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Original article

Validation of TWIST score in the diagnosis of testicular torsion in children: A Prospective study

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Abstract: ***Background:*** Early diagnosis is key in testicular torsion. This study is to validate the diagnostic value of the "Testicular Workup for Ischemia and Suspected Torsion (TWIST)" score for evaluating acute scrotum in children. ***Methods:*** Patients from 1 month old to 16 years old presented to Children's hospital No.1 with acute scrotum between June 1 st, 2020, and May 31 st, 2021 were prospectively studied. General surgeons performed an examination and recorded signs and symptoms in the collection form. After that, all patients had Scrotal Doppler Ultrasound (DUS). We calculated the sensitivity, specificity, positive predictive, and negative predictive values of the TWIST score. The ROC curve was used to find out the optimal cut-off in diagnosing Testicular torsion (TT) in Children. ***Results:*** Among 68 children with acute scrotum, 16 cases had TT (23.5%). The median age was 12.5 years in the TT group and 9 years in the non-TT group. None of 32 patients with the TWIST score ≤ 2 had TT and among 20 patients with a score of 3 – 4, only one had TT. More importantly, in the high-risk group with a score ≥ 5, 15 had TT (93.8%). ROC curve revealed an AUC of 0.987 (p<0,001) representing a high diagnostic value. The sensitivity and specificity for TT at 5-point cut-off were 93.7% and 98.1%, respectively. ***Conclusions:*** The TWIST scoring system has high sensitivity and specificity values. Therefore, it should be used as a useful tool for the diagnosis of testicular torsion. The score ≥ 5 is an indicator of testicular torsion, hence emergency surgical intervention is required.

Keywords: 3 Testicular torsion; TWIST score; acute scrotum.

1. INTRODUCTION

Acute scrotal pain and swelling is a common pediatric emergency presentation. There are different diagnostics such as testicular torsion, torsion of the appendix testis, and epididymitis [1]. Testicular torsion (TT) is the most important cause of the acute processes affecting the scrotal contents [2]. Moreover, it may lead to the loss of the testicle. As a result, TT requires early diagnosis and emergency surgical treatment. The salvage rates depend on the duration of pain, it can reach 97% if the operation is performed within 6 hours after symptoms onset and decrease to 60% if the time exceeds 12 hours [2,3].

Physical examination is important to evaluate acute scrotum. However, there is no isolated sign as well as a symptom that can confirm or exclude TT. Although the absence of a cremasteric reflex has a high sensitivity for TT, some cases of TT present with preserved reflex [4]. The scrotal Doppler Ultrasound (DUS) has got high accuracy value in diagnosis and has been considered the quality imaging to diagnose TT [5]. However, routine DUS can delay surgical exploration. On the other hand, it may burden the

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system with unnecessary tests because TT is found in 15 – 30% of children with acute scrotum [6,7].

In 2013, Barbosa [8] developed the Testicular Workup for Ischemia and Suspected Torsion (TWIST) score system for early diagnosing TT in pediatric patients who present acute scrotal pain. The aim is to screen for TT using five features: swelling, hard testicle, absent cremasteric reflex, high-riding testis, and nausea. In the first series, the cut-off scores were 2 points and 5 points for the low and high-risk groups, respectively. This score system achieved both Positive predictive value (PPV) and Negative predictive value (NPV) of 100% for diagnosing TT [8]. Prospective and retrospective studies have further evaluated this scale [9,10,11]. However, there is no study on the validation of TWIST score in Vietnam because The Twist Score has not been applied in the diagnosis of testicular torsion. The previous studies only evaluated clinical features and treatment outcomes, these studies reported a high rate of orchiectomy due to delay in diagnosis [12,13]. Therefore, this study was conducted to evaluate the value of the TWIST score system in diagnosis of TT in the children presenting with acute scrotum.

2. MATERIALS AND METHOD

2.1. Study design

Setting and design

We prospectively collected data of all male children with acute scrotum admitted to the ED of Children hospital No.1 which is one of the tertiary children's hospitals at HCMC (patients under 16-year-old).

Participants were males with scrotal acute syndrome aged 1 month to 16 years. Patients were excluded if their scrotal pain was due to trauma, undescended testis torsion and if a diagnosis of TT had already been confirmed previously.

The very first general surgeon who evaluated the patients would perform the initial physical examination and record signs and symptoms in the TWIST score system (Table 1). Then, all patients underwent a Scrotum Doppler Ultrasound by experienced radiologists in our center. The main outcome was a diagnosis of testicular torsion. In case patients were indicated for surgical exploration, the diagnosis of TT was confirmed in operation. Whereas, if patients were indicated for follow-up, the diagnosis of non-TT was confirmed by clinical and Scrotum Doppler Ultrasound follow-up on day 3 [8] (According to the primary study, for patients presenting within 72 hours of onset of symptoms, DUS was the gold standard for nonsurgical cases). We collected data on clinical characteristics, ultrasound results, and treatment results without interfering with the diagnosis and treatment process. Then, we calculated the TWIST score, classify in 3 groups, and evaluate the TWIST score. The research steps are shown in Figure 1.

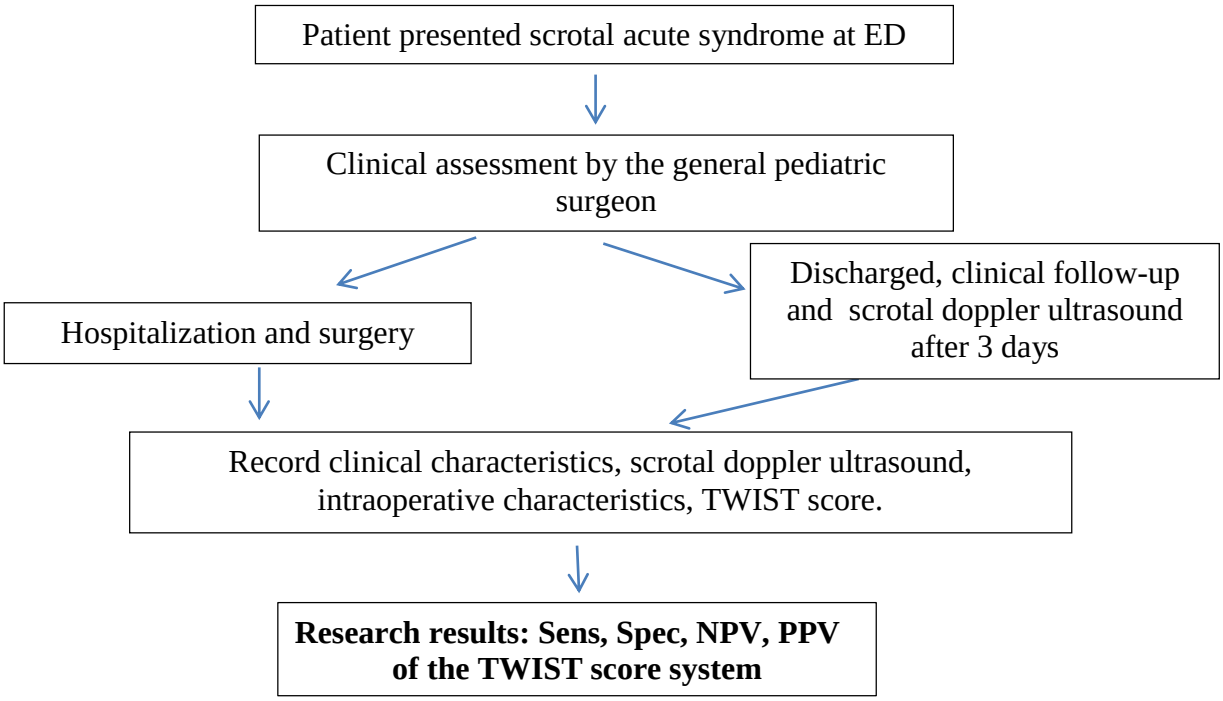

Figure 1. Our study Flow Chart

Definition of variables:

- Acute scrotal syndrome: Onset by sudden pain in the scrotum with or without redness and systemic signs.

- The TWIST score are shown in Table 1.

- Testicular torsion is defined by surgery with testicular torsion or testicular ischemia if there is no torsion (indicating recent detorsion).

- No testicular torsion was determined by clinical follow-up and scrotal doppler ultrasound-the gold Standard after 3 days without TT signs or hypoperfusion of the testicles.

Table 1. Testicular Workup for Ischemia and Suspected Torsion (TWIST) score system

Feature	Score
Testicular swelling	2
Hard testis	2
Absent cremasteric reflex	1
Nause/ vomitting	1
High-riding testis	1
Total	**7**
Low-risk	≤ 2
Intermediate-risk	3 – 4
High-risk	≥ 5

2.2. Study size

Sample size requirements are calculated based on sensitivity and specificity of the diagnosis tests:

$$Nse \geq \frac{Z^2_{(1-\frac{\alpha}{2})} \times Pse \times (1 - Pse)}{d^2 \times Pdis}$$

$$Nsp \geq \frac{Z^2_{(1-\frac{\alpha}{2})} \times Psp \times (1 - Psp)}{d^2 \times (1 - Pdis)}$$

Nse, Nsp: sample size requirements for estimates of sensitivity and specificity.

$\alpha = 0{,}05 \Rightarrow Z = 1{,}96$

d = 0,08 (the marginal error)

Pse and Psp: Predicted sensitivity and specificity. According to research by Manohar C.S. [10]: Pse =95.5%; Psp= 97.2%

Pdis: percentage of children with testicular torsion in the total number of children with acute scrotum. According to research by Manohar C.S., Pdis = 38% [10].

Nse = 68 and Nsp = 36. Therefore, the study size is 68 cases.

2.3. Sample criteria

Inclusion Criteria

• All male patients came to the clinic of Children's Hospital 1 because of acute scrotal syndrome, defined as painful scrotum or testis.

• All patients in the hospital were under 16 years, therefore, agreements from the patient's guardian were obtained.

Exclusion Criteria

• Scrotal injury [19].

• Have been diagnosed with TT at another medical center [19].

2.4. Statistical analysis

All statistical analysis was performed by using SPSS Software 25.0 (IBM, United States). Data were described in percentages for qualitative variables. We presented the continuous variables with mean and standard deviation if normally distributed and median with range if non-normal distribution. The confidence interval was 0.95. The Fisher test was used to analyze the relationship between discrete variables. The difference was statistically significant when $p < 0.05$. The Receiver operator curve (ROC) was applied to find optimal cut-off and evaluate the validity of different parameters in separating TT from non-TT. The Area under the curve (AUC) and its p-value prescribed this validity (AUC ≥ 0.9 suggests excellent test, 0.8-0.89 suggests good test, 0.7 – 0.79 suggests fair test and otherwise, unacceptable). Reliability tests (sensitivity, specificity, positive predictive value, negative predictive value) were calculated.

2.5. Ethical considerations

This was an observational study that did not impact the management of the patient. The study was approved by the ethics committee of Children's hospital No.1 (169/GCN_BVNĐ1); and accepted by The University of Medicine and Pharmacy at Ho Chi Minh City (UMP).

3. RESULTS

3.1. Research population characteristics

Sixty-eight patients were enrolled in our study, and 16 had TT (23.5%). The median age was 12.5 years (range 1-16) in TT group and 9 years (range 1-12) in non-torsion group. Testicular torsion was the third leading cause of acute scrotal syndrome, accounting for 23.5%, after torsion of testicular appendages (45.6%) and epididymitis (29.4%). The rate of orchiectomy due to torsion was 56%. The components of the TWIST score system and other clinical features are shown in Table 2.

Vomiting symptoms were related to the TT, accounting for 43.8% in the TT group compared with 5.8% in the non-TT group. This difference was statistically significant (Fisher's test, $p < 0.001$).

Similarly, high riding testicle, hard testicle, and absent cremasteric reflex accounted for a higher proportion in the TT group compared with the non-TT group. This difference was statistically significant (Fisher's test, $p < 0.001$).

Table 2. Clinical Features of Children With Acute Scrotum (N=68)

CHARACTERISTIC	TORSION (N=16)	NONE TORSION (N=52)	P
TESTICULAR SWELLING	14(87.5%)	43(82.7%)	0.16[1]
HIGH RIDING TESTES	15(93.7%)	3(5.7%)	< 0.001[1]
ABSENT CREMASTERIC REFLEX	15(93.7%)	2(3.8%)	< 0.001[1]
HARD TESTICLE	15(93.7%)	19(36.5%)	< 0.001[1]
NAUSEA AND VOMITING	7(43.7%)	3(5.7%)	< 0.001[1]

[1]FISHER TEST

3.2. Primary result-Twist score

In the TT group, the mean TWIST score was 5.9 (±0.9) whereas it was 2.6 (±1.1) in the Non-TT group. As shown in Table 3, no patient in the low-risk group (n=32) (0 – 2 points) had TT. Among 20 patients in the intermediate-risk group (3 – 4 points), we found 1 case of TT. Of 16 patients in the high-risk group (score ≥ 5), 15 were diagnosed with TT and 1 with non-TT (torsion of the appendix testis).

Table 3. Testicular Workup for Ischemia and Suspected Torsion (TWIST) Score in Children With Acute Scrotum

		Torsion (16) n (%)	Non torsion (52) n (%)
TWIST	0	0 (0%)	2 (100%)
	1	0 (0%)	1 (100%)
	2	0 (0%)	29 (100%)
	3	0 (0%)	4 (100%)
	4	1 (6.2%)	15 (93.8%)
	5	4 (80%)	1 (20%)
	6	6 (100%)	0 (0%)
	7	5 (100%)	0 (0%)
Risk group	Low	0 (0%)	32 (100%)
	Intermediate	1 (5%)	19 (95%)
	High	15 (93.8%)	1 (6.2%)

Table 4. Sensitivity, specifcity, positive predictive value and negative predictive value for diferent cutoffs of the TWIST score for diagnosis of testicular torsion

TWIST Cut-off	Sensitivity	Specifcity	cPPV[1]	NPV[2]
4	100%	69.2%	50%	100%
5	93.7%	98.1%	93.7%	98.1%
6	68.7%	100%	100%	91.2%

[1]Positive predictive value

[2]Negative predictive value

In our series, a score of 3 points or less has an NPV of 100% for testicular torsion (95% confidence). On the other hand, a score of 5 points or more exhibited a sensitivity of 93.7%, and a PPV of 98.1% (Table 4). As all 11 patients with a score ≥ 6 points had TT in this series, the specificity and PPV of 100% each. Therefore, a shift in the diagnosis cut-off from 5 to 6 points gets higher specificity and PPV. Table 4 summarizes reliability tests including sensitivity, specificity, and predictive values at different cut-offs.

The ROC curve reveals an Area Under Curve of 0.987 (95% CI 0.963–1.000; p<0.001), this was shown in Fig.2.

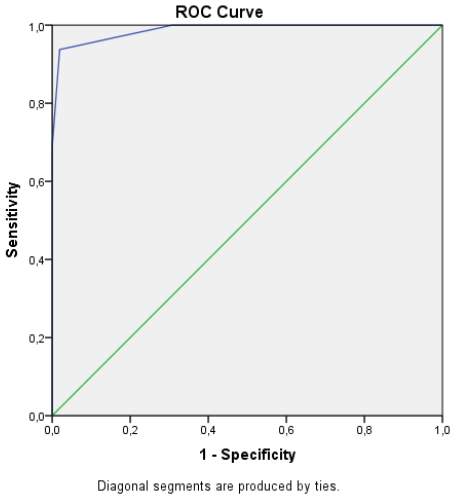

Figure 2. ROC curve for TWIST score showing the optimal cut point and each point of the score criteria. The area under curve is 0.987 (95% CI 0.963–1.000; p<0.001)

4. DISCUSSION

In this study, the median age was higher in TT group which was 12.5 years compared to 9 years for the non-TT group. This result resembles Murphy F's [14] study of 121 children, in which the median age of the TT group was 12 years and the non-TT group was 10 years. As known that there is a second peak incidence of testicular torsion in adolescent boys aged (13 – 16) years [15].

In this series, nausea/vomiting are significantly higher in the TT group (43.7% vs 5.7%) (Fisher test, p < 0.001). This result resembles the findings by Boettcher M. et al [16], Gregory J. et al [17], and Ciftci et al [18]. In our series, the high riding testis, absent cremasteric reflex, and hard testis were significantly associated with TT (93.7% in the TT vs 5.7% in the non-TT group, 93.7% vs 3.8%, and 93.7% vs 36.5% respectively), (Fisher test, p < 0.001). Boettcher M. et al [14] reported that high riding testis and absent cremasteric reflex were also significantly related to TT (41.7% in the TT vs 3.3% in the non-TT group and 50.0% vs 2.2%, respectively).

We found that the TT group has a significantly higher TWIST score compared to the non-TT group. In the TT group, the mean TWIST score was 5.9 (±0.9) whereas it was 2.6 (±1.1) score in the non-TT, Fisher test, p < 0.001. This goes with Baker's findings [11]: the median score was 6 vs 1 in the two groups. None of the patients with low-risk scores had TT. This result resembles that of Barbosa et al [8] who found none of 234 low-risk score patients had testicular torsion.

In this study, according to the ROC analysis result, the TWIST score is extremely sensitive and specific for TT. TWIST scoring promoted confirmation and exclusion of TT

with outstanding predicting value at a 5-point cut-off (specificity 98.1%, sensitivity 93.7%, PPV 93.7%, and NPV=98.1%). Furthermore, the score of 6 points exhibited a 100% PPV. However, it can increase the likelihood of missing positive patients with testicular torsion. This result is in keeping with Barbosa et al [8] found that the optimal cut point was 5 (AUC=0.98, sensitivity 76%, specificity 100%, PPV 100%, and NPV 96%).

Compare with Barbosa [8] who introduced the TWIST score system as a clinical tool to assess the risk of TT and reduce unnecessary DUS, the optimal cutoff points in their study are 2 and 5 points. The sensitivity and negative predictive value for the "2-point" cutoff were 100%. The "5-point" cutoff has a sensitivity and specificity of 76% and 100%, respectively, and a positive predictive value of 100%. With the above results, Barbosa [8] concludes that the TWIST scale can be used to diagnose and rule out TT in 80% of cases, therefore, this scale can reduce the rate of DUS indications in patients. The author commented that when applying this scale to the entire pediatric population, the assessment may be inaccurate in young children, such as the physiological absence of the scrotal reflex seen in children under 2 years of age. We only have three cases of children under 2 years old. Since our hospital is one of the tertiary hospitals, the group of patients in the study may have prolonged torsion; features on the TWIST scale such as scrotal swelling, hard testicles, and loss of scrotal reflex seem more clearly. Symptoms such as nausea/vomiting, scrotal swelling, and testicular elevation achieved similar agreement between different clinicians. However, the other two components (hard testicles, and abnormal scrotal reflex) are more difficult to assess and can be subjective. We agree with Barbosa that this score does not help distinguish the different causes of acute scrotal syndrome [8]. The ultrasound in this case provides more information.

Similarly, Manohar [10] performed a retrospective analysis of TWIST scores in a population that included adults and children (ages 8 – 28 years). Based on baseline cut-off points of 2 and 5 points, the results showed that the NPV and sensitivity in the low-risk group were 96.6% and 95.5%, respectively, while the PPV and specificity in the high-risk group were 92.8% and 97.2%. Also according to the research results, the increase in PPV from 92.8% to 100% when the cutoff is raised to 6 points. Our study also gave similar results because 100% PPV was only achieved with a positive cutoff of 6 points. In contrast to the original report, a value of 100% of PPV was achieved even when the cutoff is 5 points [8]. It should be noted that we had 1 patient with a score of 5 but false positive with the intraoperative diagnosis of epididymitis.

Unlike us and Barbosa, Sheth [11] reported a study on 128 patients under 21 years old, the optimal cutoff points were 0 and 6 points. None of the patients with a TWIST score of 0 had torsion for an NPV of 100%. With a TWIST score ≥ 6, PPV is 93.5%. Accordingly, Sheth advocated relying on history and physical symptoms to diagnose TT, reducing dependence on imaging tests, helping to reduce costs, and facilitating rapid surgical intervention. It is noteworthy in Sheth's study that patients with acute scrotal pain were assessed using the TWIST scale collected by staff who were not specialists in urology. This study suggests that the TWIST score can be accurately assessed by general practitioners who have an initial approach to pediatric patients.

Frohlich [19], conducted a prospective study of 258 children with acute scrotal presentation. In their protocol, the TWIST score is applied by pediatric emergency physicians or fellows. In this study, the authors found a lower accuracy (AUC 0.82; 95% CI 0.71 – 0.94) compared with previous reports. Based on Frohlich's results, the TWIST score can be used as a clinical tool to aid in the diagnosis of TT, especially for recommending exploratory surgery for cases with a total score of 7.

In two studies [11,19] taking the diagnostic cut-off of 7 points will give 100% of the PPV, in our study, when changing the cut-off point to 6 points, it also gives 100% of the PPV. However, the recommendations still suggest that exploratory surgery is appropriate for suspected cases [2, 3], so we still choose the cut-off point of 5 to avoid missing TT cases. Several factors need to be considered including the qualifications of the staff applying the points, population characteristics, context and available resources. According to studies, it seems that the accuracy of the score is highest when applied by urologists [11,19].

On the other hand, a score of ≤ 2 is still suitable to exclude TT. In our study, none of the patients in the low-risk group had TT, the NPV was 100% for this threshold. This parameter would be useful in excluding additional clinical indications such as DUS, particularly in settings where it is not available, or in determining a lower priority for the management of such cases.

Ridgway [20] evaluated data from four studies that directly assessed TWIST scores. They found a consistent sensitivity of 95-100% for low-risk patients, while the specificity of 97-100% for high-risk patients. This further supports the TWIST score to be considered a reliable tool for the assessment of patients with acute scrotal syndrome. The results of our research on the TWIST scale and the world's authors are presented in Table 5.

From the results, we suggest that if the TWIST score is equal to or more than 5 points, pediatric patients should be urgently referred to a specialized hospital for urgent exploratory surgery. On the opposite, the patient may not need to be hospitalized and should be monitored at home if the score is equal or less than 2 points. Doppler ultrasound performed by a qualified sonologist should be ordered early in moderate risk group.

Our study has a limited number of patients, only 16 children have testicular torsion out of a total of 68, therefore more studies are needed with a larger number of pediatric patients in the TT group and a larger sample size of acute scrotal syndrome so that the statistical tests have fewer errors and more accurate results. One further limitation of our study is that there is no follow-up for recurrent symptoms in the non-TT group or the TT group that did not have orchidectomy.

Conclusion

TWIST score exhibited high sensitivity and specificity values and should be used as a clinical tool in the diagnosis of testicular torsion in any medical setting, especially where Doppler Ultrasound is not available. We could not validate the use of TWIST score from this study since no kappa test and the small sample size, however this study suggests the usefulness of this score system for early diagnosing TT in a pediatric population who presents acute scrotal pain.

Table 5. Valuation of TWIST score in the diagnosis of testicular torsion of studies.

Author Year	Cut-off	Sens[1]	Spec[2]	PPV[3]	NPV[4]
Barbosa [8]-2013	2	100%	82%	49%	100%
	5	76%	100%	100%	96%
Sheth [11]-2016	0		47.6%		100%
	6	65.9%		93.5%	
Frohlich [17]-2017	7	21.0%	100%	100%	
Manohar [10]-2018	2	95.5%			96.6%
	5		97.2%	92.8%	
Bašković [9]-2019	2	95.1%			98.5
	5		97.7%	92.5%	
Our study 2021	2	100%			100%
	5	93.7%	98.1%	93.7%	98.1%

[1]Sensitivity
[2]Specifcity
[3]Positive predictive value
[4]Negative predictive value

LIST OF ABBREVIATIONS

TWIST: Testicular Workup for Ischemia and Suspected Torsion;

TT: Testicular Torsion;

DUS: Doppler Ultrasound

ROC: Receiver operator curve

AUC: Area under the curve

PPV: Positive predictive value

NPV: Negative predictive value.

ETHICAL STATEMENT

If abbreviations are used in the text either they should be defined in the text where first used, or a list of abbreviations can be provided.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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