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ORIGINAL RESEARCH

Risk Factors for Postoperative Neurologic Dysfunction in Patients with Spinal Tuberculosis: A Retrospective Study

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Purpose: Unexplained neurological dysfunction often occurs in patients after spinal tuberculosis(STB) surgery; therefore, this study aimed to analyze the causes of this dysfunction from the perspectives of the patient's preoperative inflammatory state, carrier bacterial state, and increased degree of autoimmunity.

Patients and Methods: We collected 247 patients with STB and 270 patients with degenerative diseases of the spine admitted from May 2015 to December 2024 at the Second Hospital of Shanxi Medical University. According to the exclusion criteria, 132 patients for each disease were included in this study. All patients with spinal STB underwent one-stage posterior lesion removal. We used the ASIA score to assess patients' neurological function and pain levels before and after surgery. We also compared the patients' pre- and postoperative changes in relevant inflammatory indicators, such as the ESR and PCT.

Results: Postoperatively, one patient developed paraplegia with an ASIA grade of A; 29 patients developed incomplete paraplegia with an ASIA score of grade B in 5 patients, grade C in 7 patients, and grade D in 17 patients. In the damaged group, LYM% decreased from 35.52 ± 10.44 preoperatively to 14.36 ± 7.27 postoperatively. NEU% increased from 54.72 ± 11.85 preoperatively to 77.72 ±7.16 postoperatively. The WBC count increased from 5.97±1.65 preoperatively to 8.34 ± 2.71 postoperatively. The LNR decreased from 0.72 ± 0.31 preoperatively to 0.18 ± 0.11 postoperatively. Neurological dysfunction was somewhat recovered in the postoperative period (6 months to 2 years) in all patients.

Conclusion: In summary, this clinical study successfully established a predictive model with significant prognostic value for postoperative neurological dysfunction in patients with spinal tuberculosis. Notably, based on the ranking of variable contributions, the use of antituberculosis drugs may play a pivotal role in the development of postoperative neurological dysfunction in spinal tuberculosis patients. A well-validated nomogram incorporating acid-fast staining and piezosurgery use may facilitate preoperative risk stratification. Prolonged exposure of the spinal cord to a highly inflammatory environment may serve as a risk factor for intraoperative spinal cord injury in these patients. Furthermore, identical or similar surgical procedures may yield differential clinical outcomes across different disease subtypes and individual patients.

Keywords: spinal tuberculosis, neurological dysfunction, immune microenvironment, inflammatory response

Introduction

Spinal tuberculosis (STB) is the most common form of osteoarticular tuberculosis, accounting for approximately 50% of all skeletal tuberculosis cases.[1–3] It is predominantly secondary to primary foci such as pulmonary or intestinal tuberculosis, with *Mycobacterium tuberculosis* typically disseminating via hematogenous spread. The lumbar spine, due to its rich vascular supply and high mobility, is most frequently affected, followed by the thoracic spine, where neurological deficits are more likely to occur.[4,5] Although the disease is more prevalent in children and adolescents, its occurrence rate in elderly

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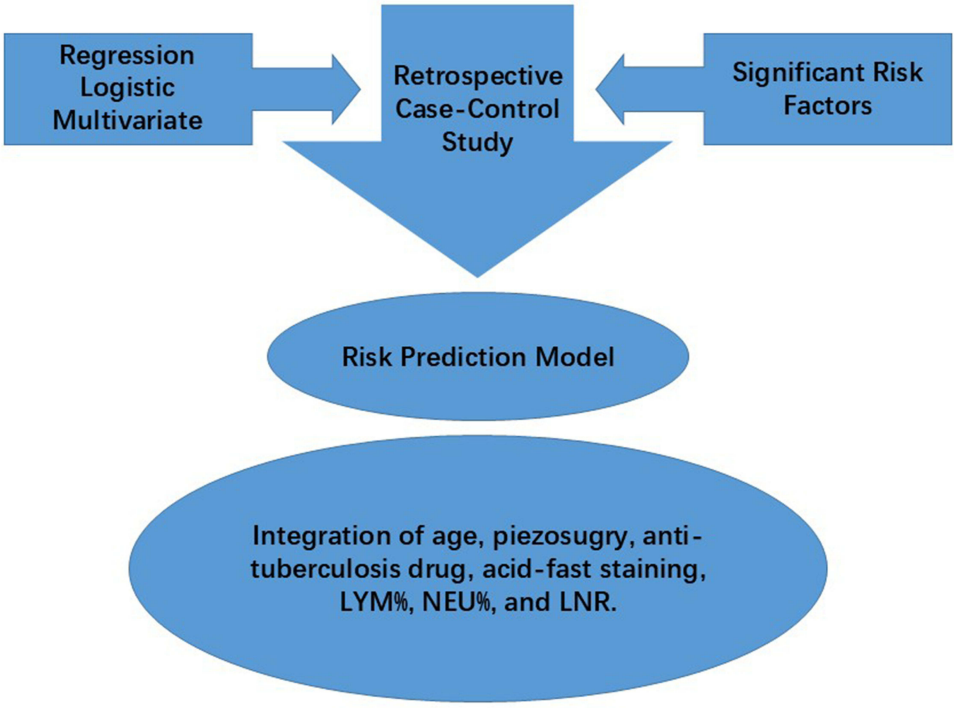
Graphical Abstract



patients has been increasing.[6] STB often leads to severe bone destruction and spinal deformities, resulting in high rates of disability and mortality.[7] Due to its insidious onset and nonspecific early symptoms, it is frequently underdiagnosed.[8] Most patients seek medical attention only after developing significant bone destruction, spinal instability, or neurological dysfunction, by which time the inflammatory response is pronounced, complicating treatment.

Advanced STB is characterized by a complex microenvironment, with elevated levels of pro-inflammatory cytokines (eg, TNF-α, IL-6) and granulomatous tissue that disrupt spinal cord blood flow autoregulation and degrade extracellular matrix integrity.[9] Preclinical models demonstrate that chronic inflammation reduces the threshold for secondary spinal cord injury by impairing axonal energy metabolism and enhancing oxidative stress.[10] Clinically, patients with extensive pre-surgical vertebral destruction and paravertebral abscesses exhibit disproportionately higher rates of postoperative neurological deficits, suggesting a potential link between preoperative inflammatory burden and surgical tolerance. However, the underlying molecular mechanisms mediating this relationship have not been elucidated.

Clinically, unlike patients with spinal tumors or degenerative conditions, some STB patients develop unexplained new-onset neurological symptoms postoperatively, such as manifestations of spinal shock, despite ruling out common causes like direct spinal cord injury, intraoperative hypotension, or postoperative hematoma compression. Intriguingly, these neurological deficits often show significant recovery within 6 months to 2 years post-surgery, differing from typical spinal shock or delayed deficits caused by disease recurrence or visceral compression.[8] It is hypothesized that advanced STB alters the local tissue microenvironment, reducing the spinal cord's tolerance threshold to surgical procedures. Thus, even routine and ostensibly safe maneuvers may induce injury. This study aims to investigate the underlying mechanisms of adverse neurological events following STB surgery.

Materials and Methods

General Situation

A total of 247 patients with STB and 270 patients with spinal degeneration admitted to the Second Hospital of Shanxi Medical University from May 2015 to December 2024 were retrospectively analyzed. According to the exclusion criteria,

132 patients with each disease were included in this study. The same operator operated on all patients. The study was conducted in accordance with the Helsinki Declaration and approved by the Ethical Review Committee of the Second Hospital at Shanxi Medical University (2024KYNO.127). Owing to the study's retrospective nature, the Institutional Review Board waived the need to obtain informed consent. Postoperative neurological-related adverse events occurred in 30 out of 132 patients (Table 1).

Inclusion and Exclusion Criteria

The inclusion criteria for patients were as follows: (1) Both male and female patients were included; (2) No age restrictions were applied; (3) Diagnosis of STB was confirmed by etiological and pathological examinations; (4) All patients underwent one-stage posterior debridement surgery; (5) Complete medical records were available, including comprehensive clinical data and perioperative laboratory test results; (6) The follow-up duration was no less than 2 years. The exclusion criteria for patients were as follows: (1) suspected STB not confirmed by pathological examination; (2) inability to tolerate chemotherapy; (3) history of previous paraplegia; (4) combination of other active tuberculosis; (5) combination of other spinal tumors and osteoporosis; (6) Patients with comorbid hypertension: Systolic blood pressure (SBP) ≥180 mmHg or diastolic blood pressure (DBP) ≥110 mmHg on three consecutive measurements; (7) Patients with comorbid diabetes mellitus: Glycated hemoglobin (HbA1c) ≥9.5% despite optimized medical therapy; neuropathic pain with a Numerical Rating Scale (NRS) score ≥7/10, which may interfere with accurate assessment of postoperative neurological recovery; (8) Other exclusion criteria: Presence of other underlying medical conditions; allergy to first-line anti-tuberculosis drugs (eg, isoniazid, rifampin). The inclusion criteria for patients with spinal degeneration were as follows:(1) Both male and female patients were included; (2) No age restrictions were applied; (3) Participants met the diagnostic criteria for spinal degeneration; and (4) Cases involved 1 or 2 degenerative segments. The exclusion criteria were as follows: (1) Spinal tumors, lower limb arthritis or other diseases not caused by spinal degeneration. (2) Patients with spinal deformities, including lumbar spondylolisthesis, lumbar scoliosis, and lumbar compression fracture; (3) Patients with comorbid hypertension: Systolic blood pressure (SBP) ≥180 mmHg or diastolic blood pressure (DBP) ≥110 mmHg on three consecutive measurements; (4) Patients with comorbid diabetes mellitus: Glycated hemoglobin (HbA1c) ≥9.5% despite optimized medical therapy; neuropathic pain with a Numerical Rating Scale (NRS) score ≥7/10,

Table 1 General Information

		Damage Group	Control Group	*P*
Age		46.20 ± 14.76	55.08 ± 15.44	0.006
Sex	Male	13(18.8%)	56(81.2%)	0.267
	Female	17(27.0%)	46(73.0%)	
Segment	C	0(0.0%)	2(100.0%)	0.935
	T upper	0(0.0%)	13(100.0%)	
	T lower	21(31.8%)	45(68.2%)	
	L	9(17.6%)	42(82.4%)	
Piezosurgery	Used	9(9.7%)	84(90.3%)	<0.001
	Unused	21(53.8%)	18(46.2%)	
ASIA	A	1(25%)	3(75%)	<0.001
	B	5(55.6%)	4(44.4%)	
	C	7(50.0%)	7(50.0%)	
	D	17(19.8%)	69(80.2%)	
	E	0(0.0%)	19(100.0%)	
Anti-Tuberculosis Drugs	Used	26(45.6%)	31(54.4%)	<0.001
	Unused	4(5.3%)	71(94.7%)	
Acid Fast Staining	Positive	25(58.1%)	18(41.9%)	<0.001
	Negative	5(5.6%)	84(94.4%)	

Abbreviations: C, cervical vertebra; T, thoracic vertebra; L, lumbar vertebra.

which may interfere with accurate assessment of postoperative neurological recovery; (5) Other exclusion criteria: Presence of other underlying medical conditions.

Preoperative Preparation

For most patients with STB, a standard quadruple chemotherapy protocol (isoniazid 0.3 g/d, rifampicin 0.45 g/d, ethambutol 0.75 g/d, pyrazinamide 0.75 g/d) is routinely used for 2 ~ 4 weeks of preoperative antituberculosis treatment, and nutritional supportive therapy is strengthened to correct anemia. In a few patients with progressive deterioration of neurological function, a short intensive chemotherapy regimen was used preoperatively (isoniazid 300 mg IV drip/d, rifampicin 600 mg IV drip/d, ethambutol 15 mg/(kg-d) morning dose/d, pyrazinamide 25 mg/(kg-d) morning dose/d). The duration of medication depends on the preoperative examination, which is usually 1–7 days. Surgery was performed when the patient's general condition improved (temperature < 37.5, hemoglobin > 100 g/L, erythrocyte sedimentation rate < 50 mm/1 h), and no other contraindications to surgery were observed. Prophylactic antibiotic therapy was administered 30 minutes before surgery to prevent nonspecific inflammation.

Postoperative Management and Follow-up

When intraoperative regional drainage was < 50 mL/d, the drain was removed. Postoperative treatment with oral antituberculosis drugs is continued for 9–12 months, and a stent is worn for 6–9 months starting one week after surgery. The patients were bedridden for 1–2 weeks; after 2–3 weeks, moderate activity with thoracolumbar support was achieved; after 3 months, functional strengthening exercises were performed; and after 6 months, normal activity without support was achieved. Blood sedimentation and C-reactive protein(CRP) levels were reviewed 3 days after surgery, and then blood sedimentation, CRP, liver, and kidney functions were reviewed monthly for 3 consecutive months and every 3 months thereafter. The patient was instructed to perform rehabilitation exercises to promote the recovery of nerve function. Frontal and lateral X-ray images were taken within one week after surgery. After that, patients visited outpatient clinics to review X-ray films during the 1st, 3rd, 6th, 9th, and 12th postoperative months. They were then reviewed every 6 months until a standard healing state was achieved. This standard healing status included (i) no recurrence of symptoms within 6 months after surgery; (ii) blood sedimentation within normal limits; (iii) X-rays showing bony healing of the diseased vertebral body; and (iv) the patient resumed normal activities and light work for 3–6 months. The total follow-up included blood sedimentation, CRP, neurological function ASIA grading, liver and kidney function tests, frontal and lateral X-rays, and additional CT in some patients.

A clear explanation of the assessment methodology is given below. The VAS score is an indicator used to assess a patient's level of pain. Patients can define their level of pain using the numbers 0--10. 0 means no pain, and 10 means the worst pain imaginable. The ASIA grading system describes the degree of impairment of neurological function. Grade A means that the patient has no sensory or motor function below the level of impairment. Grade B indicates that the patient has sensory function but no motor function below the level of impairment. In Grade C, the patient has motor function, but the strength of key muscles is below Grade 3. In Grade D, the strength of the key muscles is above or equal to Grade 3. In Grade C, the patient has motor function, but the strength of the key muscles is below Grade 3. In Grade D, the strength of the key muscles is above or equal to Grade 3. In Grade E, the patient has normal sensory and motor function. The degree of stress on key muscles is categorized into five levels. A score of 0 indicates complete paralysis. Grade 1 indicates that muscle contractions are palpable. Grade 2 means that the patient can actively use the joint but not against gravity. A grade of 3 means that the patient can actively use the joint against gravity. A grade of 4 means that the patient can actively use the joint against moderate resistance. Grade 5 means normal. Cobb's angle consists of the line between the upper and lower endplates of the end vertebral body. The Cobb angle is formed by the line of the upper and lower endplates of the end vertebrae and is also known as the posterior convexity angle. The terminal vertebrae are the upper and lower vertebrae with the greatest inclination.

Data Analysis

Data entry for this study was performed via double-entry verification. SPSS 13.0 statistical software (SPSS, USA) was used to analyze the study data statistically. The measurement data were normally distributed and are expressed as the

means ± standard deviations. Comparisons between groups of metrological data conforming to a normal distribution were performed via independent samples *t*-test, and comparisons between groups of count data were performed via chi-square tests. The lymphocyte ratio, neutrophil ratio, leukocyte ratio, and lymphocyte-to-neutrophil ratio were compared before and after surgery via one-way ANOVA and repeated-measures ANOVA. A two-sided $p< 0.05$ was used for all tests to indicate a statistically significant difference. In the multifactorial analysis, multifactorial logistic regression was used to analyze the factors affecting neurological dysfunction after STB surgery. The H–L test can be used to evaluate whether the model maximizes the fit of the model and explains the variance of the model by making full use of the available information. The results of this study indicate a good model fit superiority effect if $P>0.05$ and indicate poor model construction if $P<0.05$. In multifactor logistic regression, if $P<0.05$, this variable is significantly different from the dependent variable in the equation. The software R (4.2.1) version was used with R packages:rms [6.4.0], ResourceSelection [0.3–5]. After data cleaning, a binary logistic model was constructed using the glm function, and a Nomogram correlation model and Calibration analysis were constructed and visualized using the rms package.

Results

General Information

In this study, 247 patients with STB admitted to the Second Hospital of Shanxi Medical University from May 2015 to December 2024 were retrospectively analyzed. A total of 132 patients were included in this study according to the exclusion criteria (Figure 1). Among them, 69 were male, and 63 were female (aged 20–79 years). Among these patients, 2 were in the cervical segment, 79 were in the thoracic segment, and 51 were in the lumbar segment. All patients underwent one-stage posterior lesion removal. All patients had normal neurological function preoperatively, and 30 patients developed varying degrees of neurological dysfunction postoperatively. These neurological deficits recovered to some extent in the postoperative period, and none of the thirty patients had active tuberculosis.

ASIA Grading System

Thirty patients had normal neurological function before surgery but had different degrees of neurological dysfunction after surgery. One patient developed paraplegia after surgery with an ASIA grade of A. Twenty-nine patients developed incomplete paraplegia, with an ASIA grade of B in 5 patients, grade C in 7 patients, and grade D in 17 patients. All the above patients were operated on in a standardized manner; the process was smooth, the operation was performed without mishandling, other accidents, cerebrospinal fluid leakage, or postoperative wound infection, and all of them recovered from treatment for tuberculosis. These indicators suggest that in the case of successful surgery, the patient still presented with functional manifestations of spinal cord injury(SCI)in the postoperative period.

Patient Characteristics and Preoperative Indicators

In the present study, the mean ages of the patients in the damage group and the control group were 46.20±14.76 and 55.08 ± 15.44 years, respectively ($p<0.05$). No significant difference was found between the two groups in terms of sex. Regarding the use of piezosurgery, the use group consisted of 9 patient in the damage group and 84 patients in the control group, the nonuse group consisted of 21 patients in the damage group and 18 patients in the control group, and the chi-square test yielded $P<0.05$, suggesting that the use of piezosurgery significantly affected whether nerve function was impaired after tuberculosis surgery. With respect to the administration of anti-tuberculosis drugs, among the 26 patients in the damage group and 31 patients in the control group and the group in which only 71 patients in the control group and 4 patients in the damage group were nonadopted, the chi-square test yielded $P<0.05$, which indicated that the administration of anti-tuberculosis drugs significantly affected whether neurological function was impaired after tuberculosis surgery. This may be related to the paradoxical reactions (PRs) that often occur in antituberculosis therapy, and their clinical manifestations include central nervous system involvement, such as hemiplegia and paraplegia. In terms of acid–fast staining, the positive group consisted of 25 patients in the damage group and 18 control patients, the negative group consisted of 5 patient in the damage group and 84 control patients, and the chi-square test yielded $P<0.05$, indicating that the results of acid–fast staining significantly differed in terms of whether neurological function was impaired after

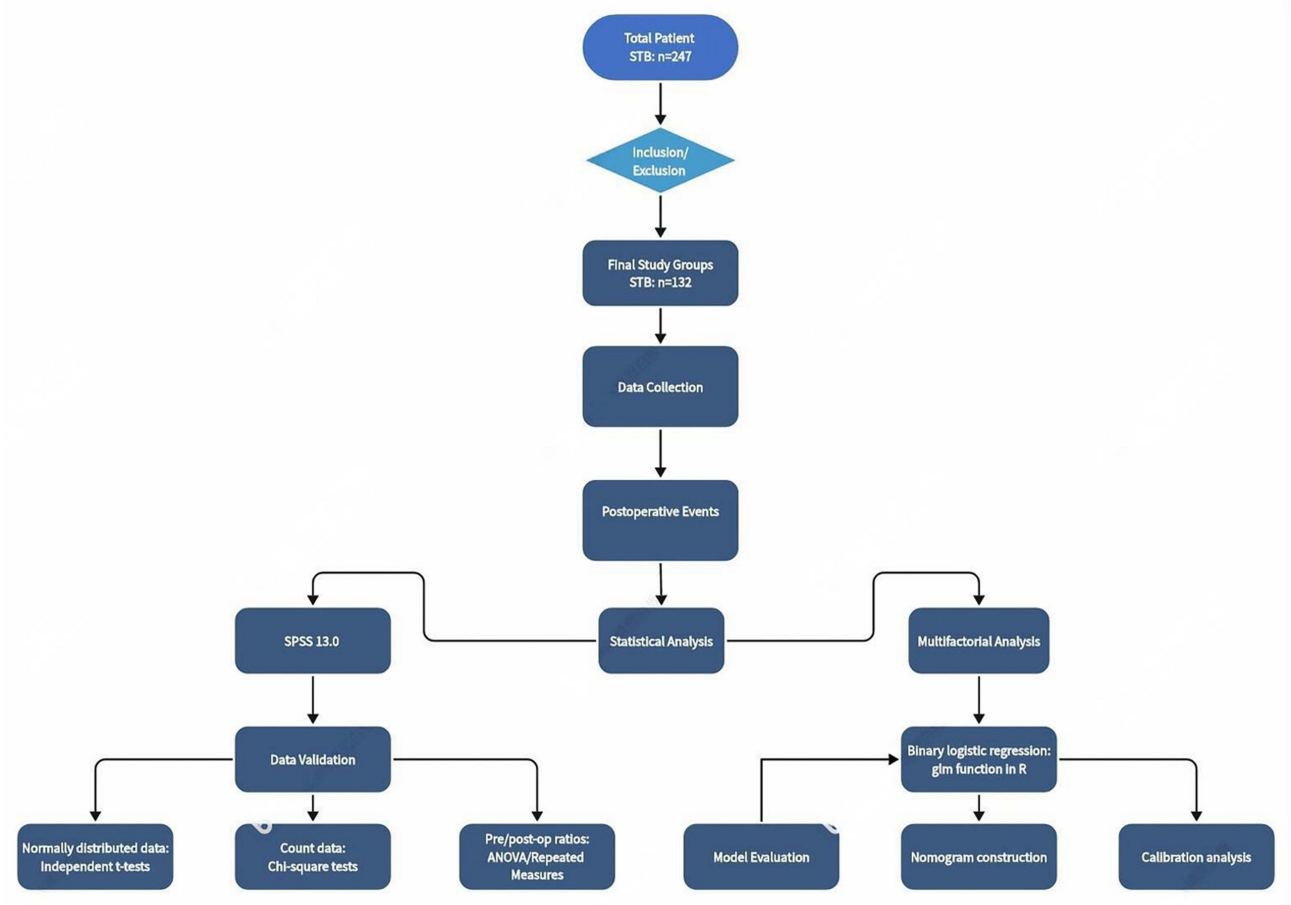


Figure 1 The flowchart of this study.

tuberculosis surgery (Table 1). The mean preoperative LYM percentage was 35.52 ± 10.44 in the damage group and 19.71±7.16 in the control group. The mean preoperative LYM percentage in the damage group was significantly greater than that in the control group (P<0.05). The mean preoperative NEU percentage was 54.72 ± 11.85 in the damage group and 70.14 ± 9.07 in the control group. The mean preoperative NEU percentage was significantly lower in the damage group than in the control group (P<0.05). The mean preoperative LNR was 0.72 ± 0.31 in the damage group and 0.28 ± 0.16 in the control group. The mean preoperative LNR in the damage group was greater than that in the control group (P<0.05). The mean preoperative CRP in the injury group was 13.81 ± 11.06, compared with 30.85 ± 36.75 in the control group. The CRP in the injury group was significantly lower than that in the control group preoperatively (P < 0.05). Except for the above indicators, no significant differences were found between the two groups (P>0.05) (Table 2).

Postoperative Factors Associated with Impaired Neurological Function

Results of Logistic Regression Analysis of Relevant Factors

Patients in both groups' postoperative indices (LYM%, NEU%, WBC, and LNR) were abnormal to different degrees than the preoperative normal values. Nevertheless, all the postoperative indices did not differ significantly between the groups (P>0.05). All relevant patient indicators were statistically analyzed, with collinearity and other confounding factors excluded. The most statistically significant variables between the damage group and control group were identified as follows (P<0.01): age, piezosurgery, anti-tuberculosis drugs, acid fast staining, LYM%, NEU%, and the LNR. Each of the above variables was included in a multifactor regression model. Multifactorial analysis was performed by backward stepwise regression. The final model constructed included piezosurgery, anti-tuberculosis drug use, and acid fast staining, all of which were significantly associated with impaired neurological function (p<0.05) (Table 3). The risk of

Table 2 Analysis of Preoperative and Postoperative Observational Indicators

		Damage Group	Control Group	*P*
Preoperative	LYM%	35.52 ± 10.44	19.71 ± 7.16	<0.001
	NEU%	54.72 ± 11.85	70.14 ± 9.07	<0.001
	LNR	0.72 ± 0.31	0.28 ± 0.16	<0.001
	CRP	13.81 ± 11.06	30.85 ± 36.75	0.014
	WBC	5.97 ± 1.65	6.71 ± 2.91	0.185
	ESR	36.60 ± 22.56	47.33 ± 35.50	0.120
Postoperative	LYM%	14.36 ± 7.27	13.56 ±7.97	0.624
	NEU%	77.72 ±7.16	77.68 ± 10.14	0.983
	WBC	8.34 ± 2.71	8.84 ± 3.06	0.417
	LNR	0.18 ± 0.11	0.20 ± 0.16	0.663

Abbreviations: LYM%, lymphocyte percentage; NEU%, neutrophil percentage; WBC, white blood cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; LNR, lymphocyte neutrophil ratio.

Table 3 Binary Logistic Regression About the Difference in Neurological Damagement

Variable	Group	b value	p value	OR Value	95% CI of OR Value
Age		−0.065	0.054	0.937	0.877–1.001
LYM%		0.070	0.605	1.073	0.823–1.398
LNR		5.426	0.251	227.261	0.021–2,413,474.097
NEU%		0.002	0.976	1.002	0.853–1.178
Acid Fast Staining	Positive Negative	2.760	0.004	15.795	2.378–104.894
Anti-Tuberculosis Drugs	Used Unused	2.073	0.043	7.952	1.069–59.147
Piezosurgery	Used Unused	−2.279	0.013	0.102	0.017–0.616

neurological impairment decreased with the use of piezosurgery (OR=0.102, 95% CI 0.017–0.616; P=0.013) and increased with positive acid fast staining (OR=15.795, 95% CI 2.378–104.894; P=0.004) and the use of anti-tuberculosis drugs (OR=7.952, 95% CI 1.069–59.147; P=0.043).

Results of Logistic Regression Analysis of Relevant Factors

To predict the probability of neurologic impairment after STB surgery, we developed a prediction model based on the following 7 risk factors and plotted a Nomogram (Figure 2). These factors included age, piezosurgery, anti-tuberculosis drugs, acid fast staining, LYM%, NEU%, and the LNR. Each factor corresponded to a specific score, and the scores of the 7 factors were summed to obtain a total score. The hazard probability of neurologic impairment is obtained by projecting the total score onto the horizontal axis of risk of neurologic impairment. A higher hazard probability indicates a higher risk of postoperative neurologic impairment in patients with STB.

We plotted the calibration curves and column line plots for the training set separately in this study. For our predicted column-line plots, the Harrell C index of the predicted model is 0.943 (Table 4). Figure 3 illustrates the calibration curves for the training set. The calibration curves are used to assess the calibration effect of the column-line plots, with the horizontal coordinate indicating the probability predicted by the model and the vertical coordinate indicating the actual observed occurrence. The blue line in the figure represents the predictive performance of the column-line graph, while the diagonal line indicates the ideal state where the model predicts the probability to be exactly the same as the actual situation. In other words, the closer the blue line is to the diagonal line, the more the predicted probability of the model matches the actual incidence and the better the model is calibrated. The adjusted deviation is shown by the red line. As

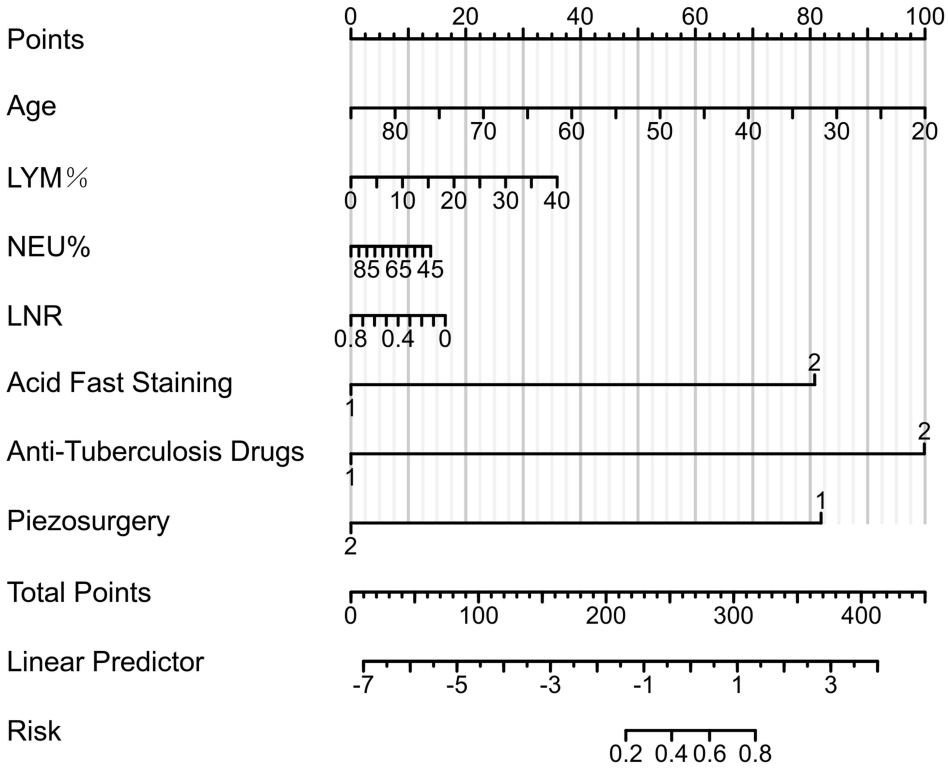


Figure 2 Postoperative neurologic impairment prediction model for spinal tuberculosis patients based on column-line plot. The graph was used to individualize the predicted risk probability. Scores were determined on the corresponding Points axis (Points) based on patient indicators (age, LYM%, NEU%, LNR, acid fast staining, anti-tuberculosis drug, and piezosurgery), which were summed to give a total score (Total Points, 0–400). The final predicted probability (0.2–0.8, ie, 20–80%) was read on the Risk axis.

shown in the figure, the calibration curve of the predictive column chart model based on the actual results of the clinical data and the predicted risk of postoperative neurological impairment presents a high degree of consistency between the predicted probability and the actual observed frequency, reflecting the accuracy of the model in the probability prediction and indicating that it is well calibrated.

Discussion

STB is the most common form of extrapulmonary tuberculosis and is a common cause of paraplegia, which has a great impact on patients' daily lives.[11] If not diagnosed and treated properly, it may lead to neurological impairment and posterior convex deformity, as well as a series of complications.[12,13] Therefore, early diagnosis, standardized antituberculosis treatment, and, if necessary, combined surgical treatment guarantee curing of STB. The incidence rates of STB in male and female patients are similar; 21–50 years is the main age group, the number of patients in rural areas is greater than the number of patients in urban areas, the number of patients with lumbar spine tuberculosis is greater than the number of patients with thoracic spine tuberculosis, and patients with more than two vertebrae are involved in most patients. From 2015.5 to 2024.12, a total of 247 STB surgeries were completed in our hospital, and the cases of

Table 4 Evaluation of the Nomogram Model

Directions for Evaluation	Evaluation Content	Statistic	p value
Model check	LR test	Chi-square: 75.638	1.06e-13
Distinction evaluation	C index	C index: 0.943 (0.898–0.987)	1.38e-87
Calibration assessment	Goodness-of-fit test	Chi-square: 3.2932	0.9146

Abbreviation: LR, likelihood ratio.

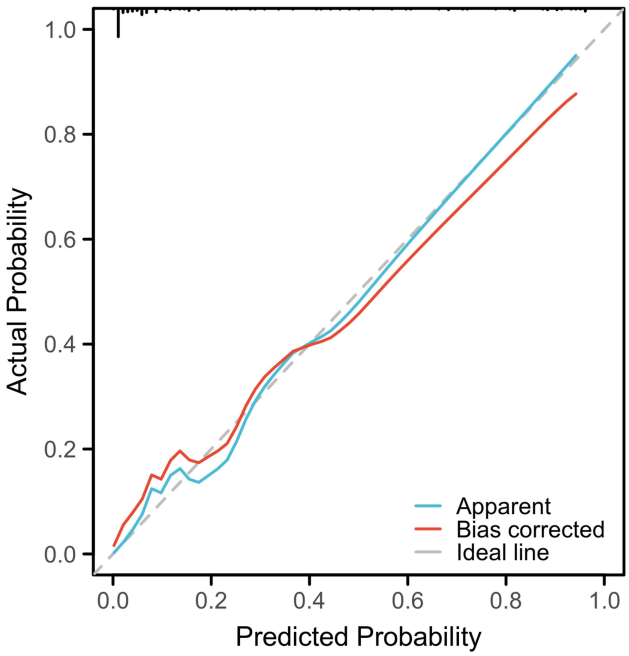


Figure 3 Training set calibration curve. The figure illustrates the agreement between the predicted probability (x-axis, Predicted Probability) and the observed probability (y-axis, Actual Probability). The plot includes the apparent line (Apparent), the bootstrap-corrected line (Bias-corrected), and the ideal reference line (Ideal line). Closer proximity of the curve to the ideal line indicates better model calibration.

neurological dysfunction accounted for 4.7% of the total. Other spinal surgeries (tumors, scoliosis, cervical spondylosis, thoracic spinal stenosis, lumbar degeneration-related diseases, etc). were performed in 1850 patients during the same period. Only 5 cases of neurological dysfunction occurred, accounting for 0.27% of the total number of cases, of which 2 cases were minor disorders and fully recovered at a later stage. One patient with cervical spondylosis had paraplegia. The patient resumed walking half a year after the operation, the muscle strength of the right limb was 5, and the muscle strength of the left limb was 4. Two patients with thoracic spine scoliosis achieved very good recovery. Table 5 indicates that the number of patients who developed neurologic dysfunction postoperatively was 30 in the STB group and 4 in the SD group, revealing a significant difference between the two groups ($p<0.05$).

Table 5 Statistics and Analysis of Data in SD and STB Group

		SD	STB	P
Age		53.92 ± 15.49	56.80 ± 12.88	0.154
Sex	Male	73	69	0.778
	Female	59	63	
Segment	C	41 (95.32%)	2(4.7%)	0.224
	T upper	2 (13.3%)	13(86.7%)	
	T lower	1(1.5%)	66(98.5%)	
	L	88(63.3%)	51(36.7%)	
Piezosurgery	Used	68(42.2%)	93 (57.8%)	0.002
	Unused	64(62.1%)	39(37.9%)	
ASIA	A	4(50%)	4(50%)	0.731
	B	2(18.2%)	9(81.8%)	
	C	16(53.3%)	14(46.7%)	
	D	96(52.7%)	86 (47.3%)	
	E	14(42.4%)	19(57.6%)	
Group	Damage	4	30	<0.001
	Control	128	102	

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These data suggest that patients with STB may be more susceptible to postoperative neurological deficits than patients with other spinal disorders. Our preliminary observations revealed that this phenomenon was not caused by direct intraoperative injury to the spinal cord or postoperative hematoma compression but may be related to the existence of a certain relationship with shock to the spinal cord during surgery. The development of STB lesions is a process of infectious inflammation, with destruction–liquefaction necrosis occurring within the lesion and sclerosis–repair–replacement–reconstruction occurring at the edge of the lesion. As the lesion progresses to the resting stable stage, sclerotic bone formation often occurs in the lesion, sometimes involving the entire vertebral body. Piezosurgery, however, exerts bone-cutting effects through the microvibration effect of ultrasound as well as the air–water cavitation effect and has been widely used in STB surgery; this method has the advantages of high bone-cutting efficiency, hemostasis of the cutting surface, and no cutting of soft tissues and has demonstrated good safety and effectiveness.[14] Nerve injury refers to destruction of the integrity of the nerve structure and impairment of nerve function. Piezosurgery avoids the irritation and damage caused by the traditional bone knife to the spine and the structures in the spinal canal, improves the safety of the osteotomy operation, and reduces the risk of nerve injury. In this study, logistic regression analysis also revealed that the use of intraoperative piezosurgery was an independent protective factor affecting postoperative neurological impairment in patients with STB (Table 3). In STB surgery, the use of piezosurgery may cause some shock to the spinal cord of the patient during the operation, damaging the spinal cord and causing corresponding neurological dysfunction. However, in other spinal surgeries, the operation method and strength of the bone knife are almost the same as those in STB surgeries, but the proportion of neurological dysfunction in patients after surgery is significantly lower, which indicates that in STB, piezosurgery shocks the spinal cord, causing spinal cord damage and resulting in neurological dysfunction, which is a hypothesis that needs to be further verified.

The diagnosis of STB at an early (inflammatory) stage is essential to prevent the development of neurological dysfunction. In STB lesions, the lesion produces a thick inflammatory exudate that surrounds the spinal cord and causes a variety of spinal cord complications, such as tuberculous radiculomyelitis, myelitis, and spinal cord cavernous disease. Each of these spinal cord complications may cause corresponding neurological dysfunction. In tuberculous myelitis, lower motor weakness is usually attributed to spinal shock. Nevertheless, the possibility of damage to the anterior horn cells of the spinal cord should also be noted, especially in patients with myelitis involving three or more segments.[15] However, the term "spinal shock" remains inappropriate in this type of myelitis because extensive involvement of the lower motor neurons in the spinal cord occurs. In contrast, some patients with parainfectious ascending myelitis develop flaccid paralysis during disease but never develop upper motor neuron signs, which often results in a poor prognosis. In posttuberculous cavernous disease of the spinal cord, however, the presence of a cystic cavity in the spinal cord alters the flow of cerebrospinal fluid in the spinal cord, further enlarging the cavity and leading to severe compression of the spinal root.

The preoperative CRP level in the control group was 30.85 ± 36.75, significantly higher than that in the damage group (13.81 ± 11.06, P=0.014; Table 2). The lower CRP levels in the damage group may be attributed to the higher proportion of patients receiving preoperative anti-tuberculosis therapy (ATT). First-line ATT drugs such as isoniazid and rifampin have been shown to suppress Mycobacterium tuberculosis-mediated inflammatory responses and reduce CRP synthesis.[16,17] Although no significant intergroup difference in postoperative CRP levels was observed, the lower preoperative CRP in the damage group suggests that ATT may have partially controlled the inflammatory response. This hyporesponsive CRP state may also reflect immune dysregulation (eg, lymphopenia with neutrophilia) in tuberculosis patients, potentially compromising spinal cord tolerance to surgical trauma.

Patients with acid-fast bacilli (AFB) positive specimens demonstrated significantly increased risk of postoperative neurological dysfunction (OR=15.795, 95% CI 2.378–104.894, P=0.004; Table 3). AFB positivity indicates higher bacterial load in lesions,[18] and active tuberculosis can induce vasculitis,[19] leading to spinal microvascular thrombosis with subsequent ischemia and hypoxia. In our study, the damage group showed both higher AFB positivity rates and more pronounced lymphocyte-to-neutrophil ratio (LNR) reduction (preoperative 0.72±0.31 → postoperative 0.18±0.11), suggesting that inflammatory-immune imbalance may contribute to this pathological process.

ATT administration was significantly associated with increased neurological complications (OR=7.952, 95% CI 1.069–59.147, P=0.043; Table 3). While ATT effectively inhibits mycobacterial proliferation, it may concurrently trigger immune activation in latent foci. Notably, isoniazid can induce vitamin B6 deficiency and peripheral neuropathy, whereas

ethambutol may cause optic nerve toxicity. Although peripheral nerve injuries were not directly observed in this study, ATT-induced metabolic disturbances might indirectly reduce spinal cord resilience to surgical stress.

STB progresses to a point where the spinal cord in the region of interest develops inflammatory edema as well as microenvironmental changes, and one of the mechanisms that may be involved is spinal vasculopathy. Vasculitis is a well-documented feature of the central nervous system, pulmonary, and renal tuberculosis.[20] However, few studies have evaluated the role of spinal vasculopathy in spinal TB (tuberculosis) lesions. From the perspective of vascular pathological changes, increased vascular permeability and protein extravasation after spinal cord injury, as well as vasospasm and hemodynamic abnormalities, interfere with the normal physiological function of the spinal cord and aggravate nerve injury, eg, the distribution of protein extravasation after spinal cord contusion in rats correlates with the degree of injury and functional status. Pathological changes such as vasospasm in human spinal cord injuries also cause further impairment of neurological function.[21] Therefore, we have accordingly proposed the hypothesis that changes in the vessel wall may lead to ischemia in the spinal vessels, resulting in spinal vasculopathy, such as inflammation of the vessels and surrounding tissues. Submucosal vascular endocarditis caused by intravascular granulomas has been reported previously, so intravascular tuberculous granulomas may also be partly responsible for spinal vasculopathy. Additionally, owing to the mechanism of granulomatous inflammation, endovascularly mechanized thrombi leading to obstruction of the lumen of the vessel may be a cause of spinal vasculopathy. For example, venous stasis is a major cause of neurologic deterioration in patients with spinal arteriovenous malformations.[22] Therefore, vascular granulomatous inflammation, as well as tissue destruction due to local ischemia caused by intravascularly mechanized thrombi, may be part of the mechanism of occurrence in patients with spinal vasculopathy. Therefore, the development of vascular inflammatory changes in patients with STB may lead to increased spinal cord vulnerability.

Another mechanism that may be involved in the alteration of the spinal cord microenvironment is the permeability of the blood–cerebrospinal fluid barrier. The presence of the blood–cerebrospinal fluid barrier is essential for proper functioning of the brain, but it is also a bottleneck in the treatment of CNS infections because it prevents 95% of the drug dose from reaching central nervous tissues such as the spinal cord. Therefore, unlike other tuberculosis diseases, STB should be treated in consideration of the permeability of the blood–cerebrospinal fluid barrier.[23,24] According to Lindsay's study, one of the earliest events that occurs in mice during PNI is the disruption of the blood–cerebrospinal fluid barrier,[25] and the use of antituberculosis drugs for treating tuberculosis can have side effects such as nerve damage. For example, isoniazid and rifampicin, in addition to causing liver damage, can cause some damage to peripheral nerves, and ethambutol can cause varying degrees of peripheral nerve invasion, which can lead to numbness of the extremities in some patients. Streptomycin can cause damage to the auditory nerve, resulting in corresponding symptoms, such as vertigo, tinnitus, or even deafness. Pyrazinamide can also cause some damage to the optic nerve, which may lead to blurred vision and vision loss. According to previous studies, peripheral nerve damage may increase the permeability of the blood–cerebrospinal fluid barrier, which may involve the production or release of one or more humoral mediators that act on the cellular and/or intercellular components that maintain an intact barrier. Alternatively, increased blood–cerebrospinal fluid barrier permeability may diffuse from the beginning of the lumbar medulla or result from the release of diffusible mediators circulating in the cerebrospinal fluid. The blood–cerebrospinal fluid (CSF) barrier is a network of endothelial cells connected by tight junctions that serve as an interface to protect the spinal cord parenchyma from circulation and peripheral influences. Dysfunction of the blood–cerebrospinal fluid (CSF) barrier may allow infiltration of inflammatory cells (eg, monocytes) and immune cells (eg, T cells) and is thought to play an important role in diseases such as traumatic brain/spinal cord injuries, stroke, and neurodegeneration. Therefore, studies on the integrity of the blood–cerebrospinal fluid barrier following peripheral nerve injury from STB, as well as other types of spinal cord inflammation, will yield a deeper understanding of the mechanism by which alterations in the spinal cord microenvironment in patients with STB lead to increased spinal cord vulnerability.

Primary injury from STB can stimulate an inflammatory response and cause secondary damage to the spinal cord, often lasting months or even years. Secondary damage to the spinal cord microenvironment at the site of injury is often accompanied by an inflammatory cascade and an adaptive immune response, which leads to impaired spinal cord function (motor, sensory, and reflex). Moreover, the inflammatory effects induce a compensatory anti-inflammatory response and play a role in repair, neuroprotection, and neuroregeneration. After SCI, inflammatory cells rapidly activate and accumulate in the injured area and release cytokines associated with the inflammatory

response, increasing vascular permeability, mediating leukocyte infiltration and inducing an inflammatory response to SCI, which further exacerbates tissue damage and disruption of the blood-spinal cord barrier (BSCB), ultimately resulting in neurological impairment of the spinal cord. Spinal cord injury is a common complication of STB, which often leads to severe neurological deficits that are difficult to recover from and seriously affects the prognosis of patients. Inflammatory cell infiltration, oxidative stress, NO, and other changes in the spinal cord microenvironment can further aggravate SCI. Therefore, it is important to further investigate and elucidate the molecular mechanisms involved in the spinal cord microenvironment in patients with spinal cord injury to improve the recovery of neurological function in patients with STB.[26]

Although the findings of this study demonstrate promising potential, several limitations must be acknowledged. Despite implementing rigorous inclusion/exclusion criteria to control for known confounding factors such as age and comorbidities to minimize bias, the retrospective nature of this study may still entail residual confounding from unmeasured variables including nutritional status (serum albumin) and socioeconomic factors (insurance type). Underreporting of certain rare comorbidities (eg, chronic kidney disease) in electronic medical records may also exist. Furthermore, the evolution of surgical proficiency over time could influence outcomes. Such biases might affect the accuracy of effect estimates regarding postoperative neurological dysfunction in spinal tuberculosis patients, necessitating validation of these conclusions through prospective studies. Future research should incorporate multicenter data synthesis and measure additional inflammatory biomarkers (eg, IL-6, TNF-α) to achieve more comprehensive confounding control. Finally, the underlying molecular mechanisms of key determinants influencing postoperative neurological outcomes in spinal tuberculosis patients remain poorly understood.

Conclusion

In summary, this clinical study successfully established a predictive model with significant prognostic value for postoperative neurological dysfunction in patients with spinal tuberculosis. Notably, based on the ranking of variable contributions, the use of antituberculosis drugs may play a pivotal role in the development of postoperative neurological dysfunction in spinal tuberculosis patients. A well-validated nomogram incorporating acid-fast staining and piezosurgery use may facilitate preoperative risk stratification. Prolonged exposure of the spinal cord to a highly inflammatory environment may serve as a risk factor for intraoperative spinal cord injury in these patients. Furthermore, identical or similar surgical procedures may yield differential clinical outcomes across different disease subtypes and individual patients.

Statement on Patient Data Confidentiality

All patient medical record data used in this study were handled in strict accordance with the ethical guidelines and regulations governing medical research, including the principles outlined in the Declaration of Helsinki. Every effort was made to ensure the confidentiality, anonymity, and privacy of all individuals involved.

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Disclosure

The authors report no conflicts of interest in this work.

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