The Predictive Value of Periostin to Diagnose Crohn's Disease

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ABSTRACT

Background: *There is still no sensitive and specific biomarker that can be used in the diagnosis and follow-up of Crohn's disease, so we aimed to assess the diagnostic accuracy of serum periostin levels in Crohn's disease.*

Methods: *The study included 40 Crohn's disease patients aged 18-70 years and considered in remission (Crohn's Disease Activity Index < 150) at admission. Forty healthy volunteers were included in the study as the control group. Crohn's patients were divided into 3 main groups as <4 years, 4-8 years, and >8 years according to the follow-up period (in the group <4 years, it was subdivided into <2 and 2-4 years). Serum periostin levels were studied by enzyme-linked immunosorbent assay.*

Results: *Forty Crohn's disease patients and 40 control participants were included in the study. In the Crohn's disease group, serum periostin level was 36.55 ng/mL, while it was 21 ng/mL in the control group, P < .001. Periostin levels in the Crohn's disease group were higher in the groups with disease duration <4 years, 4-8 years, and >8 years compared to the control group (P < .001, P < .001, P = .038, respectively). For the diagnosis of Crohn's disease independent of disease duration, the cut-off periostin level was determined as 27.8 ng/mL, while the sensitivity and specificity for this value were 72.5% and 77.5%, respectively.*

Conclusion: *Serum periostin levels of the patients followed up with the diagnosis of Crohn's disease in remission were found to be significantly higher than the healthy individuals, and cut-off values of serum periostin were obtained to both diagnose Crohn's disease and predict the course of the disease.*

Keywords: *Periostin, Crohn's disease, serum biomarkers, Crohn's disease diagnosis, inflammatory bowel disease*

INTRODUCTION

Crohn's disease (CD) is a disease with chronic inflammation and fibrosis and elevates various serum inflammation markers. Therefore, serum periostin levels may be increased in CD patients as well. Additionally, there is still no sensitive and specific biomarker that can be used in the diagnosis and follow-up of CD, so serum periostin levels may also have clinical significance in this regard.

Crohn's disease is a chronic inflammatory disease that can affect any part of the gastrointestinal tract, with flares and remissions. Although the terminal ileum is the most frequently involved site in CD, less frequent involvement of the colon, perianal region, the oral, and gastroduodenal region is observed. Chronic inflammation is typically segmental, asymmetric, and transmural. Early diagnosis and treatment prevent the development of advanced damage in the involved intestinal segment.[1] Crohn's disease is seen in 3 different clinical subtypes: inflammatory, obstructive (stenosing), and penetrating.[2] Although 70% of the patients are considered inflammatory, 15% are penetrating, and 15% are obstructive at the time of diagnosis, a large part of the patients transforms into the obstructive and/or penetrating type over time.[3]

The disease activity in CD is evaluated using a combination of symptoms, clinical examination, laboratory tests, radiological, endoscopic, and histopathological findings. In CD, the determination of disease activity is of great importance in the prognosis and treatment decisions. Many clinical and endoscopic indices have been defined to determine disease activity. The most widely accepted clinical index worldwide is the Crohn's Disease Activity Index (CDAI).[4] In CD, disease severity is determined by the CDAI score. Accordingly, a CDAI score below 150 is considered a disease in asymptomatic remission, whereas a score above 450 is considered a severe-fulminant disease.[2]

Periostin is a multi-functional extracellular matrix protein, so named because its expression was first demonstrated in the periosteum of adult mice. Periostin is mainly secreted by osteoblasts. Periostin consists of 811 amino acids, is a member of the fascicle protein family, and

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weighs 90 kDa.[5] The amino-terminal region regulates cell functions by binding to integrin in the cytoplasmic membrane. The cysteine-rich 75-amino acid module of this region binds to type I collagen and fibronectin and contributes to the organization of the architectural structure of the extracellular matrix.[6] Periostin has regulatory functions on extracellular matrix remodeling, muscle repair, repair of vascular damage, bone and tooth formation and maintenance, heart development, and tissue healing after acute myocardial infarction.[7] Studies have shown low levels of periostin expression in most normal adult tissues. However, the level of periostin is markedly increased in patients with tumors.[5]

Studies have been published showing that periostin can be used as a biomarker in Th2-dependent inflammation. It has also been shown that periostin can regulate collagen deposition in chronic inflammation, when secreted from fibroblasts, by promoting the fibrosis process and altering the mechanical properties of connective tissue.[8] It has been shown that serum periostin levels increase in various diseases with chronic inflammation and fibrosis.[9] Studies are showing that periostin plays a role in Th2-mediated inflammation. In studies conducted in the airway epithelium of patients with asthma compared to healthy controls, it was shown that the periostin gene expression of the patient group increased more.[10] Izuhara et al[11] reported that interleukin (IL)-4 and IL-13 induce the expression of periostin and that periostin is highly expressed in chronic inflammatory diseases (asthma, atopic dermatitis, eosinophilic chronic sinusitis, chronic rhinosinusitis) and allergic conjunctivitis; they also reported that periostin plays an important role in the pathogenesis of these diseases.

Crohn's disease also progresses with chronic inflammation and fibrosis and elevates various serum inflammation markers. Therefore, it is possible that patients with CD have also increased serum periostin levels. Additionally, there is still no sensitive and specific biomarker that can be used in the diagnosis and follow-up of Crohn's disease, and therefore, serum periostin levels may have clinical significance in this regard. Here, we assessed the diagnostic accuracy of serum periostin levels in the differential diagnosis of CD.

Main Points

- *Serum periostin levels of the patients followed up with the diagnosis of Crohn's disease (CD) in remission were found to be significantly higher than the healthy individuals, and cut-off values of serum periostin were obtained to both diagnose CD and predict the course of the disease.*
- *Diagnostic cut-off serum periostin level has the highest sensitivity and specificity, especially in newly diagnosed CD cases; therefore, its contribution is more valuable in terms of diagnosing CD patients earlier and noncomplicated.*
- *The most crucial and powerful aspect of this study is that it provides very accurate and reliable results, as well as the absence of any similar study in the literature.*

MATERIALS AND METHODS

Patients who applied to the Gastroenterology Outpatient Clinics between May 2020 and January 2021 were included. The study included 40 CD patients aged 18-70 years, diagnosed clinically, endoscopically, radiologically, and histopathologically, and considered in remission (CDAI < 150) at admission. Whether the disease is in remission or not was determined not only by the CDAI score but also by the current clinical, laboratory, endoscopic, and radiological evaluations of the patients. Forty healthy volunteers aged between 18 and 70 years, who applied for other reasons, and did not have a known chronic disease were included in the study as the control group. Individuals under the age of 18 or over the age of 70, pregnant women, patients, and volunteers with advanced co-morbid diseases such as diabetes mellitus, cirrhosis, heart failure, asthma, chronic obstructive pulmonary disease, and malignancy were excluded from the study.

Approval for the study was obtained from the decision of the Ethics Committee of Necmettin Erbakan University Meram School of Medicine, dated May 22, 2020, and numbered 2020/2503. Written informed consent was obtained from all patients included in the study.

All database and information of the patients in the registry system were reviewed retrospectively. Age (years), gender, disease duration (years), CD involvement and location, presence of fistula and/or abscess, anti-tumor necrosis factor (anti-TNF) treatment status, steroid dependency, steroid refractoriness, history of surgical treatment for CD, presence of ankylosing spondylitis was recorded at the time of diagnosis. The total follow-up duration of the patients was recorded; it was accepted as the time (days) between the time of diagnosis and the last admission. Crohn's patients were divided into 3 main groups as <4 years, 4-8 years, and more than 8 years according to the follow-up period (in the group <4 years, it was subdivided into <2 and 2–4 years). The steroid dependency or excess was defined as the inability to discontinue steroids below the equivalent of prednisolone 10 mg/day or budesonide 3 mg/day within 3 months of starting steroids, recurrence

or need for steroids within 3 months of discontinuation, or the need for more than one treatment within 1 year. The steroid refractoriness was defined as failure to respond to oral prednisolone equivalent of 0.75–1 mg/kg body weight within 4 weeks or intravenous steroid therapy for at least 1 week after excluding infectious complications (associated with coexisting CMV, C. difficile).

Blood samples were centrifuged and stored at –80°C until the study day; complete blood count and serum periostin levels were studied in CD patients and the control group. Serum periostin levels were studied by enzyme-linked immunosorbent assay (ELISA) (Human Periostin, POSTN ELISA Kit, E3226Hu, Shanghai Korain Biotech Co., Ltd., China).

Statistical Analysis

Statistical analysis was performed with software (Statistical Package for the Social Sciences version 25 and MedCalc version 15.8). The conformity of the variables to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Descriptive analysis was given using median and interquartile ranges for non-normally distributed variables. Since it was determined that periostin levels were not normally distributed, this parameter was compared between the groups using the Mann–Whitney *U* test. Correlation coefficients and statistical significance were calculated with Spearman's test for the relationships between variables, at least one of which was not normally distributed or ordinal.

Diagnostic decision-making properties of serum periostin values in predicting CD were analyzed by receiver operating characteristic curve analysis. In the presence of significant breakpoints, the sensitivity, specificity, positive predictive, and negative predictive values of these limits were calculated. In the evaluation of the area under the curve, the cases where the type 1 error level was below 5% were interpreted as the diagnostic value of the test was statistically significant.

In the study, the type 1 error level was used as 5% for statistical significance in all tests, and cases, where the *P* value was below .05, were considered statistically significant results.

RESULTS

Of the 40 CD patients included in the study, 15 (37.5%) were female and 25 (62.5%) were male. In the control group, 17 (42.5%) were female and 23 (57.5%) were male. While the mean age of the CD group was 37.5, the mean age of the control group was 31.5. There was no difference between the CD group and the control groups in terms of gender and age ($P = .11$ and $P = .65$, respectively). Crohn's patients were grouped according to follow-up: <2 years, 12 (30%) patients; 2-4 years, 6 (15%) patients; <4-year group, 18 (45%); 4-8-year group, 13 (32.5%) patients; >8-year group, 9 (22.5%) patients.

In terms of involvement, 19 (47.5%) of the patients had ileal, 18 (45%) had ileocolonic, and 3 (7.5%) had colonic involvement. Additionally, 11 (27.5%) patients had fistula, 4 (10%) had a perianal abscess, and 18 (45%) patients were treated with anti-TNF. Of the patients, 4 (10%) were steroid-dependent and 9 (22.5%) were steroid refractory. In the CD group, 9 patients (22.5%) had a history of CD-related surgery and 5 patients (12.5%) had ankylosing spondylitis (Table 1).

In the CD group, serum periostin level was 36.55 ng/mL, while it was 21 ng/mL in the control group; $P < .001$ (Table 2). Periostin levels in the CD group were higher in the groups with disease duration <4 years, 4-8 years, and more than 8 years compared to the control group ($P < .001$, $P < .001$, and $P = .038$, respectively). There was no significant difference between these groups in terms of periostin levels.

Periostin levels in the CD group were higher in the ileal and ileocolonic involvement group than in the control group and were similar to the control group in those with colon involvement ($P < .001$, $P < .001$, and $P = .53$, respectively). Periostin levels were higher in the CD group than the control group in both patients with and without fistula ($P < .001$ and $P = .001$, respectively). When CD patients with and without fistula were compared among themselves, no significant difference was found in periostin levels ($P = .83$). In the CD group, periostin levels were higher in those without a perianal abscess than the control group and similar to the control group in those with perianal abscess ($P < .001$ and $P = .1$, respectively). When CD patients with and without perianal abscess were compared, no significant difference was found in periostin levels ($P = .49$).

Periostin levels were higher in CD patients with and without anti-TNF therapy than in the control group ($P = .001$ and $P < .001$, respectively). When CD patients with and without fistula were compared, no significant difference was found in terms of periostin levels ($P = .09$).

Table 1. Crohn's Disease Patients' Clinical Characteristics

n = 40 (100%)	
Disease period	
<4 years	18 (45%)
4-8 years	13 (32.5%)
>8 years	9 (22.5%)
Involvement	
Ileal	19 (47.5%)
Ileocolonic	18 (45%)
Colonic	3 (7.5%)
Fistula	
Yes	11 (27.5%)
No	29 (72.5%)
Perianal abscess	
Yes	4 (10%)
No	36 (90%)
Anti-TNF	
Yes	18 (45%)
No	22 (55%)
Steroid dependency	
Yes	4 (10%)
No	36 (90%)
Steroid refractoriness	
Yes	9 (22.5%)
No	31 (77.5%)
Surgical treatment	
Yes	9 (22.5%)
No	31 (77.5%)
Ankylosing spondylitis	
Yes	5 (12.5%)
No	35 (87.5%)

In CD patients, both steroid-dependent and steroid-independent patients had higher periostin levels than the control group ($P = .002$ and $P < .001$, respectively). When steroid-dependent and steroid-refractory CD patients were compared, no significant difference was found between them in terms of periostin levels ($P = .09$).

Periostin levels were higher in CD patients, both in those with and without steroid-refractory than in the control group ($P = .001$ and $P < .001$, respectively). When CD patients with and without steroid-refractory were compared, no significant difference was found in terms of periostin levels ($P = .85$).

Table 2. Demographical and Laboratory Features of CD and Control Groups

	CD (n = 40)	Control (n = 40)	*P*
Age (years)	37.5 (25.5-51.5)	31.5 (26-39.5)	.11
Gender (F/M)	15/25	17/23	.65
Periostin	36.55 (18.7-132.3)	21 (4.2-54.2)	<.001
Hemoglobin	13.45 (9.3-18.3)	14.8 (8.9-18)	.017
Leucocyte	7.49 ± 2.51	8.03 ± 1.86	.1
Neutrophil	4.92 ± 2.23	4.46 ± 1.68	.4
Lymphocyte	1.79 (0.86-5.96)	2.51 (1.03-6.3)	<.001
Platelet	298.875 ± 87.743	278.950 ± 78.889	.31
NLR	2.94 ± 1.47	1.92 ± 1.56	<.001

CD, Crohn's disease; NLR, neutrophil-to-lymphocyte ratio.

In CD patients, periostin levels were higher than the control group in both surgical and non-surgical patients ($P = .001$ and $P < .001$, respectively). When CD patients who underwent and did not undergo surgical treatment were compared, no significant difference was found in terms of periostin levels ($P = .26$).

In CD patients, both with and without ankylosing spondylitis, periostin levels were higher than the control group ($P = .013$ and $P < .001$, respectively). When CD patients with and without ankylosing spondylitis were compared, no significant difference was found in terms of periostin levels ($P = .98$).

Hemoglobin and lymphocyte levels were lower and the neutrophil-lymphocyte ratio was higher in CD patients than in the control group ($P = .017$, $P < .001$, and $P < .001$, respectively). There was no difference in leukocyte, neutrophil, and thrombocyte count between the CD group and control groups; $P = .1$, $P = .4$, and $P = .31$, respectively (Table 2).

In Spearman's correlation analysis, a positive and moderate correlation was found between CD presence and serum periostin levels; $r = 0.545$, $P < .001$. A negative and moderate correlation was found between the duration of CD and serum periostin level; $r = -0.544$, $P < .001$ (Figure 1).

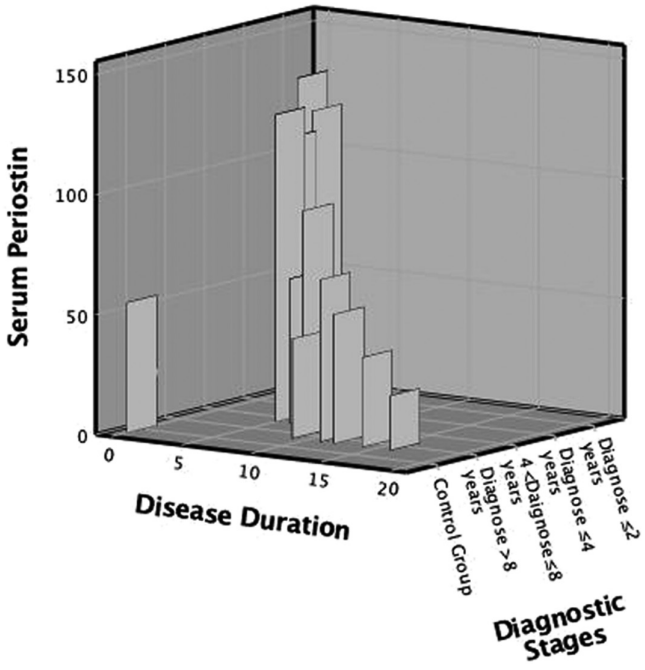

Figure 1. Interactions of periostin, Crohn's disease, and diagnostic stages in a 3D bar graph.

When the relationship between disease duration and serum periostin levels in CD patients was examined, serum periostin levels were found to be significantly higher in all patient groups than in the control group; very early diagnosis ≤2 years, early diagnosis ≤4 years, intermediate diagnosis <4 to ≤8 years, and late diagnosis >8 years (Figure 1, Table 3).

Receiver Operating Characteristic Curve Analyses

For the diagnosis of CD independent of disease duration, the cut-off periostin level was determined as 27.8 ng/mL, while the sensitivity and specificity for this value were 72.5% and 77.5%, respectively (Figure 2 and Table 4).

Table 3. Comparison of Serum Periostin Levels with Mann–Whitney *U* Test According to Diagnosis Period Between Crohn's Patients and Control Group

	Periostin	*P*
Control	21 (16.3-27.8)	<.001
Very early CD	47.95 (32.05-114.1)	<.001
Early CD	35.3 (22.8-36.1)	.043
Intermediate CD	36.6 (29.7-76.6)	<.001
Late CD	24.8 (22.6-41.4)	.038

CD, Crohn's disease; very early, diagnosis ≤2 years; early, diagnosis ≤4 years; intermediate, <4 to ≤8 years; late, diagnosis >8 years.

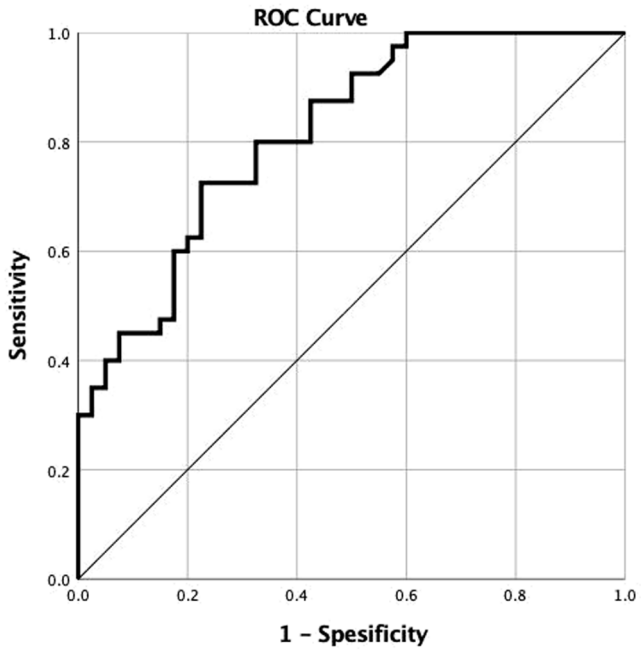

Figure 2. ROC curve for the diagnosis of Crohn's disease when serum periostin level >27.8 ng/dL; AUC = 0.815, 95% CI: 0.724-0.905, *P* < .001. ROC, receiver operating characteristic curve; AUC, area under the curve.

For the diagnosis of very early (≤2 years) CD, the periostin cut-off level was 27.8 ng/mL; the sensitivity and specificity were 83.3% and 77.5%, respectively (Figure 3 and Table 4).

Cut-off periostin level was 27.8 ng/mL for early (≤4 years) CD diagnosis; the sensitivity was 77.8% and the specificity was 77.5% (Figure 4 and Table 4).

For the diagnosis of intermediate (<4 to ≤8 years) CD, the cut-off periostin level was 24.4 ng/mL; the sensitivity was 100% and the specificity was 67.5% (Figure 5 and Table 4).

Cut-off periostin level was determined as 18.9 ng/mL for late (≥8 years) CD diagnosis; the sensitivity was 100% and the specificity was 42.5% (Figure 6 and Table 4).

DISCUSSION

In this study, higher serum periostin levels were detected in CD patients compared to the control group. While a negative correlation was found between the duration of CD and serum periostin level, the cut-off periostin level was found to be 27.8 ng/mL to diagnose CD, regardless

Table 4. ROC Analysis of the Relationship Between the Diagnosis of Crohn's Disease, Disease Duration, and Serum Periostin Levels

	Cut-off Periostin	Sensitivity	Specificity	PPV	NPV
CD diagnosis	>27.8	72.5	77.5	76.3	73.8
Very early CD	>27.8	83.3	77.5	52.6	93.9
Early CD	>27.8	77.8	77.5	60.9	88.6
Intermediate CD	>24.4	100	67.5	50	100
Late CD	>18.9	100	42.5	28.1	100

CD, Crohn's disease; very early, diagnosis ≤2 years; early, diagnosis ≤4 years; intermediate, <4 to ≤8 years; late, diagnosis >8 years; PPV, positive predictive value; NPV, negative predictive value.

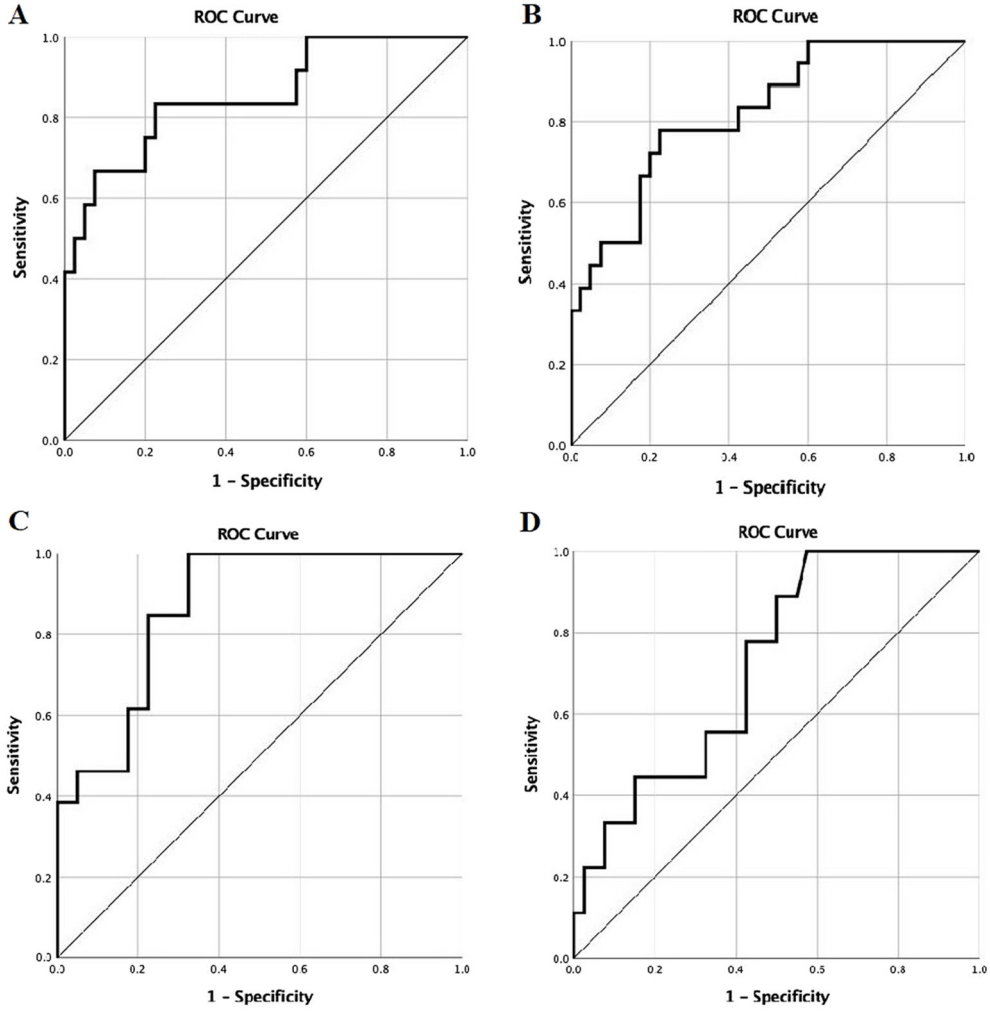

Figure 3. ROC curves for the diagnosis of Crohn's disease obtained with periostin cut-off values according to disease years. (A) ROC curve for the diagnosis of very early (≤2 years) Crohn's disease when serum periostin level >27.8 ng/dL; AUC = 0.854, 95% CI: 0.724-0.984, *P* < .001. (B) ROC curve for the diagnosis of early (≤4 years) Crohn's disease when serum periostin level >27.8 ng/dL; AUC = 0.822, 95% CI: 0.708-0.936, *P* < .001. (C) ROC curve for the diagnosis of intermediate (<4 to ≤8 years) Crohn's disease when serum periostin level >24.4 ng/dL; AUC = 0.867, 95% CI: 0.770-0.964, *P* < .001. (D) ROC curve for the diagnosis of late (>8 years) Crohn's disease when serum periostin level >18.9 ng/dL; AUC=0.724, 95% CI: 0.560-0.887, *P* = .038. ROC, receiver operating characteristic curve; AUC, area under the curve.

of the disease duration. Additionally, periostin levels were found to be higher in the ileal and ileocolonic involvement than in colonic involvement in CD patients. Periostin level was found to be lower in those with perianal abscesses than in those without. It was determined that the duration of disease, the presence of fistula, anti-TNF therapy, steroid dependency, steroid refractoriness, surgical treatment, and the presence of ankylosing spondylitis did not make a statistically significant difference to periostin levels in CD patients.

There are a limited number of studies investigating periostin levels in inflammatory bowel diseases. Koh et al[12] reported that periostin was expressed at a higher rate in the colonic mucosa of patients with ulcerative colitis than in the control group. There is no study yet about the relationship between CD and periostin. Therefore, the evaluation of serum periostin levels in terms of detection, treatment, and follow-up of CD patients is critical in terms of providing new information to the literature.

In epidemiological studies, the frequency of CD was found to be slightly higher in women than in men.[13,14] In our study, the female–male ratio in CD was found to be 0.6. This low rate was considered due to the inclusion of only a limited number of patients in remission in the study.

In CD, the most common sites of involvement are the terminal ileum and the right colon. Approximately 50% of the patients have the intestine and colon involvement (ileocolonic), 30% have only intestine involvement (ileal), and 20% have only colon involvement. In our study, ileal involvement was 47.5%, ileocolonic involvement was 45%, and colonic involvement was 7.5%. Additionally, patients with dominant intestinal involvement have higher periostin levels than those with isolated colonic involvement, which is consistent with the clinical characteristics and course of CD.

There are studies on the effect of age on periostin levels. Walsh et al[15] reported that the level of periostin was higher in the childhood age group than in adults. It has been stated that periostin levels can be determined to be high since bone development and regeneration is rapid in childhood. In our study, there was no increase in serum periostin levels associated with primary bone metabolism since only adult CD patients' serum periostin levels were studied.

In some studies evaluating serum periostin levels, it was found to be higher in women, while in some studies there was no difference between men and women.[16,17] In our study, no difference was found between serum periostin levels in the CD group according to gender. Similarly, variables such as the presence of complications (such as fistula, perianal abscess, need for surgical treatment), steroid refractoriness, steroid dependency, and anti-TNF therapies have no significant effect on serum periostin levels in CD patients; the presence of CD alone is sufficient for a significantly higher serum periostin level.

O'Dwyer et al[18] in their study investigating the role of periostin in chronic respiratory diseases such as asthma and idiopathic pulmonary fibrosis determined that periostin, which is highly expressed in the lungs of patients with asthma, contributes to mucus secretion, airway fibrosis, and remodeling and can be considered a biomarker of Th2-mediated inflammation. Periostin is highly expressed in the lungs of patients with idiopathic pulmonary fibrosis, periostin levels can predict clinical progression in this disease, and periostin contributes to lung fibrosis by increasing myofibroblast differentiation and type 1 collagen production.

In Huang et al's[7] animal model study, it was determined that periostin could be a new mediator in acute and chronic liver fibrosis induced by carbon tetrachloride and bile duct ligation, and high periostin levels were associated with the expression of transforming growth factor (TGF)-β1 and TGF-β2. It is thought that periostin, which is overexpressed in acute and chronic liver inflammation, increases collagen I and fibronectin levels and accelerates fibrillogenesis and leads to liver fibrosis.

Mael-Ainin et al's[8] experimental animal model showed that periostin mediates renal inflammation and fibrosis in response to TGF-β, but those lacking the periostin gene developed less interstitial fibrosis and inflammation.

As expected, since CD is progressing with intense inflammation and fibrosis, serum periostin level was also found to be high in our study. The fact that serum periostin level was determined at the highest level (47.95; 32.05-114.1) in patients we defined as very early disease (≤2 years) shows that periostin is more accurate in determining especially newly diagnosed CD patients. In fact, the highest diagnostic sensitivity (83.3%) and specificity (77.5%) of the serum periostin levels were similarly obtained in the very early disease group.

In the exacerbation period of CD, the presence of both clinical and laboratory findings is more evident than in the patients in the remission period. Therefore, it is more difficult to detect CD in patients who were admitted in

the remission phase. In our study, although all Crohn's patients were in remission, serum periostin levels were still found to be significantly higher in terms of detecting CD.

In cases with CD pre-diagnosis and difficulty in differential diagnosis, serum periostin evaluation and detection of elevated periostin levels can be used as a highly sensitive and highly specific method for definitive diagnosis. In our study, we found that as the duration of the disease increased, the serum periostin level was higher than the control group but decreased compared to the early stages of the disease. Therefore, when serum periostin levels of newly diagnosed CD patients are compared with the cut-off periostin levels determined in our study, it will also contribute to the prediction of the course of the disease.

The inclusion of a limited number of patients only in remission is a relatively limiting factor. Since the number of patients in remission is higher than the number of active patients, the periostin level was evaluated only in patients in remission, since working simultaneously with active and remission patients would affect serum periostin levels heterogeneously and cause inconsistent results between the groups. Obtaining a diagnostic cut-off value for serum periostin levels even in patients in remission and even being able to associate it with the disease process is the most important outcome of this study.

In conclusion, the serum periostin levels of the patients followed up with the diagnosis of CD in remission were found to be significantly higher than the healthy individuals, and cut-off values of serum periostin were obtained to both diagnose CD and predict the course of the disease. Diagnostic cut-off serum periostin level has the highest sensitivity and specificity, especially in newly diagnosed CD cases; therefore, its contribution is more valuable in terms of diagnosing CD patients earlier and noncomplicated. To evaluate the diagnosis, follow-up, and response to treatment of CD, it would be appropriate to examine the serum periostin level with studies involving more patients both in remission and in the active period.

Ethics Committee Approval: The study was approved by the medical ethics committee of Necmettin Erbakan University Meram School of Medicine (No: 2019/2012).

Informed Consent: Informed consent was obtained from all individual participants included in the study. Consent for publication was obtained for every individual person's data included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards

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Conflict of Interest: The authors declare that they have no conflict of interest.

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