Role of inflammatory indices in prognosis of carcinoma esophagus

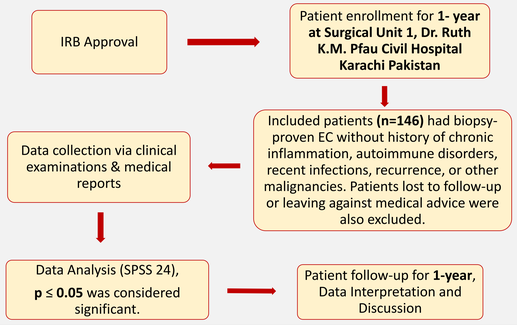
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Introduction

Esophageal carcinoma (EC) represents a significant healthcare challenge characterized by high morbidity and mortality rates. Despite advancements in treatment modalities, prognosis remains poor, largely attributed to late-stage diagnoses and variable treatment responses. Recognizing patient-specific factors influencing prognosis is imperative. Emerging evidence suggests that systemic inflammation plays a pivotal role in cancer initiation and progression. Thus, our study aims to explore the prognostic significance of various inflammatory indices, including Neutrophil to Lymphocyte Ratio **(NLR),** Platelet to Lymphocyte Ratio **(PLR),** Lymphocyte Monocyte Ratio **(LMR),** C-reactive protein **(CRP)** albumin ratio, Platelet to RDW Ratio **(P-RDW),** Systemic Immune Inflammation **(SII)** index, Systemic Inflammation Score **(SIS),** and modified Glasgow Prognostic Score **(mGPS),** in esophageal carcinoma. By elucidating the role of these inflammatory indices, our aim is to explore their potential as prognostic factors in EC.

Methodology



Results

Table 1. Optimal cut-off values of inflammatory markers for overall survival prediction

Inflammatory markers	AUC (95% CI)	Cut-off values	Sensitivity (%)	Specificity (%)
Neutrophil to lymphocyte ratio (NLR)	0.56 (0.46 - 0.65)	3.6	54.0	66.1
Platelet to lymphocyte ratio (PLR)	0.52 (0.41 - 0.60)	198.4	44.8	64.4
Lymphocyte monocyte ratio (LMR)	0.53 (0.43 - 0.63)	4.3	66.7	47.5
C-reactive protein (CRP) albumin ratio	0.57 (0.47 - 0.67)	0.17	81.6	33.9
Platelet to RDW ratio (P-RDW)	0.58 (0.48 - 0.67)	5.2	75.9	42.4
Systemic immune inflammation (SII) index	0.58 (0.48 - 0.67)	858.0	69.0	52.5
Systemic inflammation score (SIS)	0.57 (0.47 - 0.66)	2	62.1	52.5
modified Glasgow prognostic score (mGPS)	0.56 (0.46 - 0.65)	2	39.1	72.9
AUC= Area under the curve, CI= Confidence interval				

Table 2. Clinicopathological characteristics of esophageal cancer patients (n=146)

Characteristics	Total n(%)	Alive (n=59)	Expired (n=87)	p-value*
Neutrophil to lymphocyte ratio (NLR)				
< 3.6	79 (54.1)	39 (66.1)	40 (46.0)	**0.017***
≥ 3.6	67 (45.9)	20 **(33.9)**	47 **(54.0)**	
Platelet to lymphocyte ratio (PLR)				
< 198.4	86 (58.9)	38 (64.4)	48 (55.2)	**0.266***
≥ 198.4	60 (41.1)	21 **(35.6)**	39 **(44.8)**	
Lymphocyte monocyte ratio (LMR)				
< 4.3	89 (61.0)	31 (52.5)	58 (66.7)	0.086
≥ 4.3	57 (39.0)	28 (47.5)	29 (33.3)	
C-reactive protein (CRP) albumin ratio				
< 0.17	36 (24.7)	20 (33.9)	16 (18.4)	**0.033***
≥ 0.17	110 (75.3)	39 **(66.1)**	71 **(81.6)**	
Platelet to RDW ratio (P-RDW)				
< 5.2	46 (31.5)	25 (42.4)	21 (24.1)	**0.020***
≥ 5.2	100 (68.5)	34 **(57.6)**	66 **(75.9)**	
Systemic immune inflammation (SII) index				
< 858.0	58 (39.7)	31 (52.5)	27 (31.0)	**0.009***
≥ 858.0	88 (60.3)	28 **(47.5)**	60 **(69.0)**	
Systemic inflammation score (SIS)				
0	6 (4.1)	4 (6.8)	2 (2.3)	0.158
1	58 (39.7)	27 (45.8)	31 (35.6)	
2	82 (56.2)	28 (47.5)	54 (62.1)	
modified Glasgow prognostic score (mGPS)				
0	37 (25.3)	20 (33.9)	17 (19.5)	0.112
1	59 (40.4)	23 (39.0)	36 (41.4)	
2	50 (34.2)	16 (27.1)	34 (39.1)	
*p-value was calculated by Mann-Whitney test and Chi-square test.				

Table 3. Univariate and multivariate Cox regression analysis for the risk factors associated with mortality among patients with EC

Characteristics	Survival	Univariate		Multivariate	
	(%)	HR (95% CI)	p value	HR (95% CI)	p value
M stage: M0	51.5	Ref		Ref	
M1	14.0	4.35 (2.69-7.02)	**< 0.001***	3.62 (1.99-6.57)	**< 0.001***
SII: < 858.0	53.4	Ref		Ref	
≥ 858.0	31.8	1.71 (1.08-2.71)	**0.022***	1.42 (0.78-2.55)	0.245
Multivariate model adjusted for those variables whose p-value>0.25 in univariate model.					

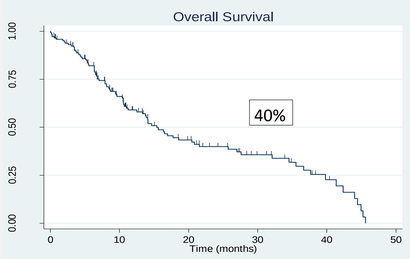


Figure. 1 Kaplan–Meier estimate of overall survival

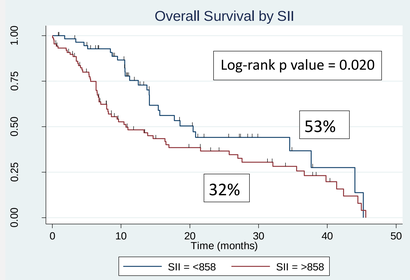


Figure. 2 Kaplan–Meier estimate of overall survival based on systemic immune inflammation index

Discussion

- Systematic review suggests NLR and CAR as potential prognostic markers for EC management **(Ishibashi et al., 2020; Tamagawa et al., 2020).**
- Recent reports proposes PLR as a potential prognostic factor for long-term outcomes in EC receiving curative treatment **(Sasahara et al., 2023; Aoyama et al., 2022).**
- Lower preoperative LMR predicted poorer prognosis in EC, identified by risk plot, AUC, and Kaplan-Meier analysis **(Wang et al., 2023; Shang et al., 2020)**
- RDW-Platelet ratio emerged as a prominent marker for predicting EC prognosis, potentially aiding clinical decision-making **(Hu et al., 2017).**
- SII independently predicts worse survival in surgical ESCC patients **(Li et al., 2022; YAN et al., 2022).** Similarly, elevated SIS also predicts poorer overall survival **(Shi et al., 2023; Aoyama et al., 2022).**
- mGPS has appeared as an independent predictor of prognosis in resectable ESCC patients **(Cui et al., 2022; Fujiwara et al., 2021).**

Conclusion

Our study highlights the potential of inflammatory markers, particularly SII, as key prognostic tools in EC. In resource-limited settings, where circulating DNA analysis is cost-prohibitive, such readily available indicator assessments hold significant promise for improving patient risk stratification and treatment decisions.