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Comparison of two combined models of cellular indices and food allergies in the screening for pediatric eosinophilic esophagitis

Julio César Moreno-Alfonso[1,2]; Rocío del Campo-Pedrosa[3]; Carlos Delgado-Miguel[4,5]; Miren Ibarzabal Arregui[6]; Ada Molina Caballero[1]; Alberto Pérez Martínez[1]; María Concepción Yárnoz Irazábal[2,7]

1: Pediatric Surgery Department. Hospital Universitario de Navarra. Calle Irunlarrea, 3. P.A. 31008. Pamplona, Navarra; Spain.

2: Doctoral School of Health Sciences. Universidad Pública de Navarra (UPNA). Pamplona, Navarra; Spain.

3: Department of Mechanical Engineering, University of La Rioja, P.A. 26006. Logroño, La Rioja; Spain.

4: Pediatric Surgery Department. Fundación Jiménez Díaz University Hospital. Avenida de los Reyes Católicos, 2, P.A 28040. Madrid, Spain.

5: Institute for Health Research IdiPAZ. La Paz University Hospital. 28046 Madrid, Spain

6: Pediatrics Department. Hospital Universitario de Navarra. Calle Irunlarrea, 3. P.A. 31008. Pamplona, Navarra; Spain.

7: General and Digestive Surgery Department. Hospital Universitario de Navarra. Calle Irunlarrea, 3. P.A. 31008. Pamplona, Navarra; Spain.

Corresponding author:

Julio César Moreno-Alfonso

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email: juliomoreno.md@gmail.com

ORCID: https://orcid.org/0000-0002-0414-2888

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Keywords: Eosinophilic esophagitis. Biomarker. Cellular indices. Food allergy. Dysphagia. Screening. Esophagus. Endoscopy. Pediatrics.

Dear Editor,

Eosinophilic esophagitis (EoE) presents with dysphagia and is associated with food allergy (FA) (1,2). Although esophagoscopy remains essential for diagnosis, predictive models based on cellular indices from the hemogram and FA history have been evaluated as screening tools for EoE; however, their theoretical comparison for EoE screening has not been analyzed (3). This study synthesizes the current literature and compares the predictive capacity of two combined models using cellular indices and FA history for EoE screening through a diagnostic study of patients <15 years old undergoing esophagoscopy for suspected EoE at a children's hospital between 2015 and 2022 (IRB approval No. 3318-0000206). Patients with histologically confirmed EoE and those with normal biopsies (NEoE) were included, while children with other esophageal diseases were excluded. Using logistic regression models, we compared FA, the eosinophil-to-lymphocyte ratio (ELR), eosinophil-to-monocyte ratio, and eosinophil-to-neutrophil ratio (ENR), calculated by dividing respective cell counts and transforming them into binary variables based on optimal cutoff values (Youden index). Several combinations of these variables were evaluated using predictive models to assess their screening performance for EoE. Internal validation was performed using bootstrap techniques (n = 1,000). Forty-six esophagoscopies were performed for suspected EoE. Ultimately, 24 patients with EoE and 17 with NEoE were included. The best predictive models included ELR+ENR and FA+ELR+ENR, with AUCs of 0.830 and 0.864, sensitivities of 88% and 79%, false negative rates of 12% and 20%, and

false positive rates of 35% and 23%, respectively (**Figure 1**). Previous studies have reported the role of cellular indices in diagnosing EoE, with the sensitivity, specificity, and PPV of ELR and ENR for diagnosing EoE reported as 54%, 94%, and 92%; and 83%, 64%, and 76%, respectively; being the ELR the marker with the highest diagnostic accuracy, with a cutoff of 0.243 and an OR of 18.9 (4). While these results are similar to ours, that study did not evaluate the indices in a screening context or analyze FA history.

Based on the results of this study, in our view, the most useful model in clinical practice would be the FA+ELR+ENR as it is more specific and fewer unnecessary endoscopies would be performed; with no impact on the prognosis of false negatives as EoE is not a malignant or time-dependent disease. Although our findings are exploratory and limited by sample size and methodological issues related to overfitting of the diagnostic analysis, combining different clinical and analytical variables through predictive models appears to have potential as a useful tool for detecting patients with possible EoE. This could help prioritize gastroenterology referrals and endoscopies in children with a positive model result or support consideration of less invasive evaluations in those with negative results.

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	NEoE (n = 17)	EoE (n = 24)
Age (years)	12 ± 3	11 ± 2.8
Female - Male, n (%)	10 (58.8%) - 7 (41.2%)	9 (37.5%)-15 (62.5%)
Food allergy history	5 (29.4%)	14 (**58.3**%)
	ELR + ENR	**FA + ELR + ENR**
AUC	0.83	0.86
Cut-off point	**ELR**= 0.25 – **ENR**= 0.12	**FA**= Yes or No – **ELR**= 0.25 – **ENR**= 0.12
Sensitivity	88%	79%
Specificity	65%	76%
PPV	78%	83%
NPV	79%	72%
LHR +	2.48 (1.28-4.8)	3.36 (1.39-8.12)
LHR -	0.19 (0.06-0.59)	0.27 (0.12-0.62)
Post-test probability for a positive result	78% (64-87%)	83% (66-92%)
Post-test probability for a negative result	21% (8-45%)	28% (14-47%)
False negative rate	12.5% (3/24)	20% (5/24)
False positive rate	35.2% (6/17)	23% (4/17)
Clinical value in screening	More endoscopies are performed (n = 27), but fewer EoE cases are missed (n = 3).	Fewer endoscopies performed (n = 24), but more patients with EoE missed (n = 5).

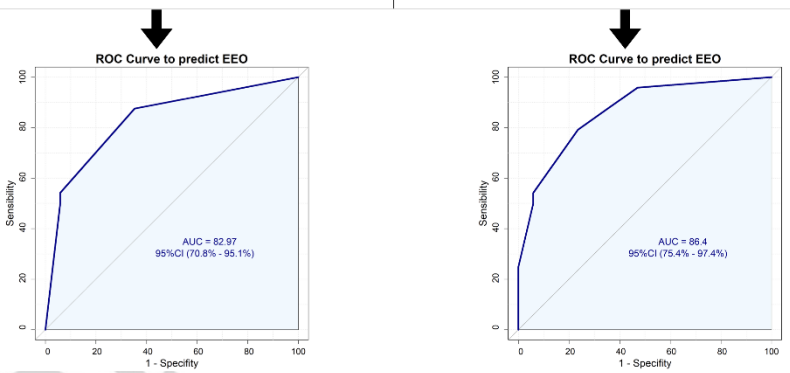

Figure 1. Demographic and analytical data of the studied population and comparison of the combined models in eosinophilic esophagitis.

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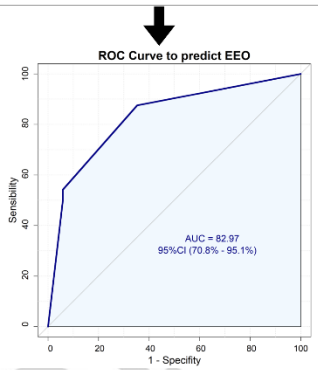

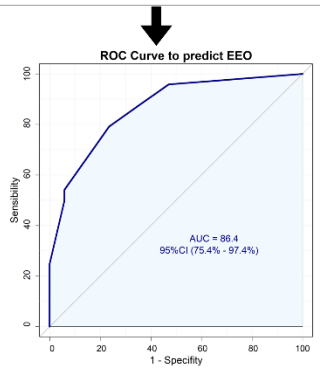

AUC: Area under the receiver operating characteristic curve; **PPV**: Positive predictive value; **NPV**: Negative predictive value; **LHR +**: Positive likelihood ratio; **LHR -**: Negative likelihood ratio.