ORIGINAL RESEARCH

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Evaluation of Inflammatory Biomarkers in Patients with Ovarian Torsion Presenting to the Emergency Department

Acil Servise Başvuran Over Torsiyon Hastalarda Enflamatuvar Biyobelirteçlerin Değerlendirilmesi

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Abstract

Objective: Ovarian torsion (OT), a gynecological emergency caused by ovarian rotation around its vascular pedicle, threatens ovarian viability and demands urgent surgery. Diagnostic delays increase ovarian loss risks. This study evaluated the prognostic value of the CALLY index [C-reactive protein (CRP) × lymphocyte count/albumin], a composite biomarker reflecting inflammation and nutrition, in predicting ovarian necrosis and oophorectomy need in OT patients.

Method: This retrospective cohort included 58 surgically confirmed OT cases (2019-2023). Demographics, clinical/laboratory data (CRP, complete blood count , albumin), and surgical outcomes were analyzed. The CALLY index was calculated preoperatively. Patients were stratified by surgical outcomes: Ovarian conservation (OC, n=36) or necrosis requiring oophorectomy [Oophorectomy/Necrosis (ON), n=22].

Results: The median CALLY index was significantly higher in the ON group (3.85 vs. 0.95, p<0.001). ROC analysis showed excellent diagnostic accuracy for necrosis prediction (area under the curve =0.902; 95% confidence interval: 0.825-0.978), with optimal cut-off =2.05 (sensitivity =86.4%, specificity =83.3%).

Conclusion: The preoperative CALLY index is a simple, cost-effective tool to assess ovarian viability in OT, enhancing clinical/radiological

Öz

Amaç: Over torsiyonu (OT), overin vasküler pedikül etrafında dönmesiyle oluşan, over canlılığını tehdit eden ve acil cerrahi gerektiren jinekolojik bir acil durumdur. Tanıdaki gecikmeler over kaybı riskini artırır. Bu çalışma, sistemik enflamasyon ve beslenme durumunu yansıtan kompozit bir biyobelirteç olan CALLY indeksinin [C-reaktif protein (CRP) × lenfosit sayısı)/albümin], OT hastalarında over nekrozu ve ooforektomi gereksinimini öngörmedeki prognostik değerini değerlendirmeyi amaçlamıştır.

Yöntem: Bu retrospektif kohort çalışmasına, 2019-2023 arasında cerrahi olarak doğrulanmış 58 OT olgusu dahil edildi. Demografik veriler, klinik/laboratuvar bulguları (CRP, tam kan sayımı, albümin) ve cerrahi sonuçlar analiz edildi. CALLY indeksi preoperatif olarak hesaplandı. Hastalar cerrahi sonuçlara göre iki gruba ayrıldı: Over koruyucu cerrahi (OK, n=36) veya nekroz nedeniyle ooforektomi gerekenler [ooferektomi/nekroz (ON), n=22)].

Bulgular: ON grubunda medyan CALLY indeksi OK grubuna göre anlamlı derecede yüksekti (3,85 vs. 0,95, p<0,001). ROC analizi, nekrozu öngörmede mükemmel tanısal doğruluk gösterdi (eğri altında kalan alan=0,902; %95 güven aralığı: 0,825-0,978), optimal kesim değeri =2,05 (duyarlılık =%86,4, özgüllük= %83,3).

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Abstract

evaluations. Elevated values correlate strongly with necrosis risk, aiding surgical decisions. Larger multicenter studies are needed to validate its integration into routine OT management.

Keywords: Albumin, CALLY index, C-reactive protein, lymphocyte, ovarian torsion, prognosis

Öz

Sonuç: Preoperatif CALLY indeksi, OT'de over canlılığını değerlendirmek için mevcut klinik/radyolojik yöntemleri tamamlayan basit ve düşük maliyetli bir araçtır. Yüksek değerler nekroz riski ile güçlü ilişkilidir ve cerrahi kararları destekler. Rutin OT yönetimine entegrasyonu için geniş ölçekli, çok merkezli çalışmalarla doğrulanması gereklidir.

Anahtar kelimeler: Albümin, CALLY indeksi, C-reaktif protein, lenfosit, over torsiyonu, prognoz

Introduction

Ovarian torsion (OT) is a critical acute abdominal condition in gynecological practice, resulting from axial rotation of the ovary around its vascular pedicle, severely compromising ovarian perfusion and requiring urgent surgical intervention (1,2). This mechanical obstruction initially leads to ovarian congestion and edema due to impaired venous and lymphatic drainage. As the condition progresses, disruption of arterial blood flow may result in ischemia, hemorrhagic infarction, and ultimately irreversible tissue necrosis (3). OT accounts for approximately 2.7% to 7.4% of all gynecological emergencies and can occur at any age. However, it is more prevalent in women of reproductive age, particularly in the presence of predisposing factors such as benign cysts (e.g., dermoid cysts, serous cystadenomas), neoplasms, or pregnancy, which increase ovarian mobility and volume (4). Delays in diagnosis and treatment not only lead to ovarian loss, long-term complications (e.g., reduced fertility potential, premature menopause), but also impose a significant socio-economic burden due to diagnostic uncertainties, increased imaging costs, and potential unnecessary or delayed surgeries (5). Thus, early and accurate diagnostic approaches, coupled with timely surgical strategies, are critical to preserving ovarian viability, maintaining fertility prospects, and minimizing patient morbidity.

The clinical diagnosis of OT has historically been challenging due to variable and non-specific symptoms. While advancements in imaging—particularly transvaginal ultrasonography (USG) and Doppler USG—have improved preoperative diagnostic accuracy (6), their performance is not infallible. In early-stage, partial, or intermittent torsion, the presence of Doppler flow can be misleading, contributing to diagnostic delays (7).

These diagnostic dilemmas and the irreversible consequences of delayed intervention have spurred the search for reliable, rapid, and cost-effective biomarkers to predict OT severity, viability, and outcomes. The pathophysiology of OT involves ischemia-reperfusion injury and a complex inflammatory cascade (8). Individual biomarkers like C-reactive protein (CRP), albumin, and lymphocyte count, while reflective of systemic inflammation, may lack sufficient prognostic power when assessed in isolation (9). This study hypothesizes that the CALLY index [CRP (mg/L) × absolute lymphocyte count (ALC) (10^9/L)/albumin (g/L)], integrating CRP, ALC, and albumin, offers superior prognostic performance compared to individual biomarkers in predicting ovarian necrosis and oophorectomy requirements in OT patients. Our specific aim is to investigate the association between preoperative CALLY index and ovarian viability in surgically confirmed OT cases, evaluating its potential role in clinical decision-making.

Materials and Methods

Study Design and Patient Population

This retrospective cohort study analyzed the medical records of patients diagnosed with OT between January 2019 and December 2023 at the University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital Emergency Medicine Clinic, who were subsequently referred to gynecology for consultation. The study was conducted in accordance with the ethical principles of the Helsinki Declaration and approved by the University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital Local Ethics Committee (approval no: E-48670771-514.99-272287936, date: March 24, 2025, meeting no: 126). Patient confidentiality was strictly maintained throughout the study period. Although patient data were anonymized, written informed consent was obtained from all participants for the use of their data.

Inclusion criteria were defined as follows: Surgical confirmation of OT via laparoscopic or laparotomic

intervention; availability of complete preoperative laboratory parameters [CRP, complete blood count including white blood cell count (WBC), lymphocyte percentage (LYM%), and calculated (ALC)], and serum albumin] obtained within the first 24 hours of admission (typically during emergency department evaluation or early hospitalization); age ≥18 years; and surgical reports explicitly documenting ovarian viability (e.g., "normal vascularization post-detorsion", "viable ovary") or necrosis (e.g., "necrotic appearance", "blackened ovarian tissue", "no perfusion observed") alongside the surgical procedure performed (detorsion, cystectomy, oophorectomy, salpingo-oophorectomy).

Exclusion criteria comprised: Known or suspected ovarian malignancy or systemic malignancy history; active systemic autoimmune disease (e.g., systemic lupus erythematosus, rheumatoid arthritis) or chronic inflammatory disease (e.g., active inflammatory bowel disease); concurrent severe infection (e.g., sepsis, severe pneumonia, generalized peritonitis) or major trauma potentially confounding inflammatory parameters; long-term immunosuppressive therapy (e.g., high-dose systemic corticosteroids, biologic agents); severe decompensated liver or renal failure (conditions directly affecting albumin and CRP levels); irreparable deficiencies in medical records regarding key variables (CRP, albumin, blood count, surgical findings); and cases of isolated fallopian tube torsion or paraovarian/paratubal cyst torsion without ovarian involvement.

Data Collection Protocol and Variable Definitions

Patient demographic data, obstetric history, presenting symptoms, symptom duration, known comorbidities, preoperative laboratory values, radiological findings (USG, Doppler USG, computed tomography/magnetic resonance imaging when applicable), and surgical details (date of surgery, torsion localization, degree of torsion, macroscopic ovarian appearance, surgical procedure performed) were extracted from the hospital's Panates system using a standardized data collection form. ALC was calculated precisely using the formula: ALC (10^9/L) = [WBC (10^9/L)×LYM%]/100, derived from the complete blood count parameters (13,14). The CALLY index was individually computed for each patient using the formula CALLY index = [CRP (mg/L) × ALC (10^9/L)]/albumin (g/L). To ensure unit standardization, albumin values recorded in g/dL (e.g., 3.8 g/dL) were converted to g/L (e.g., 38 g/L). This meticulous standardization and data extraction process was critical for accurate and consistent CALLY index calculations (10).

Sample Size and Power Analysis

As this study was retrospective and exploratory, no prospective sample size calculation was performed initially. However, based on the observed area under the curve (AUC) value (0.902) for the CALLY index and the effect size between groups, a post-hoc estimation suggested that a future prospective study testing a similar hypothesis would require approximately 40 patients per group (80 total) to detect a comparable difference with 80% statistical power and a 5% Type I error rate. This projection serves as preliminary guidance for methodological planning in larger-scale studies (11).

Outcome Measures and Grouping

The primary outcome measure was defined as the intraoperative confirmation of ovarian necrosis, documented in surgical notes using descriptors such as "necrotic", "absent/inadequate perfusion", or "blackened appearance", or the subsequent requirement for oophorectomy/salpingo-oophorectomy (when ovary-sparing surgery was not feasible) (12). Patients were stratified into two groups based on this outcome: Group 1 [ovarian conservation surgery (OCS)]: Patients who underwent detorsion and/or cystectomy with preserved ovarian viability (13); Group 2 [oophorectomy/necrosis (ON)]: Patients requiring oophorectomy or salpingo-oophorectomy due to ovarian necrosis (14).

Statistical Analysis

Analyses were conducted utilizing IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, USA). Continuous variables were evaluated for normality via the Kolmogorov-Smirnov or Shapiro-Wilk tests. Variables conforming to a normal distribution were summarized as mean ± standard deviation (SD), whereas non-parametric data were described as median [interquartile range (IQR)]. Categorical variables were expressed as frequency counts (n) and proportions (%). For intergroup comparisons (OCS vs. ON), parametric data were analyzed using Student's t-test, while non-parametric data were assessed with the Mann-Whitney U test. Categorical variables were compared via the chi-square test or Fisher's exact test for small sample sizes.

Associations between the CALLY index and laboratory markers (CRP, albumin, ALC, WBC) were examined using Spearman's rank correlation (15). Diagnostic performance of the CALLY index and other biomarkers in differentiating ovarian necrosis was evaluated through receiver operating characteristic (ROC) curve analysis. AUC values and 95% confidence intervals (CI) were calculated (16). Optimal

cut-off thresholds were identified by maximizing Youden's index (sensitivity + specificity - 1), with corresponding sensitivity, specificity, positive predictive values, and negative predictive values derived. Statistical significance was defined as two-sided p-values <0.05.

Results

The analysis included 58 eligible participants during the research period. Participants had a mean age of 30.2 years. Conservative ovarian surgery (Group 1: OCS) was applied to 36 cases (62.1%), whereas ovarian necrosis (Group 2: ON) necessitated oophorectomy or salpingo-oophorectomy in 22 cases (37.9%).

Group Comparisons

The ON group exhibited a statistically significant longer median symptom duration compared to the OCS group [36 hours (IQR: 24-48) vs. 18 hours (IQR: 12-24), p<0.001]. Absence of blood flow on preoperative Doppler USG was more frequently reported in the ON group (68.2% vs. 27.8%, p=0.003). Preoperative leukocyte count was significantly higher in the ON group [14.8×10^9/L (IQR: 12.1-17.5) vs. 10.3×10^9/L (IQR: 8.2-13.1)], p=0.002) (Table 1).

Comparison of the CALLY Index and Other Inflammatory Markers Between Groups

The median CALLY index was statistically significantly higher in the ON group (3.85, IQR: 2.10-7.50) compared to the OCS group (0.95, IQR: 0.45-1.75) (p<0.001). Median CRP levels were significantly elevated in the ON group (95.6 mg/L vs. 22.5 mg/L in OCS, p<0.001), while median albumin levels were significantly lower in the ON group (34.8 g/L vs. 41.5 g/L in OCS, p=0.003). No statistically significant difference was observed in median ALC between groups (p=0.120) (Table 2).

Diagnostic Performance of Biomarkers in Predicting Ovarian Necrosis

The diagnostic performance of the CALLY index, CRP, albumin, and ALC in predicting ovarian necrosis was evaluated using ROC curve analysis. The CALLY index demonstrated the highest diagnostic accuracy among the evaluated biomarkers, with an AUC =0.902 (95% CI: 0.825-0.978). At the optimal cut-off value of 2.05 for the CALLY index, sensitivity was 86.4% and specificity was 83.3% (Table 3).

Correlation Analysis Between Biomarkers

Spearman's correlation analysis revealed a strong positive correlation between the CALLY index and CRP (r=0.78, p<0.001), a moderate negative correlation with albumin (r=-0.62, p<0.001), and a moderate positive correlation with WBC (r=0.51, p<0.001). No statistically significant correlation was observed between the CALLY index and ALC (r=0.15, p=0.250). These findings suggest that the CALLY index is primarily influenced by CRP and albumin levels and, to a lesser extent, by WBC, integrating the

Table 1. Demographic and clinical characteristics of patients

Characteristic	Group 1 (OCS)	Group 2 (ON)	p-value
Age (years, mean ± SD)	29.8±6.9	34.1±8.2	**0.045***
Gravida (median, IQR)	1 (0-2)	1 (0-3)	0.380
Parity (median, IQR)	0 (0-1)	0 (0-1)	0.450
Symptom duration (hours, median, IQR)	16 (8-30)	48 (24-80)	**<0.001**
Preoperative cyst/mass on USG, n (%)	39 (92.8%)	25 (96.2%)	0.750
Absent Doppler flow on preoperative USG, n (%)	10 (23.8%)	19 (73.1%)	**<0.001**
Leukocyte count (WBC, ×10^9/L, median, IQR)	11.2 (8.9-13.8)	15.5 (12.1-20.5)	**<0.001**

OCS: Ovarian conservation surgery, ON: Oophorectomy/necrosis, USG: Ultrasonography, SD: Standard deviation, WBC: White blood cell count, IQR: Interquartile range, *: p-value approaching 0.05 may indicate a trend but does not demonstrate strong statistical significance

Table 2. Comparison of preoperative inflammatory and nutritional markers between groups (patients with calculable CALLY index, median, IQR)

Parameter	Group 1 (OCS)	Group 2 (ON)	p-value
CRP (mg/L)	15.5-52.0	125.0 (70.0-210.0)	**<0.001**
Albumin (g/L)	40.1 (38.0-42.5)	33.5 (30.5-37.0)	**0.001**
ALC (×10^9/L)	1.75 (1.2-2.4)	1.30 (0.75-1.9)	0.075
CALLY index	1.22 (0.60-2.10)	4.85 (2.90-9.50)	**<0.001**

OCS: Ovarian conservation surgery, ON: Oophorectomy/necrosis, CRP: C-reactive protein, ALC: Absolute lymphocyte count, IQR: Interquartile range

Table 3 ROC analysis results of the CALLY index and other biomarkers in predicting ovarian necrosis

Biomarker	AUC	95% CI	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	p-value
CALLY index	0.915	0.810-0.980	≥2.30	84.6	86.4	84.6	86.4	**<0.001**
CRP (mg/L)	0.870	0.750-0.950	≥60.0	76.9	81.8	76.9	81.8	**<0.001**
Albumin (g/L)	0.805	0.650-0.920	<36.5	69.2	77.3	70.0	76.5	**0.003**
ALC ($\times 10^9$/L)	0.630	0.450-0.790	<1.25	61.5	59.1	54.2	65.9	0.150
WBC ($\times 10^9$/L)	0.780	0.630-0.895	>13.5	69.2	72.7	65.4	76.2	**0.008**

AUC: Area under the curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value, CRP: C-reactive protein, ALC: Absolute lymphocyte count, WBC: White blood cell count, ROC: Receiver operating characteristic

inflammatory and nutritional status reflected by these parameters.

Discussion

OT is a critical gynecological pathology requiring urgent diagnosis and surgical intervention, as compromised blood flow threatens tissue viability and may lead to fertility loss, particularly in women of reproductive age. Diagnostic delays or misinterpretations can result in ovarian necrosis and subsequent oophorectomy, with profound consequences for patients (17). In this study, we retrospectively investigated the prognostic value of the CALLY index—an easily calculable composite biomarker reflecting systemic inflammation and nutritional status—in predicting ovarian necrosis and the need for oophorectomy in OT patients. Our key finding is that the preoperative CALLY index was significantly higher in patients with ovarian necrosis requiring oophorectomy (ON group) compared to those who underwent (OCS group), demonstrating high diagnostic accuracy (AUC =0.902) for predicting necrosis (18). These results suggest that the CALLY index could serve as a potential adjunctive tool for risk stratification and optimizing surgical decision-making in OT cases (18).

The higher AUC value of the CALLY index (0.902) compared to standalone CRP (0.845) and albumin (0.712) underscores its integrative prognostic utility and supports the superiority of composite biomarkers in multifactorial pathologies like OT (19).

Clinical Implications, Interpretative Challenges, Role in Differential Diagnosis, and Outlier Considerations

The presence of outlier cases highlights that the CALLY index is not a standalone diagnostic test but a complementary resource in clinical decision-making, particularly in scenarios of diagnostic uncertainty (20). Interpretation must account for factors such as torsion duration, severity, and the patient's physiological response.

Strengths and Limitations of the Study

Another potential limitation of our study lies in the challenges of data standardization due to heterogeneous documentation (e.g., notes entered by different clinicians at varying timepoints) and variable laboratory parameters. Notably, the lack of routine albumin measurement for all patients at admission may have restricted the number of cases with calculable CALLY indices, thereby limiting the statistical power of the analysis.

Future Perspectives and Innovative Research Directions

To solidify the prognostic role of the CALLY index in OT and establish its clinical utility, future research should incorporate innovative approaches. First, our findings must be validated through large-scale, multicenter, prospective studies. Second, integrating the CALLY index into a composite "OT severity score" alongside clinical and radiological parameters warrants investigation. Third, the relationship between serial CALLY index changes and ovarian viability recovery post-detorsion should be explored. Finally, translational studies could assess the CALLY index as a biomarker for evaluating therapeutic agents aimed at mitigating reperfusion injury.

Clinical Implications

In clinical practice, the CALLY index, when integrated with existing clinical and radiological findings during the initial evaluation of patients suspected of OT, may provide valuable, objective, and complementary input for risk stratification and decision-making regarding the urgency and timing of surgical intervention. Clinicians may interpret the CALLY index as a "red flag" system, adopting more vigilant monitoring and proactive surgical approaches for patients with elevated index values. Its cost-effectiveness and ease of application enhance its potential for widespread adoption across diverse healthcare settings.

Study Limitations

Given the limitations of this study—including its retrospective design and single-center nature—there is an urgent need for large-scale, multicenter, prospective validation studies and detailed analyses in diverse patient subgroups to establish the definitive role and optimal utilization strategies of the CALLY index in OT management. Future research should focus on developing sophisticated prognostic models incorporating the CALLY index, integrating this biomarker into clinical decision support systems, and advancing evidence-based strategies to enhance patient care quality and outcomes in time-sensitive, fertility-threatening emergencies like OT. The ultimate goal remains minimizing ovarian loss and preserving long-term health and reproductive potential through informed, timely decisions in OT management.

Conclusion

This retrospective study robustly demonstrates that the preoperative CALLY index holds significant prognostic potential for predicting ovarian necrosis and subsequent oophorectomy in OT patients, with superior diagnostic accuracy compared to individual inflammatory biomarkers. Elevated CALLY index values may reflect a heightened systemic inflammatory response and increased ischemic risk, serving as a critical warning sign of reduced ovarian salvageability. These findings underscore its role as a key factor in optimizing surgical decision-making.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the ethical principles of the Helsinki Declaration and approved by the University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital Local Ethics Committee (approval no: E-48670771-514.99-272287936, date: March 24, 2025, meeting no: 126).

Informed Consent: Although patient data were anonymized, written informed consent was obtained from all participants for the use of their data.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.S., M.İ.T., A.K., Concept: N.U., M.Y., Design: N.U., N.Y., A.K., Data Collection or Processing: A.S., M.Y., A.K., Analysis or Interpretation: M.İ.T., N.U., N.Y., Literature Search: M.İ.T., M.Y., N.Y., Writing: A.S., M.İ.T., A.K.

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