



# Can the PAN-Immune Inflammation Value Be Used as a Biomarker for Differentiating Epididymo-orchitis and Testicular Torsion in Children?

Nurcan Coskun<sup>1</sup>, Mehmet Metin<sup>2</sup>

<sup>1</sup>Hitit University Erol Olçok Training and Research Hospital, Department of Pediatric Surgery, Çorum, Türkiye

<sup>2</sup>Hitit University, Faculty of Medicine, Department of Pediatric Surgery, Çorum, Türkiye

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## Abstract

**Aim:** No study in the literature has investigated the role of the pan-immune inflammation value (PIV) in the differential diagnosis of epididymo-orchitis (EO) and testicular torsion (TT) in children. This study aims to evaluate the utility of PIV and other inflammatory indices in the differential diagnosis of EO and TT in children.

**Material and Method:** A retrospective analysis was conducted on 258 children who presented with scrotal pain between January 2019 and December 2023. Patients were divided into EO (n=187) and TT (n=71) groups, with the TT group further classified into orchiectomy (n=24) and detorsion (n=47) subgroups. The diagnostic power of hematological parameters, including derived indices such as PIV, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), in distinguishing TT from EO was investigated. Diagnostic performance was assessed using ROC analysis, and logistic regression models evaluated the predictive value of significant variables.

**Results:** TT patients exhibited significantly higher levels of white blood cells (WBC), neutrophil count, NLR, SIRI, and PIV compared to the EO group. PIV values were found to be significantly higher in the testicular detorsion group compared to the orchiectomy group. ROC analysis demonstrated weak diagnostic performance for NLR (AUC=0.580), SII (AUC=0.568), SIRI (AUC=0.599), and PIV (AUC=0.585), while WBC (AUC=0.673) and neutrophil count (AUC=0.634) showed poor performance. Multivariate logistic regression identified WBC (OR=2.52) and NLR (OR=2.6) as significant predictors of TT, with NLR values >3.39 associated with a 2.6-fold increased likelihood of TT.

**Conclusion:** Our study demonstrates that NLR and WBC, with high specificity, can predict TT, while SIRI and SII have limited diagnostic performance. Although PIV shows potential as a biomarker with varying sensitivity and specificity across different thresholds, its contribution in multivariate models appears less significant. However, it may be effective in predicting testicular viability in TT. Larger sample sizes and multicenter studies are required to further validate the clinical utility of these biomarkers.

**Keywords:** PAN-immune inflammation value, PIV, epididymo-orchitis, testicular torsion, diagnosis

## INTRODUCTION

Acute scrotum is one of the most critical pediatric emergencies, presenting with sudden-onset redness, swelling, and pain in the inguinoscrotal region, particularly in the neonatal and adolescent periods but occurring at any age (1). Testicular torsion (TT) and epididymo-orchitis (EO) are among the leading causes of acute scrotal pain (2). While TT is a surgical emergency characterized by sudden testicular blood flow impairment due to the torsion of the spermatic cord around its axis, infection and inflammation

play a primary role in the pathogenesis of EO (3). TT is most frequently confused with EO, as the similarity of symptoms between these two clinical conditions, especially in the early stages, complicates the differential diagnosis (4). Rapid confirmation or exclusion of TT is critical to preventing potential testicular loss. Accurate differentiation is vital for avoiding unnecessary surgical interventions and ensuring that TT is not overlooked (1). Delay or misdiagnosis can result in permanent ischemic damage and necrosis of the testis (1).

## CITATION

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**Corresponding Author:** Nurcan Coskun, Hitit University Erol Olçok Training and Research Hospital, Department of Pediatric Surgery, Çorum, Türkiye

**E-mail:** nurcannerguncoskun19@gmail.com

Doppler ultrasonography is a commonly used imaging modality in TT with high sensitivity (88.9%) and specificity (98.8%) (5). However, its limitations include operator dependency, preserved arterial flow in early stages, and challenges in examining prepubertal children (6). The primary reason for the limitations of Doppler ultrasonography in differentiating testicular torsion from epididymo-orchitis in prepubertal children is the thinner testicular vascular structures and lower blood flow in this age group (7). Additionally, nonspecific clinical findings in prepubertal patients and difficulty in patient cooperation contribute to diagnostic uncertainty (8). Additionally, delays in diagnosis using ultrasonography may lead to testicular loss, and international guidelines do not recommend relying solely on ultrasound for diagnosis (9). Therefore, more reliable diagnostic methods are being investigated.

Routine blood tests play a significant role in assessing inflammatory processes and early disease diagnosis. A complete blood count (CBC) is a routinely accessible laboratory test characterized by its simplicity of execution, affordability, and capacity to deliver critical hematological data, including quantitative measurements of leukocytes, lymphocytes, neutrophils, monocytes, platelets, and morphological indicators such as mean platelet volume. Ratios derived from these parameters are used as inflammation indices, aiding in the diagnosis, progression, and risk assessment of many diseases (10). Recently, indices such as the PIV have been investigated for their potential as prognostic biomarkers (11). However, there is no research in the literature investigating the role of PIV in differentiating EO from TT in children. This study evaluates the utility of PIV and other inflammatory markers in distinguishing EO from TT in pediatric patients.

## MATERIAL AND METHOD

Approval from the Hitit University Non-Interventional Research Ethics Committee was granted under decision number 2024-08 on 03.04.2024. In this study, children who presented with scrotal pain to Hitit University Erol Olçok Training and Research Hospital between January 1, 2019, and December 31, 2023, were retrospectively analysed. Patients were divided into two main groups: those diagnosed with EO and those with TT. Among the TT patients who underwent surgery, a further subdivision was made into two subgroups: patients who underwent testis detorsion and those who underwent orchiectomy. Demographic data such as age and gender, along with calculated values for PIV, systemic immune-inflammation index (SII), systemic immune-inflammation response index (SIRI), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), were compared between the groups. Given the retrospective nature of this study, to ensure the reliability of statistical evaluations, a negligible number of patients with missing laboratory records for key parameters were excluded as part of the exclusion criteria and were not included in the analyses. Since complete datasets for the variables of interest were available for all patients ultimately included in the study, no imputation techniques were used.

PIV, SII, and SIRI are composite biomarkers derived from routine blood parameters to assess systemic inflammation and immune response. PIV is calculated using the formula  $(\text{neutrophil} \times \text{monocyte} \times \text{platelet}) / \text{lymphocyte}$ , SII is determined as  $(\text{platelet} \times \text{neutrophil}) / \text{lymphocyte}$ , and SIRI is obtained by  $(\text{neutrophil} \times \text{monocyte}) / \text{lymphocyte}$ . These indices have been increasingly utilized in various inflammatory and oncological conditions due to their potential prognostic value. In this study, these inflammatory markers were calculated from complete blood count parameters and analysed to evaluate their diagnostic utility in differentiating EO from TT.

## Statistical Analysis

All data analyses were performed using SPSS statistics software (Version 22, SPSS Inc., Chicago, IL, USA) under Hitit University's licensed access. Categorical variables were expressed as counts (n) with corresponding percentages (%), and group comparisons for these variables were conducted using the chi-square test. For continuous variables, normality assumptions were verified through the Kolmogorov-Smirnov test, Shapiro-Wilk test, and visual inspections of histograms and Q-Q plots. Normally distributed data were reported as mean  $\pm$  standard deviation (SD), while non-normal data were presented as median (minimum–maximum) values. Variance homogeneity was assessed using Levene's test. Parametric comparisons between two independent groups were performed with the Student's t test, whereas the Mann-Whitney U test was applied for non-parametric data. For comparisons involving three or more independent groups, the Kruskal-Wallis test was utilized, followed by Dunn-Bonferroni post hoc analyses to identify pairwise differences when statistical significance was detected.

The diagnostic utility of laboratory biomarkers and composite indices (NLR, PLR, SII, SIRI, and PIV) in differentiating TT from EO was evaluated using receiver operating characteristic (ROC) curve analysis. Area under the curve (AUC) values with 95% confidence intervals (CIs) were calculated to quantify discriminatory performance. AUC interpretation followed established criteria: 0.9–1.0 (excellent), 0.8–0.9 (good), 0.7–0.8 (moderate), 0.6–0.7 (poor), and 0.5–0.6 (non-informative). Optimal cutoff thresholds were determined using the Youden index, with corresponding sensitivity and specificity values reported for the most robust predictors. To evaluate the relationships between newly categorized variables (determined using optimal cutoffs) and TT likelihood, univariate and multivariate logistic regression models were developed. Results were expressed as adjusted odds ratios (ORs) with 95% CIs. A two-tailed p-value  $<0.05$  defined statistical significance for all tests.

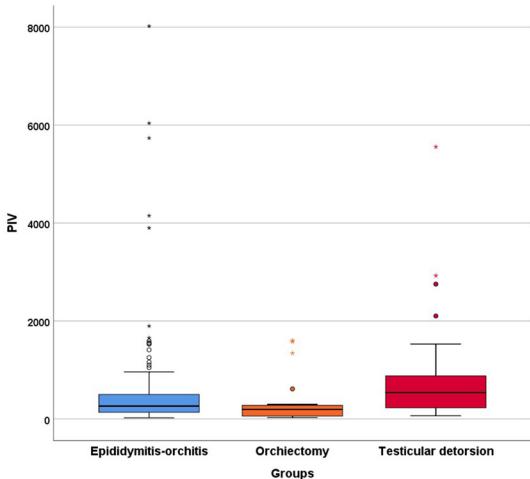
## RESULTS

Data from a total of 258 pediatric patients were analysed. The EO group consisted of 187 patients (72.5%), while the torsion group, comprising orchiectomy and testis detorsion cases, included 71 patients (27.5%). The distribution was

further subdivided into EO (n=187, 72.5%), orchiectomy (n=24, 9.3%), and testis detorsion (n=47, 18.2%). The mean age was 10.23±4.58 years (range: 0–17), and the mean hospital stay was 1.03±1.98 days (range: 0–19).

Comparisons of sociodemographic features and laboratory parameters across study groups are presented in Table 1. The torsion group had a significantly higher mean age and length of hospital stay than the EO group (P=0.001, P<0.001, respectively). No significant differences were observed for side distribution, CRP, lymphocyte, monocyte, platelet, PLR, MLR, or SII values (P>0.05). However, WBC, neutrophil count, NLR, SIRI, and PIV values were significantly higher in the torsion group (P<0.001, P=0.001, P=0.046, P=0.014, P=0.035, respectively; Table 1).

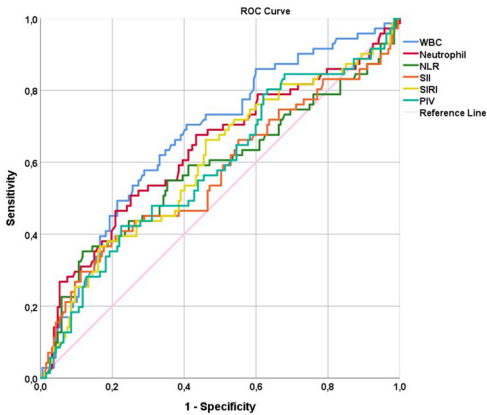
Table 2 presents the statistical findings for PIV comparisons among EO, orchiectomy, and testis detorsion groups, revealing significant differences (P<0.001). Post-hoc tests indicated that PIV values were significantly higher in the testis detorsion group compared to other groups (P<0.001 for all comparisons). No significant differences were noted between other groups (P>0.05). Figure 1 illustrates the distribution of PIV values among the groups.



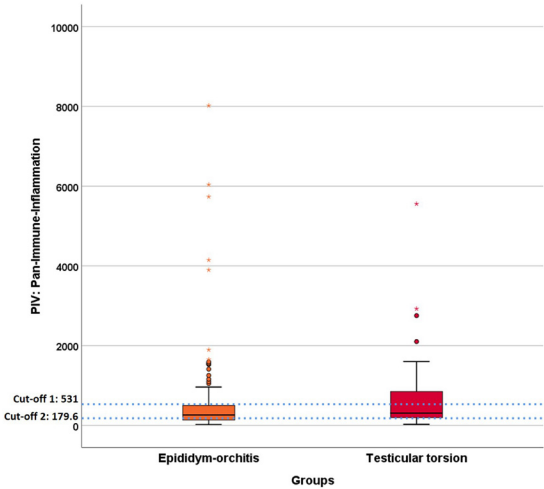
**Figure 1.** Boxplot with jitter illustrating the distribution of pan-immune-inflammation values (PIV) between epididymo-orchitis, orchiectomy and testicular detorsion groups

The findings of the ROC analysis performed to determine the success of laboratory blood values and indices in differentiating EO from TT, as well as the sensitivity and specificity values calculated using the cut-off points determined by the ROC analysis, are presented with 95% confidence intervals in Table 3. According to the ROC analysis AUC values, NLR, SII, SIRI, and PIV showed weak performance in predicting torsion (AUC=0.580, AUC=0.568, AUC=0.599, AUC=0.585, respectively), while WBC and neutrophil values exhibited poor performance (AUC=0.673, AUC=0.634; Table 2). Optimal cut-off values calculated using the Youden index were WBC 8.75, neutrophil 6.62, NLR 3.39, SII 911, SIRI 0.888, and PIV 531 and 179.6. There were two different cut-off points calculated for the PIV based on the maximum sensitivity and specificity values determined using the Youden index. Therefore, sensitivity and specificity values were calculated for both cut-off

points. According to these cut-off points, the calculated sensitivity and specificity values were 70.4% and 59.4% for WBC, 46.5% and 79.1% for neutrophil count, 35.2% and 88.2% for NLR, 36.6% and 82.4% for SII, 66.2% and 54% for SIRI, 42.3% and 77.5% for the first PIV cut-off (PIV-1), and 80.3% and 36.9% for the second PIV cut-off (PIV-2), respectively. The ROC curves plotted to evaluate the success of significant laboratory blood values and indices in distinguishing between EO and TT are presented in Figure 2. Additionally, boxplots showing the distribution of PIV values for the proposed two different cut-off points among the study groups are shown in Figure 3.



**Figure 2.** ROC curves illustrating the predictive performance of significant biomarkers in diagnosing epididymo-orchitis and testicular torsion



**Figure 3.** Boxplot with jitter illustrating the distribution of pan-immune-inflammation values (PIV) between epididymo-orchitis, and testicular torsion groups

Univariate and multivariate binary logistic regression analysis results, performed to determine the effects of laboratory blood values and indices on TT using the new categorical variables created based on the cut-off points determined by the ROC analysis, are presented in Table 4. In the univariate model, the effect of age was significant at the P<0.10 level (P=0.066). In the univariate model, WBC, neutrophil, NLR, SII, SIRI, PIV-1, and PIV-2 values were significant at the P<0.01 level (P<0.001, P<0.001, P<0.001, P=0.001, P=0.004, P=0.002, P=0.009, respectively). Since neutrophils were used in calculating the PIV index and NLR, SII, and SIRI were highly correlated with PIV (r=0.852, r=0.927, r=0.959, P<0.001, respectively), they were not

included simultaneously in the multivariate model despite being significant in the univariate model. In the model established with age, WBC, and PIV-1 index, PIV-1 was not significant (P=0.463). Similarly, PIV-2 was not significant (P=0.469) in the model with age, WBC, and PIV-2. In the multivariate model established with age, WBC, and SIRI index, SIRI was not significant (P=0.509). In the model with age, WBC, and SII index, SII was not significant (P=0.373).

In the model with age, WBC, and NLR index, age was not significant (P=0.188). Therefore, the final multivariate model was established with the WBC and NLR index, as presented in Table 4. In the multivariate model, the odds ratio (OR) for WBC was 2.52 (95% CI: 1.33–4.8), and for NLR, it was 2.6 (95% CI: 1.26–5.34). Patients with an NLR value greater than 3.39 were 2.6 times more likely to have TT compared to those with an NLR value less than 3.39 (Table 4).

| Table 1. Statistical findings for the comparison of sociodemographic characteristics and laboratory blood values between epididymo-orchitis, and testicular torsion groups                                                                                                                                                                                               |                                   |                                   |                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|-----------------------------------|------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                          | Groups                            |                                   | P values                     |
|                                                                                                                                                                                                                                                                                                                                                                          | Epididym-orchitis (n=187)         | Testicular torsion (n=71)         |                              |
| Side (right/left)                                                                                                                                                                                                                                                                                                                                                        | 100 (53.5%) /87 (46.5%)           | 34 (47.9%)/37 (52.1%)             | 0.422 <sup>a</sup>           |
| Age                                                                                                                                                                                                                                                                                                                                                                      | 10 (0-17) (9.90±4.008)            | 13 (0-17) (11.08±5.766)           | <b>0.001<sup>c</sup></b>     |
| Length of stay                                                                                                                                                                                                                                                                                                                                                           | 0 (0-19) (0.95±2.273)             | 1 (0-3) (1.24±0.746)              | <b>&lt;0.001<sup>c</sup></b> |
| CRP                                                                                                                                                                                                                                                                                                                                                                      | 3.22 (0.20-153.60) (9.07±21.24)   | 3.22 (3.05-39.90) (6.62±9.059)    | 0.926 <sup>c</sup>           |
| WBC                                                                                                                                                                                                                                                                                                                                                                      | 8.25 (2.36-25.71) (8.76±3.318)    | 10.78 (1.88-20.52) (10.66±3.498)  | <b>&lt;0.001<sup>c</sup></b> |
| Lymphocyte count                                                                                                                                                                                                                                                                                                                                                         | 2.77 (0.66-11.62) (3.16±1.701)    | 2.78 (0.66-10.13) (3.36±2.109)    | 0.947 <sup>c</sup>           |
| Neutrophil count                                                                                                                                                                                                                                                                                                                                                         | 4.14 (0.48-22.70) (4.84±3.197)    | 5.92 (0.38-17.39) (6.40±3.668)    | <b>0.001<sup>c</sup></b>     |
| Monocyte count                                                                                                                                                                                                                                                                                                                                                           | 0.62 (0.17-3.30) (0.69±0.364)     | 0.65 (0.31-1.94) (0.73±0.319)     | 0.243 <sup>c</sup>           |
| Platelet count (10 <sup>3</sup> )                                                                                                                                                                                                                                                                                                                                        | 310.1±85.34 (302 (107-517))       | 294.7±85.40 (292 (102-648))       | 0.200 <sup>b</sup>           |
| NLR                                                                                                                                                                                                                                                                                                                                                                      | 1.420 (0.064-19.824) (2.13±2.575) | 1.829 (0.193-12.56) (3.05±2.982)  | <b>0.046<sup>c</sup></b>     |
| PLR                                                                                                                                                                                                                                                                                                                                                                      | 108.8 (25.47-483.7) (119.7±62.72) | 102.5 (24.06-419.6) (116.9±69.08) | 0.367 <sup>c</sup>           |
| MLR                                                                                                                                                                                                                                                                                                                                                                      | 0.21 (0.06-1.52) (0.27±0.212)     | 0.22 (0.06-1.46) (0.28±0.213)     | 0.253 <sup>c</sup>           |
| SII                                                                                                                                                                                                                                                                                                                                                                      | 414 (27.47-7097) (636.4±792.1)    | 439.8 (43.06-3268) (854.1±815.7)  | 0.090 <sup>c</sup>           |
| SIRI                                                                                                                                                                                                                                                                                                                                                                     | 0.86 (0.05-23.40) (1.69±2.99)     | 1.13 (0.10-16.63) (2.21±2.65)     | <b>0.014<sup>c</sup></b>     |
| PIV                                                                                                                                                                                                                                                                                                                                                                      | 261.9 (22.9-8019) (515.5±943.3)   | 309.9 (25.8-5555) (639.4±835.1)   | <b>0.035<sup>c</sup></b>     |
| <sup>a</sup> Chi-square test, <sup>b</sup> Student's t test, <sup>c</sup> Mann-Whitney U test, CRP: C-reactive protein, WBC: white blood cell count, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, PIV: pan-immune-inflammation value, M: male, F: female |                                   |                                   |                              |

| Table 2. Statistical findings for the comparison of PIV values between epididymo-orchitis, orchiectomy and testicular detorsion groups |                                   |                           |                                    |                  |                       |
|----------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|---------------------------|------------------------------------|------------------|-----------------------|
|                                                                                                                                        | Epididymo-orchitis (1)<br>(n=187) | Orchiectomy (2)<br>(n=24) | Testicular detorsion (3)<br>(n=47) | P value          | Post-hoc P value      |
| PIV                                                                                                                                    |                                   |                           |                                    |                  |                       |
| Median                                                                                                                                 | 261.8                             | 195.6                     | 537.3                              |                  | 1-2: 0.224            |
| (min-max)                                                                                                                              | (22.88-8019)                      | (25.84-1601)              | (63.94-5555)                       | <b>&lt;0.001</b> | <b>1-3: &lt;0.001</b> |
| (mean±SD)                                                                                                                              | (515.5±943.2)                     | (340.7±470.6)             | (791.8±938.1)                      |                  | <b>2-3 &lt;0.001</b>  |
| Kruskal-Wallis test following Dunn-Bonferroni post-hoc tests, PIV: pan-immune-inflammation value                                       |                                   |                           |                                    |                  |                       |

| Table 3. Results of ROC analysis for laboratory blood values and inflammatory indices in distinguishing testicular torsion from Epididymo-orchitis, with sensitivity and specificity values based on cut-off points                                                                                   |       |             |             |         |                   |                   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|-------------|-------------|---------|-------------------|-------------------|
| Variables                                                                                                                                                                                                                                                                                             | AUC   | 95% CI      |             | Cut-off | Sensitivity       | Specificity       |
|                                                                                                                                                                                                                                                                                                       |       | Lower bound | Upper bound |         |                   |                   |
| WBC                                                                                                                                                                                                                                                                                                   | 0.673 | 0.600       | 0.746       | 8.75    | 70.4% (58.2-80.4) | 59.4% (51.9-66.4) |
| Neutrophil count                                                                                                                                                                                                                                                                                      | 0.634 | 0.553       | 0.715       | 6.62    | 46.5% (34.7-58.6) | 79.1% (72.5-84.6) |
| NLR                                                                                                                                                                                                                                                                                                   | 0.580 | 0.495       | 0.666       | 3.39    | 35.2% (24.5-47.5) | 88.2% (82.5-92.3) |
| SII                                                                                                                                                                                                                                                                                                   | 0.568 | 0.484       | 0.653       | 911     | 36.6% (25.7 - 49) | 82.4% (76 - 87.4) |
| SIRI                                                                                                                                                                                                                                                                                                  | 0.599 | 0.519       | 0.679       | 0.888   | 66.2% (53.9-76.7) | 54% (46.6-61.3)   |
| PIV-1                                                                                                                                                                                                                                                                                                 | 0.585 | 0.505       | 0.665       | 531     | 42.3% (30.8-54.5) | 77.5% (70.8-83.2) |
| PIV-2                                                                                                                                                                                                                                                                                                 |       |             |             | 179.6   | 80.3% (68.8-88.4) | 36.9% (30-44.3)   |
| CRP: C-reactive protein, WBC: white blood cell count, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, PIV: pan-immune-inflammation value, AUC: area under curve, CI: confidence interval |       |             |             |         |                   |                   |

| Table 4. Results of univariate and multivariate binary logistic regression analyses to evaluate the effect of risk factors in distinguishing testicular torsion from epididymo-orchitis                                                                                                                                 |            |                     |                            |                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|---------------------|----------------------------|---------------------|
|                                                                                                                                                                                                                                                                                                                         | Univariate |                     | Multivariate (Final model) |                     |
|                                                                                                                                                                                                                                                                                                                         | P values   | OR (CI 95%)         | P values                   | OR (CI 95%)         |
| Age                                                                                                                                                                                                                                                                                                                     | 0.066      | 1.061 (0.996-1.131) | ns                         |                     |
| WBC ≥8.75                                                                                                                                                                                                                                                                                                               | <0.001     | 3.477 (1.933-6.256) | 0.005                      | 2.521 (1.325-4.798) |
| Neutrophil ≥6.62                                                                                                                                                                                                                                                                                                        | <0.001     | 3.296 (1.836-5.914) | ni                         |                     |
| NLR ≥3.39                                                                                                                                                                                                                                                                                                               | <0.001     | 4.076 (2.108-7.883) | 0.010                      | 2.596 (1.262-5.340) |
| SII ≥911                                                                                                                                                                                                                                                                                                                | 0.001      | 2.696 (1.462-4.972) | ni                         |                     |
| SIRI ≥0.888                                                                                                                                                                                                                                                                                                             | 0.004      | 2.300 (1.301-4.065) | ni                         |                     |
| PIV-1 ≥531                                                                                                                                                                                                                                                                                                              | 0.002      | 2.526 (1.410-4.525) | ni                         |                     |
| PIV-2 ≥179.6                                                                                                                                                                                                                                                                                                            | 0.009      | 2.381 (1.236-4.587) | ni                         |                     |
| Multivariate model: Nagelkerke R Square=0.136, Classification accuracy: 74%                                                                                                                                                                                                                                             |            |                     |                            |                     |
| Values below P<0.05 were shown bold, ni: not included, ns: not significant (P>0.05); WBC: white blood cell count, NLR: neutrophil-to-lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammatory response index, PIV: pan-immune-inflammation value, OR: odds ratio, CI: confidence interval |            |                     |                            |                     |

DISCUSSION

TT accounts for 10–15% of acute scrotal diseases in children and results in an orchiectomy rate of 42% among patients undergoing surgery for TT (12). Rapid and accurate diagnosis of TT is critical (13). However, TT must be distinguished from other conditions that can cause acute scrotal pain, particularly EO (14). The diagnosis of TT primarily relies on clinical symptoms, physical examination, and color Doppler ultrasonography (15). Scrotal color Doppler ultrasonography is an effective method for diagnosing TT, with sensitivity (88.9%) and specificity (98.8%) (5). However, in cases of early or partial torsion, as well as atypical presentations that may be influenced by the operator’s subjective assessment, there is a risk of misdiagnosis or missed diagnosis (16). In addition to operator dependency, it has disadvantages such as limited accessibility and delays in emergencies. Preparation for surgery and the duration of the operation may also narrow the critical therapeutic window for testicular salvage.

The European Association of Urology (EAU) pediatric urology guidelines recommend manual detorsion without anesthesia in patients with testicular torsion (TT). Despite successful manual detorsion, the guidelines emphasize the necessity of emergency surgical intervention and contralateral testicular fixation within the first 24 hours (17). A recent study evaluating the approaches of pediatric surgeons and urologists in Türkiye reported that only 14.7% of participants performed manual detorsion, while 70.5% never attempted it, and 14.7% considered it only when immediate surgery was unavailable. Additionally, among those who performed manual detorsion, 71.4% still proceeded with surgical intervention within 24 hours. The low utilization of manual detorsion may be attributed to concerns about incomplete detorsion, the risk of recurrent torsion, and delayed definitive management (18).

In recent years, it has been reported that hematological parameters (MPV, PLR, NLR, PLT, and leukocytes) at admission may differ between patients with TT and EO (19-24). These parameters hold potential as diagnostic

markers for TT. In our study, we investigated the usability of hematological parameters and systemic inflammatory indices in distinguishing between TT and EO in children. Notably, our study is original in that it is the only study in the literature to examine the diagnostic value of PIV in this context.

Our findings show similarities with those of Yılmaz et al. (2022) but also exhibit some differences. In the study by Yılmaz et al. (2022), which included pediatric and adult patients over the age of 12, the AUC values were reported as good for NLR and SIRI and poor for PLR in differentiating TT (22). In our study, PLR was found to be insignificant, and the performance of NLR, SII, and SIRI indices in distinguishing TT was determined to be poor. When comparing the sensitivity and specificity values of NLR with the study by Yılmaz et al. (2022), our study achieved higher specificity but lower sensitivity. While the OR for NLR was reported as 3.27 in the study by Yılmaz et al., the OR for NLR in our study was calculated as 4.076 (95% CI: 2.1–7.9) in the univariate model and 2.6 (95% CI: 1.26–5.34) in the multivariate model. This finding supports that, despite the low sensitivity (35.2%) and high specificity (88.2%) of NLR in our study, it remains a significant predictor in the multivariate model and may be an important marker for TT.

In the study by Yiğman et al. (2024) examining hematological parameters in the differential diagnosis of TT and EO in adult patients, WBC, neutrophil, and platelet levels were reported as insignificant, whereas lymphocyte, monocyte, eosinophil, MPV, NLR, and PLR levels were significant, with AUC values ranging from poor to weak (23). In our study, lymphocyte, monocyte, and platelet levels were found to be insignificant in distinguishing TT from EO, while NLR, SII, SIRI, and PIV indices were significant at a poor level, and WBC and neutrophil levels showed weak significance. Unlike Yiğman et al.’s findings, our study identified WBC as a significant marker for distinguishing TT, and consistent with their findings, the NLR results showed similar AUC values and cut-off points. In logistic regression analyses, Yiğman et al. reported only MPV as significant in their

multivariate model (OR 1.85, 95% CI: 1.33–2.57), whereas in our study, WBC (OR 2.52, 95% CI: 1.33–4.8) and NLR (OR 2.6, 95% CI: 1.26–5.34) were significant predictors. These results suggest that WBC and NLR could also be considered important predictors of TT in children.

In the meta-analysis conducted by Zhu et al. (2019), it was reported that parameters such as NLR and PLT showed significant differences in distinguishing TT from EO, whereas no significant differences were found for WBC, MPV, and PLR between TT and EO patients (24). The pooled results from the meta-analysis indicated that TT patients had lower NLR compared to EO patients (WMD=−1.66, 95% CI=−3.25 to −0.06,  $p=.042$ ; SMD=−0.26, 95% CI=−0.51 to −0.02,  $p=.036$ ) and lower PLT (WMD=−27.39, 95% CI=−48.03 to −6.75,  $p=.009$ ; SMD=−0.31, 95% CI=−0.55 to −0.07,  $p=.011$ ). Similarly, in our study, we found that NLR values were significant in distinguishing TT in children; however, in contrast, TT patients in our study had higher NLR values. The finding that PLR did not show a significant difference in diagnosing TT aligns with Zhu et al. (2019).

In the study by Yucel et al. (2019), which included children over 12 years old and adults, NLR and PLR were found to be significant at good and moderate levels, respectively, in distinguishing TT from EO (4). Similar to the findings of Yucel et al. (2019), our study also calculated the NLR cut-off as 3.39. However, in our study, the AUC and sensitivity values were lower in children. The specificity values, on the other hand, were calculated to be very high, consistent with the study by Yucel et al. (2019).

In our study, we also observed that the PIV index showed high specificity (77.5%) at the PIV-1 cut-off point in distinguishing TT, but with low sensitivity. This finding suggests that when high, it is useful in confirming testicular torsion (TT), as false positives are rare. However, its low sensitivity suggests that PIV alone cannot reliably exclude TT, and additional diagnostic tools (e.g. Doppler ultrasonography, clinical assessment) are necessary in cases with low PIV values. At the PIV-2 cut-off point, however, it showed high sensitivity (80.3%) but with low specificity. These findings suggest that PIV may be a potential biomarker when distinguishing either EO or TT alone. However, the fact that PIV was not significant in our multivariate model indicates that it provides limited contribution when used alongside other biomarkers. Additionally, in our study, PIV values were significantly higher in the testis detorsion group compared to the orchiectomy group, suggesting that it may be an effective marker for predicting testicular viability in TT.

The decision between orchiectomy and testicular preservation in testicular torsion (TT) remains a matter of debate, primarily due to the lack of objective criteria to determine testicular viability. Factors such as symptom duration, degree of torsion, ischemic appearance, and intraoperative findings are commonly used in clinical decision making. However, a recent multicenter study re-evaluating orchiectomy specimens using histopathologic

classification revealed that some cases with severe perioperative findings, late hospital admission or high degree of torsion still exhibited reversible histopathologic changes. These findings suggest that testicular viability assessment based solely on clinical and perioperative parameters may not always be reliable (25). In this context, the significant difference in PIV values between the detorsion and orchiectomy groups in our study suggests that PIV may serve as a complementary marker in assessing testicular viability and guiding surgical decision-making in TT cases.

In conclusion, this study highlights the diagnostic value of biomarkers such as NLR, WBC, and PIV in distinguishing TT and EO. However, it also reveals the limited effectiveness of the SIRI and SII indices and underscores the need for further validation in studies with larger sample sizes.

One limitation of this study is its single-center design. However, the use of a 5-year sample from a single center, covering the period from 2019 to 2023, can be seen as a strength. It provides depth and consistency to the study by ensuring more homogeneous data from the same hospital conditions. This approach can serve as a foundation for future multi-center studies.

## CONCLUSION

This study emphasizes the diagnostic value of biomarkers such as NLR, WBC, and PIV in distinguishing TT and EO in children. Our findings suggest that NLR and WBC, especially with high specificity, can serve as important predictors for TT, while indices such as SIRI and SII demonstrate limited diagnostic performance. Although PIV shows potential as a biomarker with varying sensitivity and specificity across different thresholds, its contribution appears less significant in multivariate models. However, it can be considered an effective biomarker for predicting testicular viability in TT. To enhance the clinical utility of these biomarkers, further validation through larger sample sizes and multicenter studies is required.

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