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Complete Blood Count Markers and C-Reactive Protein as Predictors of Testicular Viability in the Event of Testicular Torsion in Adults

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Keywords
Testicular torsion · Orchiectomy · C-reactive protein · Platelet-lymphocyte ratio · Neutrophil-lymphocyte ratio

Abstract
Introduction: The association between blood markers and testicular viability after testicular torsion (TT) is not well known. We evaluated the role of complete blood count markers and C-reactive protein (CRP) in predicting testicular viability after TT. ***Methods:*** Fifty men, ≥18 years of age, operated for TT between the years 2015–2020 were enrolled. Blood markers including neutrophil-, lymphocyte-, and platelet count, and CRP were obtained. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were calculated. The study outcome was testicular salvage. ***Results:*** Median age was 23 years (interquartile range [IQR]: 21, 31). Median duration of torsion was 10 h (IQR: 6, 42). Sonographic texture of the testis was homogenous in 27 (56%) patients and heterogenous in 21 (44%). During scrotal exploration, 36 patients (72%) underwent orchiopexy and 14 (28%) underwent orchiectomy. Patients who underwent orchiopexy were younger (22 years vs. 31 years, $p = 0.009$), had a shorter duration of torsion (median 8 h vs. 48 h, $p < 0.001$), and a homogenous texture on scrotal ultrasound (76.5 vs. 7.1%, $p < 0.001$). Median NLR, PLR, and CRP were higher among patients who underwent orchiectomy; however, these differences did not reach statistical significance. Patients with heterogenous echotexture were significantly more likely to undergo orchiectomy (odds ratio = 42, 95% confidence interval: 7, 831, adjusted p value = 0.009). ***Conclusions:*** We found no association between blood-based biomarkers and testicular viability after TT; however, testicular echotexture significantly predicted outcome.

Introduction

Testicular salvage rates after an event of torsion range from 41% to 77% in adults who are 21 years old or older [1, 2]. Predictors of testicular salvage include initial misdiagnosis, degree of torsion, duration of ischemia, and sonographic findings [3–8]. Almost all testes are salvaged within the first 6 h after the onset of symptoms; however, with later treatment, salvage rates rapidly decrease [9]. Among patients who underwent ultrasonography prior to surgery, homogenous echogenicity of the affected testis was associated with a significantly higher

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salvage rate (64–89 vs. 0%) [4, 7]. A minimal degree of torsion was also associated with testicular viability [3, 10].

Complete blood count and C-reactive protein (CRP) measurements are inexpensive and widely available; therefore, if associated with testicular viability, they may serve as a simple tool for counseling patients presenting with testicular torsion (TT) as to the outcome of scrotal exploration. Few studies examined the correlation between blood tests, the diagnosis of TT and testicular viability at scrotal exploration [11–14]. In a study conducted by Bitkin et al. [11] WBC, mean platelet volume (MPV), and neutrophil-lymphocyte ratio (NLR) values were significantly higher in both epididymitis and torsion, hence helpful in the diagnosis of these diseases but not for the differentiation between them. Jang et al. [12] found that, in children with delayed TT diagnosis, NLR could serve as a predictor of testicular viability. He et al. [13] reported that MPV was an independent risk factor for orchiectomy. Finally, Gunes et al. [14] compared platelet-lymphocyte ratio (PLR) and NLR in TT with a control group and found they were significantly higher in patients with torsion. Previous studies showed inconsistent results and only one study evaluated the association between CRP and testicular viability. In the current study, we aimed to evaluate the association between complete blood count markers and CRP and testicular viability at scrotal exploration.

Materials and Methods

After obtaining Institutional Review Board approval (registration # TLV-0539-20), we reviewed the electronic medical records of 50 men, 18 years of age and older, who underwent scrotal exploration for TT at our center between the years 2015–2020. Baseline characteristics collected included patient age in years, side of torsion, duration of torsion in hours, testicular position at the time of evaluation, and a history of a cryptorchid testis. Most patients evaluated at our center that are suspected to have a TT undergo a scrotal ultrasound (US) with Doppler, performed by a radiologist, prior to scrotal exploration. Imaging findings collected included testicular echotexture stratified as homogenous and heterogenous, and the presence of testicular blood flow on color Doppler. All patients had a complete blood count prior to scrotal exploration and the white blood count (10^9/L, normal range 4.0–11.0 × 10^9/L), absolute neutrophil count (10^9/L, normal range 1.4–6.0 × 10^9/L), absolute lymphocyte count (10^9/L, normal range 1.2–3.0 × 10^9/L), and platelet count (10^9/L, normal range 150–450 × 10^9/L) were obtained. These values were then used to calculate the NLR and the PLR. CRP values (μg/mL, normal range <0.03–5.0 μg/mL) were also collected when available.

All patients underwent scrotal exploration, the diagnosis of TT was confirmed, and the degree of torsion was noted. The ipsilateral testis was de-torsed and evaluated for its viability. If there was a concern regarding testicular viability, the testis was wrapped in a warm, moist, gauze for 15–30 min and reevaluated. Testis viability was then evaluated based on improvement in the color of the testis after revascularization. In controversial cases, a fasciotomy was performed in the tunica albuginea to decompress the testis and assess blood flow. If the testis was deemed nonviable, orchiectomy of the ipsilateral testis was performed. In all patients, the contralateral testis underwent orchiopexy.

The study outcome was testicular preservation at the time of scrotal exploration. Descriptive statistics were used to report the clinical characteristics of the study cohort stratified by treatment outcome (orchiectomy vs. orchiopexy). Continuous variables were assessed for normal distribution using visual inspection of the density plot and the Shapiro-Wilk test of normality. Normally distributed data were reported using the mean and standard deviation and compared with the Student's t test. Nonparametric data were reported as median and interquartile range (IQR) and compared with the Mann-Whitney U test. Categorical variables were reported as number and percent and compared with the Fisher's exact and χ^2 tests. Univariable logistic regression analyses were conducted to evaluate the association between preoperative baseline characteristics including age, side of torsion, duration of torsion, testicular position at presentation, testicular echotexture on US, white blood cell count, neutrophil count, lymphocyte count, platelet count, NLR, PLR, CRP, and outcome during scrotal exploration. Due to multiple testing, we used the Bonferroni method to adjust the p values. All statistical analyses were two-sided, and significance was defined as $p < 0.05$. All analyses were conducted using R Statistical Software (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria).

Results

The study cohort comprised of 50 men with a median age of 23 years (IQR: 21, 31). The median duration of torsion between the time of presentation and the time of scrotal exploration was 10 h (IQR: 6, 42). The sonographic texture of the testis was homogenous in 27 (56%) patients and heterogenous in 21 (44%). Testicular blood flow was absent in most patients (43/49, 88%). During scrotal exploration, 36 patients (72%) underwent orchiopexy and 14 patients (28%) underwent orchiectomy. As can be seen in Table 1, patient who underwent orchiopexy were younger (22 years vs. 31 years, $p = 0.009$), had a shorter duration of torsion (median 8 h vs. 48 h, $p < 0.001$), and had a homogenous texture on scrotal US (76.5% vs. 7.1%, $p < 0.001$).

White blood cell and platelet counts were normally distributed; mean and standard deviation values were 10.53 × 10^9/L (±3.14 × 10^9/L) and 214 × 10^9/L (±48 × 10^9/L), respectively. Median and IQR values of the neutrophil and lymphocyte counts were 7.30 × 10^9/L (5.03, 9.50) and 1.90 × 10^9/L (1.50, 2.48), respectively. Median NLR value was 3.41 (IQR: 2.29, 5.88) and median PLR was 108 (IQR: 77, 150). CRP measurements were available for 44

Table 1. Preoperative characteristics of men who underwent scrotal exploration for testicular torsion stratified by outcome of surgery (n = 50)

Variable	Orchiopexy (n = 36)	Orchiectomy (n = 14)	p value
Age, years	22 [20, 28]	31 [25, 43]	0.009
Side of torsion			
Right	22 (61)	9 (64)	1
Left	14 (39)	5 (36)	
Duration of torsion (hours, n = 46)	7.50 [5, 12]	48 [19, 168]	<0.001
Testicular position at presentation (n = 46)			
Normal	9 (26.5)	5 (42)	0.467
Elevated	25 (73.5)	7 (58)	
Testicular echotexture on US (n = 48)			
Homogenous	26 (76.5)	1 (7)	<0.001
Heterogenous	8 (23.5)	13 (93)	
Blood flow on Doppler US (n = 49)			
Present	6 (17)	0 (0)	0.164
Absent	29 (83)	14 (100)	
Cryptorchidism			
Absent	36 (100)	12 (86)	0.074
Present	0 (0)	2 (14)	
Degree of torsion (n = 42)	360 [180, 720]	510 [360, 720]	0.369
White blood cell count (10^9/L)	10.62 [±3.31]	10.31 [±2.76]	0.745
Neutrophil count (10^9/L)	7.10 [4.45, 9.50]	7.70 [5.35, 9.50]	0.681
Lymphocyte count (10^9/L)	2.00 [1.58, 2.62]	1.60 [1.25, 1.95]	0.076
Platelet count (10^9/L)	218 [±46]	205 [±51]	0.431
NLR	3.11 [2.06, 5.42]	4.98 [2.91, 6.03]	0.139
PLR	105 [76, 137]	129 [84, 163]	0.266
C-reactive protein (μg/mL, n = 44)	0.60 [0.24, 2.69]	6.96 [0.33, 38.54]	0.136

Continuous variables are reported as mean and standard deviation when parametric and median and interquartile range when nonparametric; categorical variables are reported as number and percent. US, ultrasound; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio.

patients; median CRP level was 0.90 μg/mL (IQR: 0.28, 8.05). Median NLR, PLR, and CRP were higher among patients who underwent orchiectomy (4.98 vs. 3.11, 129 vs. 105, and 6.96 vs. 0.60, respectively); however, these differences did not reach statistical significance (Table 1).

On univariable logistic regression analyses, testicular echotexture prior to exploration was a significant predictor of surgical outcome. Patients with heterogenous echotexture were significantly more likely to undergo orchiectomy (odds ratio [OR] = 42, 95% confidence interval [CI]: 7, 831, adjusted p value = 0.009); 1/27 (4%) men with homogenous echotexture underwent orchiectomy compared to 13/21 (62%) men with heterogenous echotexture (online suppl. Fig. 1; for all online suppl. material, see https://doi.org/10.1159/000531145). None of the blood-based markers evaluated were found to be significantly associated with outcome on univariable analyses (Table 2). The sensitivity, specificity, positive predictive value, and negative predictive value of heterogenous echotexture on testicular US in identifying patients with nonviable testes who underwent orchiectomy were 93%, 76%, 62%, and 96%, respectively.

Discussion

In the current study, we found an orchiopexy rate of 72% at scrotal exploration due to TT. Heterogeneous testicular echotexture was a significant predictor of outcome; however, none of the blood-based markers evaluated were significantly associated with testicular viability at time of surgery.

Established predictors of outcome in patients undergoing scrotal exploration for TT include time from symptom onset to surgery, degree of torsion, and parenchymal echotexture [3, 7]. In the current study, consistent with previous reports, patients who underwent orchiopexy had a shorter duration of torsion and a higher rate of homogenous testicular echotexture on US. Furthermore, on univariable analyses adjusted for multiple testing, homogenous testicular echotexture remained a

Table 2. Univariable logistic regression analyses evaluating the association between preoperative characteristics and orchiectomy at surgery in men who underwent scrotal exploration for testicular torsion

Variable	Group	OR	95% CI		*p* value	Adjusted *p* value*
Age (per 1 year)		1.09	1.02	1.18	0.013	0.152
Side	Right	Ref				
	Left	0.87	0.23	3.09	0.84	1
Duration of torsion (per 1 h)		1.03	1.01	1.05	0.009	0.112
Testicular position	Normal	Ref				
	Elevated	0.504	0.13	2.07	0.33	1
US texture	Homogenous	Ref				
	Heterogenous	42.25	6.87	830.65	0.001	0.009
WBC count (per 10^9 cells/L)		0.97	0.79	1.18	0.76	1
Neutrophil count (per 10^9 cells/L)		1.003	0.82	1.22	0.98	1
Lymphocyte count (per 10^9 cells/L)		0.53	0.21	1.09	0.13	1
Platelet count (per 10^9 cells/L)		0.99	0.98	1.007	0.39	1
NLR (per 1 unit)		1.008	0.86	1.15	0.91	1
PLR (per 1 unit)		1.002	0.99	1.01	0.64	1
CRP (per 1 μg/mL)		1.004	0.99	1.02	0.56	1

OR, odds ratio; CI, confidence interval; Ref., reference; US, ultrasound; WBC, white blood cell; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio. *p value adjusted using the Bonferroni method.

significant predictor of orchiopexy. These findings support the role of scrotal US when counseling patients and their families regarding the expected outcome of scrotal exploration for TT and emphasize the importance of including testicular echotexture in future studies evaluating predictors of outcome after TT.

Few studies evaluated the role of blood-based markers in predicting testicular outcome during exploration (Table 3) [11–14]. Jang et al. recruited 60 men to their research and found that both WBC and NLR were significantly lower in patients who underwent orchiopexy ($p < 0.001$). NLR independently predicted testicular viability, particularly for patients with marginally delayed diagnosis [12]. In a study conducted by Bitkin et al. which included 153 patients, WBC, MPV, and NLR values were significantly higher in both epididymitis and torsion ($p < 0.001$), hence helpful in the diagnosis of these diseases but not in the differentiation between the two. They also reported NLR identified TT with a sensitivity and specificity of 70.1% and 76.9%, respectively. Thus, the authors concluded that CBC is a cheap, rapid, and easily accessible test that may be used to aid in the differential diagnosis of acute scrotum, especially in centers where Doppler US cannot obtained or properly used in a short time [11]. Gunes et al. compared platelet count, PLR, and NLR in TT with a control group and found they were significantly higher in patients with torsion ($p < 0.001$). In the same study, NLR was significantly associated with duration of torsion ($p = 0.01$, beta coefficient, 0.380). Interestingly, Gunes et al. [14] mentioned the lack of CRP in their database as a limitation of their study. Finally, He et al. reported that MPV is an independent significant predictor of orchiectomy (OR = 3.697, $p = 0.044$) and therefore can provide valuable information before scrotal exploration. The study also showed that symptom duration (OR = 1.11, $p < 0.001$), and the degree of spermatic cord torsion (OR = 1.006, $p = 0.002$) are indicators of testicular viability at surgery [13]. In the current study, we observed higher NLR and PLR values in patients who underwent orchiectomy; however, this difference did not reach statistical significance. Furthermore, our study was the second to evaluate the role of CRP in predicting outcome at time of surgical exploration. While the median CRP value was higher among patients undergoing orchiectomy (6.96 vs. 0.60), the difference did not reach statistical significance ($p = 0.136$) and we did not find an association between CRP and outcome on univariable logistic regression analysis.

The study is limited by its retrospective nature and small cohort size possibly limiting the significance of our findings. In addition, we did not include patients under the age of 18 years within our cohort, despite the high prevalence of TT in this population, since we did not have preoperative complete blood count consistently collected for these patients. Nevertheless, TT may occur at any age, with 39% of all torsion cases occurring in adulthood [1], and the prevalence of torsion in adults hospitalized with acute scrotal pain is 25–50% [15, 16]. Scrotal USs were performed by several radiologists, and did not undergo centralized review; thus, it is possible that some variability exists between the sonographic readers. Finally, we did not have long-term follow-up of our patients but rather

Table 3. Summary of findings from studies evaluating the association between blood markers and the diagnosis of testicular torsion and testicular viability after an event of testicular torsion

Study	Cohort size	Blood markers evaluated	Associations found with blood markers	Additional findings
Gunes et al. [14] 2015	75 patients with testicular torsion and 56 aged matched healthy subjects	NLR, PLR, MPV, platelet count	Higher NLR, PLR, and platelet count were significantly associated with testicular torsion ($p < 0.001$ for all). NLR was significantly associated with duration of torsion ($p = 0.01$)	
Bitkin et al. [11] 2018	153 patients divided into 3 groups. 51 patients who underwent surgery for testicular torsion, 50 patients treated for epididymitis and a control group of 52 healthy individuals	WBC, neutrophil count, lymphocyte count, platelet count, NLR, PLR, MPV	WBC, MPV, and NLR values were higher in both the epididymitis and torsion groups compared to the controls ($p < 0.001$) and did not differ between torsion and epididymitis. Platelet counts and PLR were significantly higher in the epididymitis group compared to the other two groups ($p < 0.001$)	
Jang et al. [12] 2019	60 patients with testicular torsion. 38 underwent orchiectomy and 22 orchiopexy	Hb, WBC, neutrophil count, lymphocyte count, platelet count, NLR, PLR, CRP	WBC and NLR were significantly lower in the orchiopexy group ($p < 0.001$). NLR independently predicted testicular survival after surgical intervention especially for patients with marginally delayed diagnosis	Symptom duration was significantly lower in the orchiopexy group
He et al. [13] 2019	112 patients with testicular torsion. 58 underwent orchiectomy and 54 orchiopexy	WBC, neutrophil count, lymphocyte count, monocyte count, platelet count, NLR, PLR, MPV	Higher MPV was found to be a significant predictor of orchiectomy (OR = 3.697, $p = 0.044$)	Longer symptom duration (OR = 1.11, $p < 0.001$), and higher degree of torsion (OR = 1.006, $p = 0.002$) were significant predictors of orchiectomy
Current study	50 patients with testicular torsion ≥18 years of age	WBC, neutrophil count, lymphocyte count, platelet count, NLR, PLR, CRP	Complete blood count markers and CRP were not significantly associated with testicular viability at scrotal exploration	Heterogenous testicular echotexture was significantly associated with orchiectomy during exploration (OR = 42, 95% CI 7, 831, adjusted p value = 0.009)

WBC, white blood cell; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; MPV, mean platelet volume; Hb, hemoglobin; CRP, C-reactive protein; OR, odds ratio; CI, confidence interval.

relied on surgical outcome to evaluate whether the testicle was viable or not, thus, the rate of viable testes may be lower than identified in our study. Similarly, the lack of long-term follow-up limits our ability to evaluate long-term outcomes including testicular atrophy, testicular pain, testosterone levels, and pregnancy rates.

Conclusion

Our findings do not suggest an association between blood-based biomarkers and testicular outcome after scrotal exploration for TT but rather supports the role of previously reported baseline characteristics including

testicular echotexture and duration of torsion as predictors of outcome. Specifically, scrotal US findings may be used when counseling patients and their families regarding the outcome of scrotal exploration.

Due to the inconsistent association between blood-based biomarkers and outcome in multiple studies, there is still no consensus regarding the association between these markers and testicular viability after an event of TT. Further research, especially large-scale, prospective studies are needed to evaluate this association.

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Statement of Ethics

This study protocol was reviewed and approved by the Tel Aviv Sourasky Medical Center Ethics Committee, approval number [0539-20]. The study has been granted an exemption from requiring written informed consent by the Ethics Committee.

Conflict of Interest Statement

Roy Mano is a paid consultant for NIXIO LTD. All other authors have no conflicts of interest to declare.

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Author Contributions

E.B., A.B., and R.M. contributed to study concept and design. E.B. and S.D. were involved in data collection. E.B., S.D., and R.M. performed analysis and interpretation of data. E.B. and R.M. drafted the manuscript. O.Y., J.B.-C., Y.B.-Y., and A.B. provided critical revision of the manuscript for important intellectual content.

Data Availability Statement

The data that support the findings of this study are not publicly available due to institutional policy. Data can be made available on request from the corresponding author [R.M.].

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