

Systemic Inflammatory and Immunonutritional Indices for Discriminating Ruptured From Non-Ruptured Endometriomas at Presentation: A Retrospective Study

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Abstract

Objective: Ruptured endometrioma is an uncommon but clinically important emergency that often mimics other causes of acute abdomen, making timely diagnosis challenging. This study aimed to assess whether readily available systemic inflammatory and immunonutritional indices measured at presentation could discriminate ruptured from non-ruptured endometriomas during initial clinical assessment, and secondarily to compare unilateral and bilateral endometriomas. **Methods:** This retrospective cohort study included 77 women diagnosed with endometrioma between January 2020 and May 2026. Demographic characteristics, laboratory findings, surgical data, and inflammatory indices were analyzed, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), aggregate index of systemic inflammation (AISI), derived NLR (dNLR), neutrophil percentage-to-albumin ratio (NPAR), albumin-to-C-reactive protein ratio (ACR), prognostic nutritional index (PNI), hemoglobin-albumin-lymphocyte-platelet score (HALP), and C-reactive protein-to-lymphocyte ratio (CLR). All indices were calculated from raw laboratory values using a single, explicit unit convention. Patients were compared according to rupture status and, secondarily, disease laterality. Univariate logistic regression analyses were performed to evaluate unadjusted associations with rupture status, whereas receiver operating characteristic (ROC) curve analysis was used to assess discriminatory performance. P values were adjusted for multiple comparisons using the Benjamini-Hochberg false discovery rate (FDR) procedure within each table-specific analysis family. **Results:** Among the included patients, 57 (74.0%) had unilateral and 20 (26.0%) had bilateral endometriomas. Seven patients (9.1%) experienced spontaneous rupture. No significant differences were observed between unilateral and bilateral disease regarding demographic features, cyst size, hematological parameters, or inflammatory/immunonutritional indices; for the 11 index comparisons, none was significant after FDR correction. In contrast, patients with ruptured endometriomas had significantly higher SII, SIRI, NLR, NPAR, AISI, and dNLR values than those without rupture, and all six indices remained significant after FDR correction (adjusted $p \leq 0.004$). SIRI (AUC 0.865), AISI (AUC 0.861), and dNLR (AUC 0.861) demonstrated the highest discriminatory performance for identifying rupture status at presentation, whereas indices incorporating nutritional or non-neutrophil-dominant components, including PNI (AUC 0.643) and ACR (AUC 0.616), showed limited discriminatory ability that did not survive correction for multiple comparisons. **Conclusions:** Routine blood count-derived inflammatory indices, particularly SIRI, AISI, and dNLR, may serve as simple, inexpensive, and widely available adjunctive biomarkers for identifying rupture status at presentation among women with endometrioma. Although these associations remained significant after correction for multiple comparisons, the findings require external validation in larger prospective cohorts and should be regarded as hypothesis-generating given the exploratory design and small rupture group. These indices should not be interpreted as tools for future rupture prediction or as stand-alone diagnostic tests.

Keywords: Endometrioma; Endometrioma rupture; Systemic inflammatory index; SIRI; AISI; dNLR; Neutrophil-to-lymphocyte ratio; Immunonutritional index; Acute abdomen

1. Introduction

Endometriosis is a chronic, estrogen-dependent, inflammatory disease affecting approximately 5-10% of women of reproductive age, characterized by the presence of endometrial glands and stroma outside the uterine cavity¹. Experimental endometriosis models also support the inflammatory nature of the disease and have been used to evaluate anti-inflammatory and antioxidant therapeutic approaches². The disease can present with symptoms that severely impair quality of life, such as chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility^{1,3}. Endometrioma is a cystic ovarian manifestation of endometriosis that may involve one or both ovaries and contains dark-colored viscous fluid resulting from recurrent cyclic bleeding of ectopic endometrial implants within ovarian tissue³.

Endometriomas can present with unilateral or bilateral ovarian involvement. However, there are a limited number of comparative studies in the literature regarding the extent to which unilateral and bilateral endometrioma cases differ in terms of demographic characteristics, cyst size, surgical approach, and systemic inflammatory response.

One of the rare but clinically significant acute complications of endometrioma is cyst rupture. Spontaneous endometrioma rupture is reported in approximately 2-3% of cases and can lead to sudden onset of severe pelvic pain, peritoneal irritation, and rarely hemoperitoneum or sepsis as a result of leakage of cyst contents into the peritoneal cavity^{4,5}. The overlap of clinical findings with other acute abdominal causes such as ovarian torsion, ruptured ectopic pregnancy, or acute appendicitis makes the preoperative diagnosis of ruptured endometrioma difficult and can lead to diagnostic delays^{4,5}. Larger cyst diameter and lower body mass index have been reported to be associated with spontaneous rupture⁶. Because clinical and imaging findings may overlap with other causes of acute abdomen, simple and readily available biomarkers may be useful as adjunctive tools for discriminating ruptured from non-ruptured endometriomas at presentation and supporting timely clinical decision-making.

Chronic inflammation plays a central role in the pathophysiology of endometriosis. Ectopic endometrial implants and increased macrophage activation in peritoneal fluid have been characterized by elevated levels of pro-inflammatory cytokines such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-17 (IL-17), and tumor necrosis factor-alpha (TNF- α)^{1,3}. This local inflammatory process can also have a systemic repercussion, leading to measurable changes in circulating hematological parameters.

In recent years, the use of systemic inflammatory and immunonutritional indices derived from routine complete blood count parameters as inexpensive, rapid, and easily accessible adjunctive diagnostic or prognostic tools in various diseases has become increasingly common. In endometriosis-related studies, markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) have been reported to contribute to differentiating endometrioma from other benign ovarian cysts, with SIRI showing high diagnostic performance in this differentiation^{7,8}. Similar complete blood count-derived inflammatory parameters have also been evaluated as clinically accessible markers in obstetric populations, supporting the broader clinical interest in hematological indices⁹. In addition, SII has been associated with the presence of endometriosis¹⁰, and NLR may reflect systemic inflammation associated with endometrioma and infertility¹¹. Newer indices such as the neutrophil percentage-to-albumin ratio (NPAR), aggregate index of systemic inflammation (AISI), derived NLR (dNLR), albumin-to-C-reactive protein ratio (ACR), prognostic nutritional index (PNI), hemoglobin-albumin-lymphocyte-platelet score (HALP), and C-reactive protein-to-lymphocyte ratio (CLR) reflect both inflammatory and nutritional status and have been investigated in various clinical conditions¹².

Additional comparative data on endometrioma and benign ovarian cysts further support the interest in serum inflammatory markers in this clinical field¹³.

However, the role of these systemic inflammatory and immunonutritional indices in discriminating ruptured from non-ruptured endometriomas at presentation, and, secondarily, in revealing differences between unilateral and bilateral endometrioma cases, has not yet been sufficiently investigated. Early and non-invasive identification of rupture status at presentation may be clinically useful for prioritizing appropriate diagnostic and surgical decision-making, while avoiding any interpretation as prediction of future rupture.

In this study, the diagnostic value of systemic inflammatory and immunonutritional indices such as NLR, PLR, SII, SIRI, NPAR, AISI, dNLR, ACR, PNI, HALP, and CLR for discriminating ruptured from non-ruptured endometriomas at presentation was evaluated as the primary aim; the demographic, clinical, and surgical characteristics of patients diagnosed with unilateral and bilateral endometrioma were compared as a secondary aim. The study aimed to determine whether these readily available and low-cost markers could serve as adjunctive clinical decision-support tools during the initial assessment of patients with suspected rupture.

2. Materials and Methods

2.1. Study Design and Patient Population

This study was designed as a retrospective observational cohort study. Study data were obtained from the electronic medical records of patients who presented between January 2020 and May 2026 and were diagnosed with endometrioma by ultrasonography and/or surgical-histopathological assessment. The study was evaluated by the Acibadem Mehmet Ali Aydınlar University Medical Research Evaluation Board (ATADEK) and found to be ethically appropriate (Decision No: 2026-10/422, Date: 11.06.2026). The study was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for additional written informed consent was waived by the ethics committee because of the retrospective design and anonymized nature of the data.

To protect patient privacy, all data were anonymized and analyzed. Inclusion criteria for the study were: being 18 years of age or older, having a diagnosis of endometrioma, and having complete access to necessary clinical, laboratory, and imaging data. Patients with incomplete clinical or laboratory data, cases diagnosed with malignancy, patients with active infection, individuals with hematological disease, patients receiving treatment for chronic inflammatory or autoimmune diseases, and cases with concomitant ovarian masses were excluded from the study. Patients included in the study were primarily divided into two groups based on the presence or absence of endometrioma rupture; they were also secondarily grouped according to unilateral versus bilateral disease. Rupture was defined as intraoperative evidence of cyst wall disruption with leakage of endometriotic cyst content into the pelvic/peritoneal cavity, accompanied by compatible acute clinical presentation and/or imaging findings. Intraoperative assessment was used as the reference standard for rupture classification. A total of 77 patients followed up with a diagnosis of endometrioma were included in the study based on inclusion and exclusion criteria. Of these patients, 57 (74.0%) had unilateral endometrioma and 20 (26.0%) had bilateral endometrioma. Furthermore, endometrioma rupture was detected in 7 patients (9.1%) in the study population, while rupture was not observed in 70 patients (90.9%).

2.2. Data Collection

Patient data including age, gravida, parity, body mass index, symptoms, ultrasonographic findings, endometrioma localization, cyst size, surgical treatment information, and histopathological results were obtained from patient files. For laboratory evaluation,

the first available complete blood count and biochemical parameters obtained at presentation before any surgical intervention were used. White blood cell count, neutrophil count, lymphocyte count, monocyte count, platelet count, hemoglobin, C-reactive protein (CRP), and albumin levels were recorded.

2.3. Inflammatory and Immunonutritional Indices

The following inflammatory and immunonutritional indices were calculated from routine laboratory parameters. For every index, neutrophil, lymphocyte, monocyte, and total leukocyte counts were expressed in $\times 10^9/L$ and platelet counts in $\times 10^9/L$; albumin and CRP were expressed in g/L and mg/L, respectively. Hemoglobin values recorded in g/dL were converted to g/L for HALP calculation. Neutrophil percentage used for NPAR was expressed as percentage (%).

Neutrophil/Lymphocyte Ratio (NLR) = Neutrophil / Lymphocyte

Platelet/Lymphocyte Ratio (PLR) = Platelet / Lymphocyte

Derived Neutrophil/Lymphocyte Ratio (dNLR) = Neutrophil / (Leukocyte – Neutrophil)

Systemic immune-inflammation index (SII) = Neutrophil $\times$ Platelet / Lymphocyte

Systemic inflammation response index (SIRI) = Neutrophil $\times$ Monocyte / Lymphocyte

Aggregate index of systemic inflammation (AISI) = Neutrophil $\times$ Monocyte $\times$ Platelet / Lymphocyte

Neutrophil percentage-to-albumin ratio (NPAR) = Neutrophil percentage / Albumin

Albumin-to-C-reactive protein ratio (ACR) = Albumin / CRP

Prognostic Nutritional Index (PNI) = Albumin (g/L) + 5 $\times$ Lymphocyte count ($\times 10^9/L$)

Hemoglobin-albumin-lymphocyte-platelet score (HALP) = Hemoglobin (g/L) $\times$ Albumin (g/L) $\times$ Lymphocyte ($\times 10^9/L$) / Platelet ($\times 10^9/L$)

C-reactive protein-to-lymphocyte ratio (CLR) = CRP / Lymphocyte

The primary endpoint of the study was to evaluate the discriminatory performance of inflammatory and immunonutritional indices for identifying rupture status at presentation.

The secondary endpoint was to compare clinical, laboratory, and surgical characteristics between unilateral and bilateral endometrioma cases and to explore whether these indices differed by disease laterality.

2.4. Statistical Analysis

Statistical analysis of the data was performed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA) and Python 3 (SciPy, statsmodels, scikit-learn) software. The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov and Shapiro–Wilk tests, assessed separately within each comparison group. Data showing normal distribution in both groups being compared were presented as mean $\pm$ standard deviation and compared with the independent-samples Student t-test; all other continuous data were presented as median (interquartile range [IQR]) and compared with the Mann–Whitney U test. Categorical variables were expressed as number and percentage and compared using Pearson's chi-square test or Fisher's exact test, as appropriate for expected cell counts.

To explore unadjusted factors associated with endometrioma rupture status, univariate logistic regression analyses were performed. Continuous predictors were standardized (z-scored) prior to regression so that odds ratios (ORs) are expressed per 1-standard-deviation increase, allowing meaningful comparison across indices measured on very different native scales (e.g., SII in the hundreds-to-thousands versus NPAR around 1.5); results are presented as OR with 95% confidence interval (CI). Receiver operating characteristic (ROC) curve analysis was used to evaluate the discriminatory performance of

inflammatory and immunonutritional indices for distinguishing ruptured from non-ruptured endometriomas at presentation. The area under the curve (AUC) was calculated together with 95% confidence intervals using the DeLong method. Optimal cut-off values were determined using the Youden index (maximizing sensitivity + specificity – 1).

This study involved multiple comparisons. To limit the inflation of type I error from these multiple, related tests, Benjamini-Hochberg false discovery rate (FDR) correction was applied within each table-specific analysis family: the 11 laterality-based index comparisons in Table 3, the 11 rupture-status index comparisons in Table 4, the 16 univariate logistic regression analyses in Table 5, and the 11 ROC analyses in Table 6. Both the nominal p value and the FDR-adjusted p value (p-FDR) are reported. Given this exploratory, multiple-comparison design and the modest overall sample size — particularly the rupture group (n=7) — all findings, including those that remained significant after FDR adjustment, should be interpreted as hypothesis-generating rather than confirmatory. A nominal two-sided $p < 0.05$ was used as the threshold for statistical significance, interpreted alongside the corresponding p-FDR.

3. Results

A total of 77 patients were included in the study. Among them, 57 patients (74.0%) had unilateral endometrioma and 20 patients (26.0%) had bilateral endometrioma; spontaneous rupture was detected in seven patients (9.1%). Descriptive and secondary laterality-based comparisons are summarized first in Tables 1–3, followed by the rupture-status analyses in Tables 4–6, which represent the primary focus of this study.

Table 1. Comparison of demographic characteristics, endometrioma-related features, and surgical outcomes between patients with unilateral and bilateral endometrioma.

	Unilateral Endometrioma N=57	Bilateral Endometrioma N=20	P value
Age (years)	40.0 ± 9.1	37.1 ± 9.1	0.203
Gravida	2.0 (0.0, 3.0)	2.0 (0.0, 2.0)	0.548
Parity	2.0 (0.0, 2.0)	2.0 (0.0, 2.0)	0.237
Nulliparity	16 (28.1%)	6 (30.0%)	0.869
BMI (kg/m ²)	27.2 ± 4.2	25.9 ± 5.3	0.298
Smoking	5 (8.8%)	3 (15.0%)	0.432
Rupture of Endometrioma	7 (12.3%)	0 (0.0%)	0.180
Total Length of Endometrioma (mm)	101 ± 38.3	106 ± 35.4	0.627
Surgery Type			0.167
Laparoscopy	38 (66.7%)	16 (80.0%)	
Laparotomy	19 (33.4%)	4 (20.0%)	

Data are presented as mean ± standard deviation, median (interquartile range), or n (%), as appropriate. Continuous variables were compared using the independent samples t-test or Mann-Whitney U test according to data distribution. Categorical variables were compared using the χ^2 test or Fisher's exact test

BMI: body mass index.

3.1. Laterality: Unilateral Versus Bilateral Endometrioma

The unilateral and bilateral endometrioma groups were comparable with respect to age, gravida, parity, nulliparity ratio, body mass index, smoking status, total endometrioma length, and surgical approach ($p > 0.05$ for all comparisons; Table 1). Although all rupture events occurred in the unilateral group, the distribution of rupture status did not differ significantly between unilateral and bilateral endometriomas (7/57 [12.3%] vs. 0/20 [0.0%], $p = 0.180$; Table 1). No significant differences were observed between the unilateral and bilateral groups in hematological or biochemical parameters, including hemoglobin,

white blood cell count, neutrophil count, lymphocyte count, monocyte count, platelet count, albumin, CA 125, anti-Müllerian hormone, and C-reactive protein levels (Table 2).

Table 2. Comparison of hematological, biochemical, and inflammatory parameters between patients with unilateral and bilateral endometrioma.

	Unilateral Endometrioma N=57	Bilateral Endometrioma N=20	P value
Hemoglobin (g/dL)	11.6 ± 1.7	11.9 ± 1.30	0.494
WBC (×10 ⁹ /L)	8.626 ± 2.590	8.496 ± 2.332	0.843
Neutrophil (×10 ⁹ /L)	5.874 ± 2.679	5.692 ± 2.066	0.784
Lymphocyte (×10 ⁹ /L)	2.050 ± 0.681	1.984 ± 0.682	0.713
Monocyte (×10 ⁹ /L)	0.554 ± 0.175	0.585 ± 0.159	0.503
Platelet (×10 ⁹ /L)	298 ± 87	304 ± 98	0.781
Albumin (g/L)	43.7 (40.2, 46.0)	42.3 (38.6, 46.6)	0.697
CA 125 (U/mL)	55.6 (22.8, 82.6)	45.8 (26.7, 130.0)	0.798
AMH (ng/mL)	1.76 (1.19, 2.40)	1.69 (1.21, 2.78)	0.803
CRP (mg/L)	3.08 (1.60, 4.47)	3.68 (1.96, 4.41)	0.426

Data are presented as mean ± SD for normally distributed variables and median (interquartile range [IQR]) for non-normally distributed variables. Comparisons between groups were performed using the independent samples t-test or Mann-Whitney U test, as appropriate. Statistical significance was defined as $p < 0.05$.

WBC: white blood cell count; AMH: anti-Müllerian hormone; CRP: C-reactive protein; CA125: cancer antigen 125.

Similarly, none of the 11 systemic inflammatory or immunonutritional indices differed significantly between unilateral and bilateral endometrioma. SII, SIRI, NLR, PLR, NPAR, AISI, dNLR, ACR, PNI, HALP, and CLR were all comparable between the two groups by nominal p values, and no index remained significant after Benjamini-Hochberg false discovery rate correction (all p -FDR=0.821; Table 3). These findings indicate that disease laterality was not a major determinant of the systemic inflammatory or immunonutritional profile in this cohort.

Table 3. Comparison of systemic inflammatory and immunonutritional indices between patients with unilateral and bilateral endometrioma.

	Unilateral Endometrioma N=57	Bilateral Endometrioma N=20	P value	P-FDR
SII	742.31 (493.25–1078.73)	758.21 (626.74–1000.60)	0.776	0.821
SIRI	1.22 (0.88–2.18)	1.42 (1.11–2.45)	0.400	0.821
NLR	2.26 (1.72–3.95)	2.47 (2.14–3.50)	0.447	0.821
PLR	140.17 (118.65–197.50)	143.04 (119.78–227.94)	0.550	0.821
NPAR	1.49 (1.36–1.70)	1.60 (1.40–1.66)	0.646	0.821
AISI	369.74 (255.59–706.04)	428.96 (353.36–752.82)	0.475	0.821
dNLR	1.77 (1.36–2.70)	1.78 (1.57–2.34)	0.821	0.821
ACR	14.09 (9.99–26.88)	12.09 (9.44–21.72)	0.400	0.821
PNI	53.37 ± 4.73	52.52 ± 5.92	0.564	0.821
HALP	32.82 (23.42–45.70)	33.62 (25.58–44.12)	0.821	0.821
CLR	1.53 (0.75–2.15)	2.19 (0.81–3.09)	0.338	0.821

Data are presented as mean ± SD or median (IQR), as appropriate, based on per-group Shapiro-Wilk normality testing. Comparisons between groups were performed using the independent samples t-test or Mann-Whitney U test according to data distribution. To account for multiple comparisons across the 11 indices tested in this table, p values were additionally adjusted using the Benjamini-Hochberg false discovery rate (FDR) procedure; adjusted p values (p -FDR) are reported alongside nominal p values.

SII: systemic immune-inflammation index; SIRI: systemic inflammation response index; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; NPAR: neutrophil percentage-to-albumin ratio; AISI: aggregate index of systemic inflammation; dNLR: derived neutrophil-to-lymphocyte ratio; ACR: albumin-to-CRP ratio; PNI: prognostic nutritional index; HALP: hemoglobin, albumin, lymphocyte, and platelet score; CLR: CRP-to-lymphocyte ratio.

3.2. Rupture Status: Systemic Inflammatory and Immunonutritional Indices

In patients with ruptured endometriomas, SII, SIRI, NLR, NPAR, AISI, and dNLR values were significantly higher than in patients without rupture. The median SII value was 2186.2 (IQR, 1025.6–2576.8) in the rupture group and 721.9 (IQR, 497.0–1021.1) in the non-rupture group ($p=0.002$, $p\text{-FDR}=0.004$). SIRI was also higher in ruptured cases than in non-ruptured cases (4.19 [2.65–6.30] vs. 1.21 [0.88–2.09], $p<0.001$, $p\text{-FDR}=0.003$), as were NLR (6.07 [4.23–9.84] vs. 2.25 [1.81–3.44], $p=0.001$, $p\text{-FDR}=0.004$), NPAR (1.89 [1.74–2.04] vs. 1.48 [1.36–1.65], $p=0.002$, $p\text{-FDR}=0.004$), AISI (935.3 [811.1–1734.9] vs. 388.7 [248.7–594.2], $p<0.001$, $p\text{-FDR}=0.003$), and dNLR (4.23 [2.75–6.05] vs. 1.74 [1.36–2.39], $p<0.001$, $p\text{-FDR}=0.003$; Table 4). In contrast, PLR, ACR, PNI, HALP, and CLR did not differ significantly between rupture groups after FDR correction. HALP showed a non-significant trend toward lower values in ruptured cases (27.25 [21.89–31.38] vs. 34.40 [23.49–48.02], $p=0.056$, $p\text{-FDR}=0.087$; Table 4).

Table 4. Comparison of systemic inflammatory and immunonutritional indices between patients with ruptured and non-ruptured endometrioma.

	Endometrioma with Rupture N=7	Endometrioma without Rupture N=70	P value	P-FDR
SII	2186.23 (1025.61–2576.79)	721.93 (497.04–1021.07)	0.002	0.004
SIRI	4.19 (2.65–6.30)	1.21 (0.88–2.09)	<0.001	0.003
NLR	6.07 (4.23–9.84)	2.25 (1.81–3.44)	0.001	0.004
PLR	202.05 (150.38–212.17)	135.87 (117.47–197.01)	0.088	0.120
NPAR	1.89 (1.74–2.04)	1.48 (1.36–1.65)	0.002	0.004
AISI	935.26 (811.13–1734.87)	388.66 (248.67–594.20)	<0.001	0.003
dNLR	4.23 (2.75–6.05)	1.74 (1.36–2.39)	<0.001	0.003
ACR	11.06 (3.15–21.15)	12.86 (10.03–26.76)	0.324	0.324
PNI	50.80 ± 5.13	53.38 ± 5.00	0.243	0.267
HALP	27.25 (21.89–31.38)	34.40 (23.49–48.02)	0.056	0.087
CLR	2.15 (1.81–16.07)	1.44 (0.75–2.40)	0.102	0.125

Data are presented as mean ± SD or median (IQR), as appropriate, based on per-group Shapiro-Wilk normality testing. Comparisons between groups were performed using the independent samples *t*-test or Mann-Whitney *U* test according to data distribution. To account for multiple comparisons across the 11 indices tested in this table, *p* values were additionally adjusted using the Benjamini-Hochberg false discovery rate (FDR) procedure; adjusted *p* values (*p*-FDR) are reported alongside nominal *p* values.

SII: systemic immune-inflammation index; SIRI: systemic inflammation response index; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; NPAR: neutrophil percentage-to-albumin ratio; AISI: aggregate index of systemic inflammation; dNLR: derived neutrophil-to-lymphocyte ratio; ACR: albumin-to-CRP ratio; PNI: prognostic nutritional index; HALP: hemoglobin, albumin, lymphocyte, and platelet score; CLR: CRP-to-lymphocyte ratio.

In univariate logistic regression analysis, continuous predictors were standardized to allow comparison across variables measured on different native scales. The same six indices were significantly associated with rupture status: SII (OR 2.15 per 1-SD increase, 95% CI 1.17–3.92, $p=0.013$, $p\text{-FDR}=0.035$), SIRI (OR 2.49, 95% CI 1.31–4.73, $p=0.005$, $p\text{-FDR}=0.030$), NLR (OR 2.17, 95% CI 1.20–3.92, $p=0.011$, $p\text{-FDR}=0.035$), NPAR (OR 2.60, 95% CI 1.25–5.44, $p=0.011$, $p\text{-FDR}=0.035$), AISI (OR 2.55, 95% CI 1.35–4.80, $p=0.004$, $p\text{-FDR}=0.030$), and dNLR (OR 2.35, 95% CI 1.28–4.30, $p=0.006$, $p\text{-FDR}=0.030$; Table 5). Age, BMI, smoking, and total endometrioma length were not significantly associated with rupture status. The odds ratio for bilaterality could not be estimated because no rupture occurred among the 20 bilateral cases; Fisher's exact test for the corresponding 2×2 table was also non-significant ($p=0.180$; Table 5).

Table 5. Univariate associations between demographic, clinical, and inflammatory variables and rupture status at presentation.

	OR (95% CI)	P value	P-FDR
Age (years) (per 1-SD)	0.511 (0.215–1.216)	0.129	0.229
BMI (kg/m ²) (per 1-SD)	0.749 (0.338–1.657)	0.476	0.507
Smoking	4.267 (0.677–26.893)	0.122	0.229
Total endometrioma length (mm) (per 1-SD)	1.121 (0.515–2.438)	0.774	0.774
SII (per 1-SD)	2.145 (1.174–3.920)	0.013	0.035
SIRI (per 1-SD)	2.493 (1.314–4.730)	0.005	0.030
NLR (per 1-SD)	2.166 (1.198–3.916)	0.011	0.035
PLR (per 1-SD)	1.478 (0.762–2.867)	0.247	0.304
NPAR (per 1-SD)	2.605 (1.248–5.439)	0.011	0.035
AISI (per 1-SD)	2.547 (1.353–4.797)	0.004	0.030
dNLR (per 1-SD)	2.349 (1.283–4.300)	0.006	0.030
ACR (per 1-SD)	0.571 (0.143–2.269)	0.426	0.487
PNI (per 1-SD)	0.599 (0.274–1.310)	0.199	0.266
HALP (per 1-SD)	0.277 (0.062–1.232)	0.092	0.210
CLR (per 1-SD)	1.387 (0.841–2.287)	0.200	0.266
Bilaterality of endometrioma	NE	0.180	0.266

Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using univariate logistic regression. To make coefficients comparable and interpretable across indices measured on very different native scales (e.g., SII in the hundreds-to-thousands vs. NPAR around 1.5), all continuous predictors except the binary variable Smoking were standardized (z-scored) prior to regression; OR is therefore expressed per 1-SD increase in the predictor. OR > 1 indicates an increased likelihood of endometrioma rupture, whereas OR < 1 indicates a decreased likelihood. NE = not estimable: the OR for Bilaterality of endometrioma could not be estimated because of complete separation (0 of 20 bilateral cases ruptured); the reported p value for this variable is instead from Fisher's exact test on the corresponding 2×2 table. To account for multiple comparisons across the 16 predictors tested in this table, p values were additionally adjusted using the Benjamini-Hochberg false discovery rate (FDR) procedure; adjusted p values (p-FDR) are reported alongside nominal p values. Given the exploratory nature of this analysis and the limited sample size (particularly n=7 in the rupture group), results should be interpreted as hypothesis-generating.

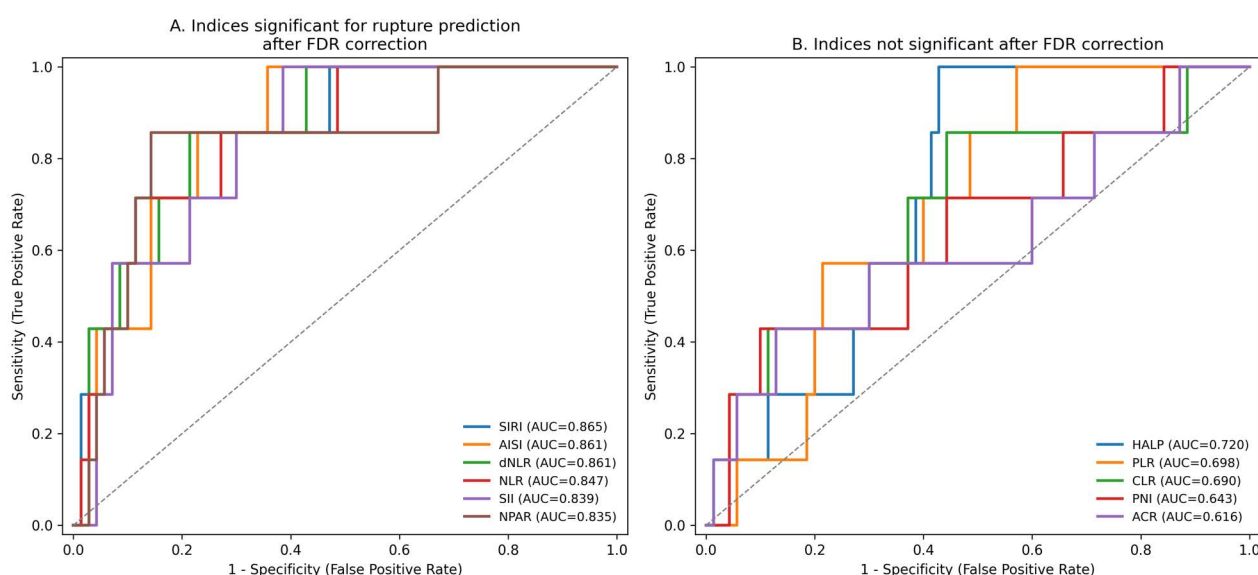


Figure 1. Receiver operating characteristic curves (ROC) for discriminating ruptured from non-ruptured endometriomas at presentation. (A) The six indices that remained statistically significant after Benjamini-Hochberg FDR correction (SIRI, AISI, dNLR, NLR, SII, NPAR). (B) The five indices that were not statistically significant after correction (HALP, PLR, CLR, PNI, ACR). AUC values are DeLong point estimates; see Table 6 for 95% confidence intervals and exact p values.

In ROC analysis, using Youden-index-derived cut-offs, SIRI, AISI, and dNLR showed the highest discriminatory performance for identifying rupture status at presentation. The

AUC values were 0.865 for SIRI (95% CI 0.734–0.996), 0.861 for AISI (95% CI 0.754–0.968), and 0.861 for dNLR (95% CI 0.740–0.982). NLR, SII, and NPAR also demonstrated significant discriminatory performance, with AUC values of 0.847 (95% CI 0.711–0.983), 0.839 (95% CI 0.719–0.959), and 0.835 (95% CI 0.659–1.000), respectively. All six indices remained significant after FDR correction ($p\text{-FDR} \leq 0.004$). At their respective Youden-optimal cut-offs, sensitivity ranged from 71% to 100%, and specificity ranged from 61% to 89% for these six indices (Table 6, Figure 1A).

By contrast, HALP showed moderate but non-significant discriminatory performance after correction for multiple comparisons (AUC 0.720, 95% CI 0.581–0.860, $p=0.056$, $p\text{-FDR}=0.087$), with lower values observed in ruptured cases. PLR (AUC 0.698, 95% CI 0.539–0.857), CLR (AUC 0.690, 95% CI 0.458–0.922), PNI (AUC 0.643, 95% CI 0.401–0.884), and ACR (AUC 0.616, 95% CI 0.355–0.877) showed limited, non-significant discriminatory ability after FDR correction (all $p\text{-FDR} \geq 0.120$; Table 6, Figure 1B).

Table 6. ROC-based discriminatory performance of systemic inflammatory and immunonutritional indices for identifying ruptured versus non-ruptured endometrioma at presentation.

	Direction	AUC (95% CI)	Sensitivity	Specificity	Cut-off	P value	P-FDR
SIRI	higher risk	0.865 (0.734–0.996)	86%	79%	2.19	<0.001	0.003
AISI	higher risk	0.861 (0.754–0.968)	100%	64%	494.3	<0.001	0.003
dNLR	higher risk	0.861 (0.740–0.982)	86%	79%	2.48	<0.001	0.003
NLR	higher risk	0.847 (0.711–0.983)	71%	89%	5.13	0.001	0.004
SII	higher risk	0.839 (0.719–0.959)	100%	61%	867.2	0.002	0.004
NPAR	higher risk	0.835 (0.659–1.000)	86%	86%	1.71	0.002	0.004
HALP	lower value = higher risk	0.720 (0.581–0.860)	100%	57%	32.31	0.056	0.087
PLR	higher risk	0.698 (0.539–0.857)	100%	43%	128.9	0.088	0.120
CLR	higher risk	0.690 (0.458–0.922)	86%	56%	1.64	0.102	0.125
PNI	lower value = higher risk	0.643 (0.401–0.884)	43%	90%	47.45	0.243	0.267
ACR	lower value = higher risk	0.616 (0.355–0.877)	43%	87%	4.69	0.324	0.324

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the ability of inflammatory indices to discriminate between ruptured and non-ruptured endometrioma. The area under the ROC curve (AUC) is presented with DeLong 95% confidence intervals (CI). Optimal cut-off values were determined using the Youden index (maximizing sensitivity + specificity – 1), consistent with the Statistical Analysis section. For HALP, PNI, and ACR, lower values (not higher values) were associated with rupture; AUC, sensitivity, and specificity for these three indices are reported in that direction, and the cut-off represents the threshold below which risk is increased. P values correspond to the Mann-Whitney U test comparing marker distributions between the rupture and non-rupture groups (Table 4), which is mathematically equivalent to testing whether AUC = 0.5. To account for multiple comparisons across the 11 indices tested in this table, p values were additionally adjusted using the Benjamini-Hochberg false discovery rate (FDR) procedure; adjusted p values ($p\text{-FDR}$) are reported alongside nominal p values.

4. Discussion

In this study, the diagnostic value of systemic inflammatory and immunonutritional indices for discriminating ruptured from non-ruptured endometriomas at presentation was evaluated as the primary aim, and unilateral and bilateral endometriomas were compared as a secondary aim. SII, SIRI, NLR, NPAR, AISI, and dNLR levels were significantly higher in ruptured than in non-ruptured cases, and these associations remained significant after correction for multiple comparisons in the rupture-status comparison, univariate regression, and ROC analysis families. ROC curve analysis, using Youden-index-derived cut-offs, showed that SIRI, AISI, and dNLR had the highest discriminatory performance (AUC 0.86–0.87), with sensitivity of 86–100% and specificity of 64–79% at their optimal cut-offs. PLR, ACR, PNI, HALP, and CLR did not show a significant difference according to rupture status after correction for multiple testing. No significant differences

were observed between the unilateral and bilateral endometrioma groups for any demographic, hematological, biochemical, or inflammatory/immunonutritional variable examined; because this comparison was uniformly negative and is not the focus of the study's contribution, it is discussed only briefly below.

Systemic inflammatory indices have previously been evaluated as non-invasive markers for endometriosis and endometrioma, including differentiation from benign ovarian cysts^{7,8,10,11,13}. Our findings extend this literature by suggesting that these indices may also support discrimination of rupture status among patients already diagnosed with endometrioma. This distinction is important: because blood samples were obtained at presentation, after symptom onset, the observed elevations should be interpreted as markers accompanying the rupture episode rather than as evidence of future rupture prediction.

The diagnostic interpretation of the present findings should be positioned within the broader evidence on non-invasive biomarkers in endometriosis. Current ESHRE guidance does not recommend biomarkers measured in endometrial tissue, blood, menstrual fluid, uterine fluid, or urine as stand-alone tests for diagnosing endometriosis¹⁴. A recent systematic review and meta-analysis similarly concluded that no blood or urine biomarker has yet demonstrated sufficient and reproducible accuracy for routine clinical use, although panel-based approaches may be more promising than isolated markers¹⁵. Therefore, the indices evaluated in the present study should be understood as adjunctive rather than substitutive: they may help refine clinical suspicion when a patient with endometrioma presents with acute pain, but they should not replace imaging, pelvic examination, or surgical judgment^{14,15}. This cautious interpretation is also consistent with rupture-specific studies showing elevations of markers such as CA 125, CRP, and other inflammatory parameters after spontaneous ovarian endometrioma rupture, while isolated biomarkers remain insufficient for definitive decision-making^{16,17}.

The higher discriminatory performance of SIRI, AISI, and dNLR compared with other indices can be explained by the inclusion of neutrophil and lymphocyte counts, as well as monocyte and/or platelet counts, in the calculation of these indices; this may allow for a more comprehensive reflection of the acute inflammatory response (neutrophilia, monocytosis, and relative lymphopenia) due to leakage of endometriotic cyst contents into the peritoneal cavity and the accompanying acute peritoneal inflammatory response. The relevance of AISI in endometriosis has also been supported by a recent logistic regression-based analysis of endometriosis risk¹⁸, and the broader use of composite systemic inflammatory indices in other inflammatory or fibrotic conditions supports the biological plausibility of these findings¹².

In contrast, indices incorporating nutritional or non-neutrophil-dominant components, such as ACR, PNI, HALP, CLR, and PLR, were not found to be significant after correction for multiple comparisons. The relatively long half-life of albumin as a negative acute phase reactant may have made it difficult to show a measurable change in the short time between rupture and blood sampling; this suggests that indices based on rapidly responding cellular components (neutrophils and platelets) may be more sensitive for discriminating acute rupture status than albumin-dominant indices. Similarly, the fact that NLR was found to be significant while PLR was not suggests that neutrophilic response, rather than platelet increase, may be dominant in the acute rupture response. One of the most important strengths of our study is that all patients underwent diagnosis, treatment, and surgery at a single center and by a single clinician. This eliminates inter-observer variability in terms of rupture diagnosis, determination of surgical indication, surgical technique, and sampling protocol, thus increasing the consistency of the data. Furthermore, the simultaneous evaluation of 11 different systemic inflammatory and immunonutritional indices instead of a single marker, together with explicit correction for the resulting

multiple comparisons, allows for a direct and appropriately conservative comparison of the discriminatory performance of these indices. The use of standardized univariate logistic regression estimates together with Youden-index-based ROC cut-offs also improves the interpretability of the exploratory results.

Our study also has some important limitations. First, the retrospective and single-center design limits the establishment of causal relationships and carries the risk of selection bias; the generalizability of findings from a single center to different populations and different surgical/laboratory protocols may be limited. Second, the small number of patients, especially in the rupture group ($n=7$), significantly reduces statistical power, widens confidence intervals (including for the ROC-derived cut-offs, which should be regarded as provisional), and increases the risk of type II errors for non-significant markers (PLR, ACR, PNI, HALP, CLR); although the six significant indices survived Benjamini-Hochberg FDR correction in the rupture-status comparison, univariate regression, and ROC analysis families, this correction cannot fully compensate for the limited sample size, and our findings should be considered hypothesis-generating and validated in larger, multicenter, prospective cohorts. Third, blood samples were taken at the time of hospital admission after rupture had occurred and symptoms had begun; this cross-sectional sampling makes it difficult to distinguish whether the measured indices reflect a pre-existing inflammatory predisposition to rupture or, more plausibly, a reactive response secondary to rupture itself. Therefore, these results should not be interpreted as evidence of future rupture prediction. Prospective studies with serial measurements are needed to clarify this causality issue. Fourth, the lack of a healthy control group without endometriomas limits the determination of disease-specific reference values for these indices. Fifth, potential confounding factors that could affect hematological indices (such as subclinical infection, drug use, and menstrual cycle phase at sampling time) were not controlled for with a multivariate model; only univariate analysis was performed, and the small number of events precluded a multivariable model that could adjust for several covariates simultaneously without overfitting. Finally, this study tested eleven indices across two grouping schemes, sixteen univariate predictors, and eleven ROC analyses; although we addressed this directly with Benjamini-Hochberg FDR correction within each table-specific family and report both nominal and adjusted p values throughout, the overall exploratory, multiple-comparison nature of the analysis means these results require confirmation in an independent, adequately powered cohort before any diagnostic threshold is applied clinically.

5. Conclusion

Endometrioma rupture remains a difficult preoperative diagnosis because it may mimic other causes of acute abdomen. In this study, ruptured cases had significantly higher blood count-derived inflammatory indices than non-ruptured cases, and these associations remained significant after correction for multiple comparisons in the rupture-focused analyses; unilateral and bilateral endometriomas, evaluated as a secondary aim, showed similar clinical and inflammatory profiles.

Among the inflammatory markers, SIRI, AISI, and dNLR demonstrated the best discriminatory performance and may serve as simple, low-cost adjunctive markers during the initial assessment of patients with suspected rupture. However, given the retrospective design, the exploratory multiple-comparison analysis, and the small rupture group, these findings should be considered hypothesis-generating and validated in larger prospective studies. They should not be interpreted as evidence of future rupture prediction or as stand-alone diagnostic tools.

Ethics approval: The study was evaluated by the Acibadem Mehmet Ali Aydınlar University Medical Research Evaluation Board (ATADEK) and found to be ethically appropriate (Decision No: 2026-10/422, Date: 11.06.2026).

Informed Consent: The requirement for additional written informed consent was waived by the ethics committee because of the retrospective design and anonymized nature of the data.

genAI: No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

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

Availability of data and materials : Due to institutional privacy policies, the datasets generated and/or analyzed during the current study are not publicly available, but they are available from the corresponding author upon reasonable request.

Author contributions: Aşkın Evren Güler: Conceptualization, methodology, patient recruitment, clinical management, data curation, investigation, supervision, project administration, and critical revision of the manuscript. Ayberk Çakır: Data analysis, formal analysis, literature review, interpretation of the data, original draft preparation, and manuscript editing. Both authors contributed to the study design, reviewed and approved the final version of the manuscript, and agree to be accountable for all aspects of the work.

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