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Can the Delta Neutrophil Index (DNI) be used as a marker to predict whether the ovaries are viable or not in cases of ovarian torsion before surgery?

Delta Nötrofil İndeks (DNI), over torsiyonu olgularında cerrahi öncesinde over canlılığını tahmin etmek için bir belirteç olarak kullanılabilir mi?

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ABSTRACT

Aim: To assess the predictive capability of the preoperative Delta Neutrophil Index (DNI) value in deciding whether to pursue an ovarian-preserving approach.

Materials and Methods: This retrospective cohort study was conducted on 81 women diagnosed with ovarian torsion. All patients underwent surgery, with 48 undergoing surgical detorsion and 33 undergoing oophorectomy. The latter group had available final pathology results. Patients were categorized based on final pathology results into groups with and without necrosis. None of the detorsion patients required reoperation within the first month. Surgery type , number of ovarian twists, preoperative admission hemogram parameters and final histological diagnosis were recorded, and it was evaluated whether the DNI values could be used as a predictive marker of ovarian viability in cases of ovarian torsion.

Results: A DNI value cut-off of 0.70 yielded 95.7% specificity, 83.3% sensitivity, 97.1% negative predictive value, and 83.3% positive predictive value for predicting necrosis. For neutrophil to lymphocyte ratio (NLR) values, a cut-off of 7.53 resulted in 77% specificity, 91.7% sensitivity, 98% negative predictive value, and 39% positive predictive value for predicting necrosis. No significant association was observed between necrosis and ovarian enlargement, the duration of time between the initial onset of pain and surgery, or the number of adnexal twists. However, the necrosis group exhibited significantly higher leukocyte counts, especially neutrophil counts($p<0.01$).

Conclusion: Our study suggests that having DNI and NLR values lower than the preoperative total blood count cut-off levels may serve as valuable guidance to surgeons in assessing the absence of ovarian necrosis.

Keywords: Ovarian torsion, delta neutrophil index, necrosis

ÖZ

Amaç: Delta Nötrofil İndeksi'nin (DNI), cerrahi öncesinde overlerin canlılığını tahmin etmedeki etkinliğini değerlendirmek ve over koruyucu cerrahi yaklaşımları desteklemedeki rolünü incelemek.

Gereç ve Yöntemler: Bu retrospektif kohort çalışması, over torsiyonu tanısı konmuş 81 kadın üzerinde gerçekleştirildi. Hastaların 48'ine cerrahi detorsiyon, 33'üne ise ooferektomi yapıldı ve ooferektomi grubunda nihai patoloji sonuçları incelendi. Hastalar, patoloji sonuçlarına göre nekroz olan ve olmayan olarak iki gruba ayrıldı. Detorsiyon uygulanan hiçbir hasta, ilk ay içinde yeniden cerrahiye ihtiyaç duymadı. Çalışmada, cerrahi türü (detorsiyon veya ooferektomi), torsiyon sayısı, cerrahi öncesi tam kan parametreleri ve nihai histopatolojik sonuçlar kaydedildi. DNI'nin, over torsiyonu durumlarında overlerin canlılığını öngörmek için kullanılıp kullanılamayacağı değerlendirildi.

Bulgular: DNI için belirlenen 0.70 eşik değerin, nekroz tahmininde; %95,7 özgüllük, %83,3 duyarlılık, %97,1 negatif prediktif değer ve %83,3 pozitif prediktif değer sağladığı belirlendi. Nötrofil-lenfosit oranı (NLR) için belirlenen 7.53 eşik değeri ise %77 özgüllük, %91,7 duyarlılık, %98 negatif prediktif değer ve %39 pozitif prediktif değer gösterdi. Nekroz ile over boyutu, ağrının başlangıcından cerrahiye kadar geçen süre veya torsiyone tur sayısı arasında anlamlı bir ilişki bulunmadı. Bununla birlikte, nekroz grubunda lökosit ve özellikle nötrofil sayıları anlamlı derecede yüksek bulundu ($p < 0.01$).

Sonuç: Bu çalışma, cerrahi öncesi DNI ve NLR değerlerinin belirlenen eşik değerlerin altında olması durumunda, over nekrozu bulunmadığını değerlendirme konusunda cerrahlara önemli bir yol gösterici olabileceğini ve over koruyucu cerrahi yaklaşımlara rehberlik edebileceğini ortaya koymaktadır.

Anahtar Kelimeler: Over torsiyonu, delta nötrofil indeks, nekroz

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INTRODUCTION

Ovarian torsion is a gynecological emergent situation which has a 2.7% prevalence (1). Prompt diagnosis and urgent surgical intervention are required to avoid necrosis and serious consequences on ovarian function and subsequent fertility (2-4). But diagnosis is often difficult. The most common presentation is lower abdominal pain, with other associated symptoms including nausea, vomiting and fever (5). The first preferred imaging method is ultrasound with doppler. The sensitivity of this method has been reported as 84% (6). Computed tomography (CT) and magnetic resonance imaging (MRI) are often used to rule out other abdominal pathologies, rather than diagnose. Surgical treatment is indicated, and in reproductive-age women, preserving ovarian function is crucial. The assessment of ovarian viability usually involves direct visualization during surgery, but no parameter or marker has reliably indicated existence of necrosis. The assessment of viability often involves direct visualization of a twisted ovary. An enlarged and darkened appearance of the ovary with hemorrhagic lesions is often considered a necrotic sign but can usually be salvaged (7). Despite the common belief among surgeons that the ovary image suggests necrosis, no specific parameter, imaging method, or marker has been proven to reliably indicate necrosis (8).

Delta Neutrophil Index (DNI) is a marker showing the number of immature granulocytes. In a limited number of studies, the DNI was investigated in patient groups with inflammatory processes such as sepsis, acute appendicitis, meningitis, decompensated heart failure, acute gout attack and acute pancreatitis. With this viewpoint, it was thought that it may guide physicians in determining severity of diseases (9). Researchers have recently begun to focus on DNI in diseases characterized by ischemia and necrosis. To our knowledge, this is the first study in the literature to examine the DNI as a sign of ovarian viability in ovarian torsion cases.

The aim of this study is to assess the predictive capability of the preoperative DNI value in deciding whether an oophorectomy is necessary, based on its relation with the final pathology result. If a specific cut-off value can be established, it could provide valuable guidance to surgeons regarding ovarian vitality and the likelihood of necrosis before the planned surgery.

MATERIALS AND METHODS

This retrospective cohort study was conducted in 81 women, aged between 18 and 45 years, who were diagnosed with ovarian torsion in a gynecology department of a tertiary hospital between September 2019 and July 2023. The study was approved by the hospital's Ethical Committee (E2-23-4702). Patients who applied to the emergency department as soon as the pain started, whose complete blood parameters were recorded at the time of admission, and who were diagnosed with ovarian torsion and undergone surgery were included in the study. Patients with any additional diseases which are likely to affect the DNI value (immunological diseases, rheumatological diseases, chronic diseases, or chronic inflammatory diseases, etc.) were excluded from the study. Patients who were pregnant, had to take any kind of medication, were addicted to drugs, or consumed alcohol or tobacco were also excluded. 48 of them had surgical detorsion while 33 of them underwent oophorectomy. Those who had oophorectomy had final pathology results. Patients were first compared as those with detorsion and those with oophorectomy. Then, according to the final pathology results, they were divided into two groups as those with and without necrosis. None of the patients who underwent detorsion required reoperation within the first month. Since there was no material taken in the detorsion group, pathological examination was not performed. The oophorectomy group was reported as congestion and necrosis according to the pathology results. Patients' age, gravida, parity, body mass indexes (BMI), surgery type (detorsion or oophorectomy), how many times the ovary twisted, the time from the first onset of pain to the operation, final histological diagnose and the first onset total blood parameters including the DNI values were reached from hospital records. DNI is calculated using automated hematology analyzers during a complete blood count . It is determined by subtracting the proportion of mature neutrophils from the total granulocyte count. The formula is as follows: DNI = (Total granulocyte count) - (Mature neutrophil count). Both the total granulocyte count and mature neutrophil count are automatically obtained through optical systems and channel-based measurements during CBC analysis(10). In this study, we tried to compare the total blood parameters measured at the time of first admission from the emergency department with the diagnosis of ovarian torsion in both groups (necrosis and congestion) and investigated their usefulness as an auxiliary laboratory indicator in determining the type of surgery to be performed. We aimed to associate the final pathology result and the patients' preoperative admission hemogram parameters especially the DNI values, and evaluated the predictive power of these values in the decision on ovarian-preserving approach.

All statistical analyses were performed using the SPSS for Windows 21.0 (SPSS Inc. IL, USA) software package. A p-value of <0.05 was considered to indicate statistically significant difference. The normality of distribution for variables was assessed using the Shapiro-Wilk test. Data are presented as means ± SD for continuous variables. For all comparisons, the $P<0.05$ value was determined as statistically significant. Independent samples t-test and Mann–Whitney U test were used for comparing groups.

Power analysis was implemented using G-power software (G-power v3.1.9.2, Universitat Kiel, Kiel, Germany). The difference between two independent mean power analyzes indicated that the study achieved a power of 0.93. This analysis was performed using a comparison of preoperative DNI levels between 21 women with congestion and 12 women with necrosis according to the pathology results.

RESULTS

Table 1 represents the demographic features of women diagnosed with ovarian torsion according to the type of surgery, including age, gravidity, BMI, smoking status, ovarian enlargement, pain onset to surgery and number of ovarian twists. Parameters other than the number of ovarian twists did not statistically significant in deciding the type of operation. It was demonstrated that the kind of procedure changed toward oophorectomy as the number of ovarian twists increased (p<0.05).

Table 2 illustrates the hemogram parameters, ovarian enlargement, time to surgery and number of adnexial twists of the groups according to pathology results. It has been demonstrated that leukocyte count, especially neutrophil count, hematocrit, neutrophil/lymphocyte ratio, delta neutrophil index(%), and number of ovarian twists are statistically significantly higher in patients with necrosis in the pathological examination (p<0.05).

Figure 1 shows a receiver operating characteristic curve which was constructed to select the optimal cut-off values of the DNI and NLR for the identification of necrosis in ovarian torsion cases. For the DNI value, the Area Under the Curve (AUC) was 0.902 with a 95% confidence interval of (0.77 to 1.00; p < 0.001). The optimal cut-off value of 0.70 yielded a specificity of 95.7%, sensitivity of 83.3%, a negative predictive value of 97.1%, and a positive predictive value of 83.3%. For the NLR value, AUC was 0.85 with a 95% confidence interval of (0.76 to 0.941; p < 0.001). The optimal cut-off value of 7.53 resulted in a specificity of 77%, sensitivity of 91.7%, a

Table 1. Demographic features of women diagnosed with ovarian torsion according to the type of surgery

Characteristics	Detorsion Group n=48	Oophorectomy group n=33	p value
Age (year) mean±SD	25.74±5.85	26.2±6.5	0.72
Gravidity mean±SD	0.04±0.2	0.15±0.43	0.15
BMI (kg/m²) mean±SD	23.5±3.37	24.3±3.2	0.24
Smoking +/-	4/43 % (8.5/91.5)	4/30 % (11.8/88.2)	0.71
Over enlargement (mm) mean±SD	73.6±37.1	77.5±32.2	0.62
Pain onset to surgery (hours) mean±SD	38.75±13.92	35.5215.84±0.66	0.63
Twist number (median +IQR)	2(8)	3(6)	**0.044***

*p <0.05 was considered as statistically significant
BMI, body mass index IQR: Inter Quantile Range SD:Standart deviation

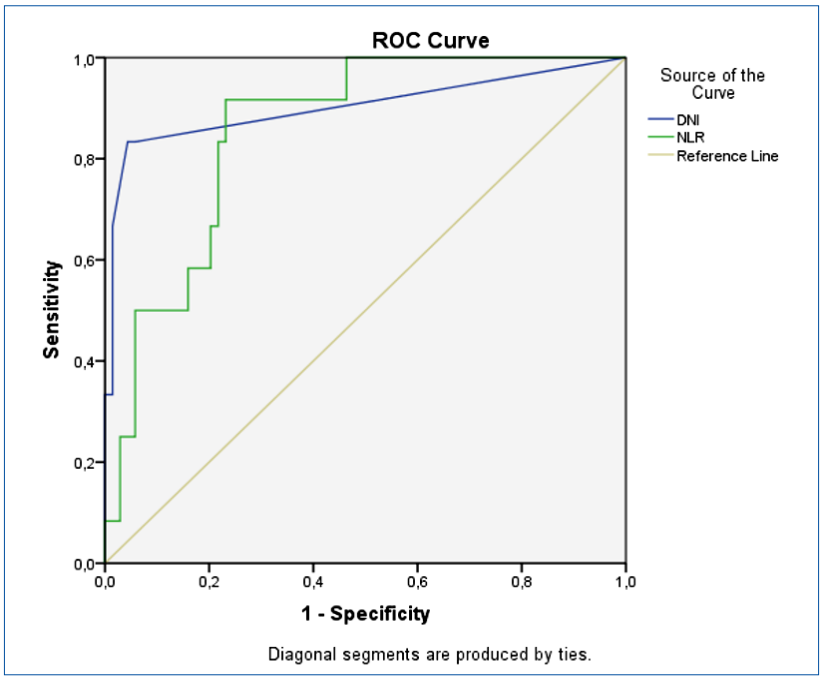

Figure 1. ROC curve for DNI and NLP in torsion cases for the identification of necrosis

Table 2. Hemogram parameters, ovarian enlargement, time to surgery and number of adnexial twists of the groups according to pathology results

Parameters	Congestion group n=21	Necrosis group n=12	p value
Leukocyte count, x10^9 /L	10.4±3.85	14.4±3.96	**0.008***
Neutrophil count, x10^9 /L	8.27±3.73	13.8±3.48	**0.0001***
Lymphocyte count, x10^9 /L	1.53±1.13	1.12±0.59	0.24
Monocyte count, x10^9 /L	0.46±0.28	0.46±0.31	0.99
Hemoglobin, g/dL	12.1±1.57	12.9±1.02	0.09
Hematocrit	36.78±3.9	39.7±2.11	**0.022***
MCV, fL	84.6±8.02	87.3±5.56	0.30
RDW	14.6±2.39	14.4±2.55	0.89
PLT, x10^9 /L	314±72	313±58	0.97
MPV	8.66±0.95	8.40±0.91	0.45
PCT	0.27±0.075	1.01±2.6	0.19
PDW, fL	53.1±8.37	50.1±5.81	0.28
NLR	9.18±9.08	15.5±8.05	**0.048***
DNI(%)	0.3±0.82	3.34±2.98	**0.0001***
PLT/MPV ratio	36.6±8.7	37.8±8.55	0.71
Over enlargment(mm)	81.2±31.8	70.8±34.6	0.38
Pain onset to surgery (hours)	1.48±0.75	1.50±0.52	0.91
Twist number (median +IQR)	3(3)	4(5)	**0.017***

*p <0.05 was considered as statistically significant
MCV, mean corpuscular volume;RDW, red cell distribution width; PLT, platelet count; PCT, plateletcrit; MPV, mean platelet volume; PDW, platelet distribution width; NLR, neutrophil/lymphocyte ratio; DNI, delta neutrophil index; IQR: Inter Quantile Range

Table 3. The area under the receiver operating characteristic curve for DNI and NLR

Variables	Cut-off	AUC ± SE	95%CI	Sensitivity %	Specivity %	PPV %	NPV %	p-value
DNI	0.70	0.902±0.65	0.77-1.0	83.3	95.7	83.3	97.1	**<0.001***
NLR	7.53	0.85± 0.047	0.76-0.94	91.7	77	39	98	**<0.001***

*p<0.05 was considered as statistically significant. AUC ± SE,Area Under the Curve±Standart error. 95% CI, Confidence Interval. PPV,Positive Predictive Value. NPV,Negative Predictive Value. NLR, neutrophil/lymphocyte ratio; DNI, delta neutrophil index; NLR, neutrophil to lymphocyte ratio

negative predictive value of 98%, and a positive predictive value of 39%. Receiver operating characteristic(ROC) curve information for NLR and DNI is presented in Table 3.

DISCUSSION

The diagnosis of ovarian torsion is difficult. Generally, the surgeon makes a certain diagnosis by visually during the operation. Although the treatment is surgical, many factors should be considered for the type of surgery. The patient's age, fertility desire, whether she is in reproductive age or not and the appearance of the ovary during surgery are among these factors (11). When the torsion occurs; the first stage is stoppage of blood flow. This is followed by hemorrhage and congestion and ends with necrosis (12,13). There is no method to detect this necrosis before and even during surgery. In this study, we aimed to evaluate the predictive power of preoperative hemogram parameters especially the DNI values in the decision of surgical approach based on its relation with the final pathology result.

Studies so far have tried to find an answer to the question of whether there is a marker that shows necrosis in ovarian torsion before or during surgery. Doppler ultrasound is tradiationally the first choice

imaging method for the diagnosis of torsion. In a prior study, which evaluated ovarian flow and correlated it with histopathologic findings, no association between the ovarian flow on ultrasound and histopathological evidence of necrosis was found (14). Another parameter that can be evaluated with ultrasound is ovarian size. Although studies have argued that ≤5 cm ovarian size may exclude the diagnosis of torsion, the relationship between size and necrosis has not been demonstrated (14,15). In our study, there was no association observed between ovarian enlargement and necrosis.

The relationship between the onset of pain until the surgery starts and necrosis was investigated, but a specific timeframe could not be given. Studies have suggested that the surgery should be performed as early as possible in women who are thought to be torsion, and that it should not be exceeded 24 hours if possible (13,16,17). In our study the onset of pain till the surgery was evaluated and there was no statistically significant difference for choosing the type of surgery between the detorsion or oophorectomy groups (p=0.062). When the histopathological results were evaluated in terms of answering the question of the presence of necrosis or congestion, it was found that onset of pain till the surgery had no statistically significant difference between study groups (p=0.91).

The relation between the number of twist and result in necrosis was also evaluated in our study. There was a statistical significant difference between the congestion and necrosis groups. As the number of rotations increased, the possibility of necrosis also increased ($p<0.05$).

Although the decision for oophorectomy is made by the surgeon's visual assessment of necrosis during the operation; the previous studies have shown that visual assessment has a low positive predictive value. Novoa et all. stated that only 16% of 33 patients, who were evaluated as visually necrotic and underwent oophorectomy, had histopathologically confirmed necrosis (14). Although there are similar studies, the American College of Obstetricians and Gynecologists (ACOG) recommends against oophorectomy regardless of the appearance of the ovary (18-20).

In a recent study with MRI, one of the advanced imaging modalities, Renganathan et al. conducted a retrospective study on 42 patients to determine whether the ultra-short optimized MRI protocol predicted ovarian necrosis. They concluded that a hypointensity score of 2 or more can diagnose necrosis with high sensitivity and specificity (21). Although the results of this study seem very satisfactory, may not be widely available because the lack of widespread use of MRI and examination costs.

In a study conducted by Mazouni et al., predictive factors for adnexal necrosis in torsion cases were investigated, but no specific predictive factors were identified (8). However, they did emphasize the significance of hyperleukocytosis, with positive and negative predictive values for adnexal necrosis at 21% and 77%, respectively. In our study, we observed similar trends; leukocyte count was significantly higher in the necrosis group ($p<0.01$).

The DNI is a marker showing the number of immature granulocytes (IGs). IGs are simple to quantify using automatic hematological analyzers and are inflammatory markers that rise after infection and inflammation. Granulocytes with polymorphonuclear neutrophils serve as the initial line of defense for the host against infectious diseases. Within 7–10 days, the progenitor cells in the bone marrow mature into segmented neutrophils. After reaching full maturity, they migrate into the peripheral blood. As a result, sepsis-related enhanced bone marrow activation is indicated by IG formation in the blood. DNI assesses the percentage of IGs in blood circulation. Researchers are investigating the DNI for sepsis severity and inflammatory processes; recently, it has begun to be investigated by some researchers in cases of ischemia and necrosis. Unal et al. found that the DNI effectively aided in the diagnosis of necrotizing pancreatitis. They also argue that the DNI is meaningful in distinguishing between complicated appendicitis and normal appendicitis (22). Another study reported significantly higher DNI levels in the diagnosis of intestinal necrosis due to irreducible hernia (23). According to Cha et al., the DNI was significantly higher during intestinal ischemia caused by strangulation (24). Similarly, Durak et al., mentioned that the DNI can be used to evaluate intestinal necrosis in mesenteric ischemia (25). In light of these findings, we sought to determine if DNI might assist the surgeon in identifying necrosis in ovarian torsion patients before the surgery. In our study, when neutrophil to lymphocyte ratio (NLR) and DNI values were evaluated with histopathological results, both levels were found remarkable higher in patients with histopathologically confirmed necrosis when compared to the patients with congestion and hemorrhage. Notably, when we established a cut-off value of 0.7 (%) for the DNI, the positive predictive value for histopathological necrosis was 83.3%, while the negative predictive value was notably higher at 97.1% ($p<0.001$). For NLR, using a cut-off value of 7.53, the positive predictive value for histopathological necrosis was 39%, with a highly reliable negative predictive value of 98% below this threshold ($p<0.001$). These findings suggest that both the DNI and the NLR with the DNI having a greater specificity and negative predictive value and the NLR having a higher sensitivity, are both capable of distinguishing between positive and negative cases for necrosis. Thus, based on our study, having both DNI and NLR values lower than the preoperative total blood count cut-off levels may serve as a guide to surgeons for the absence of necrosis during the surgical evaluation process.

This study has some limitations. It is well established that inflammatory processes have an impact on DNI and NLR. Although those with chronic co-morbidities at the time of administration were excluded from the study, it is unclear whether they had additional acute inflammatory diseases at the time of diagnosis since the study is retrospective.

Additionally, considering this study was conducted with data from a single hospital, the sample size was small. But to minimize potential biases, we investigated every patient with ovarian torsion admitted to our hospital ever since the DNI level became measurable in our hospital.

In conclusion, our study highlights the importance of the DNI, which can easily be calculated using automatic hematological analyzers, as a potential indication for ovarian necrosis in cases of torsion. It also helps the surgeon decide on the operation. While the NLR demonstrates greater sensitivity, the DNI demonstrates higher specificity and a stronger negative predictive value in determining the presence of necrosis. Establishing cut-off values for DNI and NLR can aid in distinguishing necrosis from congestion, prior to proceeding to the surgical process. Surgeons may use readings below the cut-off limits for the preoperative total blood count as helpful guidelines for determining whether necrosis is absent during surgery.

Conflict of interest statement
The authors have no conflicts of interest relevant to this article.

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