95% CI 1.04 - 2.46, p=0.032) remained significant on multivariate analysis.
### Image 1: Patient, tumour and treatment characteristics

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Fig. 2: Overall survival, freedom from recurrence, freedom from locoregional failure, and freedom from distant metastasis for the cohort stratified by neutrophil-to-lymphocyte ratio (NLR)

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Fig. 3: Overall survival according to human papilloma virus (HPV) status

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Conclusion

Pre-treatment NLR is an independent prognostic factor in patients with oropharyngeal cancer regardless of HPV status. Patients with lower NLR had more favorable OS and disease control. Further studies evaluating the incorporation of systemic inflammation indicators to further stratify patients for treatment personalisation is required.
Dr. Sweet Ping Ng is a radiation oncologist at the Peter MacCallum Cancer Centre. She recently completed her fellowship at the University of Texas MD Anderson Cancer Center. She is also completing her PhD studies in imaging and blood biomarkers in head and neck cancer in a joint study between MD Anderson Cancer Centre and Peter MacCallum Cancer Centre.
References
