Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2026;51(1):361-368
DOI: 10.17826/cumj.1848421

RESEARCH

The predictive value of laboratory parameters in diagnosing gastrointestinal malignancy in older adults

Yaşlı bireylerde gastrointestinal malignite tanısında laboratuvar parametrelerinin prediktif değeri

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Abstract

Purpose: This retrospective study aimed to evaluate the predictive value of pre-endoscopic biochemical parameters for detecting malignant lesions in older adults undergoing upper and lower gastrointestinal (GI) endoscopies.

Materials and Methods: We retrospectively analyzed 419 individuals aged 60 and above. Of these, 109 older adult patients who underwent both upper and lower GI endoscopies were included in the study. Patients with a prior history of GI cancer or those who could not complete the procedure due to intolerance were excluded. Patients were categorized based on the presence of benign or malignant lesions.

Results: Malignant lesions were identified in 10.1% of patients (11/109). Statistically significant differences were observed between the benign and malignant groups in terms of hemoglobin (Hb), neutrophil count, mean corpuscular volume (MCV), neutrophil-lymphocyte ratio (NLR), iron (Fe), 25-hydroxyvitamin D [25(OH)D], C-reactive protein (CRP), total protein, albumin (Alb), blood urea nitrogen (BUN), CRP/albumin ratio (CAR), and aspartate aminotransferase (AST). The ROC curve analysis suggests that MCV, NLR, 25(OH)D, Fe, and CAR are valuable indicators for predicting malignant lesions in older adults, with optimal cut-off values of 79.5 fL, 3.28, 12 μg/L, 22 μg/dL, and 5.93, respectively.

Conclusion: Laboratory parameters such as MCV, NLR, 25(OH)D, Fe, and CAR can support risk stratification when interpreted alongside clinical assessment and guideline-based recommendations.

Keywords:. Gastrointestinal malignancy; gastrointestinal endoscopy; predictive; older adult; laboratory parameters

Öz

Amaç: Bu çalışmada, üst ve alt gastrointestinal (GI) endoskopi uygulanan yaşlı bireylerde malign lezyonların saptanmasında endoskopi öncesi biyokimyasal parametrelerin prediktif değerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmada 60 yaş ve üzeri toplam 419 birey retrospektif olarak analiz edilmiştir. Bunlar arasından hem üst hem de alt GI endoskopi yapılan 109 yaşlı hasta çalışmaya dahil edilmiştir. Daha önce GI kanser öyküsü olan veya intolerans nedeniyle işlemi tamamlayamayan hastalar çalışma dışı bırakılmıştır. Hastalar benign veya malign lezyon varlığına göre gruplandırılmıştır.

Bulgular: Hastaların %10,1'inde (11/109) malign lezyon saptanmıştır. Benign ve malign gruplar arasında hemoglobin (Hb), nötrofil sayısı, ortalama eritrosit hacmi (MCV), nötrofil-lenfosit oranı (NLR), demir (Fe), 25-hidroksivitamin D [25(OH)D], C-reaktif protein (CRP), total protein, albümin (Alb), kan üre nitrojeni (BUN), CRP/albümin oranı (CAR) ve aspartat aminotransferaz (AST) açısından istatistiksel olarak anlamlı farklılıklar bulunmuştur. ROC eğrisi analizi, MCV, NLR, 25(OH)D, Fe ve CAR'ın yaşlı bireylerde malign lezyonların öngörülmesinde anlamlı göstergeler olduğunu ortaya koymuştur. Bu parametreler için optimal kesim değerleri sırasıyla 79,5 fL, 3,28, 12 μg/L, 22 μg/dL ve 5,93 olarak belirlenmiştir.

Sonuç: MCV, NLR, 25(OH)D, Fe ve CAR gibi laboratuvar parametreleri, klinik değerlendirme ve kılavuz temelli öneriler ile birlikte yorumlandığında risk sınıflandırmasını destekleyebilir.

Anahtar kelimeler: Gastrointestinal malignite; gastrointestinal endoskopi; prediktif; yaşlı birey; laboratuvar parametreleri.

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Received: 27.12.2025 Accepted: 09.03.2026

INTRODUCTION

Gastrointestinal (GI) cancers account for over a quarter of all cancer diagnoses and are responsible for one-third of cancer-related deaths worldwide[1]. Colorectal cancer is one of the most commonly detected cancers in older adults in our country, ranking third in men and second in women aged 70 years and above[2]. Additionally, along with colorectal cancer, gastric cancer is another of the most common causes of cancer-related death[1].

Early diagnosis and treatment are critical to improving survival and longevity in GI cancers, as in most cancers[3]. Therefore, early diagnosis and treatment through screening tests to detect and remove precancerous lesions or to discover cancer at a curable stage is essential in managing GI cancers. Guidelines recommend colonoscopy screening for asymptomatic individuals, with recent recommendations suggesting that screening start at age 45 rather than 50[4]. However, there is no universally recommended screening program for gastric cancer except in populations with a high incidence[5,6]. Nevertheless, combined upper and lower endoscopy may be preferred in geriatric patients who require screening due to advanced age.

While colonoscopy and upper endoscopy are standard screening and diagnostic tools for detecting gastrointestinal malignancies, these procedures can be invasive and sometimes burdensome for older or frail patients. Therefore, it is clinically important to identify individuals at higher risk of malignancy and who may benefit most from endoscopic evaluation. Iron deficiency anemia (IDA) can be a marker of gastrointestinal malignancy in older adults[7]. Consequently, when anemia is detected in this population, upper and lower gastrointestinal endoscopes are performed to identify potential malignancies or bleeding lesions[8]. Laboratory parameters, including serum ferritin, transferrin saturation (TSAT), sedimentation rate, albumin (Alb), and lactate dehydrogenase (LDH), may also be associated with gastrointestinal malignancies[9,10]. Given the well-established link between inflammation and cancer, recent studies have examined associations between certain cancers and systemic inflammation markers, such as the C-reactive protein (CRP)/Albumin ratio (CAR) and the neutrophil-to-lymphocyte ratio (NLR)[11,12]. Pre-investigation biochemical parameters, including markers of anemia, malnutrition, and systemic inflammation, could help stratify patients by malignancy risk and assist clinicians in deciding who may benefit most from invasive endoscopic procedures. However, research explicitly focusing on older adult patients remains limited.

Unlike previous studies that have primarily focused on prognostic biomarkers after a confirmed cancer diagnosis and have included heterogeneous adult populations, the present study specifically targets older adults. It evaluates pre-investigation biochemical parameters as potential predictors of premalignant and malignant gastrointestinal lesions before diagnostic endoscopic procedures. This study aims to evaluate whether the pre-investigation biochemical parameters can predict the presence of premalignant/malignant disease in patients undergoing upper and lower gastrointestinal endoscopy. Identifying a potential biochemical predictor of malignancy in older adults could offer valuable insights for clinicians and enhance early detection and intervention strategies.

MATERIALS AND METHODS

Sample

This retrospective study included 419 patients aged 60 years and older who presented to our geriatric outpatient clinic with iron-deficiency anemia (IDA) or persistent gastrointestinal symptoms. These patients, for whom upper and lower gastrointestinal endoscopies were planned, were seen between September 2016 and January 2021. A total of 109 older adult patients who underwent both upper and lower gastrointestinal endoscopies were included. Patients with a history of gastrointestinal malignancy (n = 14) or those who could not tolerate the procedure and withdrew (n = 18) were excluded from the study. All endoscopic procedures were performed at Gazi University Hospital by experienced gastroenterologists, with support from trained nurses, in accordance with institutional protocols.

Procedure

This study was approved by the Gazi University Ethics Committee (05.10.2020/663) and conducted according to the Declaration of Helsinki. Demographic data, comorbidities, indications for endoscopy, and presenting complaints were collected retrospectively from outpatient clinic records. Blood

samples were obtained from patients after their outpatient clinic evaluations, when indicated by routine laboratory testing. Samples were collected under fasting conditions when possible, processed immediately in the hospital laboratory, and analyzed on the same day. All results were recorded in the hospital information system on the day of collection.

Pre-endoscopy routine laboratory tests were collected, including complete blood count; iron (Fe, 33-193 μg/dL); total iron-binding capacity (TIBC, 135-392 μg/dL); serum ferritin (13–150 ng/mL); transferrin saturation (TS, 15-45 %); vitamin B12 (197-771 ng/L); folate (3.89-26.8 μg/L); liver enzymes (AST and ALT 0-35, U/L); lactate dehydrogenase (LDH, 135–214 U/L); electrolytes; total protein (TP, 6–8 g/dL); albumin (Alb, 3.5–5 g/dL); renal function markers (BUN 7–20 and creatinine, 0.6–1.3 mg/dL); 25-hydroxyvitamin D [25(OH)D, 20–50 μg/L]; and inflammatory markers, including erythrocyte sedimentation rate (ESR, 0–20 mm/h) and C-reactive protein (CRP, 0–5 mg/L). The recorded values were the most recent laboratory assessments conducted before the endoscopic procedures. Hemoglobin concentrations under 13 g/dL in men and 12 g/dL in women were used to define anemia[13]. The neutrophil-lymphocyte ratio (NLR) was calculated by dividing the neutrophil count (*10^9/L) by the lymphocyte count (*10^9/L). The C-reactive protein/albumin ratio (CAR) was calculated by dividing CRP (mg/L) by albumin (g/dL). Laboratory tests were performed according to standard hospital protocols using automated analyzers.

Gastrointestinal endoscopies

Experienced gastroenterologists performed all upper and lower gastrointestinal endoscopic procedures. Before the procedure, patients received full information and provided informed consent. During the procedures, vital signs, including ECG, blood pressure, and oxygen saturation, were continuously monitored. A Fujinon endoscopy system was used. When indicated, sedation was administered under the supervision of an anesthesiologist. All findings were documented in the hospital information system.

Endoscopic imaging and, when available, biopsy results were reviewed for all patients. In upper gastrointestinal endoscopy, gastritis, ulcers, and Helicobacter pylori were considered benign, while intestinal metaplasia was considered premalignant. Colonoscopy findings categorized hemorrhoids, diverticula, tubular adenoma, tubulovillous adenoma, villous adenoma, and angiodysplasia as benign conditions. Malignancy was confirmed in cases with cancerous lesions.

For the primary analyses, patients with premalignant lesions, including intestinal metaplasia, were combined with those having malignant lesions and analyzed as a single premalignant/malignant group.

Statistical analysis

All statistical analyses were performed using SPSS software (version 24.0; IBM Corp., Armonk, NY, USA). Descriptive features were summarized as numbers and percentages for categorical variables. The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test and by visual inspection of histograms. Data showing a normal distribution were reported as mean ± standard deviation, whereas non-normally distributed variables were stated as median values with minimum and maximum ranges. Group comparisons for normally distributed continuous variables were performed using the Student's t-test, while the Mann–Whitney U test was applied for variables with non-normal distributions. Categorical variables were evaluated using the chi-square test. This approach ensured that the statistical tests were appropriately selected for each variable's type and distribution. Descriptive features were summarized as numbers and percentages for categorical variables and as mean ± standard deviation or median (minimum–maximum) for continuous variables, as appropriate. Statistical significance was defined as a p-value below 0.05.

Receiver operating characteristic curves were conducted using MedCalc software (version 22.023) to evaluate the discriminative performance of biochemical markers in identifying malignant lesions. For each parameter, we calculated the optimal cutoff values and the corresponding sensitivity, specificity, and predictive values (positive and negative). The area under the curve (AUC) was assessed with a type I error rate set at 5%, and p-values less than 0.05 were considered statistically significant. A post hoc power analysis using G*Power, based on the total sample size and the observed number of malignant cases (n = 11), indicated a statistical power of approximately 53% for detecting associations between laboratory parameters and malignant lesions. While this reflects

limited power due to the small number of events, the study provides valuable exploratory insights into potential predictors in older adults.

RESULTS

The mean age was 77.7 ± 6.5 years, and 58.7% of the participants were female. Baseline characteristics and laboratory results, stratified by benign versus malignant lesion status, are exhibited in Table 1.

Malignant lesions were identified in 10.1% of the study population (11/109). Significant differences among the groups were observed in Hb, MCV, NLR, Fe, 25(OH)D, CRP, TP, Alb, BUN, CAR, and AST levels.

Table 1. Demographics and baseline characteristics of the patients

Parameters	All participants (n=109)	Malignant (n=11)	No Malignant (n=98)	*P* value
Age, year, (SD)	77.9±6.6	79.6±7	77.7±6.5	0.356
Gender, female, n (%)	64 (58.7%)	5 (45.5%)	59 (60.2%)	0.346
DM, n (%)	41 (36%)	5 (45.5%)	36 (36.7%)	0.706
HTN, n (%)	60 (55%)	6 (54.5%)	54 (55.1%)	0.728
CKD, n (%)	8 (7.3%)	0	8 (8.2%)	0.303
CHF, n (%)	7 (7.5%)	1 (9.1%)	6 (6.1%)	0.754
Dementia, n(%)	7 (6.4%)	0	7 (7.1%)	0.369
Anemia, n (%)	73 (67%)	8 (72.7%)	65 (66.3%)	0.093
Weight loss, n (%)	52 (47.7%)	6 (54.5%)	46 (46.9%)	0.725
Hb (g/dL)	10.7 (6.3-18.4)	8.8 (6.3-18.4)	11 (7.1-15.7)	**0.050**
WBC, *10^9/L	7.06 (3.03-26.6)	8,17 (5.11-16.4)	7.01 (3.03-26.6)	0.075
Neut, *10^9/L	4.7 (1.9-13.1)	5.27 (2.91-12.2)	4.5 (1.9-13.1)	**0.030**
Lymph, *10^9/L	1.52 (0.58-3.23)	1.4 (0.8-3.2)	1.53 (0.58-3.23)	0.903
NLR	3.13 (1.14-14.56)	3.81 (1.72-8.75)	3 (1.14-14.56)	**0.044**
MCV (fL)	84.3 (26.5-129)	74 (26.5-96.1)	85.5 (31.6-129)	**0.009**
Fe (µg/dL)	41 (3-182)	21 (3-93)	41 (11.7-182)	**0.028**
TIBC (µg/dL)	246 (81-509)	247 (116-509)	245.5 (81-494)	0.794
Ferritin (ng/mL)	51 (5-1083)	26 (5-458)	53.5 (5-1083)	0.288
TSAT (%)	16.3 (0.91-224.7)	8.2 (0.91-41.4)	16.7 (3.7-224.7)	0.278
Vitamin B12 (ng/L)	341 (50-2804)	158 (92-894)	345.5 (50-2804)	0.141
Folic acid (µg/L)	8 (2.9-24)	7.4 (4.7-13)	8 (2.9-24)	0.866
25(OH)D (µg/L)	22 (5.4-63)	10 (8.3-51)	23.5 (5.4-63)	**0.011**
ESR (mm/h)	42 (1-140)	48.5 (13-106)	42 (1-140)	0.254
CRP (mg/L)	8 (1-341)	42 (3.1-206)	6.9 (1-341)	**0.020**
TP (g/dL)	7 (3.8-8.4)	6.2 (3.8-7.1)	7 (5-8.4)	**0.006**
Alb (g/dL)	3.8 (2-5.1)	3.4 (2-4.5)	3.8 (2.3-5.1)	**0.031**
BUN (mg/dL)	23 (7-73)	30 (16-44)	22 (7-73)	**0.008**
Cr (mg/dL)	0.95 (0.43-7)	1.15 (0.6-3.34)	0.92 (0.43-7)	0.364
CAR	2.25 (0.22-92.2)	12.35 (0.91-55.7)	1.85 (0.22-92.2)	**0.015**
ALT (U/L)	15 (1-68)	15 (4-26)	15 (1-68)	0.251
AST (U/L)	20 (7-85)	13 (8-35)	21 (7-85)	**0.011**
LDH (U/L)	209 (70-646)	219 (134-326)	203 (70-646)	0.535

Data were reported as numbers and percentages for categorical variables, mean ± SD* for normally distributed continuous variables, and median (min-max) for non-normally distributed continuous variables. *SD: standard deviation; DM: Diabetes Mellitus, HTN: Hypertension, CKD: Chronic Kidney Disease, CHF: Congestive heart failure, Hb: Hemoglobin, NLR: neutrophil/lymphocyte ratio, MCV: Mean Corpuscular Volume, Fe: Iron, TIBC: Total Iron Binding Capacity, TSAT: Transferrin Saturation, 25(OH)D: 25-hydroxyvitamin D, ESR: Erythrocyte sedimentation rate, CRP: C-Reactive protein, TP: Total Protein, Alb: Albumin, BUN: Blood urea nitrogen, Cr: Creatinine, CAR: C-reactive protein/albumin ratio, AST: Aspartate Aminotransferase, ALT: Alanine Transaminase, LDH: Lactate dehydrogenase

Table 2 presents the endoscopic findings of the study participants. Gastric cancer was identified in 4 patients (3.7%), while intestinal metaplasia was detected in 21 patients (19.2%). Colonic polyps, including hyperplastic polyps, tubular, tubulovillous, and villous adenomas, were found in 31 patients (28.4%), and colorectal cancer was identified in 7 patients (6.4%). Malignancy was detected in 8 out of

the 73 patients with anemia (10.9%). Of these, three patients had gastric malignancies, and 5 had colorectal malignancies. Among these patients, 88.9% were anemic at the time of malignancy diagnosis.

Table 2. Endoscopic data of the patients

Upper Gastrointestinal Endoscopies	**All participants (n=109)**
Chronic Gastitis, n (%)	69 (63.3%)
Peptic Ulcer, n (%)	7 (6.4%)
Helicobacter Pylori, n (%)	11 (12.4%)
Intestinal Metaplasia, n (%)	21 (19.2%)
Gastric Cancer, n (%)	4 (3.7%)
Lower Gastrointestinal Endoscopies	**All participants (n=109)**
Colonic Polyps, n (%)	31 (28.4%)
Angiodysplasia, n (%)	3 (2.8%)
Hemorrhoid, n (%)	20 (18.3%)
Colitis, n (%)	5 (4.6%)
Colorectal Cancer, n (%)	7 (6.4%)

Data were presented as numbers and percentages for categorical variables.

Table 3. ROC curve of laboratory parameters in the diagnosis of malignant lesions in older adults

Parameters	**Cut-off**	**AUC**	**SE**	**P**	**95%CI**	**Sensitivity**	**Specificity**	**+PV**	**-PV**
MCV (fL)	≤79.5	0.740	0.102	**0.018**	0.647-0.820	72.73	78.35	27.6	96.2
NLR	>3.28	0.686	0.080	**0.021**	0.589-0.772	81.82	59.79	18.8	96.7
25(OH)D (µg/L)	≤12	0.759	0.107	**0.015**	0.661-0.840	77.78	79.55	28.0	97.2
CAR	>5.93	0.723	0.067	**0.001**	0.629-0.806	72.73	67.71	20.5	95.6
Fe (µg/dL)	≤22	0.702	0.105	**0.029**	0.606-0.787	63.64	88.54	38.9	95.5

MCV: Mean Corpuscular Volume, NLR: neutrophil/lymphocyte ratio, 25(OH)D: 25-hydroxyvitamin D, CAR: C-reactive protein/albumin ratio, Fe: Iron, AUC: area under the curve, SE: Standard Error, CI: Confidence interval, PV: Predictive Value

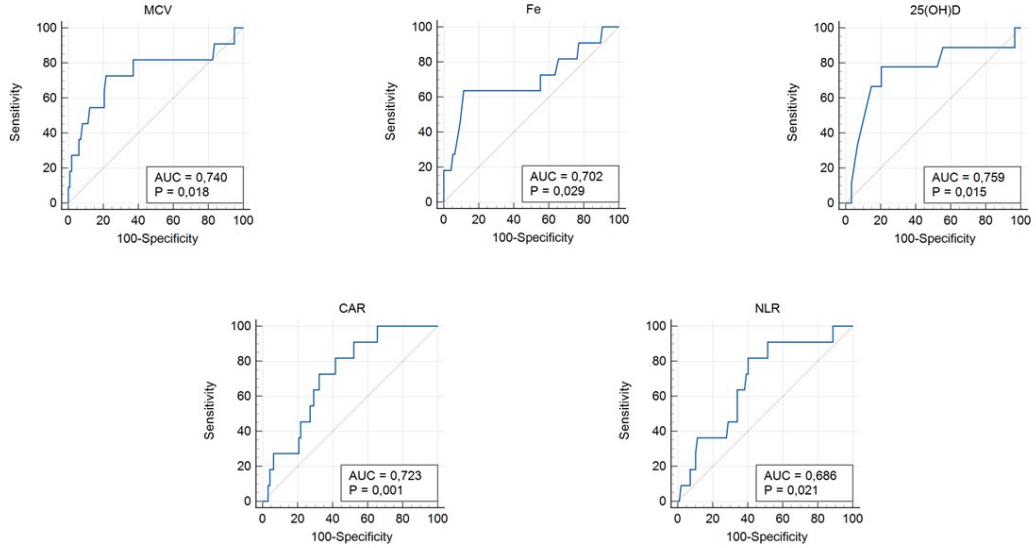

Figure 1. ROC curves of MCV, NLR, 25(OH)D, CAR, Fe level for diagnosing malignancy in all patients with 95% confidence intervals. AUC is the area under the curve.

Figure 1 displays the ROC curves for MCV, NLR, 25(OH)D, CAR, and Fe in diagnosing gastrointestinal malignant lesions. Table 3 presents the values and predictive metrics for the parameters used to identify malignant lesions among older adults, with optimal cutoffs of ≤79.5 fL for MCV, >3.28 for NLR, <12 μg/L for 25(OH)D, >5.93 for CAR, and ≤22 μg/L for Fe.

Notably, the negative predictive values of MCV, NLR, 25(OH)D, Fe, and CAR were relatively high, indicating that patients with values outside the predictive cut-offs are unlikely to have malignant lesions.

DISCUSSION

The present study identified significant differences between the groups concerning NLR, MCV, 25(OH)D, Fe, and C-reactive protein/albumin ratio (CAR) levels before diagnosis. Notably, ROC curve analysis indicates that NLR and CAR are valuable predictors of malignant lesions in older adults, with optimal cutoff values of 3.28 and 5.93, respectively. To our knowledge, this is the first study to investigate pre-diagnosis laboratory parameters for predicting malignant gastrointestinal lesions, specifically in older adults.

In recent years, systemic inflammatory response markers such as NLR, CRP, and CAR have been shown to predict prognosis in patients diagnosed with cancer[9,14,15]. Additionally, studies have demonstrated that the Glasgow Prognostic Score (derived from serum CRP and Alb levels) is a reliable prognostic factor in patients with non-small cell lung cancer as well as gastric and colorectal cancers[16,17]. While previous studies have primarily focused on the prognostic role of these markers after cancer diagnosis, our findings suggest that NLR and CAR may also have predictive value in identifying malignant gastrointestinal lesions before diagnosis in older adults undergoing endoscopic evaluation. This distinction is clinically important, as it supports the potential utility of inflammation-based biomarkers not only in outcome stratification but also in pre-diagnostic risk assessment.

A study of 222 adult patients with unintentional weight loss, 22 of whom were diagnosed with gastrointestinal cancer, demonstrated that ferritin above 100 mcg/L could rule out colon cancer but not gastric or rectal cancer[18]. In our study, ferritin was >100 mcg/L in 18% of patients with malignancies, including cases of colon and gastric cancer. However, as ferritin is an acute-phase reactant that can rise with inflammation and its prevalence increases with age, relying on elevated ferritin to exclude cancer may lead to missed diagnoses[19]. Some findings also suggest that ferritin levels in many elderly individuals with iron deficiency anemia may be normal or elevated[20]. Therefore, we recommend using other laboratory parameters, such as Fe, alongside ferritin to provide a more reliable prediction of gastrointestinal cancer, particularly in older adults. We hypothesize that Fe may be a more appropriate biomarker than ferritin in this population.

A recent large cohort study examining patients with stage II/III colorectal cancer reported that both low and high preoperative MCV values were independently associated with recurrence-free survival, further supporting the clinical significance of MCV as a potential predictive marker in gastrointestinal malignancies[21]. Consistent with these findings, our study's ROC curve indicates that MCV may be a helpful indicator for predicting gastrointestinal malignancies in older adults, with a cut-off value of ≤79.5 fL.

Growing evidence has related 25-hydroxyvitamin D [25(OH)D] to cancer risk, clinical outcomes, and survival across multiple malignancies[22,23]. In a large randomized, placebo-controlled trial of 25,871 adults aged 50 years and older in the United States, participants received vitamin D_3 (cholecalciferol, 2000 IU/day) with or without omega-3 fatty acids (1 g/day) to assess the role of these agents in cancer and cardiovascular disease prevention[24]. Over a median follow-up of 5.3 years, invasive cancer developed in 1,617 individuals, with no statistically significant difference between the vitamin D and placebo groups[24]. Despite these findings, 25(OH)D is thought to contribute to gastrointestinal carcinogenesis by activating the vitamin D receptor (VDR) and regulating key cellular pathways, including differentiation, proliferation, invasion, metastasis, angiogenesis, and apoptosis[25]. In our study, significantly lower 25(OH)D levels in patients with malignancy further support these findings.

Several limitations of this study should be acknowledged. First, because of the retrospective design, comprehensive adjustment for potential confounding factors that may influence inflammatory markers in older adults such as chronic inflammatory diseases, acute infections, and nutritional status was not possible. Second, the relatively small number of

patients with malignant lesions may confine the generalizability of the findings. Finally, because this was a single-center study, the results may not fully reflect those of broader populations. Therefore, the outcomes should be interpreted with prospective, multicenter studies with larger sample sizes and comprehensive clinical data are needed to validate our results.

In conclusion, this study suggests that laboratory parameters, including MCV, NLR, 25(OH)D, Fe, and CAR, are associated with premalignant and malignant gastrointestinal lesions in older adults. These findings suggest that routinely available, minimally invasive biomarkers may contribute to risk stratification before endoscopic evaluation. In frail older patients or those with significant comorbidities, where invasive procedures carry increased risk, such markers may help clinicians prioritize high-risk individuals while potentially reducing unnecessary procedures in lower-risk patients. Future prospective multicenter studies with larger sample sizes are required to validate the proposed cutoff values and to establish standardized predictive models that integrate biochemical markers with clinical variables such as frailty status, comorbidity burden, and nutritional parameters. The development of such comprehensive risk algorithms may improve individualized decision-making and optimize endoscopic referral strategies in geriatric populations.

Author Contributions: Concept/Design : FYB, HDV; Data acquisition: MY, BT; Data analysis and interpretation: FYB, MY, BT, ÖG, BG; Drafting manuscript: FYB; Critical revision of manuscript: ÖG, BG, HDV; Final approval and accountability: FYB, MY, BT, ÖG, BG, HDV; Technical or material support: -; Supervision: HDV; Securing funding (if available): n/a.
Ethical Approval: Ethical approval and consent to participate: This study was approved by the Gazi University Ethics Committee (05.10.2020/663)..
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support
Acknowledgement: Use of AI Statement: Artificial intelligence–based language assistance was used only for language editing and grammar improvement during the manuscript revision process.

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