

## Mean platelet volume is the most valuable hematologic parameter in differentiating testicular torsion from epididymitis within the golden time

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**Background:** We aimed to assess the diagnostic value of hematologic parameters in the differential diagnosis of testicular torsion and epididymitis within and after the golden time.

**Methods:** We retrospectively reviewed the records of 250 patients aged <25 years who were diagnosed with epididymitis (n=119) or testicular torsion (n=131). The characteristics and hematologic parameters of patients in the two groups were analyzed. Receiver operating characteristic (ROC) curves were used to assess the validity of hematologic parameters as differential diagnostic tools with respect to the golden time (defined as 6 h of symptom duration). Further, we evaluated the predictive factors associated with orchiectomy in patients with testicular torsion.

**Results:** The mean patient age was 14.4 years. Among patients with testicular torsion, 91.40% (53 of 58) underwent detorsion and orchiopexy within the golden time, whereas only 27.40% (20 of 73) of the affected testes were preserved after the golden time. Within the golden time, mean platelet volume (MPV) seemed to be the most valuable hematologic parameter [area under the curve (AUC) 0.855, 95% confidence interval (CI): 0.778–0.932]. In a multivariate analysis, symptom duration (symptoms beyond the golden time) was associated with orchiectomy in patients with testicular torsion.

**Conclusions:** MPV showed the greatest hematologic value in the early stage of testicular torsion and epididymitis, suggesting its potential use for the differential diagnosis of these two conditions within the golden time.

Keywords: Diagnosis; epididymitis; hematologic tests; mean platelet volume (MPV); spermatic cord torsion

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## Introduction

The onset of unilateral scrotal pain is commonly caused by acute testicular torsion or epididymitis (1). The annual incidence of testicular torsion has been reported as 1 per 4,000 males by age 25 years, however, a recent study reported as 3.8 per 100,000 males younger than 18 years (2). Testicular torsion is a surgical emergency requiring prompt intervention. Several studies have reported the impact of testicular torsion on the function of the affected testis and the possibility of damage to the contralateral testis (3). The duration of symptoms is essential for the prognosis of testicular torsion. The risk rate of testicular loss is approximately 5%, 20%, 40%, 60%, 80%, and 90% at 0-6, 7-12, 13-18, 19-24, >24, and >48 h after the onset of pain, respectively (4). Prompt diagnosis of testicular torsion is crucial to the preservation of the affected testis. However, clinical overlap in symptoms and physical examination findings may preclude the differential diagnosis between testicular torsion and epididymitis. Furthermore, the evaluation of an acute scrotum, including ultrasonography, could be challenging owing to various situations (5,6), and there may be differences between doctors in how ultrasound is performed and in interpreting the results.

Complete blood count (CBC) evaluation is relatively inexpensive and included in the routine biochemical evaluation. Moreover, the results are usually available within 30 min. Although analyzed along with other CBC indices, several hematologic parameters are often overlooked by clinicians. Recent studies have reported the possible predictive role of hematologic parameters in patients with testicular torsion and epididymitis (7,8). However, to our knowledge, there has been no report about the role of hematologic parameters in differentiating testicular torsion from epididymitis according to symptom duration, especially within the golden time.

Hence, in the present study, we aimed to investigate the diagnostic value of hematologic parameters in the differential diagnosis of testicular torsion and epididymitis within the golden time. In addition, we also aimed to evaluate the predictive factors associated with orchiectomy in patients with testicular torsion. We present the following article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/ view/10.21037/tau-21-1112/rc).

#### **Methods**

#### Patients and diagnosis

This was a retrospective cohort study conducted at the urologic department of Chonnam National University Hospital between January 2008 and December 2020. The study was performed in accordance with the Declaration of Helsinki (as revised in 2013) and the Ethical Guidelines for Clinical Studies. The study protocol was reviewed and approved by the institutional review board of Chonnam National University Hwasun Hospital (approval No. CNUHH-2020-160) and individual consent for this retrospective analysis was waived.

Patients aged <25 years diagnosed with testicular torsion or epididymitis were enrolled in the study (Figure 1). The following patients were excluded from the study: patients who had been diagnosed with hematologic diseases, chronic kidney diseases, neurogenic voiding dysfunction, or urethral abnormalities; patients who were taking any medications; and patients who were diagnosed with appendage torsion and other infectious diseases at the time of presentation. A total of 250 patients were enrolled; of these patients, 131 were diagnosed with testicular torsion, and 119 with epididymitis. All patients underwent physical examination and color Doppler ultrasonography. Testicular torsion was defined as twisting of the spermatic cord detected on scrotal exploration. Epididymitis was diagnosed on the basis of the findings of physical examination and scrotal exploration or color Doppler ultrasonography, as well as according to clinical findings such as localized epididymal enlargement, tenderness, increased epididymal blood flow, and intact testicular blood flow, compared with the contralateral side.

# Assessments of clinical characteristics and hematologic parameters

The patients' clinical characteristics, including age, laterality, symptom duration, and seasonality, were evaluated. Biochemical evaluation and ultrasonography were performed at the time of visit. We evaluated the following CBC parameters: hemoglobin (Hgb) level, mean corpuscular volume (MCV), white blood cell (WBC) count, platelet count, neutrophil count, lymphocyte count, monocyte count, platelet distribution width (PDW), mean platelet volume (MPV), neutrophil ratio, lymphocyte ratio,

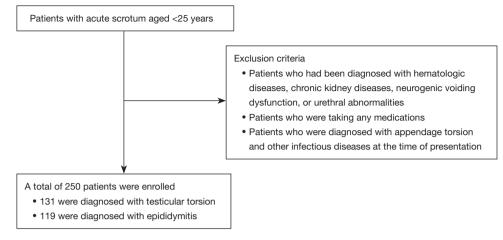


Figure 1 A flow diagram of the study.

monocyte ratio, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR).

The patients' characteristics and CBC parameters were compared between the two groups (epididymitis group and testicular torsion group). The golden time was defined as within 6 h of symptom duration, and receiver operating characteristic (ROC) curves were used to assess the validity of hematologic parameters as differential diagnostic tools according to symptom duration. Among the various CBC parameters, the predictive hematologic parameters [area under the curve (AUC) >0.6] for the differential diagnosis of testicular torsion from epididymitis were further evaluated according to symptom duration. Further, we evaluated the predictive factors associated with orchiectomy in patients with testicular torsion before 24 h of symptom duration.

## Statistical analysis

Statistical analyses were performed using SPSS software for Windows (version 25.0; SPSS Inc., Chicago, IL, USA). All data were analyzed in terms of means  $\pm$  standard deviations. Comparisons between groups were performed using an independent-samples *t*-test for continuous variables and a chi-square test for categorical variables. ROC curve analysis was performed to identify the optimal cutoff values of hematologic parameters. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using standard methods. Values of P<0.05 were considered statistically significant.

## Results

The clinical and hematologic parameters of the testicular torsion and epididymitis groups are shown in Table 1. The mean patient age was 14.4±5.3 years, and the symptom duration was 44.4±59.5 h. The percentage of patients who arrived at the hospital within 6 h of symptom duration was 41.6% (104 of 250). The two groups showed no significant differences in age, laterality, symptom duration, seasonality, Hgb level, platelet count, WBC count, monocyte count, lymphocyte count, and MCV. However, neutrophil count, NLR, PLR, neutrophil ratio, and MPV were significantly higher in the testicular torsion group than in the epididymitis group. PDW, monocyte ratio, and lymphocyte ratio were significantly higher in the epididymitis group than in the testicular torsion group. Among patients with testicular torsion, 91.4% (53 of 58) underwent detorsion and orchiopexy within 6 h of symptom duration, whereas only 27.4% (20 of 73) of the affected testes were preserved after 6 h of symptom duration.

We divided the patients into two groups (within 6 h and after 6 h of symptom duration) to compare the hematologic parameters between patients with epididymitis and patients with testicular torsion according to symptom duration (*Table 2*). We found no significant differences in WBC count, lymphocyte count, monocyte count, and MCV between the epididymitis and testicular torsion groups regardless of symptom duration. Within 6 h of symptom duration, Hgb level (P=0.029), MPV (P=0.001), neutrophil ratio (P=0.005), NLR (P=0.001), and PLR (P=0.008) were

Table 1 Comparison of clinical and hematologic parameters between the testicular torsion and epididymitis groups

Variables	Epididymitis (n=119)	Testicular torsion (n=131)	P value	
Age (years)	14.6±6.1	14.7±4.3	0.291	
Laterality (%)			0.059	
Right	58 (48.7)	57 (43.5)		
Left	57 (47.9)	74 (56.5)		
Both	4 (3.4)	0 (0)		
Symptom duration (h)	46.8±50.1	42.4±66.7	0.598	
Within 6 h (%)	46 (38.7)	58 (44.3)	0.368	
Seasonality (%)			0.495	
Spring	34 (28.6)	38 (29.0)		
Summer	29 (24.4)	22 (16.8)		
Autumn	20 (16.8)	26 (19.8)		
Winter	36 (30.3)	45 (34.4)		
WBC count (×10³/µL)	11.3±21.1	10.9±2.9	0.810	
Neutrophil count (×10³/µL)	6.1±4.1	7.7±3.2	0.001	
Hemoglobin level (g/dL)	14.0±1.3	14.2±1.3	0.229	
Platelet count (×10³/µL)	272.2±60.7	252.7±629	0.002	
Lymphocyte count (×10³/µL)	2.6±1.0	2.7±6.1	0.847	
Monocyte count (×10³/µL)	0.7±0.3	0.7±0.3	0.700	
PDW (fL)	13.8±5.8	11.5±2.2	0.001	
MPV (fL)	8.5±1.2	9.8±0.9	0.001	
MCV (fL)	84.9±5.3	84.7±5.8	0.740	
Neutrophil ratio (%)	59.9±13.6	69.6±15.0	0.001	
Lymphocyte ratio (%)	30.2±12.5	22.0±12.3	0.001	
Monocyte ratio (%)	7.0±2.2	6.1±2.4	0.004	
NLR (%)	3.2±4.6	4.8±3.9	0.003	
PLR (%)	121.0±56.1	141.8±82.5	0.022	

WBC, white blood cell; PDW, platelet distribution width; MPV, mean platelet volume; MCV, mean corpuscular volume; NLR, neutrophil-tolymphocyte ratio; PLR, platelet-to-lymphocyte ratio; fL, femtoliter.

higher, whereas platelet count (P=0.001), lymphocyte ratio (P=0.003), and monocyte ratio (P=0.026) were lower in the testicular torsion group than in the epididymitis group. After 6 h of symptom duration, neutrophil count (P=0.006), MPV (P=0.001), and neutrophil ratio (P=0.001) were higher, whereas PDW (P=0.001) and lymphocyte ratio (P=0.001) were significantly lower in the testicular torsion group than in the epididymitis group.

The diagnostic performance of the hematologic

parameters for the differential diagnosis regardless of symptom duration is summarized in Table S1. Among the various CBC parameters, WBC count, neutrophil count, neutrophil ratio, MPV, and NLR were predictive (AUC >0.6) of the differential diagnosis of testicular torsion from epididymitis regardless of symptom duration. The AUC value of WBC count, neutrophil count, neutrophil ratio, NLR, and MPV was 0.648 [95% confidence interval (CI): 0.597–0.716], 0.682 (95% CI: 0.615–0.750), 0.700 (95%

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Table 2 Comparison of hematologic parameters between the testicular torsion and epididymitis groups according to 6 h of symptom duration

	Within 6 h of symptom duration (n=104)			After 6 h o	After 6 h of symptom duration (n=146)		
Variables	Epididymitis (n=46)	Testicular torsion (n=58)	P value	Epididymitis (n=73)	Testicular torsion (n=73)	P value	
WBC count (×10 <sup>3</sup> /µL)	10.15±2.97	10.78±3.38	0.324	12.10±26.82	11.00±2.53	0.726	
Neutrophil count (×10 <sup>3</sup> /µL)	6.40±2.94	7.78±3.91	0.043	5.97±4.66	7.72±2.55	0.006	
Hemoglobin level (g/dL)	13.88±1.30	14.43±1.22	0.029	14.05±1.30	13.99±1.38	0.786	
Platelet count (×10 <sup>3</sup> /µL)	283.37±61.96	242.48±64.53	0.001	274.99±60.07	262.55±60.65	0.215	
Lymphocyte count (×10 <sup>3</sup> /µL)	2.93±1.03	3.37±9.11	0.745	2.42±1.00	2.22±1.03	0.226	
Monocyte count (×10 <sup>3</sup> /µL)	0.62±0.23	0.56±0.28	0.268	0.68±0.35	0.75±0.36	0.176	
PDW (fL)	13.11±6.45	11.64±2.28	0.111	14.24±5.27	11.46±2.22	0.001	
MPV (fL)	8.58±1.19	10.11±0.97	0.001	8.53±1.16	9.57±0.81	0.001	
MCV (fL)	84.83±4.74	85.11±4.63	0.768	84.95±5.70	84.33±6.56	0.54	
Neutrophil ratio (%)	60.76±12.80	69.35±17.80	0.005	59.33±14.18	69.85±12.37	0.001	
Lymphocyte ratio (%)	30.40±11.70	22.62±14.05	0.003	30.12±12.98	21.46±10.77	0.001	
Monocyte ratio (%)	6.19±1.77	5.33±2.04	0.026	7.51±2.35	6.82±2.42	0.081	
NLR (%)	2.57±1.73	5.17±4.80	0.001	3.57±5.69	4.44±2.89	0.247	
PLR (%)	106.20±35.51	141.37±90.19	0.008	130.34±64.37	142.22±76.38	0.311	

WBC, white blood cell; PDW, platelet distribution width; MPV, mean platelet volume; MCV, mean corpuscular volume; NLR, neutrophil-tolymphocyte ratio; PLR, platelet-to-lymphocyte ratio; fL, femtoliter.

CI: 0.634–0.766), 0.686 (95% CI: 0.620–0.753), and 0.803 (95% CI: 0.749–0.858), respectively. These hematologic parameters were further evaluated for their role in differential diagnosis according to symptom duration.

The ROC curves of hematologic parameters (WBC count, neutrophil count, neutrophil ratio, MPV, and NLR) within and after the golden time are shown in Figure 2. Within the golden time of 6 h, MPV seemed to be the most valuable hematologic parameter (AUC 0.855, 95% CI: 0.778-0.932, cutoff value 9.35 fL, sensitivity 80.0%, specificity 76.1%, PPV 82.5, NPV 72.9). The AUC value of WBC count, neutrophil count, neutrophil ratio, and NLR was 0.565 (95% CI: 0.457-0.672), 0.631 (95% CI: 0.527-0.735), 0.695 (95% CI: 0.598-0.793), and 0.678 (95% CI: 0.579–0.778), respectively. After the golden time of 6 h, the AUC value of WBC count, neutrophil count, neutrophil ratio, and MPV was 0.698 (95% CI: 0.610-0.786), 0.726 (95% CI: 0.640-0.812), 0.706 (95% CI: 0.618-0.795), 0.758 (95% CI: 0.680-0.836), and 0.700 (95% CI: 0.611-0.789), respectively.

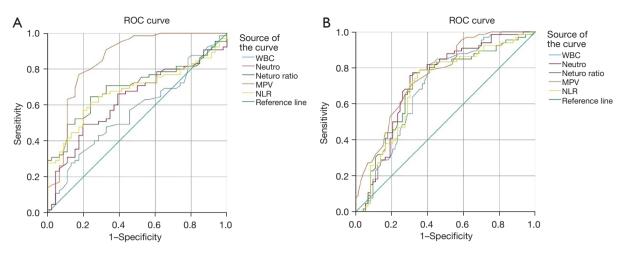
The predictive factors associated with orchiectomy before 24 h of symptom duration in patients with testicular

torsion are summarized in *Table 3*. In the univariate analysis, age (P=0.015), symptom duration (P=0.001), WBC count (P=0.033), neutrophil count (P=0.035), Hgb (P=0.046), monocyte count (P=0.036), and MPV (P=0.043) were significantly associated with orchiectomy in patients with testicular torsion. In the multivariate analysis, only symptom duration (P=0.020) was significantly associated with orchiectomy in patients with testicular torsion.

## Discussion

In the present study, among various hematologic parameters, MPV showed the greatest diagnostic performance for differentiating testicular torsion from epididymitis during the golden time. In addition, neutrophil count, neutrophil ratio, and NLR could be useful parameters for the diagnosis of testicular torsion within the golden time. These results would be a useful reference for physicians dealing with patients aged <25 years with an acute scrotum in the early stage.

Most cases of acute scrotal pain are caused by testicular torsion or epididymitis (1). The treatment methods and



**Figure 2** Receiver operator characteristic curves of hematologic parameters (leucocyte, neutrophil, neutrophil ratio, MPV, NRL) within 6 hours (A, n=104) and after 6 hours (B, n=146) of symptom duration. (A) Within 6 hours of symptom duration (B) Over 6 hours of symptom duration. ROC, receiver operating characteristic; WBC, white blood cell; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio.

prognosis differ between epididymitis and testicular torsion. Antibiotics and conservative treatment are required for epididymitis, whereas immediate surgical treatment is required in the case of testicular torsion (2,9). The golden time for testicular torsion is known to be within 6 h of symptom onset, and the testicular salvage rate decrease to 50% if symptoms are present for more than 12 hours, and are typically less than 10% if symptom duration is 24 hours or more (2,10). Therefore, rapid diagnosis and treatment are required in patients with acute scrotal pain. However, the diagnosis and treatment are often delated for various reasons (5,6). Clinical overlap in symptoms and physical examination findings may preclude the differential diagnosis between testicular torsion and epididymitis (11). Therefore, recently, several studies were conducted on the rapid differential diagnosis of testicular torsion and epididymitis (8,12,13).

CBC examination is relatively inexpensive, and the results are usually available within 30 min. In addition, because blood tests, which include CBC evaluation, is a part of preoperative or admission examinations, it is routinely performed in patients with an acute scrotum. A few studies have been performed on the usefulness of hematologic parameters for the differential diagnosis of testicular torsion and epididymitis (8,12,13). However, most of them were small-scale studies, and no study identified which factors are the most important within the golden time.

A recent study reported that WBC count is important

for the differential diagnosis between testicular torsion and epididymitis (14). Similarly, in our study, WBC count showed meaningful diagnostic value regardless of symptom duration; however, its diagnostic performance was not consistent within the golden time. Epididymitis can cause inflammatory reactions, and Testicular torsion can cause both inflammatory resections and ischemic reactions of blood vessels (15,16). Therefore, the WBC count could be increased in both testicular torsion and epididymitis, however, there could be a difference in the degree of increasing to differentiate between the two diseases. Neutrophils and monocytes are subtypes of WBCs and are also known to be associated with inflammation. In the case of Monocytes, there have been reported to play a role in the post-ischemic process (14). NLR is also an inflammatory marker known to increase with the progression of the inflammatory reaction (17). Based on these findings, neutrophil count, lymphocyte count, monocyte count, and NLR were found to significantly differ between patients with testicular torsion and controls (18). Also, several studies have shown that NLR could be a useful parameter for the discrimination of patients with testicular torsion from a healthy group and are a significant factor affecting testicular salvage within 12 h of symptom duration in patients with testicular torsion (7,19). Similarly, in our study, neutrophil count, monocyte count, and NLR differed between the testicular torsion and epididymitis groups. Neutrophil count and NLR showed a predictive diagnostic value regardless of

Table 3 Predictive facto	ors associated with	n orchiectomy in	patients with	testicular torsion

Variable –	Univariate analy	Multivariate ana	Multivariate analysis		
	OR (95% CI)	P value	OR (95% CI)	P value	
Age	0.825 (0.71–0.96)	0.015	0.81 (0.64–1.03)	0.082	
Laterality					
Right	Reference				
Left	2.242 (0.76–6.65)	0.145	2.558 (0.55–12.01)	0.234	
Symptom duration	1.165 (1.08–1.25)	0.001	1.21 (1.03–1.43)	0.020	
Within 6 h	Reference				
After 6 h	8.106 (2.52–26.04)	0.001	1.09 (0.10–12.38)	0.023	
WBC count	1.21 (1.02–1.44)	0.033	0.92 (0.36–2.36)	0.858	
Neutrophil count	1.18 (1.01–1.38)	0.035	1.31 (0.47–3.67)	0.606	
Hemoglobin level	0.68 (0.47–0.99)	0.046	0.80 (0.37–1.70)	0.555	
Platelet count	1.00 (0.99–1.01)	0.630			
Lymphocyte count	0.90 (0.55–1.47)	0.660			
Monocyte count	6.10 (1.13–32.89)	0.036	3.26 (0.06–166.94)	0.556	
PDW	1.09 (0.89–1.32)	0.409			
MPV	0.467 (0.22–0.98)	0.043	0.70 (0.27–1.79)	0.458	
MCV	0.95 (0.88–1.02)	0.144			
Neutrophil ratio	1.03 (0.99–1.07)	0.094	1.05 (0.73–1.53)	0.786	
Lymphocyte ratio	0.96 (0.91–1.00)	0.072	1.02 (0.64–1.63)	0.934	
Monocyte ratio	1.13 (0.88–1.44)	0.346			
NLR	1.03 (0.92–1.16)	0.574			
PLR	1.00 (0.99–1.01)	0.812			

OR, odds ratio; CI, confidence interval; WBC, white blood cell; PDW, platelet distribution width; MPV, mean platelet volume; MCV, mean corpuscular volume; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

symptom duration and remained significant with respect to the golden time.

Several studies have reported the association between MPV and various diseases including inflammation (20). Moreover, MPV is known to be an indirect marker of platelet function and has been reported to be associated with vascular pathologies such as thrombosis and cardiovascular diseases, including acute myocardial ischemia (21-23). Urologic diseases with a vascular pathology, such as erectile dysfunction and ischemic priapism, have been reported to be associated with an increase in MPV (24). In addition, studies in children reported that elevated MPV was associated with acute ischemic stroke and acute pyelonephritis (25,26). As testicular torsion can also be considered a type of vascular pathology causing an ischemic response and thrombosis, it is believed that MPV increases in the presence of testicular torsion. Given that testicular torsion induces both ischemic and acute inflammatory responses, it could result in a higher MPV than that when epididymitis is present. Previously, studies about the relationship of MPV and testicular torsion reported results without considering the symptom duration, especially in terms of the golden time. Cicek *et al.* reported that MPV was the most valuable hematologic parameter for the diagnosis of testicular torsion when a patient group was compared with a healthy group (AUC =0.800) (27). Another study also reported that MPV could be an indicator of testicular viability in patients with testicular torsion (AUC =0.722, cutoff value 10.6, sensitivity 47.8%, specificity

92.6%) (28). In our study, the AUC of MPV regardless of symptom duration was 0.803 (95% CI: 0.749-0.858). In addition, the diagnostic value of MPV in differentiating testicular torsion from epididymitis was more prominent than that of the other parameters during the golden time (AUC =0.855, 95% CI: 0.778-0.932). These results could be a valuable reference when dealing with patients with an acute scrotum before and after the golden time. Over time, after the onset of a testicular ischemic event, tissue hypoxia occurs and leads to an inflammatory response, which is a secondary injury mechanism (14). In a study on children with acute appendicitis, MPV was significantly lower in pediatric patients with acute appendicitis than in the control group (29). Similarly, in our study, MPV tended to be lower after the golden time than within the golden time in both the testicular torsion and epididymitis groups. These results could be related to the fact that MPV was not a predictive factor associated with orchiectomy in patients with testicular torsion in the multivariate analysis.

This study had several limitations. This was a retrospective study conducted at a single tertiary care center in a specific region in Asia and could be affected by selection bias. Second, the symptom duration of an acute scrotum could be affected by recall bias. The patients' self-reporting of symptom duration is subjective owing to various emergent circumstances. Third, because surgical exploration was not performed in all patients, epididymitis associated with the spontaneous resolution of testicular torsion might have been overlooked. Finally, the changes in hematologic parameters before and after the event and treatment were not evaluated because of clinical circumstances. Thus, it could be difficult to uniformly apply the cutoff value of this study. Nevertheless, our study has great relevance in that this is the first study to evaluate the diagnostic value of hematologic parameters in differentiating testicular torsion from epididymitis with respect to the golden time and is the largest study to date in these patient populations.

## Conclusions

MPV is the most valuable hematologic parameter in the early stage of testicular torsion and epididymitis, suggesting its potential use in the differential diagnosis of these conditions within the golden time of 6 h of symptom duration. Our study results would be a useful reference for physicians dealing with patients with an acute scrotum in the early stage.

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#### Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-21-1112/rc

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-21-1112/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was performed in accordance with the Declaration of Helsinki (as revised in 2013) and the Ethical Guidelines for Clinical Studies. The study protocol was reviewed and approved by the institutional review board of Chonnam National University Hwasun Hospital (approval No. CNUHH-2020-160) and individual consent for this retrospective analysis was waived.

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