

Investigation of the Relationship Between Delta Inflammatory Markers and Prognosis in Head and Neck Squamous Cell Carcinoma

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Background

- Squamous Cell Carcinoma of the Head and Neck (HNSCC) is the largest and most commonly occurring subset of Head and Neck Cancer (HNC) [1, 2].
- Classic prognostic factors include tumor differentiation, site, size, nodal involvement, metastasis, tumor grading, in addition to age and various comorbidities [3–5].
- Smoking and alcohol usage status have classically been useful in indicating tumor prognosis.
- Lately, there has been increased interest in the use of inflammatory biomarkers as prognostic indicators for HNC. The neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR) have all been shown to be potentially reliable values in the prediction of HNC outcomes [6–11].
- Markers of systemic inflammation have been shown to be associated with tumor stage and progression, likely due to inflammatory reactions throughout tumor development [12].
- Studies have shown the utility of such markers in the prognosis of HNC. In laryngeal cancer patients treated with induction chemotherapy, a high pre-treatment NLR was shown to be associated with poorer survival, independent of the response to chemotherapy [13]. These findings have shown the predictive significance of the monitoring of inflammatory values throughout the course of treatment, pointing to the use of the delta (Δ) ratio (pre-treatment subtracted from post-treatment value) as a potential prognostic indicator. In the past, the delta ratio has been used in cancers of the breast, lung, colon, and brain, showing delta NLR to be an independent prognostic indicator of overall survival [14-17].
- There are fewer studies that focus on the use of such values in patients with HNSCC.
- Therefore, the aim of our study was to evaluate the delta NLR, delta PLR, and delta LMR in patients that have undergone treatment for HNSCC. These values are easily obtainable and affordable, further adding to their potential utility as prognostic factors.

Methods

- This retrospective cohort study included patients with HNC treated at the Northwell Health System from 2010 to 2017.
- 89 patients met criteria and were included in the study.
- Patients with HNSCC had their medical records analyzed for data on both Allscripts and Sunrise.
- Pre-treatment, defined as anywhere within a month before treatment, and post-treatment, defined as within one to three months after treatment, data was obtained. Data collected includes pre- and post-treatment values for neutrophil (count and percentage), lymphocytes (count and percentage), and monocyte (count and percentage), time of last follow-up and cancer recurrences.
- Overall Survival (OS) and Event-Free Survival (EFS) were chosen as endpoints.
- A receiver operating characteristic (ROC) curve was constructed to determine the cutoff for lab values. Then, the area under the ROC curve (AUC) was included to assess the predictability of the model. AUC values range from 0.0 which denotes a nonpredictive model to 1.0 which denotes a predictive model.
- A Kaplan Meier curve was then constructed to estimate survival endpoints. If a lab variable was significant on univariate analysis, it was selected for multivariate analysis. The alpha value was set to 0.05, and all analyses were performed using MedCalc for Windows, version 15.0.

Results

Variable	Univariate analysis		p value	Multivariate analysis		p value
	HR	95% CI		HR	95% CI	
Pre-treatment PLR	2.59	0.87 - 7.72	0.0869			ns
Pre-treatment NLR	0.45	0.17 - 1.24	0.1217			ns
Pre-treatment LMR	3.11	1.23 - 7.90	0.0169*			ns
Post-treatment PLR > 173.8	2.00	0.82 - 4.88	0.1271			ns
Post-treatment NLR > 3.3	N/A					ns
Post-treatment LMR <= 1.71	1.31	0.64 - 2.68	0.4536			ns
Delta PLR	1.00	1.00 - 1.00	0.9975			ns
Delta NLR	0.96	0.91 - 1.02	0.2275			ns
Delta LMR	1.18	0.93 - 1.50	1.688			ns
Delta PLR > 173.8	0.52	0.20 - 1.35	0.1779			ns
Delta NLR < 0.18	3.05	1.28 - 7.28	0.0119*			ns
Delta LMR > -1.48	4.75	1.40 - 16.15	0.0125*	4.17	1.21 - 14.41	0.0241*

Table 1. Univariate and multivariate analysis of event-free survival (EFS), *p values < 0.05 are considered statistically significant

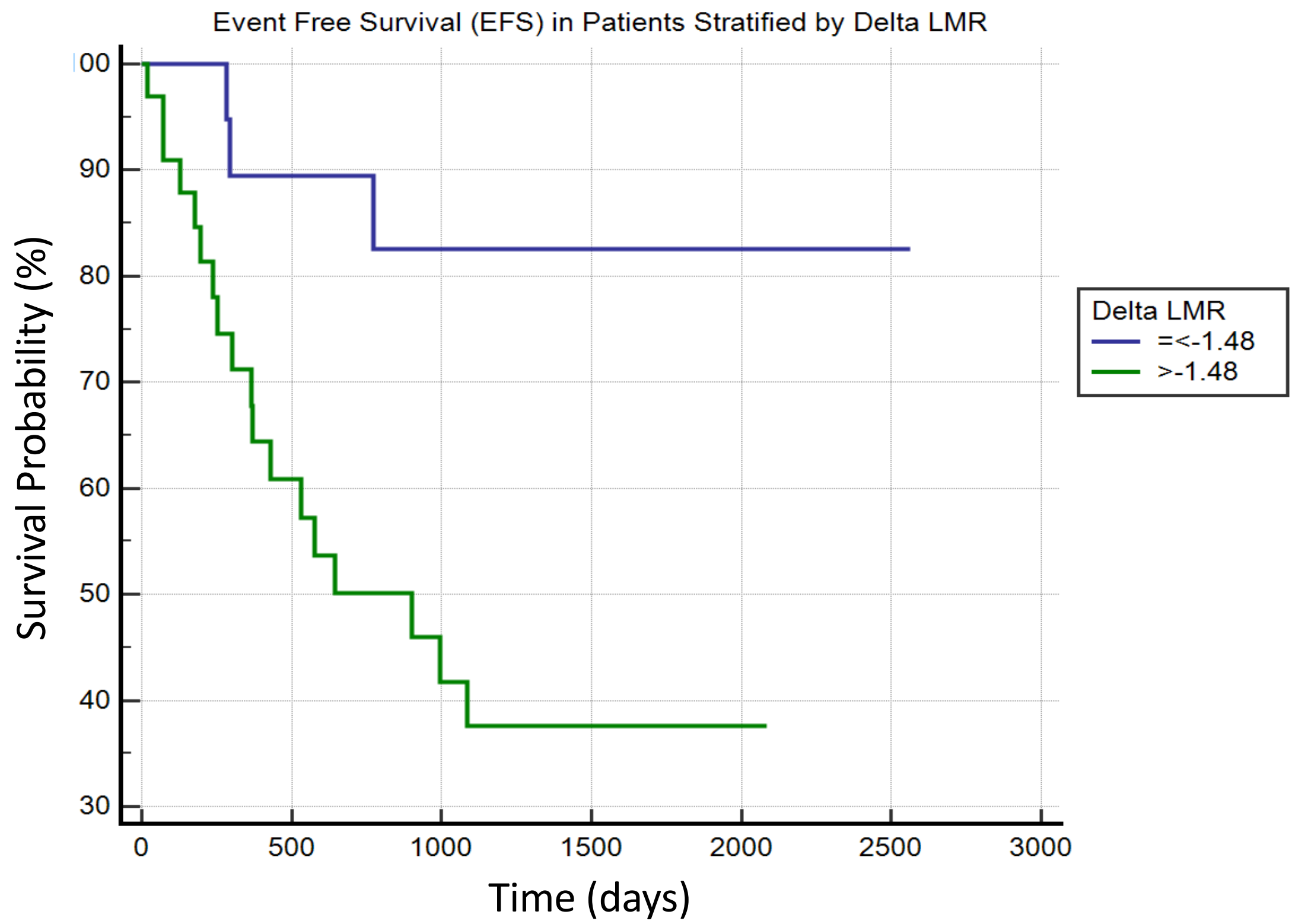


Figure 1. Kaplan Meier curve depicting patient survival over time against Delta LMR

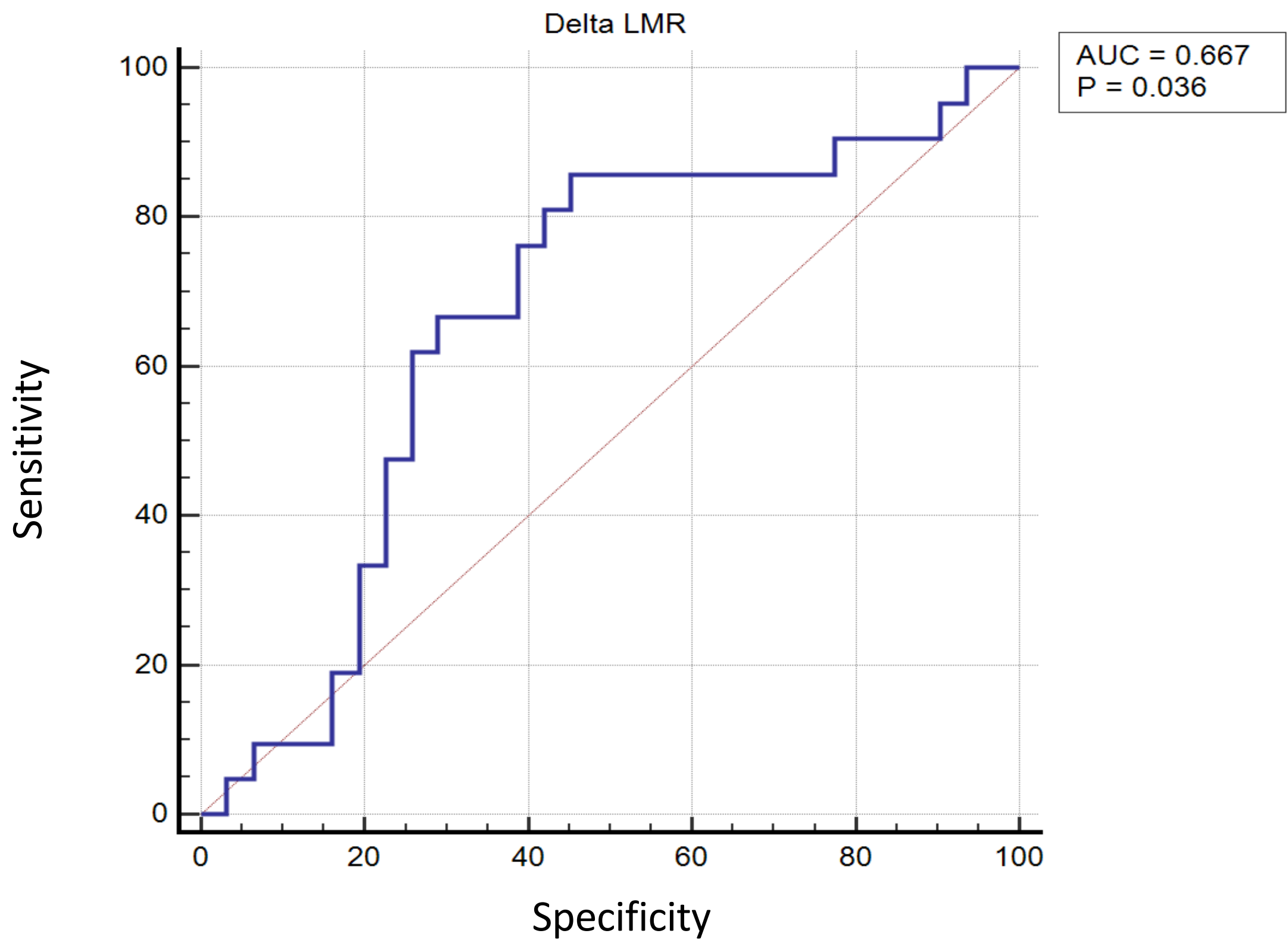


Figure 2. ROC curve depicting sensitivity and specificity of Delta LMR data

Conclusions

- Overall survival (OS) could not be predicted by the NLR, LMR, or PLR as the variables were not statistically significant.
- However, event- free survival (EFS) showed that binary LMR, delta LMR, and delta NLR were statistically significant upon univariate analysis.
- Upon multivariate analysis, delta LMR was the only variable shown to have statistical significance on predicting EFS.
- A higher delta LMR value (> -1.48) was associated with poorer EFS (p=0.0241, HR= 4.17, 95% CI, 1.21 to 14.41).

Resources

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