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Original Research

Pathological re-evaluation of testicular torsion specimens: Implications for surgical intervention strategies

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Summary

Objective
This study aims to conduct a retrospective pathological analysis of testicular tissue specimens excised due to testicular torsion, to reassess the validity of previous surgical decisions and provide a comprehensive summary of the appropriate surgical indications for orchiectomy.

Methods
Medical records of patients who underwent orchiectomy due to testicular torsion at XXX Hospital between 2015 and 2023 were reviewed, and the excised testicular specimens were re-evaluated using the Mikuz grading system.

Results
113 patients who underwent orchiectomy were included in this study. Following the Mikuz classification, 14 patients were classified as Grade 1, 31 as Grade 2, and 68 as Grade 3. A longer duration of symptoms was associated with a lower proportion of patients with Grade 1 testicular injury while increasing age was correlated with a higher likelihood of developing Grade 1. In the Grade 1 group, 78.6 % of patients had a monocyte count of less than 0.5×10^9/L, whereas the monocyte counts in the Grade 2 and Grade 3 groups were significantly higher than those in the Grade 1 group.

Conclusion
The findings of this study indicate that 12.4 % (14/113) of patients who underwent orchiectomy had low-grade testicular injury. Currently, objective measures are deficient for assessing the extent of testicular injury post-torsion, necessitating cautious decision-making regarding orchiectomy during surgical intervention. Patients presenting with brief symptom duration and low monocyte count may be more suitable candidates for orchiopexy as opposed to orchiectomy.

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Background

Testicular torsion is a critical urological emergency characterized by the twisting of the spermatic cord, leading to compromised blood flow to the testicle. Timely intervention is crucial to restore blood flow and viability of the testis through orchiopexy. In cases where testicular vitality is irreversibly compromised, orchiectomy is advised to prevent reperfusion and autoimmune damage [1]. At present, most studies mainly judge testicular viability according to the bleeding of testicular parenchyma after testicular tunica albuginea incision [2]. Additional research has explored the potential predictors of testicular salvage, such as the duration of symptoms, severity of spermatic torsion, testicular color, and hematological parameters [3—6]. Regrettably, there is a lack of standardized criteria to guide clinicians in determining whether to proceed with orchiectomy or attempt testicular retention. Consequently, some clinicians may inaccurately assess the extent of testicular tissue damage, resulting in unnecessary orchiectomies [7]. This study conducted a retrospective analysis of the clinical data of patients who underwent orchiectomy at XXX Hospital, re-evaluating the extent of testicular injury through a pathological perspective. Additionally, the study aims to investigate the likelihood of orchiectomy in cases of low-grade injury and identify strategies to prevent such occurrences.

Materials and methods

The Ethics Board of Shenzhen Children's Hospital (IRB No. 2022014) approved the study protocol. The research examined the medical records of patients with testicular torsion who underwent surgical intervention at XXX Hospital between June 2015 and December 2023. In this study, the participants comprised patients who had undergone orchiectomy following testicular torsion. During the surgical procedure, all patients were diagnosed with testicular torsion and subsequently underwent orchiectomy due to the extent of testicular damage, except for cases involving neonatal testicular torsion and those lacking medical documentation. Data about the patient's age at onset, duration of symptoms, presence of cryptorchidism, hematological parameters, degree of spermatic torsion, surgical approach, and other relevant medical information were gathered. The excised testicular specimens were subjected to histological evaluation by a pathologist using hematoxylin-eosin staining under a light microscope, and subsequently graded according to the histological grading system of testicular torsion proposed by Mikuz (Table 1) [8].

During the study, the double-blind method was employed, with clinicians retrieving the medical records of the children using hospitalization numbers. Histological evaluation results were not accessible. The pathologist assessed testicular samples from the specimen bank using pathological specimen numbers, without access to the children's medical records. Subsequently, another doctor collected and organized the final results. In Mikuz's classification, Grade 1 denotes a mild impairment of testicular germ cells that is potentially reversible, while Grade 2 indicates necrosis of a portion of the testicular parenchyma with some potential for salvage. Grade 3 signifies hemorrhagic infarction of the testis and complete necrosis of the testicular parenchyma. In this study, patients categorized as Grade 1 were considered to have mild testicular injury, whereas those classified as Grade 2 and Grade 3 were deemed to have severe testicular injury.

Table 1 The Mikuz grading system.

Grade	Histomorphological changes
Grade 1	Testicular interstitial edema and telangiectasia were observed, with Leydig cells, spermatogonia, and Sertoli cells exhibiting normal morphology, spermatocytes, spermatids, and spermatozoa were exfoliated.
Grade 2	Diffuse hemorrhage in the testicular interstitium, partial necrosis of germ cells and interstitial cells, and partial contraction of testicular tubules. Germ cells displayed extensive desquamation, with some persisting spermatogonia and Sertoli cells coexisting with necrotic spermatogonia.
Grade 3	Complete hemorrhagic infarction of the testicular parenchyma, resulting in blurred and indiscernible parenchymal structure. All germ cells, including spermatogonia, were found to be necrotic.

The Kolmogorov—Smirnov test was employed to assess the normal distribution of the data. The Kruskal—Wallis test is utilized for comparing groups with non-normally distributed data, while univariate analysis of variance (ANOVA) is employed for comparing groups with normally distributed data. Median (interquartile range) is used to represent measurement data with non-normal distribution, whereas mean $\pm$ standard deviation is used for data conforming to a normal distribution. The observed difference was found to be statistically significant ($P < 0.05$).

Results

Over the period from June 2015 to December 2023, a total of 203 patients underwent surgical intervention for testicular torsion at our institution. Following the identification of testicular torsion during the surgical procedure, prompt and accurate restoration was achieved. After a 20-min application of warm saline gauze externally, alterations in testicular color were monitored, followed by a minor incision into the testicular parenchyma. Orchiopexy was conducted in cases where fresh blood outflow was present, while orchiectomy was performed with parental consent in instances of no blood outflow [3]. Fifteen neonates with testicular torsion and nine individuals lacking medical documentation were excluded from the study. In this study, 113 patients underwent orchiectomy. The specimens obtained after orchiectomy were classified according to Mikuz grade into Grade 1, Grade 2, and Grade 3 groups (Fig. 1) [8]. The distribution of patients in these groups was as follows: 14 (12.4 %) in Grade 1, 31 (27.4 %) in Grade 2, and 68 (60.2 %) in Grade 3. The median age of patients in the Grade 1, Grade 2, and Grade 3 groups was 12.78, 7.01, and 9.20 years, respectively. The median duration of symptoms in the Grade 1 group was 10.5 h, while in the Grade 2 and Grade 3 groups, it was 24 h

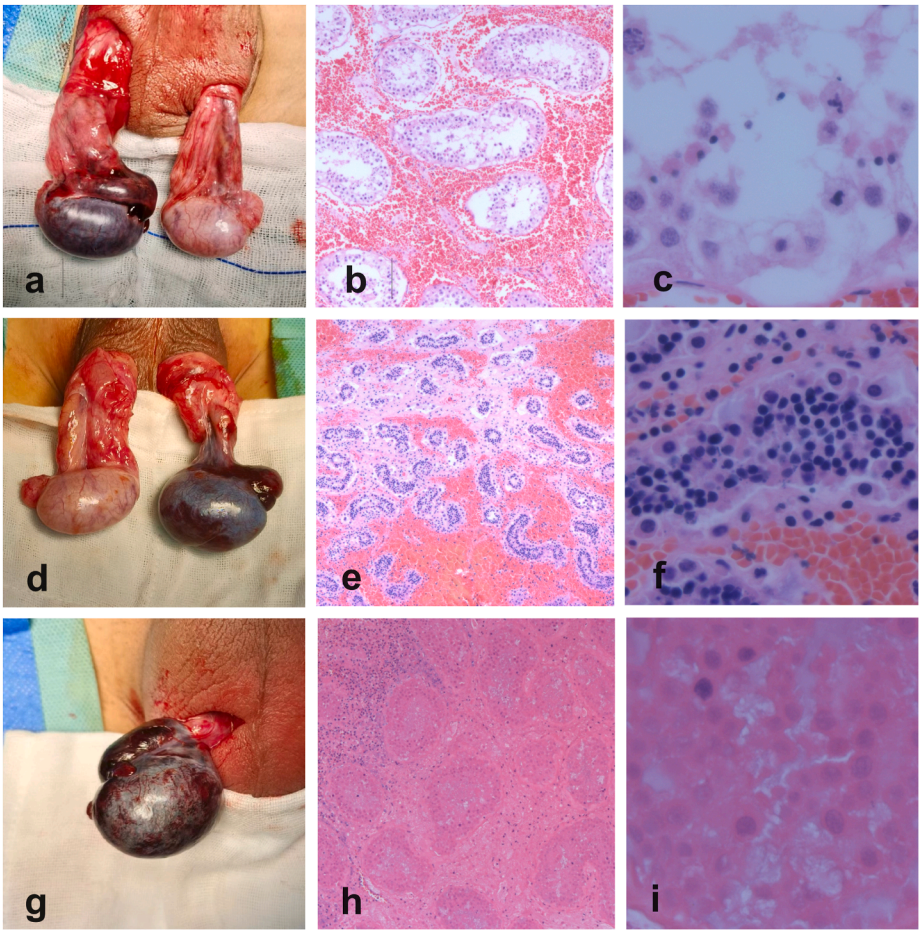

Fig. 1 (a) Intraoperative appearance of the testis for Grade 1 testicular injury. (b, c) testis sections at 50x and 400x magnification for Fig.a. Interstitial edema and mild hemorrhage. Germ cells exhibit spermatocytes, spermatids, and sloughing spermatocytes, while spermatogonia and Sertoli cells remain unchanged. Interstitial cells appear intact. (d) Intraoperative appearance of the testis for Grade 2 testicular injury. (e, f) testis sections at 50x and 400x magnification for Fig.d. Diffusely hemorrhagic and congested interstitial tissue, with partially necrotic germ cells and interstitial cells. Shedding is evident in germ cells and some spermatogonia. (g) Intraoperative appearance of the testis for Grade 3 testicular injury. (h, i) testis sections at 50x and 400x magnification for Fig.d. The tissue exhibits complete hemorrhage and infarction, with the parenchymal structure only minimally discernible. All germ cells, including spermatogonia, are affected by infarction.

and 72 h, respectively. Based on the established grouping criteria, all patients were categorized into either the low-degree testicular injury group or the high-degree testicular injury group (Table 2). A comparative analysis between these groups revealed significant age differences ($P < 0.002$), symptom duration ($P < 0.001$), NLR (neutrophil-lymphocyte ratio) ($P < 0.001$), and monocyte count ($P < 0.001$). A bar chart was utilized to visually represent the distribution of patients across three levels of injury severity (Fig. 2). Within the Grade 1 group, symptom duration was less than 12 h in 9 cases, 12—24 h in 3 cases, 24—48 h in 1 case, and 48—72 h in 1 case (Fig. 1). Our study revealed a negative correlation between the duration of symptoms and the proportion of patients with Grade 1 testicular injury, as well as a positive correlation between age and the likelihood of postoperative Grade 1 testicular pathological scores. Further analysis of monocyte counts showed that 78.6 % of Grade 1 patients had a count of less than 0.5×10^9/L, while Grade 2 and Grade 3 patients had significantly higher counts compared to Grade 1 patients (Fig. 2).

Discussion

Testicular torsion has the potential to result in testicular ischemic injury, which, if left untreated, can progress to testicular atrophy and necrosis [9]. Clinicians typically assess the extent of testicular damage during surgery by evaluating testicular color and bleeding following parenchymal incision, ultimately determining whether orchiectomy or orchidopexy is necessary [2]. Current research efforts primarily concentrate on identifying prognostic indicators for successful testicular salvage, particularly in cases where testicular retention is feasible. Limited research has been conducted on the potential for testicular preservation following severe testicular injury. This study involved the assessment of excised testicles from patients with testicular torsion, categorizing the degree of testicular tissue damage. The findings revealed that 12.4 % (14/113) of patients exhibited mild testicular injury, suggesting potential errors in surgical decision-making. This comprehensive

Table 2 Baseline of patients with low-grade and high-grade testicular injury.

	Grade 1 (n = 14)	Grade 2/3 (n = 99)	*P*
Age (y)	12.78 (11.94, 13.50)	7.35 (2.75, 12.73)	0.002
Symptom duration (h)	10.5 (4, 24)	48 (24, 72)	<0.001
Spermatic cord torsion degree (°)	360 (360, 585)	540 (360, 720)	0.082
Cryptorchidism	0	14	0.225
WBC (10^9/L)	10.28 (9.06, 13.05)	11.54 (9.94, 14.02)	0.268
NLR	6.94 (4.48, 10.59)	2.27 (1.26, 4.52)	<0.001
Monocyte count (10^9/L)	0.38 (0.27, 0.48)	0.75 (0.59, 0.93)	<0.001
MPV (fl)	10.10 (9.23, 10.95)	9.6 (9.10, 10.40)	0.100

WBC, white blood cell; MPV, mean platelet volume; NLR, neutrophil-lymphocyte ratio.
Note: Median (interquartile range) is used to represent measurement data with non-normal distribution, whereas mean ± standard deviation is used for data conforming to a normal distribution.

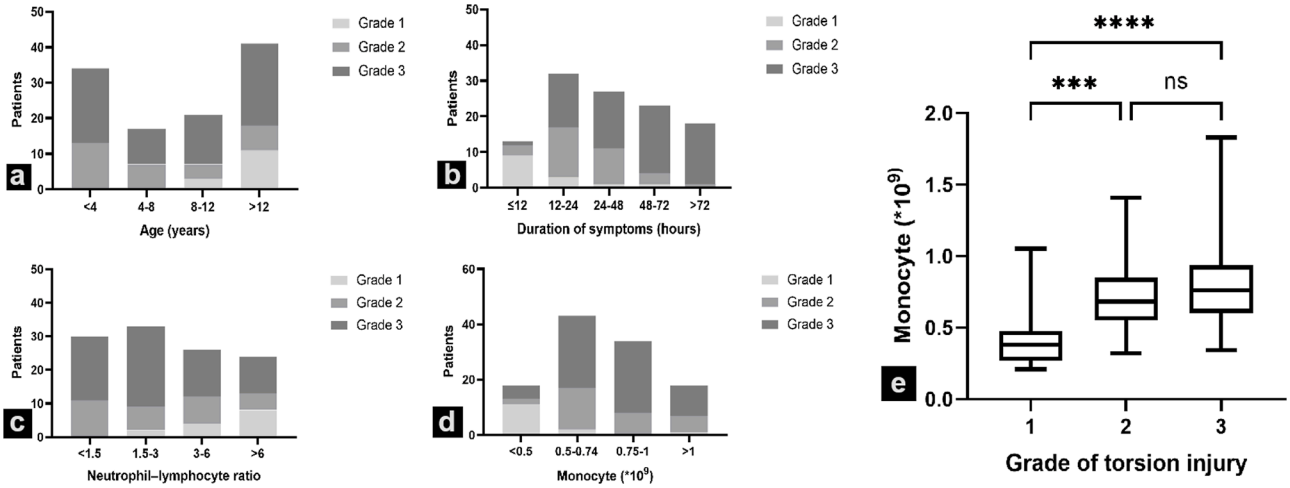

Fig. 2 (a) age distribution of patients with varying degrees of testicular injury. (b) the distribution of symptom duration among patients with varying degrees of testicular injury. (c) the distribution of NLR among patients with varying degrees of testicular injury. (d, e) the distribution of monocyte counts among patients with varying degrees of testicular injury.

investigation serves as a significant case study on the pathological analysis and associated factors of testicular outcomes post-testicular torsion.

To date, limited research has been conducted on the pathological grading of testicular specimens following testicular torsion [1,7,10,11]. Marcou's study found that 10.4 % (5/48) of patients with Grade 1 injuries [7], while Aworanti reported a 6.0 % incidence of mild testicular tissue injury post-orchiectomy [1]. Kuzu's study revealed that 9.5 % of patients with Grade 1 injuries [10], leading to a subsequent multicenter follow-up study by their team. Upon pathological assessment of 228 testes removed due to testicular torsion, it was determined that 8.8 % (20/228) exhibited Grade 1 injuries, with the remaining 91.2 % (208/228) classified as Grade 2 or Grade 3 injury [11]. Based on data from multiple institutions, approximately 10 % of patients diagnosed with testicular torsion underwent orchiectomy despite experiencing only mild testicular injury. This phenomenon has prompted a reassessment of the appropriateness of such surgical decisions. In our study, we encountered a patient with testicular torsion presenting with a 360° rotation, a symptom duration of 72 h, dark discoloration of the testicle during surgery, and absence of fresh blood flow following incision of the testicular membrane. Despite these severe clinical indicators, the pathological assessment revealed only Grade 1 injury. This study suggests that relying solely on the duration of symptoms and intraoperative testicular hemorrhage is insufficient for assessing testicular vitality in cases of testicular torsion. It highlights the need for more comprehensive evaluation criteria to preserve the functional testicles of affected patients. Samson et al. proposed a method for predicting testicular viability by comparing the heterogeneity index between ipsilateral and contralateral testes using Doppler ultrasound. They also noted that a testicular heterogeneity index difference of 0.394 or greater could accurately predict the viability of torsional testis with a sensitivity of 100 % and specificity of 94.5 % [12]. However, the accuracy of ultrasound examination is contingent upon the operator's level of experience. Furthermore, ultrasound examination may prolong the time to surgical intervention and potentially decrease the rate of testicular salvage [13,14].

Our study demonstrates variations in age, symptom duration, monocyte count, and NLR between patients with mild and severe testicular injury. Olderly children with mild testicular injury may exhibit a stronger tolerance to testicular ischemia and hypoxia, potentially due to age-related physiological changes [15]. The duration of

symptoms can serve as an indicator of the extent of testicular ischemia. Prolonged symptoms in cases of complete testicular ischemia are associated with more severe testicular injury [6]. Recent research has highlighted the significance of hematological parameters in predicting testicular viability following testicular torsion. The findings of these studies vary, with current reports indicating that significant predictors include NLR, MPV (mean platelet volume), and monocyte count [4,16,17]. Our prior research confirmed the predictive value of monocyte count in the context of testicular salvage following torsion [3,4]. In the present study, it was observed that 78.6 % (11/14) of patients with mild testicular injury had a monocyte count below 0.5×10^9/L. Building upon existing literature, we hypothesize that the monocyte count in individuals with testicular torsion may serve as an indicator of the extent of testicular damage, particularly in cases of minor injury, where the monocyte count of patients is less than 0.5×10^9/L. Several studies have indicated an elevated monocyte count in individuals with acute myocardial infarction, suggesting a potential involvement of monocytes in myocardial infarction pathogenesis, particularly in ischemia/reperfusion injury [18]. Additionally, some studies have linked increased monocyte levels to reduced high-density lipoprotein levels and compromised renal function in patients with coronary heart disease [19]. While these findings confirm the important role of monocytes in ischemia/reperfusion injury, the lack of basic or clinical studies on testicular ischemia/reperfusion injury hinders the confirmation of our conjecture.

In the clinical setting, pathological biopsy is suggested as the most precise method for evaluating the extent of testicular injury. We advised that patients with testicular torsion undergo intraoperative pathological biopsy to assess the degree of testicular injury during surgery. In cases of mild testicular tissue injury, preservation of the testis is recommended, while in instances of severe injury resulting in extensive necrosis of the testicular parenchyma, testicular excision is advised. Nevertheless, the availability of such facilities may vary among different healthcare institutions, and ensuring consistent availability of round-the-clock pathological examination in all hospitals poses a challenge [20]. Nevertheless, we strongly advised that, when feasible, intraoperative pathological results be utilized as a crucial reference standard for orchiectomy.

Numerous studies have demonstrated the efficacy of substances with anti-inflammatory and antioxidant properties in mitigating testicular ischemia/reperfusion injury [21—23]. Modalities such as hyperbaric oxygen therapy, ozone therapy, ischemic preconditioning, and post-treatment of the testis have been shown to play a significant role in reducing testicular ischemia/reperfusion injury in animals [22,24]. Nevertheless, the absence of clinical randomized controlled trials to substantiate the findings of animal experiments underscores the need for further research in the form of clinical randomized controlled trials for the treatment of testicular torsion. We recommended that these trials prioritize safety while aiming to enhance testicular salvage rates through drug administration or clinical intervention.

Given the retrospective nature of this study, it is important to acknowledge the inherent limitations. The variability in subjective criteria for orchiectomy between different operations may be attributed to the involvement of multiple doctors in this study. With a sample size of 113 in this study and a total combined sample size of just over 400 when considering data from other similar studies, there is a need for further research in histopathological assessment post-orchiectomy. This research is crucial for enhancing the decision-making process surrounding orchiectomy procedures. Furthermore, further research is necessary to evaluate the potential implications of retaining severely damaged testes following testicular torsion on the contralateral testis and fertility of individuals. If the presence of retained testes does not have a negative impact on patients, it may be prudent to prioritize orchiopexy in surgical decision-making.

Conclusion

A retrospective histological analysis conducted in this study revealed that 12.4 % (14/113) of patients who underwent orchiectomy had a low-grade testicular injury, suggesting the possibility of erroneous surgical decisions in these cases. Our study revealed that patients with low-grade testicular injury exhibited a brief duration of symptoms and a low monocyte count. When making surgical decisions for these patients, preference may be given to orchiopexy over orchiectomy.

Author contributions

Conceptualization: Pengyu Chen, Shoulin Li. Data curation: Pengyu Chen, Yue Wang, Qiulin Miao. Formal analysis: Weipeng Huang, Pengyu Chen. Funding acquisition: Shoulin Li. Investigation: Jiahong Su, Zhilin Yang. Methodology: Shoulin Li. Supervision: Weimo Li. Validation: Xuerui Sun. Visualization: Pengyu Chen, Yue Wang, Qiulin Miao. Writing — original draft: Pengyu Chen. Writing — review & editing: all authors.

Ethics

This study obtained approval from the Ethics Committee of Shenzhen Children's Hospital (NO.2022014).

Declaration of Generative AI and AI-assisted technologies in the writing process

Generative AI and AI-assisted technologies were NOT used in the preparation of this work.

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Competing interest

All authors declare no competing interests.

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