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ORIGINAL ARTICLE

Male Health

Establishment and internal validation of preoperative nomograms for predicting the possibility of testicular salvage in patients with testicular torsion

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This study aimed to establish nomograms to preoperatively predict the possibility of testicular salvage (TS) in patients with testicular torsion. The clinical data of 204 patients with testicular torsion diagnosed at Xijing Hospital and Tangdu Hospital (Xi'an, China) between August 2008 and November 2019 were retrospectively analyzed. Univariate and multivariate logistic regression analyses were used to determine the independent predictors of TS. Based on multivariate regression coefficients, nomograms to predict possibility of TS were established. The predictive ability of the nomograms was internally validated by receiver operating characteristic (ROC) curves and calibration plots. The duration of symptoms ranged from 2 h to 1 month, with a median of 3.5 days. Thirty (14.7%) patients underwent surgical reduction and contralateral orchiopexy, while the remaining 174 (85.3%) underwent orchiectomy and contralateral orchiopexy. Finally, long symptom duration was an independent risk predictor for TS, while visible intratesticular blood flow and homogeneous testicular echotexture under color Doppler ultrasound were independent protective predictors. Internal validation showed that the nomograms, which were established by integrating these three predictive factors, had good discrimination ability in predicting the possibility of TS (areas under the ROC curves were 0.851 and 0.828, respectively). The calibration plots showed good agreement between the nomogram-predicted possibility of TS and the actual situation. In conclusion, this brief preoperative prediction tool will help clinicians to quickly determine the urgency of surgical exploration.

Asian Journal of Andrology (2021) 23, 97–102; doi: 10.4103/aja.aja_31_20; published online: 17 July 2020

Keywords: nomogram; testicular salvage; testicular torsion

INTRODUCTION

Testicular torsion is a common urological emergency and one of the most common causes of testicular loss in adolescents. Surgical exploration and testicular reduction are the primary methods used to save the testis. Time is a key factor affecting the possibility of testicular salvage (TS). However, relying solely on this variable cannot meet the needs of clinical decision-making. Patients with a short duration of symptoms may undergo orchiectomy, while those with a relatively long duration of symptoms may successfully retain the testis. This study aimed to predict the possibility of TS using routine preoperative findings to help clinicians quickly determine the urgency of surgical exploration.

PATIENTS AND METHODS

General information

A total of 220 patients with a median age of 16 (interquartile range [IQR]: 14–21) years with testicular torsion were treated in Xijing Hospital and Tangdu Hospital (Xi'an, China) between August 2008

and November 2019. Of them, 204 patients with a median age of 16 (IQR: 14–20) years were finally enrolled in our study. Patients older than 30 years old ($n = 16$) were excluded because comorbidities such as diabetes, smoking, and hypertension can affect the status of their testes. All patients had unilateral testicular torsion. Cryptorchidism was observed in three patients. One patient had cryptorchidism with testicular torsion and underwent cryptorchidectomy. In other two patients, testicular torsion occurred in the normal side, and they underwent orchiectomy and fixation of contralateral cryptorchidism. None of the patients had a retractile testis. Of these 204 patients, 145 (71.1%) and 59 (28.9%) cases occurred on the left and right sides, respectively. The initial symptoms were scrotal pain (198 patients), scrotal swelling (2 patients), and lower abdominal pain (4 patients). The median duration of symptoms was 3.5 (IQR: 1.0–7.0) days. No typical intermittent testicular torsion was observed in all patients. Preoperative scrotal color Doppler ultrasound was used to assess the intratesticular blood flow of the affected testis, testicular parenchymal echotexture of

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Received: 28 September 2019; Accepted: 27 April 2020

the affected testis, and maximum diameter of twisted spermatic cord. Moreover, the bilateral testicular dimensions in the anteroposterior, mediolateral, and craniocaudal axes were measured in 187 patients, and testicular volume was calculated using an ellipsoid volume formula, multiplying the three diameters by 0.523.¹ Preoperative laboratory parameters of inflammation were routinely evaluated, including white blood cell count, neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR). No manual detorsion attempts were performed before operation. During the operation, the testes were untwisted and rewarmed with warm saline for more than 10 min. If the testes turned ruddy, testicular fixation was performed using three polyethylene sutures to provide a three-point fixation.² If the testes remained black and purple, according to Arda's classification,³ the tunica albuginea was incised and orchiectomy was performed if arterial blood leakage did not occur within 10 min.

All patients who participated in this study provided written informed consent. Moreover, the present study conformed to the 1964 Helsinki Declaration and its later amendments and was conducted in accordance with the ethical standards of the Research Committees of Xijing Hospital (KY20203295-1).

Statistical methods

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as median (IQR). The distribution of continuous variables between the orchiectomy and salvage groups was compared using the Mann-Whitney U test, while the distribution of categorical variables between the two groups was compared using the Chi-square tests.

Univariate and multivariate logistic regression analyses were conducted to identify the independent predictors of TS. Continuous variables were converted to categorical variables according to median or clinical experience. Variables that achieved statistical significance in the univariate analysis were entered into the multivariate analysis. Two nomograms were developed using R software (version 3.5.2, <http://www.r-project.org/>) by integrating all variables with

independent predictive significance for TS. One nomogram covers all patients ($n = 204$), while the other covers patients whose symptom duration is within 24 h ($n = 51$). In our study, differences with two-sided $P < 0.05$ were considered significant.

The discrimination ability of the nomograms, namely, their predictive accuracy, was measured using analysis of the area under the receiver operating characteristic (ROC) curve (AUC), whose value ranged from 0.5 to 1. An AUC value equal to 0.5 indicates that the nomogram has no discriminative ability, while a value equal to 1 implies that the nomogram can perfectly distinguish patients with different possibilities of TS. Furthermore, calibration plots were constructed to elucidate the relationship between the nomogram-predicted possibility and the actual rate of TS, and the predictions were expected to fall on a 45° diagonal line in a perfect calibrated model. Bootstrapping with 200 resamples was performed to estimate the optimism and to reduce the overfitting bias of the nomograms.

RESULTS

Distributions of clinical parameters in the orchiectomy and salvage groups

Among the 204 patients with testicular torsion, 30 (14.7%) patients aged 4–30 years underwent orchiopexy, while 174 (85.3%) patients aged 2–30 years underwent orchiectomy. **Table 1** presents the clinical parameters of the orchiectomy and salvage groups. There were significant differences in symptom duration ($P < 0.001$), intratesticular blood flow ($\chi^2 = 18.102$, $P < 0.001$), and testicular parenchymal echotexture ($\chi^2 = 11.074$, $P = 0.001$) between the two groups. In contrast, no significant differences were observed in age, history of sexual activities, side of the twisted testicle, testicular volume of affected testis, testicular volume ratio of affected to contralateral testes, maximum diameter of twisted spermatic cord, white blood cell count, NLR, or LMR between groups (all $P > 0.05$).

Independent predictors of salvage possibility

Univariate and subsequent multivariate logistic regression analyses showed that a long symptom duration (odds ratio [OR] = 0.755, 95%

Table 1: Comparisons of clinical parameters between the orchiectomy group and salvage groups

Parameters	Orchiectomy group	Salvage group	P
Age (year), median (IQR)	16 (14–20)	20 (16–22)	0.052
History of sexual activities, <i>n</i> (%)			0.914
No	161 (92.5)	27 (90.0)	
Yes	13 (7.5)	3 (10.0)	
Duration of symptoms (day), median (IQR)	4.0 (2.0–8.3)	0.2 (0.3–1.8)	0.000
The side of the twisted testicle, <i>n</i> (%)			0.888
Left	124 (71.3)	21 (70.0)	
Right	50 (28.7)	9 (30.0)	
Intratesticular blood flow, <i>n</i> (%)			0.000
Invisible	168 (96.6)	22 (73.3)	
Visible	6 (3.4)	8 (26.7)	
Testicular parenchymal echotexture, <i>n</i> (%)			0.001
Nonhomogeneous	141 (81.0)	16 (53.3)	
Homogeneous	33 (19.0)	14 (46.7)	
Testicular volume of affected testis (cm ³), median (IQR)	16.2 (11.3–21.0)	14.7 (11.7–18.6)	0.625
Testicular volume ratio (affected testis/contralateral testis)	1.75 (1.19–2.19)	1.46 (1.41–1.70)	0.411
Maximum diameter of twisted spermatic cord (cm), median (IQR)	2.5 (2.1–3.2)	2.4 (1.7–3.1)	0.501
White blood cell count (10 ⁹ l ⁻¹), median (IQR)	9.85 (7.90–11.68)	9.33 (7.09–12.39)	0.721
NLR, median (IQR)	3.76 (1.90–5.70)	4.26 (1.68–8.26)	0.429
LMR, median (IQR)	2.78 (1.99–4.48)	3.34 (1.93–5.05)	0.420

A total of 17, 63, and 82 patients with unknown information were not considered when comparing testicular volume of affected testis, testicular volume ratio, and maximum diameter of twisted spermatic cord, respectively. IQR: interquartile range; NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio

confidence interval [CI]: 0.630–0.904, $P = 0.002$) was an independent risk factor for TS, while visible intratesticular blood flow (OR = 8.367, 95% CI: 2.260–30.968, $P = 0.001$) and homogeneous testicular echotexture in the affected testis (OR = 3.422, 95% CI: 1.357–8.626, $P = 0.009$) were independent protective factors for TS, as shown in **Table 2**.

Establishment and internal validation of nomograms

According to the multivariate logistic regression coefficients, two nomograms were established using the rms package in R software (**Figure 1a** and **1b**). In both two nomograms, duration of symptoms made the largest contribution to predictive outcomes, and intratesticular blood flow and testicular parenchymal echotexture had moderate impacts on predictive outcomes.

Excellent discrimination of the nomograms was yield in internal validation (AUC was 0.851 and 0.828, respectively), as shown in **Figure 2a** and **2b**. In addition, the nomograms both calibrated well, as the nomogram-predicted possibilities of TS were in close agreements with actual rates, as shown in **Figure 2c** and **2d**.

DISCUSSION

Testicular torsion is the most common scrotal emergency in urology. It can occur at any age, most commonly during adolescence, with an incidence of 1/4000 in patients aged <25 years.⁴ The disease can be classified as intravaginal or extravaginal. The intravaginal type is

common in adolescents and adults, while the extravaginal type rarely occurs during the perinatal period.⁵ Unilateral testicular torsion is common, mostly on the left side, while bilateral testicular torsion is extremely rare.⁶ Testicular torsion initially obstructs testicular venous blood flow and then impairs the arterial blood flow due to the balance of venous and arterial pressure, leading to testicular ischemia.⁷ Bell-clapper deformity (BCD) is a predisposing factor for testicular torsion, in which the testis lacks adhesion to the parietal tunica vaginalis. The tunica vaginalis has a higher termination point on the spermatic cord; thus, the spermatic cord has greater mobility.⁸ Other causes, such as exercise, injury, and cold temperatures,^{9,10} may lead to excessive contraction of the cremaster muscle, causing testicular elevation or even transverse position.

Testicular torsion has different clinical manifestations. Scrotal pain and swelling on the affected side commonly occur. Other manifestations include marked scrotal tenderness, hard testis, and no pain relief after scrotal elevation. Barbosa *et al.*¹¹ devised and validated the Testicular Workup for Ischemia and Suspected Torsion scoring system. This scoring system considers the following parameters to evaluate the risk of testicular torsion: testis swelling, hard testis, absent cremasteric reflex, nausea/vomiting, and high-riding testis. This scoring system was examined by another study,¹² which also reported its limited applicability. More importantly, the lack of imaging results is not convincing and can easily lead to medical disputes.

Table 2: Univariate and multivariate logistic regression analyses of related factors related to testicular salvage

Parameters	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age (year)	1.067 (0.987–1.152)	0.101		
History of sexual activities				
No	1 (reference)			
Yes	1.376 (0.368–5.151)	0.635		
Duration of symptoms (day)	0.747 (0.626–0.892)	0.001	0.755 (0.630–0.904)	0.002
The side of the twisted testicle				
Left	1 (reference)			
Right	1.063 (0.456–2.479)	0.888		
Intratesticular blood flow				
Invisible	1 (reference)		1 (reference)	
Visible	10.182 (3.230–32.092)	0.000	8.367 (2.260–30.968)	0.001
Testicular parenchymal echotexture				
Nonhomogeneous	1 (reference)		1 (reference)	
Homogeneous	3.739 (1.661–8.415)	0.001	3.422 (1.357–8.626)	0.009
Testicular volume of affected testis (cm ³)				
≤15.0	1 (reference)			
>15.0	0.593 (0.216–1.633)	0.312		
Testicular volume ratio (affected testis/contralateral testis)				
≤1.70	1 (reference)			
>1.70	0.570 (0.177–1.835)	0.346		
Maximum diameter of twisted spermatic cord (cm)				
≤2.0	1 (reference)			
>2.0	0.765 (0.221–2.642)	0.672		
White blood cell count (10 ⁹ l ⁻¹)	0.979 (0.868–1.104)	0.727		
NLR	1.057 (0.970–1.151)	0.209		
LMR	1.109 (0.938–1.310)	0.225		

Analyzing results of patients with unknown information were not listed as no clinical significance. OR: odds ratio; CI: confidence interval; NLR: neutrophil-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio

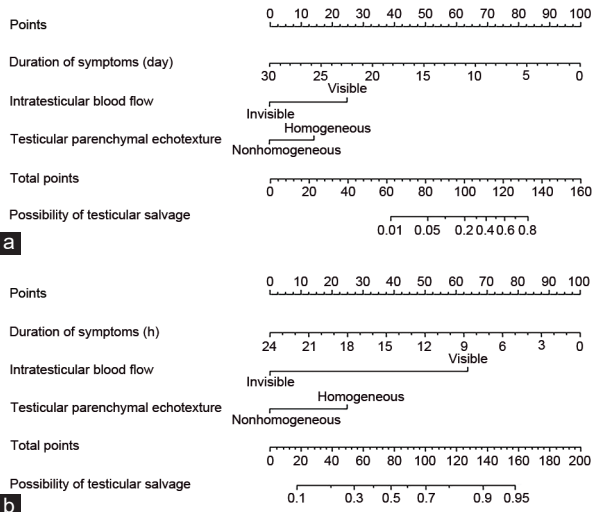


Figure 1: Prognostic nomograms including the duration of symptoms, intratesticular blood flow, and testicular parenchymal echotexture. (a) Nomogram for patients whose duration of symptoms is 0–30 days. (b) Nomogram exclusive for patients whose duration of symptoms is 0–24 h. The testicular salvage possibility is determined according to a combination of covariates. The nomogram is used by locating the patient’s duration of symptoms and drawing an upward vertical line upward to the “Points” axis to determine the score. The process is repeated for the other covariates, and the scores are summed to calculate the total points. Finally, a downward vertical line is drawn to determine the possibility of testicular salvage.

Color Doppler ultrasound can accurately display the anatomical information and blood flow of scrotal contents in a limited time. This examination method is commonly used to determine scrotal emergencies, particularly to distinguish testicular torsion from acute epididymitis, with a sensitivity and specificity of up to 88.9% and 98.8%, respectively.¹³ Patients with testicular torsion usually show decreased or loss of intratesticular blood flow; however, in the early stage, blood flow signals may remain unchanged or may even increase due to arterial compensation, leading to misdiagnosis as inflammatory lesions.^{14,15} In a multicenter study of 208 children with testicular torsion, 50 (24%) children showed normal or high intratesticular blood flow at the early stage of torsion;¹⁶ thus, comparative analysis of the contralateral blood flow is necessary to reduce the rate of misdiagnosis. The gray-scale findings vary depending on the symptom duration. In the early stage, the testis may appear normal. Over time, the testicular echotexture may appear enlarged and inhomogeneous. Hemorrhage may occur as the disease progresses, with necrotic and hemorrhagic areas showing hypoechoic and hyperechoic features. When infarction finally occurs, the testis may be diffusely hypoechoic with cystic areas and may eventually shrink.¹⁷ Kaye *et al.*¹⁸ concluded that a heterogeneous parenchymal echotexture indicated late torsion and testicular nonviability among 34 of 37 patients with heterogeneous echoes in the testicular parenchyma who underwent orchiectomy. In our study, we observed significant differences between the two groups in terms of intratesticular blood flow and testicular parenchymal echotexture under color Doppler ultrasound; therefore, we included these two variables into our nomograms. Spiral torsion of the spermatic cord is a characteristic change in testicular torsion detected on ultrasound.¹⁹ Vijayaraghavan²⁰ described it as “whirlpool sign” and considered it as the most specific sign of testicular torsion. Our data showed no significant correlation between the maximum diameter of twisted spermatic cord and the rescue rate. Ultrasound can also show changes

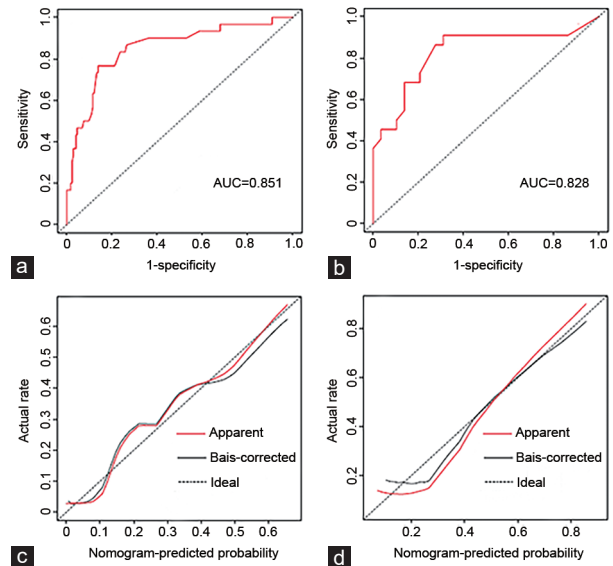


Figure 2: Discrimination and calibration of the nomograms. (a) Receiver operating characteristic curve of the nomogram for patients whose duration of symptoms is 0–30 days. (b) Receiver operating characteristic curve of the nomogram exclusive for patients whose duration of symptoms is 0–24 h. (c) Calibration curve of the nomogram for patients whose duration of symptoms is 0–30 days. (d) Calibration curve of the nomogram exclusive for patients whose duration of symptoms is 0–24 h. The dotted line represents the performance of an ideal nomogram (predicted outcome perfectly corresponds to the actual outcome). The red solid line indicates the apparent accuracy of the nomogram without correction for overfitting. The black solid line is the bootstrap-corrected nomogram. AUC: area under the curve.

in the size of scrotal contents. Our analysis did not show a significant correlation between the testicular volume and the possibility of TS. Furthermore, to evaluate the relationship between testicular volume change and the possibility of TS, we used the testicular volume ratio of the affected testis to the contralateral testis as a parameter to determine whether the testicles were enlarged or shrunk to eliminate the interference of self-development. The analysis showed no significant correlation between them, which may be related to the tendency for testicular swelling followed by necrosis and atrophy.

The third and most important variable included in our nomograms was the duration of symptoms. There is a significant negative correlation between duration of symptoms and the possibility of TS. Patients suspected of testicular torsion should be examined promptly to avoid treatment delays. The possibility of TS within 6 h after the onset of symptoms is 90%, while that after 24 h is <10%.²¹ Another study reported an orchiectomy rate of 67% for testicular pain lasting more than 12 h.²² In our study, 33 patients had symptoms that lasted for no more than 12 h, 19 (57.6%) of whom retained their testicles, and 14 (42.4%) had their testicles removed. Of the 171 patients with symptoms that lasted for more than 12 h, 160 (93.6%) underwent orchiectomy and only 11 (6.4%) retained their testicles. The difference was statistically significant ($\chi^2 = 30.060, P < 0.001$). The degree of spermatic cord torsion may also affect the possibility of TS.²³ Sessions *et al.*²⁴ retrospectively analyzed the operation conditions of 186 patients with testicular torsion. The median torsion in 70 patients who underwent orchiectomy was 540° (IQR: 180°–1080°), compared with 360° (IQR: 180°–1080°) in the 116 patients with TS. Another study showed that patients whose testicles have 720° of torsion may not survive within 4 h, but they may survive after 3 weeks of incomplete torsion.²⁵ Similarly, patients with intermittent testicular torsion have small degrees of torsion and could

survive longer than 3 months.²⁶ In our study, 162 patients had data on the degrees of torsion, ranging from 90° to 1080°. In this group, the degree of torsion was associated with the possibility of TS (OR = 0.998, 95% CI: 0.996–1.000, $P = 0.076$). However, the degree of torsion was not an independent predictor in our study, as there was a clear correlation between the degree of torsion and intratesticular blood flow (OR = 0.990, 95% CI: 0.984–0.996, $P = 0.001$). Whether hematological indicators can predict the possibility of TS warrants further exploration. NLR alone can predict the need for orchiopexy in patients whose symptom duration is 3–12 h.²⁷ Our study also explored the predictive value of preoperative hematological parameters in testicular torsion. White blood cell count, NLR, and LMR did not have a predictive value, which is consistent with the idea that these systemic inflammation markers can be influenced by various factors.²⁸ Another possible reason is that our study had a longer duration, while the inflammation markers were more limited to the “window period” of their study, *i.e.*, 3–12 h.

In this study, we established predictive models for testicular torsion to predict the possibility of TS before surgical exploration. We included only three variables, which can be easily obtained through color Doppler ultrasound before surgery rather than extracting variables from complex examinations. The duration of symptoms showed a time effect. The visibility of intratesticular blood flow directly reflects the severity of testicular torsion, while the homogeneity of the testicular parenchymal echotexture more likely reflects testicular tolerance to ischemia. In this way, we determined the possibility of saving the testis from three different dimensions. To our knowledge, this is the first model to predict the possibility of TS rate using the combination of these three variables. We did not consider the degree of spermatic cord torsion as a research variable because it can only be determined during surgery and can not be accurately judged by preoperative imaging examinations. In particular, the spermatic cord may show no rotation under color Doppler ultrasound in some cases of partial torsion with small degrees of twist (<270°).²⁹ Consistent with our expectations, the results of internal validation showed that the two nomograms established based on these three variables reflect the real-world setting. According to **Figure 1a**, if the duration of symptoms is more than 18 days, the possibility of TS is <5% regardless of the other two variables, which confirms that time is the most critical factor affecting the possibility of TS. If the duration of symptoms is close to 7 days, with invisible intratesticular blood flow and nonhomogeneous testicular parenchymal echotexture, the possibility of TS is about 4%. The possibility of TS in patients with visible intratesticular blood flow and homogeneous testicular parenchymal echotexture increases to 50%. If the duration of symptoms is 6 h, according to **Figure 1b**, the possibility of TS is only 48% in patients with invisible intratesticular blood flow and nonhomogeneous testicular parenchymal echotexture and increases to > 95% in those with visible intratesticular blood flow and homogeneous testicular parenchymal echotexture. Therefore, our nomograms have good discrimination in patients with both long torsion time and short torsion time, which can be used for accurate preoperative predictions. A previous study has suggested that the duration of symptoms and testicular parenchymal echotexture are also predictive factors of testicular atrophy after TS following torsion.³⁰

This study has several limitations. First, this is a retrospective study. Color Doppler ultrasound was performed by different ultrasonologists, which possibly influenced the heterogeneity and homogeneity of the results. Similarly, surgery was performed by different surgeons with different surgical experiences and judgments regarding testicular excision. Second, relevant indicators of physical examination were not included because these indicators were often missing and were

strongly subjective. Finally, due to the small sample size, the predictive effectiveness of our models requires further verification.

CONCLUSION

We established preoperative nomograms for predicting the possibility of TS. The visualization effect of the nomograms is also helpful to more intuitively understand the weight of various factors affecting the possibility of TS and for preoperative communication with patients and their families. Testicular torsion patients with a high possibility of TS require timely surgical exploration to preserve their fertility. In contrast, testicular torsion patients with a very low probability of TS do not require urgent surgical exploration.

AUTHOR CONTRIBUTIONS

WXZ contributed to the conception of the study, performed data collection and analysis, and drafted the manuscript. GDH participated in the statistical analysis and figure design and assisted in drafting the manuscript. WZ performed data collection. DW and XLG participated in the design of the study. LGH participated in data collection. FL, LY, GZ, FY, and MHC contributed to acquisition of data and critically appraised the manuscript. JLY and BZ participated in the design of the study and directed the related work. All authors have read and approved the final version of the manuscript and agree with the order of presentation of authors.

COMPETING INTERESTS

All authors declared no competing interests.

ACKNOWLEDGMENTS

This work was supported by the Military Medicine Research Projects of Xijing Hospital (XJZT18D05).

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