

**Review Article** 

# Association of MPV, NLR, PLR and CRP on testicular salvage in testicular torsion: A systematic review and meta-analysis

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# Abstract

Testicular torsion, a critical urological emergency caused by twisting of the spermatic cord, poses a risk of ischemia, particularly in children who often struggle to pinpoint symptoms onset. Delay in managing testicular torsion can lead to the need for orchiectomy. The aim of this study was to assess the association between hematologic parameters-mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and C-reactive protein (CRP)-and testicular salvage in cases of testicular torsion. Four databases (PubMed, Embase (Ovid), Science Direct, and Scopus) were systematically searched for eligible studies published up to November 4, 2024. The primary outcome was testicular salvage. Sensitivity analysis was performed using leaveone-out plot. Subgroup analysis was performed based on age, country, region, duration to orchiopexy and duration to orchiectomy. Heterogeneity was examined using  $I^2$  statistics, and a random-effect model was applied. Out of 363 studies identified, nine observational studies involving 796 patients were included, with 338 (42.3%) in orchiopexy group. The meta-analysis indicated that MPV value was significantly elevated in orchiectomy group (mean difference (MD): -0.4; 95% confidence interval (95%CI): -0.62–(-0.18); p<0.01), with higher MPV levels associated with an increased likelihood of orchiectomy (odds ratio (OR): 2.12; 95%CI: 1.35-3.33; p<0.01). NLR, PLR, and CRP showed no significant association with testicular salvage, as demonstrated by pooled MD and OR analyses (p>0.05). No significant differences were observed after sensitivity and subgroup analysis (p>0.05). These findings suggest that elevated MPV levels are associated with nonsalvageable testis, requiring orchiectomy highlighting its potential utility in clinical evaluation for testicular torsion.

**Keywords**: Testicular torsion, mean platelet volume, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, C-reactive protein

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# Introduction

T esticular torsion is a critical urological emergency caused by the twisting of the spermatic cord, which disrupts blood flow to the testicle and leads to testicular ischemia [1]. As a leading cause of irreversible testicular ischemia, testicular torsion can be effectively managed with timely intervention [2], which can prevent the need for orchiectomy in 97.2% of cases when treated within the first six hours of symptom onset [3]. However, this rate significantly drops to 7.4% after 48 hours [3]. This shows that delays in managing testicular torsion can lead to the need for orchiectomy [4].

Since testicular salvage is highly time-sensitive in testicular torsion [5], determining the exact time of onset can be challenging, as it often relies on the patient's memory, which can be especially unreliable in young children [6]. Testicular echogenicity can be a helpful imaging tool for assessing testicular salvageability [7], but its reliability largely depends on the operator. Furthermore, the test is not definitive, as incorrect judgment of non-salvageability in a viable testicle can have serious consequences [7]. Therefore, additional tests are needed to aid in clinical evaluation and decision-making in testicular torsion.

Oxidative stress and irreversible oxidative damage following testicular torsion may lead to alterations in hematologic parameters [8,9]. Recent studies have highlighted that hematologic parameters such as mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and C-reactive protein (CRP) are associated with testicular salvage, indicating systemic inflammatory response and ischemic damage [10,11]. Altered MPV, along with elevated NLR and PLR, has been correlated with prolonged symptoms and non-salvageability risk [12]. While NLR has been shown to be a beneficial parameter to differentiate the diagnosis between testicular torsion and epididymo-orchitis [9,13], its association with testicular salvage remains inconclusive. The aim of this study was to assess the association between these hematologic parameters with testicular salvage in testicular torsion.

# **Methods**

### **Protocol registration**

The protocol of this systematic review was registered on PROSPERO on November 19, 2024, under the registration number CRD42024611757. The systematic review and meta-analysis were performed and written following the 2020 preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [14].

#### Data source and search strategy

A systematic literature search was carried out on PubMed, Embase (Ovid), ScienceDirect and Scopus as of November 4, 2024, to identify studies of testicular torsion and hematologic parameters: MPV, NLR, PLR and CRP. Keywords such as "testicular torsion", "mean platelet volume", "neutrophil-to-lymphocyte ratio", "platelet-to-lymphocyte ratio", "C-reactive protein", "platelet" "neutrophils", "lymphocytes", "orchiopexy", "orchiectomy" and "viability", along with their synonyms as defined by subject headings, were used to search for relevant articles.

### **Eligibility criteria**

All studies included in the analysis met the specified inclusion criteria: (1) the study involved human participants diagnosed with testicular torsion; (2) the study examined NLR, MPV, PLR, or CRP levels to compare between orchiopexy and orchiectomy or to assess the likelihood of testicular salvage; and (3) blood parameters were collected prior to surgical intervention. Conversely, studies were excluded if: (1) overlapping study; (2) study with insufficient or low-quality data; (3) study with neonates under one-month-old; (4) patients with comorbidities that affect their blood parameter results; (5) patients' age was not specified in both groups; (6) the study was of inappropriate article types, such as meeting reports, reviews, or non-human studies; (7) unavailable full-text publication; and (8) full-text articles were not in English.

# Selection of studies and data extraction

The articles identified in the initial search were collected, and duplicates found across different databases were removed. The titles and abstracts of the remaining articles were then assessed using the inclusion and exclusion criteria. Two independent investigators (BT and TF) conducted the comprehensive search, resolving any disagreements about study inclusion through in-depth discussion with the third investigator (SRB).

Data extraction was independently carried out by two investigators (BT and TF) using a standardized data extraction spreadsheet. Information extracted from each eligible study included the first author's name, publication year, country, study design, number of orchiopexy and orchiectomy patients, patients' age, duration of symptoms, blood parameters, and their association with the outcome.

### **Risk of bias assessment**

Two investigators (IWD and NY) independently evaluated the risk of bias in the included studies using the Newcastle-Ottawa Scale (NOS) with three main categories: selection, comparability, and outcome [15]. Studies were considered to be of "Good" quality with a score of seven points or higher, "Fair" quality with a score between two and six points, and "Poor" quality with a score of one point or less. All studies with good quality were included for further analysis.

### Data synthesis and statistical analysis

Statistical analysis was conducted using RevMan 5.4.1 software (Cochrane Collaboration London, United Kingdom) and StataMP 17 (StataCorp LLC, Texas, USA). The associations of MPV, NLR, PLR, and CRP with testicular salvage were measured using mean difference (MD) with 95% confidence interval (95%CI), while the likelihood of orchiectomy was measured using odds ratio (OR) with 95% CI. For data with a non-normal distribution, parameter levels reported as medians with ranges or interquartile ranges were converted to mean values with standard deviation using the equation described previously [16,17]. Studies were excluded from pooled MD analysis if the data were not normally distributed and were reported as medians with interquartile range or full range. Likewise, studies were excluded from pooled OR analysis if the methods used to calculate the OR were not clearly specified. The OR with 95%CI for orchiopexy, derived from binary logistic regression analysis, was converted to represent the odds for orchiectomy by calculating the reciprocal (1/OR) and its corresponding confidence interval [18].

A random-effects model was employed for further analysis to pool the effect sizes of MD with 95%CI in blood parameters between orchiopexy and orchiectomy, as well as the OR with 95%CI for the likelihood of orchiectomy. Heterogeneity among studies was assessed using Cochran's Q test and the  $I^2$  index, with p<0.10 indicating significant heterogeneity [19] and  $I^2$  more than 50% suggesting substantial heterogeneity [20]. In cases of significant heterogeneity, sensitivity analysis was performed [21]. Publication bias was evaluated by constructing and examining a funnel plot for asymmetry [22].

# Results

# Literature search

The database search initially yielded 363 studies, and after removing duplicates, 326 articles remained (**Figure 1**). After excluding irrelevant titles and abstracts, 25 full-text articles were assessed thoroughly. Out of these, ten studies did not have the outcome of interest [23-32], two studies were not in English [33,34], two studies had different outcome classifications [35,36], one study had comorbidity that affects blood parameters result [37], and one study did not specify patients' age [12]. Therefore, only nine studies [6,38-45] met the predefined eligibility criteria (**Figure 1**).

### **Characteristics of included studies**

Nine included studies [6,38-45] examined the relationship of MPV, NLR, PLR, and CRP with testicular salvage, involving 796 patients (**Table 1**). All of the included studies were conducted in Asia and were retrospective studies. A total of 338 (42.5%) patients were treated with orchiopexy and 458 (57.5%) patients were treated with orchidectomy. Four studies measured MPV [38,39,41,43], seven studies measured NLR level [6,38,39,42-45], five studies measured PLR [6,38,39,42,43], and four studies measured CRP level [6,40-43].

In all nine studies [6,38-45], data from four studies [42-45] were not normally distributed and were not presented as median and standard deviation, making data conversion potentially inaccurate. Therefore, these four studies [42-45] were excluded from the forest plot of MD, leaving only five studies [6,38-41] included in the meta-analysis of MD (**Table 1**). Of the nine studies [6,38-45], all studies provided OR data except Merder *et al.* [39], which only included parameter rate data. Jang *et al.* [6], Barkai *et al.* [42] and Zheng *et al.* [45] reported OR for orchiopexy. To convert these into the odds for orchiectomy, the calculation of reciprocal (1/OR) and its corresponding confidence interval was performed [18].



Figure 1. PRISMA flowchart showing the study selection.

# **Risk of bias assessment**

The risk of bias assessment in each study is summarized in **Table 1**. All included studies had good methodological quality [6,38-45]. Five studies [38,41-45] scored 8, while four studies [6,39,40,44] scored 7. The studies that did not achieve a full score were missing either a selection component or an outcome component. Jang *et al.* [6], Merder *et al.* [39], and Gang *et al.* [44] had already demonstrated the outcome of interest at the start of the study, while Tanaka *et al.* [40] did not conduct sufficient follow-up. Due to the good methodological quality of most studies, none was excluded based on the risk of bias assessment.

### Association between MPV and incidence of orchiectomy

Among the four studies [38,39,41,43] that reported the association of MPV levels with testicular salvage, two studies [38,41] found higher MPV levels in the orchiectomy group, while the other two studies [39,43] found no association between MPV level and testicular salvage after torsion. Of these four studies [38,39,41,43], only three [38,39,41] were included in the forest plot, as the data in Deng *et al.* [43] had no mean values with standard deviations. When the MD between groups from the included studies were pooled, a significant difference in MPV levels was found between orchiopexy and orchiectomy (MD: -0.40; 95%CI: -0.62–(-0.18); p<0.01) (**Figure 2**).

# Table 1. Characteristics of included studies

Author	Year	Country	Orchiopexy			Orchiec	tomy		Parameter	Association	NOS
			n	Age (years)	Duration (hours)	n	Age (years)	Duration (hours)	_	with increase	
										in parameter	
Data presented in mean	ı ± stand	ard deviation	1								
He <i>et al</i> . [38]	2019	China	54	11.3±3.6	21.4±36	58	9.9±5.0	84.4±90.8	NLR	Orchidopexy	8
									PLR	Orchidopexy	
									MPV	Orchiectomy	
Jang <i>et al</i> . [6]	2019	Korea	22	14.6±2.0	3.2±1.8	38	14.7±2.7	11.1±3.8	NLR	Orchiectomy	7
									PLR	Orchiectomy	
									CRP	N/S	
Merder <i>et al</i> . [39]	2020	Turkey	61	17.6±4.3	$3.8 \pm 4.8$	27	17.8±4.6	21.3±20.2	NLR	N/S	7
		·							PLR	N/S	
									MPV	N/S	
Tanaka <i>et al</i> . [40]	2020	Japan	23	$11.1 \pm 3.7$	14.2±19.9	15	10.5±3.6	84.3±128.0	CRP	Orchiectomy	7
Zhang et al. [41]	2023	China	42	$8.32 \pm 4.87$	N/A	60	$6.89 \pm 5.50$	N/A	MPV	Orchiectomy	8
0	-						,		CRP	N/S	
Data presented in medi	an (inter	quartile rang	e or rang	e)						,	
Barkai <i>et al</i> . [42]	2023	Israel	36	22(20, 28)	7.5 (5, 120)	14	31(25, 43)	48 (19, 168)	NLR	N/S	8
	0		0		,		0 ( 0) 10)		PLR	N/S	
									CRP	N/S	
Deng <i>et al.</i> $[43]$	2024	China	27	12(7.5, 13)	8 (3, 22)	40	5.1(0.4, 12)	48 (24, 120)	NLR	Orchidopexy	8
0 2103			,			•	0 1 1 /		PLR	N/S	
									MPV	N/S	
Gang et al. [44]	2024	China	43	14.4 (9–18)	N/A	32	12.5 (2-18)	N/A	NLR	Orchidopexy	7
Zheng et al. [45]	2021	China	30	20 (16-22)	4.8 (7.2, 43.2)	174	16(14-20)	96 (48-199.2)	NLR	N/S	8

CRP: C-reactive protein; MPV: mean platelet volume; N/A: not available; N/S: not significant; NLR: neutrophil-to-lymphocyte ratio; NOS: Newcastle-Ottawa Scale; PLR: platelet-to-lymphocyte ratio

As Merder *et al.* [39] did not provide OR data, only two studies [38,41] were available for pooled OR analysis. From the pooled OR analysis, high MPV levels were found to be associated with the incidence of orchiectomy (OR: 2.12; 95%CI: 1.35-3.33; *p*<0.01) (**Figure 3**).

Study	SE	Orchiopexy T	Orchiectomy otal			Std. Mean Difference Weig with 95% Cl (%	ght 。)
He et al, 2019 [38]	0.15	54	58			-0.32 [ -0.62, -0.02] 54.2	23
Merder et al, 2020 [39]	0.27	61	27			-0.41 [ -0.94, 0.12] 17.2	22
Zhang et al, 2023 [41]	0.21	42	60			-0.56 [ -0.97, -0.15] 28.5	55
Overall	0.11				-	-0.40 [ -0.62, -0.18]	
Heterogeneity: $\tau^2 = 0.00$	, <b>I</b> <sup>2</sup> = 0.0	0%, H² = 1.0	0				
Test of $\theta_i = \theta_j$ : Q(2) = 0.8	85, p = 0	.65					
Test of $\theta = 0$ : $z = -3.60$ ,	o = 0.00						
				-1	5	0	
Random-effects REML m	odel						

Figure 2. Forest plot of studies assessing mean difference (MD) in mean platelet volume (MPV) levels between those who had orchiopexy and orchiectomy.



Figure 3. Forest plot of studies evaluating the association between mean platelet volume (MPV) levels and the incidence of orchiectomy.

#### Association between NLR and incidence of orchiectomy

Out of the seven studies [6,38,39,42-45] assessing the association between NLR and testicular salvage, three studies reported higher NLR levels in the orchiopexy group [38,43,44], one study found higher NLR levels in the orchiectomy group [6], while three studies found no association between NLR and testicular salvage. Out of the seven studies [6,38,39,42-45], only three studies [6,38,39] were included in the forest plot of MD, as the data from four studies [42-45] did not present data in mean values with standard deviation. However, when the MD between groups from the included studies were pooled, no significant difference in NLR levels was identified between orchiopexy and orchiectomy (MD: 0.44; 95%CI: -1.19-2.06; p=0.60) (**Figure 4**).



Figure 4. Forest plot of studies assessing mean difference (MD) of neutrophil-to-lymphocyte ratio (NLR) levels between those who had orchiopexy and orchiectomy.

Among the seven studies [6,38,39,42-45], Merder *et al.* [39] did not provide OR data, leaving six studies [6,38,42-45] included in the forest plot analysis of OR. From the pooled OR analysis, no association was observed between NLR levels and incidence of orchiectomy (OR: 1.09; 95%CI: 0.93–1.27; p=0.27) (**Figure 5**). The MD and OR for the NLR forest plot showed significant heterogeneity, requiring sensitivity analysis.



Figure 5. Forest plot of studies evaluating the association of neutrophil-to-lymphocyte ratio (NLR) levels with incidence of orchiectomy.

# Association between PLR with incidence of orchiectomy

Out of five studies [6,38,39,42,43] reporting PLR association with testicular salvage, one study reported higher PLR levels in the orchiopexy group [38], one study found higher PLR levels in the orchiectomy group [6], while three studies [39,42,43] found no association between PLR levels and testicular salvageability. Out of five studies [6,38,39,42,43], only three studies [6,38,39] were included in the forest plot of MD, as two studies [42,43] did not present the data in mean values with standard deviation. When the MD between groups from the included studies were pooled [6,38,39], no significant difference in PLR levels was found between orchiopexy and orchiectomy (MD: 14.63; 95%CI: -47.30–76.56; p=0.64) (**Figure 6**).



Figure 6. Forest plot of studies assessing mean difference (MD) for platelet-to-lymphocyte ratio (PLR) level between those who had orchiopexy and orchiectomy.

Only three studies [6,38,42] reported OR data. From the pooled OR analysis, there was no association between PLR levels and the incidence of orchiectomy (OR: 1.00; 95%CI: 1.0–1.01; p=0.20) (**Figure 7**).

#### Association between CRP and incidence of orchiectomy

Out of four studies [6,40,41,42] reporting the association between CRP levels and testicular salvage, one study [40] reported higher CRP levels in the orchiectomy group, while the other studies did not show significant differences [6,41,42]. Barkai *et al.* [42] did not present the data

in mean values with standard deviation, resulting in only three studies [6,40,41] being included in the forest plot. The pooled studies showed no significant MD in CRP levels between orchiopexy and orchiectomy groups (MD: 0.0; 95%CI: -0.29–0.28; p=0.98) (**Figure 8**).



Figure 7. Forest plot of studies evaluating the association of platelet-to-lymphocyte ratio (PLR) levels with incidence of orchiectomy.

Jang *et al.* [6], Zhang *et al.* [41] and Barkai *et al.* [42] did not report the OR for orchiectomy based on CRP levels. As a result, pooled OR analysis of CRP could not be performed due to an insufficient number of studies.

Study	SE	Orchiopexy T	Orchiectomy				Std. Mean Difference with 95% CI	Weight (%)
Jang et al, 2019 [6]	0.27	22	38				-0.14 [ -0.67, 0.39]	29.21
Tanaka et al, 2020 [40]	0.33	23	15		-		0.26 [ -0.39, 0.91]	18.90
Zhang et al, 2023 [41]	0.20	42	60		<b></b>		-0.02 [ -0.42, 0.37]	51.89
Overall	0.14						-0.00 [ -0.29, 0.28]	
Heterogeneity: τ <sup>2</sup> = 0.00	$I^2 = 0.0$	0%, H² = 1.0	0					
Test of $\theta_i = \theta_j$ : Q(2) = 0.8	8, p = 0	64						
Test of $\theta = 0$ : z = -0.02, j	o = 0.98							
				5	Ó	.5	י <b>1</b>	
Bandom-effects BEML m	odel							

Figure 8. Forest plot of studies assessing mean difference (MD) for C-reactive protein (CRP) level between those who had orchiopexy and orchiectomy.

#### Sensitivity analysis

For analyses demonstrating substantial heterogeneity, including MD and OR in NLR as well as MD in PLR, sensitivity analysis was conducted. The leave-one-out approach revealed no significant findings for NLR and PLR (**Table 2**), indicating that no individual study was solely responsible for rendering the analysis insignificant. The OR for NLR remained insignificant, even after excluding studies outside the funnel plot (OR 0.96; 95%CI: 0.89–1.04; p=0.32).

### Subgroup analysis

The inclusion of six studies [6,38,42-45] enabled subgroup analysis for OR of NLR. Groups were categorized by age, ethnicity, region, and duration of orchiopexy and orchiectomy, but the results of the subgroup analysis remained statistically insignificant (**Table 3**). For other analyses, subgroup analysis was not feasible due to the limited number of studies included in the forest plot.

Table 2. Sensitivity	analysis of t	the association	between	neutrophil-to	-lymphocyte 1	ratio	(NLR) and	platelet-to	o-lymphocyte	ratio (P	LR) with	n testicular	salvage	in
testicular torsion														

Leave-one-out plot in NLR								
Omitted study	MD (95%CI)	<i>p</i> -value	Heterogeneity		OR (95%CI)	<i>p</i> -value	Heterogeneity	
			$I^{2}(\%)$	<i>p</i> -value			$I^{2}(\%)$	<i>p</i> -value
Jang <i>et al.,</i> 2019 [6]	1.18 (-0.46–2.82)	0.157	64.6%	0.092	1.04 (0.91–1.19)	0.617	57.3%	0.079
He et al., 2019 [38]	-0.36 (-1.47–0.75)	0.526	62.9%	0.100	1.101 (0.94–1.31)	0.238	74.5%	0.006
Merder <i>et al.</i> , 2020 [39]	0.54 (-2.24–3.33)	0.701	92.2%	< 0.001	N/A	N/A	N/A	N/A
Barkai <i>et al.</i> , 2023 [42]	N/A	N/A	N/A	N/A	1.12 (0.92–1.36)	0.264	69.4%	0.005
Deng et al., 2024 [43]	N/A	N/A	N/A	N/A	1.11 (0.93–1.33)	0.238	74.8%	0.006
Gang et al., 2024 [44]	N/A	N/A	N/A	N/A	1.04 (0.90–1.2)	0.632	56.3%	0.090
Zheng <i>et al.</i> , 2021 [45]	N/A	N/A	N/A	N/A	1.15 (0.96–1.37)	0.128	53.8%	0.070
Leave-one-out plot in PLR								
Omitted study	MD (95%CI)	<i>p</i> -value	Heterogeneity		OR (95%CI)	<i>p</i> -value	Heterogeneity	
			$I^{2}(\%)$	<i>p</i> -value			$I^{2}(\%)$	<i>p</i> -value
Jang <i>et al.</i> , 2019 [6]	40.75 (-13.75–95.25)	0.143	88.3%	0.003	N/A	N/A	N/A	N/A
He et al., 2019 [38]	-11.28 (-66.65–44.09)	0.690	89.9%	0.002	N/A	N/A	N/A	N/A
Merder <i>et al.,</i> 2020 [39]	14.54 (-95.64–124.72)	0.796	95.4%	<0.001	N/A	N/A	N/A	N/A
AT / A								

N/A: not available

# Table 3. Subgroup analysis of the association between neutrophil-to-lymphocyte ratio (NLR) and testicular salvage in testicular torsion

Subgroup analysis of NLR using C	DR						
Group	Reference	Number of studies	OR (95%CI)	<i>p</i> -value	Heterogeneity		
					$I^{2}$ (%)	<i>p</i> -value	
Age (in median or mean)							
<15 years	[6,38,43,44]	4	1.21 (0.99, 1.48)	0.065	42.5%	0.163	
>15 years	[42,45]	2	0.96 (0.89, 1.04)	0.345	0.01%	0.512	
Ethnicity							
Chinese	[38,43-45]	4	1.05 (0.86, 1.28)	0.626	62.9%	0.040	
Non-Chinese	[6,42]	2	1.18 (0.84, 1.66)	0.337	78.5%	0.031	
Region							
East Asian	[6,38,43-45]	5	1.12 (0.91, 1.36)	0.264	69.4%	0.005	
Non-East Asian	[42]	1	1.01 (0.86, 1.19)	0.903	N/A	N/A	
Duration of orchiopexy							
<6 hours	[6,45]	2	1.14 (0.77, 1.70)	0.516	87.3%	0.005	
>6 hours	[38,42,43]	3	1.00 (0.87, 1.14)	0.957	0%	0.934	
<12 hours	[6,39,40,42]	4	1.05 (0.89, 1.23)	0.569	62.4%	0.047	
>12 hours	[35]	1	0.92 (0.53, 1.60)	N/A	N/A	N/A	
Duration of orchiectomy							
<24 hours	[6]	1	1.43 (1.09, 1.88)	N/A	N/A	N/A	
>24 hours	[38,42-45]	4	0.96 (0.89, 1.04)	0.321	0%	0.928	
<48 hours	[6,42,43]	3	1.11 (0.89, 1.40)	0.367	62.4%	0.073	
>48 hours	[38,45]	2	0.95 (0.87, 1.04)	0.240	0%	0.910	

N/A: not available

# Summary of findings and publication bias

Among all blood parameters, only the MPV level demonstrated a significant association with nonsalvageable testis, requiring orchiectomy. No evidence of publication bias was detected for any of the outcomes of interest, as indicated by *p*-values greater than 0.10 for both Egger's test and Begg's tests (**Table 4**).

Variable	Number of	Effect of	<i>p</i> -value	Egger's	test		Begg's	test
	studies and	estimate	_	Т	<i>p</i> -value	95%CI	Z	<i>p</i> -value
	reference	(95%CI)			-			_
MPV	3 [38,39,41]	MD: -0.40	< 0.001	-0.54	0.687	-33.27-30.58	-	1
		(-0.62–(-0.18))					1.04	
	2 [38,41]	OR: 2.12	0.001	N/A	N/A	N/A	N/A	N/A
		(1.35-3.33)						
NLR	3 [6,38,39]	MD: 0.44	0.599	2.35	0.256	-21.76-31.65	1.04	0.290
		(-1.19–2.06)						
	6 [6,38,42-45]	OR: 1.09	0.269	0.27	0.800	-3.46-4.2	-	1
		(0.93–1.27)					0.38	
PLR	3 [6,38,39]	MD: 14.63	0.643	0.09	0.940	-124.32-126.17	0	1
		(-47.3–76.56)						
	3 [6,38,42]	OR: 1.01	0.195	-0.09	0.944	-24.23–23.89	-	1
		(1.00–1.01)					1.04	
CRP	3 [6,40,41]	MD: 0.0	0.983	0.52	0.695	-34.45-37.39	0	1
		(-0.29-0.28)						

Table 4. Summar	y of findings and	publication bias	test for bloo	d parameters
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CRP: C-reactive protein; MPV: mean platelet volume; N/A: not available; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio

# Discussion

Testicular torsion involves the twisting of the spermatic cord, leading to intratesticular venous congestion, interstitial edema, and vascular changes that compromise the testicular microcirculatory system [46]. This results in hypoxia, inflammation, thrombosis and potential testicular injury [38,47], which may alter blood parameters. Our analysis revealed that elevated MPV levels were associated with non-salvageable testis, requiring orchiectomy in testicular torsion cases.

MPV, an indicator of platelet turnover [48], is elevated due to increased production of larger, younger platelets during pathological conditions such as testicular torsion [48]. The present meta-analysis revealed that patients with high MPV levels were twice as likely to undergo orchiectomy compared to orchiopexy. The spermatic cord torsion induces platelet activity and production due to microthrombi formation in the testicular tissue [38]. Prolonged torsion led to more platelet consumption and extensive thrombosis, resulting in the elevation of MPV in the orchiectomy group. Similar associations have been observed in thromboembolic events such as acute ischemic stroke [49] and coronary artery disease [50], where higher MPV is linked to increased clot formation in the coronary arteries, potentially leading to myocardial infarction [51]. MPV also serves as a marker of stroke severity, with elevated levels in the acute phase correlating with decreased 1-year mortality after stroke [52].

In addition to its association with testicular salvageability, MPV could also differentiate between testicular torsion and epididymitis during the golden period [12]. Higher MPV levels were observed in testicular torsion due to both ischemia and inflammation, whereas epididymitis involved only inflammation [12]. Two studies [38,41] reported that high MPV levels were associated with an increased likelihood of orchiectomy following testicular torsion. However, Lee *et al.* [12] found that MPV levels were decreased in both the testicular torsion and epididymitis groups after six hours of symptoms. This study was excluded from the meta-analysis due to the unclear patients' age and the unspecified number of cases undergoing orchiectomy or orchiopexy [12]. A subgroup analysis comparing time to orchiopexy and orchiectomy at different cut-off points could address these discrepancies, but the limited number of available studies prevented such analysis.

The ischemic event due to testicular torsion can lead to tissue hypoxia, cellular damage, and, if prolonged, testicular infarction—complete tissue necrosis due to irreversible ischemia [53].

This event leads to the release of intracellular contents and damage-associated molecular patterns (DAMPs) triggering a more intense inflammatory response than ischemia alone [53]. The immune system responds with leukocyte activation, release of pro-inflammatory cytokines, and acute-phase reactants [53]. Based on this principle, NLR [54], PLR [55] and CRP [56] levels should be changed due to testicular infarction.

In this meta-analysis, markers such as NLR, PLR, and CRP, which are typically elevated in response to infarction, did not reach statistical significance in cases of testicular infarction. Sensitivity and subgroup analyses were conducted to explore the potential impact of heterogeneity on observed summary effects, particularly in groups with significant heterogeneity or sufficient data for subgroup analysis. Despite performing a leave-one-out analysis, heterogeneity persisted for both NLR and PLR. When the number of studies was sufficient, analysis was performed, excluding studies outside the funnel plot, but this exclusion did not result in significant findings for NLR. Subgroup analyses considering factors such as age, ethnicity, region, and time to orchiopexy and orchiectomy also failed to demonstrate a significant association between NLR and testicular salvageability. Persistent heterogeneity in some subgroups reflects the variability in study results, highlighting the need for more studies to clarify the relationship between blood markers and testicular salvageability.

The high heterogeneity in the study may be attributed to unreported comorbidities or other conditions, such as chronic inflammatory diseases (e.g., diabetes or autoimmune diseases), which could elevate markers like NLR and PLR, potentially masking the specific effect of testicular infarction [57]. Moreover, considerable variability in the duration of testicular torsion reported across studies [6,38-40,42,43,45] is significant since testicular torsion is time-sensitive, and inflammatory markers may change depending on the ischemic duration before intervention [10]. Delayed presentations could cause a plateau in inflammatory marker levels, affecting their observed effect [58], contributing to the variability seen in the analysis.

Inflammatory markers like NLR, PLR, and CRP change dynamically over time, with their peak levels occurring at different points depending on the duration of ischemia and infarction [59]. NLR peaks early during acute inflammatory response but may normalize quickly in resolved cases or plateau in chronic damage [58,59]. PLR reflects cumulative inflammation but might be less responsive to acute testicular injury than other conditions [60,61]. CRP typically rises 24–48 hours after inflammation onset, potentially missing peak levels if measured too early or late [61,62]. The timing of blood sample collection across studies likely obscured significant associations.

The main limitation of this meta-analysis is the relatively small number of included studies, with only nine studies meeting the eligibility criteria. All studies were retrospective, which inherently limits the ability to derive definitive conclusions. Furthermore, the predominance of studies from Asian countries may limit the generalizability of the findings to broader populations. The lack of standardization in blood parameter measurement methods across studies limits the interpretability of the findings. Future research should prioritize larger, multicenter prospective studies with standardized methodologies to validate the role of hematologic parameters in testicular torsion management. Efforts should also focus on establishing standardized protocols, defining clinically relevant cutoff values, and assessing their utility in guiding clinical decisions.

# Conclusion

MPV demonstrated a significant association with non-salvage testis, requiring orchiectomy, whereas NLR, PLR, and CRP showed no such association. These findings highlight its utility in clinical evaluation for testicular torsion. However, further research is needed to establish standardized protocols, define cut-off values, and validate its role in guiding management decisions for testicular torsion.

# **Ethics approval**

Not required.

#### Acknowledgments

We have no acknowledgments to declare.

# **Competing interests**

All the authors declare that there are no conflicts of interest.

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### **Underlying data**

Derived data supporting the findings of this study are available in the article.

#### Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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