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A retrospective study on unfavorable 28-day neurological outcomes of stage II TB meningitis

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Tuberculous meningitis (TBM) is often associated with adverse neurological outcomes, however, there is a lack of relevant research. The aim of this study is to explore the risk factors that affect the poor prognosis of 28-day neurological function in patients with stage II TBM. A retrospective analysis was conducted on the clinical data of patients with stage II TBM who visited our hospital from January 1st, 2018 to August 1st, 2019 based on the staging criteria of the Medical Research Council. The neurological function prognosis after 28 days of follow-up was determined to establish independent risk factors. A total of 138 patients (82 male and 56 female) were included, with an average onset age of 37.01 ± 17.30 years. Forty patients had poor prognosis (Modified Rankin Scale [MRS] score, 3–6 points), while 98 patients had a good prognosis (MRS score, 0–2 points). Multivariate logistic regression analysis showed that peripheral nerve dysfunction (odds ratio [OR], 6.315; 95% confidence interval [CI] 2.319–17.196; $p < 0.001$), Quick Sequential Organ Failure Assessment (QSOFA) score (OR 7.343; 95% CI 2.984–18.066; $p < 0.001$), and hydrocephalus (OR 2.685; 95% CI 1.020–7.068; $p = 0.045$) were independent risk factors. The area under the curve for predicting the 28-day neurological prognosis of patients with stage II TBM using the QSOFA score was 0.766 (95% CI 0.680–0.853; $p < 0.001$). Peripheral nerve dysfunction, QSOFA score, and hydrocephalus are independent risk factors for 28-day neurological dysfunction in patients with stage II TBM. The QSOFA score had good predictive ability of the prognosis in terms of 28-day neurological function of patients with stage II TBM.

Keywords Tuberculous meningitis, Prognosis, Disease staging, Risk factors

Abbreviations

AUC	Area under the curve
CI	Confidence interval
COVID-19	Coronavirus disease 2019
CT	Computed tomography
HIS	Hospital information system
HIV	Human immunodeficiency virus
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MRS	Modified Rankin Scale
OR	Odds ratio
ROC	Receiver operating characteristic
TB	Tuberculosis
TBM	Tuberculous meningitis
WHO	World Health Organization

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According to the 2022 global tuberculosis (TB) report of the World Health Organization (WHO), TB is the second most deadly infectious disease after coronavirus disease 2019 (COVID-19), the thirteenth leading cause of death worldwide, and a serious global public health problem[1]. TB meningitis (TBM) is a nonpurulent inflammatory disease of the meninges and spinal membranes caused by *Mycobacterium tuberculosis*, with a mortality rate of 24.7%. Furthermore, 50.9% of the survivors experience residual neurological sequelae[2], including cognitive impairment, intellectual disability, limb paralysis, and epilepsy. TBM accounts for only 1–5% of all types of TB; however, it is the most serious type of extrapulmonary TB[3], causing great financial burden for families of affected patients. A previous study has reported that the average cost of treatment for each patient with TBM in China is as high as $9484 United States dollars (USD)[4]. Therefore, reasonable clinical treatment plans are needed, with targeted, scientific, and meticulous care being key to improving patient compliance and treatment effects[5].

The onset of TBM is not obvious; therefore, early diagnosis is difficult. Most patients with TBM have stage II or stage III disease at the time of diagnosis (stage I: conscious, only fever, headache, other nonspecific symptoms, no neurological impairment, Glasgow Coma Scale (GCS) score of 15; stage II: somnolence or cranial nerve paralysis, GCS score of 11–14; stage III: coma, severe paralysis or paralysis, GCS score ≤ 10)[6–8]. A previous study reported that two-thirds of deaths and neurological sequelae occur immediately after the first admission for TBM[9]. Late disease stage, hydrocephalus, change in the level of consciousness, advanced age, cerebral infarction, tuberculoma, focal neurological deficit, cranial nerve paralysis, and human immunodeficiency virus (HIV) infection are generally believed to be related to poor prognosis[2,10,11]. In 2020, a meta-analysis determined the clinical stages of 4761 cases of TBM, wherein stage II accounted for 48% of these cases[12]. In patients with stage II disease, the condition is serious, disease progression is rapid, and disease development is uncertain; therefore, it is difficult to treat and provide nursing care for such patients. If active and effective intervention is provided at this stage, then the patient's condition can be gradually improved. In contrast, with disease progression to stage III[13], coma, seizures, paralysis, and death can occur[14]. Therefore, the disease direction of stage II TBM can result in better or worse conditions and is significant to the prognosis; however, relevant reports are lacking. Therefore, this study aimed to explore the risk factors influencing the unfavorable prognosis of this disease in terms of the 28-day neurological function in patients with stage II TBM. Herein, we conducted a retrospective analysis of the clinical data of 138 patients with stage II TBM to provide insights that can be used to guide targeted interventions at an early stage, restrict disease progression, and prevent adverse prognosis.

Methods

Research objectives

In this retrospective study, we selected patients with TBM at West China Hospital of Sichuan University in Chengdu, China, from January 1st, 2018 to August 1st, 2019. The inclusion criteria were as follows: age 18 years or older, complete laboratory tests and imaging examinations performed after admission, Patients were classified as microbiologically confirmed or probable TBM according to the standardized diagnostic criteria proposed by Marais et al.[15]. Fulfilled the British Medical Research Council (Medical Research Council [MRC]) criteria for stage II disease[16] (stage I: conscious, only fever, headache, other nonspecific symptoms, no neurological impairment, GCS score of 15; stage II: somnolence or cranial nerve paralysis, GCS score of 11–14; stage III: coma, severe paralysis or paralysis, GCS score ≤ 10). The exclusion criteria were as follows: pregnancy or lactation, previous neuropsychiatric diseases (sequelae of stroke, postoperative brain tumOR history of severe craniocerebral trauma), severe underlying diseases (malignant tumors, organ failure), failure to complete follow-up, and incomplete clinical data.

The study was performed in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of West China Hospital of Sichuan University (ethical code no. 2018-598). The need for written informed consent was waived by the institutional review board owing to the retrospective nature of the study.

Research methods

The general data and clinical symptom data of the patients were collected through the Hospital Information System (HIS). General data included data on sex, age, history of contact with TB patients, delayed treatment time, body temperature at admission (°C), heart rate (beats/min), respiratory rate (breaths/min), and blood pressure (mmHg; 1 mmHg = 0.133 kPa). Clinical symptom data included data on fever (> 5 days), night sweats, cough (> 2 weeks), headache, nausea, vomiting, convulsions, weight loss, change in the level of consciousness, cognitive impairment, meningeal irritation neck ankylosis, pathologic reflex, peripheral nerve dysfunction, Quick Sequential Organ Failure Assessment (QSOFA) score, and GCS score. To minimize potential confounding due to concurrent bacterial sepsis, all patients underwent routine investigations upon admission to identify other sources of infection. These included peripheral blood cultures, urinalysis, and chest radiography or CT scans. Patients with confirmed bacterial infections or meeting clinical diagnostic criteria for bacterial sepsis were excluded from the final analysis. Peripheral neuropathy was identified based on a combination of clinical symptoms and physical examination findings. Diagnostic criteria included limb weakness, numbness, paresthesia, or gait disturbance, along with neurological signs such as diminished deep tendon reflexes or reduced distal sensation. In cases with atypical symptoms or diagnostic uncertainty, nerve conduction studies were performed to assess peripheral nerve function. To exclude spinal involvement, all patients underwent cerebrospinal fluid examination and spinal imaging when clinically indicated. Moreover, auxiliary examination-related information, such as laboratory test results and imaging examination results, was collected. Clinical symptom definitions were standardized as follows: "change in the level of consciousness" was evaluated by the Glasgow Coma Scale (GCS), with scores < 15 considered indicative of alteration; "cognitive dysfunction" referred to impairments in memory, orientation, or attention; and "pathological signs" referred to abnormal neurological reflexes such as positive Babinski sign. Clinical symptom data included Laboratory test results included blood potassium (mmol/L),

blood glucose (mmol/L), serum albumin (g/L), blood sodium (mmol/L), cerebrospinal fluid chloride (mmol/L), cerebrospinal fluid glucose (mmol/L), and cerebrospinal fluid protein (g/L) levels; platelet ($\times 10^9$/L), red blood cell ($\times 10^{12}$/L), white blood cell ($\times 10^9$/L), and lymphocyte counts ($\times 10^9$/L); absolute value of neutrophils ($\times 10^9$/L); cerebrospinal fluid glucose/plasma glucose ratio; and nucleated cell number in the cerebrospinal fluid. Imaging examination results included intracranial changes (cerebral infarction, hydrocephalus, meningeal enhancement, basal exudates, intracranial enhanced vasculitis or infection, intracranial tuberculoma) observed on magnetic resonance imaging (MRI) and computed tomography (CT).

Follow-up and outcome index

Within 28 days of discharge, the hospital inpatients were followed-up, and their electronic medical records were reviewed to obtain prognostic indicators. Discharged patients were followed-up by telephone to obtain prognostic indicators. Patients who did not participate in the follow-up were excluded from the study. Failure to attend the telephone follow-up more than three times was considered loss to follow-up. Outcome indicators were scored according to the MRS as follows[17]: 0 points, no neurological dysfunction and normal daily life; 1 point, mild neurological dysfunction that does not affect daily life; 2 points, mild neurological dysfunction affecting daily life; 3 points, moderate neurological dysfunction requiring daily assistance; 4 points, severe neurological dysfunction that causes the inability to care for oneself; 5 points, bedridden status and incontinence; and 6 points, death. The patients were classified into the good prognosis group and poor prognosis group, based on their modified Rankin scale (MRS) scores; scores of 0–2 indicated a good prognosis, whereas scores of 3–6 points indicated poor prognosis.

Statistical analysis

Statistical analysis was performed using the SPSS 22.0 (IBM Corp., Armonk, NY, USA) statistical software. Data with normal distribution are expressed as mean ± standard deviation; for intergroup comparisons, the independent samples t-test was performed. Data with non-normal distribution are expressed as median (lower quartile–upper quartile). The Mann–Whitney test was performed for group comparisons. The chi-squared test was performed for categorical data. Factors with $p < 0.05$ in the univariate analysis model were included in the multivariate logistic regression analysis. Binary multivariate logistic regression was used to identify independent risk variables for poor 28-day neurological function in patients with stage II TBM. The odds ratio (OR) and 95% confidence interval (CI) were evaluated, and the Hosmer–Lemeshow test was performed to determine whether the results of the regression model were consistent with the overall data. The predictive efficiency of the QSOFA score was evaluated using a receiver operating characteristic (ROC) curve and area under curve (AUC). $p < 0.05$ was considered statistically significant.

Treatment protocol

All patients received anti-tuberculosis treatment based on the national TB guidelines, including a standard quadruple regimen: isoniazid, rifampin, pyrazinamide, and ethambutol. Dexamethasone was routinely co-administered to all patients to slow down the inflammatory response and pyridoxine (vitamin B6) was routinely co-administered to all patients to prevent isoniazid-induced peripheral neuropathy. In cases of liver dysfunction or drug intolerance, adjustments were made accordingly. For hydrocephalus, medical therapy involved mannitol to reduce intracranial pressure. Patients who failed to respond to medical management underwent ventriculoperitoneal shunting. Supportive therapies, including nutritional support and electrolyte balance, were provided as needed.

Results

Microbiological classification and drug resistance

Among the 138 patients included in the study, 45 (32.6%) were microbiologically confirmed cases based on positive cerebrospinal fluid (CSF) culture or nucleic acid amplification test (NAAT) results. The remaining 93 patients (67.4%) were classified as probable TBM. Drug susceptibility testing was conducted for all microbiologically confirmed cases, and no drug-resistant TBM was detected in this cohort.

Comparison of the general conditions and clinical symptoms

In this study, 138 patients were included. The average age at onset was 37.01 ± 17.30 years. There were 82 male (59.4%) and 56 female (40.6%) patients. No patients exhibit drug resistance and no patients showed evidence of spinal arachnoiditis based on clinical and radiological evaluations. The patients were classified into the good prognosis group (n = 98 patients; 71.0%) and poor prognosis group (n = 40; 29.0%), based on their MRS scores (MRS score 0–2, good prognosis; MRS score 3–6, poor prognosis). Seven patients died. Univariate analysis of the general condition and clinical symptoms showed that diastolic blood pressure ($p = 0.046$), incidence of peripheral nerve dysfunction ($p < 0.001$), change in the level of consciousness ($p = 0.021$), and QSOFA score ($p = 0.000$) were significantly higher in the poor prognosis group than in the good prognosis group; however, the GCS score was significantly lower in the poor prognosis group than in the good prognosis group ($p = 0.015$). Other general information and clinical symptoms showed no statistically significant differences ($p > 0.05$) (Tables 1 and 2).

Comparison of auxiliary inspection results

The absolute value of neutrophils was significantly lower in the poor prognosis group than in the good prognosis group ($p = 0.042$). Furthermore, the incidence of hydrocephalus was significantly higher in the poor prognosis group than in the good prognosis group ($p < 0.001$). Single-factor comparisons between the groups indicated no significant differences ($p > 0.05$) (Table 3).

Index	Good prognosis group	Poor prognosis group	*p*
Sex			0.499
Male	60 (61.2%)	22 (55.0%)	
Female	38 (38.8%)	18 (45.0%)	
Age (years)	36.42 ± 16.58	38.45 ± 19.11	0.533
History of tuberculosis exposure	3 (3.1%)	1 (2.5%)	1.000
Delayed treatment time (days)	45.35 ± 61.53	67.58 ± 121.70	0.27
Vital signs at the time of admission			
Temperature (°C)	37.11 ± 0.87	36.95 ± 0.81	0.310
Heart rate (beats/min)	85.84 ± 16.29	84.53 ± 18.85	0.683
Breathing (breaths/min)	20.10 ± 1.74	20.50 ± 1.71	0.222
Diastolic blood pressure (mmHg)	73.22 ± 13.70	78.40 ± 13.61	0.046
Systolic blood pressure (mmHg)	125.93 ± 64.11	124.63 ± 19.49	0.900

Table 1. Univariate analysis of the prognosis of stage II TBM. SD, standard deviation; TBM, tuberculosis meningitis.

Index	Good prognosis group	Poor prognosis group	*p*
Fever > 5 days	81 (82.7%)	34 (85.0%)	0.737
Night sweats	26 (26.5%)	8 (20.0%)	0.419
Cough > 2 weeks	26 (26.5%)	8 (20.0%)	0.419
Headache	91 (92.9%)	36 (90.0%)	0.829
Neck ankylosis	72 (73.5%)	29 (72.5%)	0.907
Pathological reflexes	36 (36.7%)	21 (52.5%)	0.088
Peripheral nerve dysfunction	22 (22.4%)	25 (62.5%)	< 0.001
Cognitive dysfunction	20 (20.4%)	12 (30.0%)	0.226
Change in the level of consciousness	45 (45.9%)	27 (67.5%)	0.021
Cranial nerve paralysis	29 (29.6%)	13 (32.5%)	0.736
Weight loss	38 (39.2%)	15 (37.5%)	0.855
Vomiting	60 (61.2%)	29 (72.5%)	0.209
Nausea	52 (53.1%)	26 (65.0%)	0.199
Convulsion	19 (19.4%)	14 (35.0%)	0.051
Focal epilepsy	7 (7.1%)	8 (15.0%)	0.152
QSOFA score, median (LQ–UQ)	1 (1–2)	2 (1–2)	0.000
GCS score, median (LQ–UQ)	15 (14–15)	14 (12–15)	0.015

Table 2. Single-factor analysis of stage II clinical symptoms affecting the prognosis of TBM. GCS, Glasgow Coma Scale; LQ, lower quartile; QSOFA, Quick Sequential Organ Failure Assessment; TBM, tuberculosis meningitis; UQ, upper quartile; Pathological reflexes refer to clinical signs of corticospinal tract damage such as positive Babinski or Chaddock signs; Change in the level of consciousness was assessed by GCS (Glasgow Coma Scale), while Cognitive dysfunction refers to deficits in memory, orientation, or attention.

Results of the multifactor analysis

Multivariate logistic regression analysis was conducted using seven significant factors: hydrocephalus, change in the level of consciousness, peripheral nerve dysfunction, diastolic blood pressure, absolute neutrophil count, GCS score, and QSOFA score, as independent variables and 28-day neurological prognosis of patients with stage II TBM as the dependent variable. According to the results of the Hosmer–Lemeshow test ($\chi^2 = 6.387$; $p = 0.381$), the regression model results were well-fitted to the overall data. The results showed that QSOFA score (OR 7.343; 95% CI 2.984–18.066; $p < 0.001$), peripheral nerve dysfunction (OR 6.315; 95% CI 2.319–17.196; $p < 0.001$), and hydrocephalus (OR 2.685; 95% CI 1.020–7.068; $p = 0.045$) were independent risk factors (Table 4).

Efficacy of the QSOFA score for predicting the stage II TBM prognosis

Analysis of the ROC curve for the prognosis of TBM in terms of the 28-day neurological function using the QSOFA score showed that the QSOFA score could predict the neurofunctional prognosis of patients with stage II TBM (AUC, 0.766; 95% CI 0.680–0.853; $p < 0.001$). When the cutoff point was 2, sensitivity was 75.0% and specificity was 73.5% (Table 5, Fig. 1).

Index	Good prognosis group	Poor prognosis group	*p*
Laboratory examination			
Lymphocyte count, median (LQ–UQ)	0.97(0.68–1.30)	0.84(0.36–1.46)	0.364
Absolute value of neutrophil	6.26 ± 2.76	5.11 ± 3.43	0.042
Red blood cell count, $\times 10^9$/L	4.41 ± 0.61	4.41 ± 0.67	0.996
Platelets, $\times 10^9$/L	238.20 ± 93.20	227.98 ± 82.34	0.547
Serum potassium (mmol/L)	3.69 ± 0.51	3.53 ± 0.41	0.08
Blood leukocyte count, $\times 10^9$/L	7.99 ± 3.02	7.30 ± 3.81	0.263
Blood sugar (mmol/L)	6.05 ± 1.32	6.27 ± 1.52	0.389
Blood sodium (mmol/L)	131.72 ± 6.79	131.86 ± 6.82	0.911
Human serum albumin (g/L)	38.87 ± 4.27	38.06 ± 6.11	0.378
Nucleated cells in cerebrospinal fluid	212.63 ± 213.79	194.45 ± 238.67	0.662
Cerebrospinal fluid blood glucose	1.90 ± 0.84	1.96 ± 1.04	0.771
Cerebrospinal fluid protein (g/L)	3.48 ± 7.72	3.70 ± 5.07	0.87
Cerebrospinal fluid chlorine (mmol/L)	113.87 ± 7.20	111.48 ± 7.97	0.088
Cerebrospinal fluid sugar ratio, median (LQ–UQ)	0.30 (0.21–0.44)	0.28 (0.17–0.51)	0.825
Imaging examination			
Hydrocephalus	23 (23.5%)	25 (62.5%)	0.000
Cerebral infarction	39 (39.8%)	21 (52.5%)	0.172
Basal exudates	6 (6.1%)	3 (7.5%)	1.000

Table 3. Univariate analysis of the influence of laboratory and imaging examination results on the prognosis of stage II TBM. LQ, lower quartile; QSOFA, Quick Sequential Organ Failure Assessment; TBM, tuberculosis meningitis; UQ, upper quartile.

Prediction factors	Partial regression coefficient	Standard error of the partial regression coefficient	*p*	OR	95% CI
QSOFA	1.994	0.459	< 0.001	7.343	2.984–18.066
Peripheral nerve dysfunction	1.843	0.511	< 0.001	6.315	2.319–17.196
Hydrocephalus	0.988	0.494	0.045	2.685	1.020–7.068
Constant	− 5.083	0.867	< 0.001	0.006	

Table 4. Analysis of independent prognostic factors for poor outcomes of stage II TBM. CI confidence interval; OR odds ratio; QSOFA, Quick Sequential Organ Failure Assessment; TBM, tuberculosis meningitis.

Index	AUC	95% CI	*p*	Cutoff value	Sensitivity	Specificity	Youden index
QSOFA	0.766	0.680–0853	0.000	2	0.75	0.735	0.485

Table 5. Analysis of the predictive value of the QSOFA score. AUC, area under the curve; CI confidence interval; QSOFA, Quick Sequential Organ Failure Assessment.

Discussion

We examined the risk factors influencing the unfavorable prognosis of this disease in terms of the 28-day neurological function in patients with stage II TBM. TBM develops more rapidly than other types of TB. Even after anti-TB treatment, more than half of the patients die or experience neurological sequelae; for those with HIV, the outcome is often fatal[18]. Therefore, identification of risk factors is particularly important to guide treatment and improve the prognosis. This study found that peripheral nerve dysfunction, high QSOFA score, and hydrocephalus were independent risk factors for unfavorable 28-day neurological function of patients with stage II TBM. Moreover, the QSOFA score showed good predictive ability for the prognosis in terms of 28-day neurological function of patients with stage II TBM. The average age at disease onset in patients was 37.01 ± 17.30 years in this study, and the proportion of male patients was higher than that of female patients. Similar to the findings of previous studies[1,4,7], the main clinical symptoms in our study were headache (92.0%), fever (83.3%), cervical stiffness (73.2%), and vomiting (64.5%). However, the overall poor prognosis incidence was lower than that reported in previous studies[19–23]. The primary reason for this is that our hospital is a diagnosis and treatment center for challenging and critical diseases, and some patients had been diagnosed with TB and treated with anti-TB therapy at other hospitals before presenting to our hospital. Furthermore, none of the patients in this study had HIV. Additionally, previous studies included a certain proportion of patients with

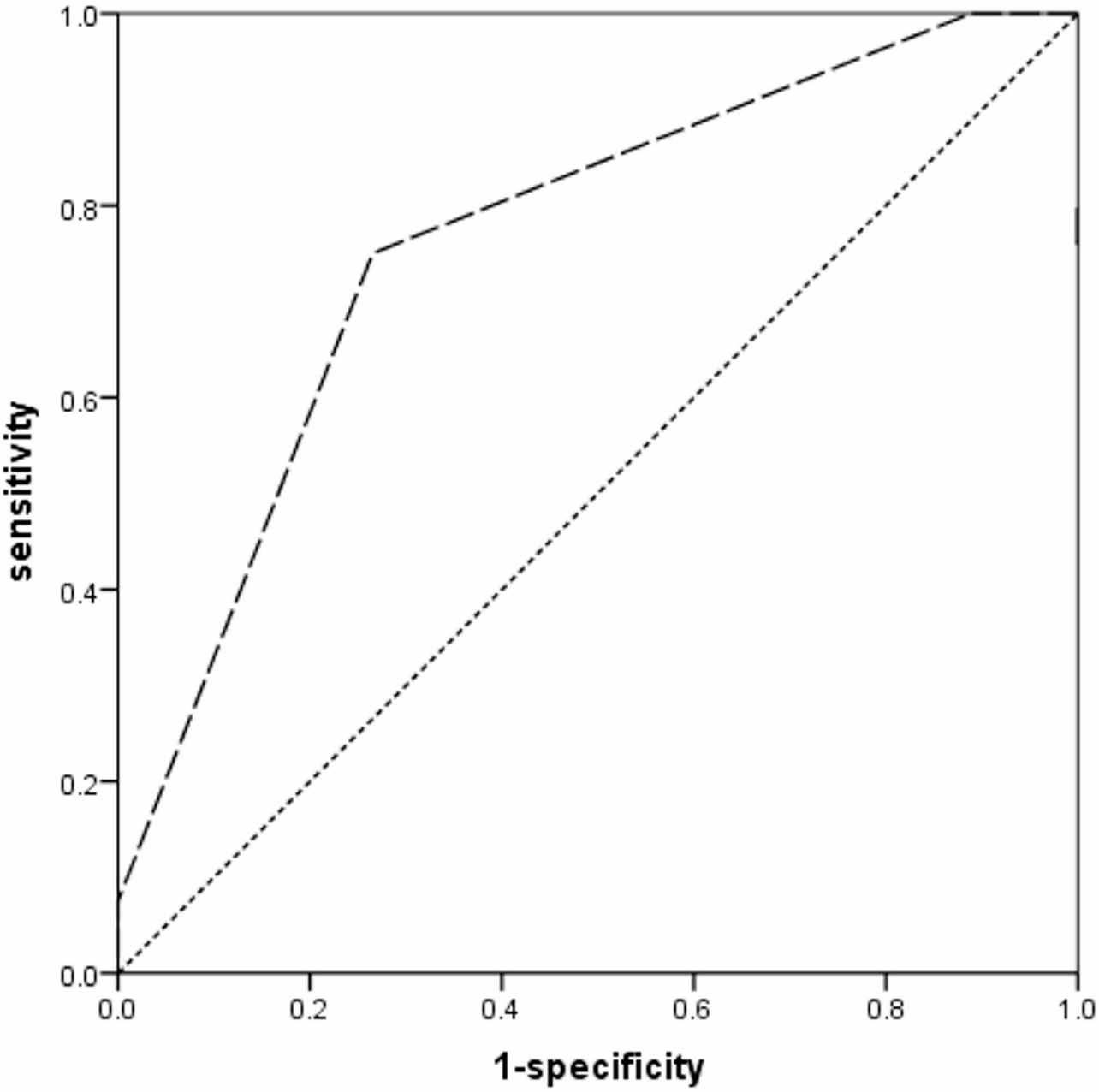

Fig. 1. The predictive value of the QSOFA score of neurological outcomes. The figure illustrates a plot of the receiver operating characteristic (ROC) curve of the Quick Sequential Organ Failure Assessment (QSOFA) score predicting the 28-day neurological outcomes of patients with stage II tuberculosis meningitis (TBM).

stage III TBM. Stage III TBM is more critical than stage II TBM, with a worse prognosis and high mortality rate of up to 64.8%[2]. In our study, the 28-day mortality rate of patients with stage II TBM was 5.07%.

We found that the QSOFA score is an independent risk factor for poor prognosis of patients with stage II TBM. The QSOFA score is commonly used for early identification and to determine prognosis of patients with sepsis, and it includes the following three items: systolic blood pressure ≤ 100 mmHg, respiratory rate ≥ 22 beats per minute, and change in the level of consciousness (GCS score ≤ 14). Each of these items are assigned a score of 1, and a total score of ≥ 2 indicates a high risk of intensive care unit admission or death[24]. Because data collection for the QSOFA is easy to perform, convenient, and fast, and because there is no need to wait for laboratory test results, the use of the QSOFA score in emergency departments is extensive[25]. However, the efficacy of the QSOFA score in evaluating patients with TBM has not been reported. During this study, the QSOFA score was used to evaluate the prognosis of patients with stage II TBM; the median QSOFA score of the good prognosis group was 1, the median QSOFA score of the poor prognosis group was 2: the QSOFA score of the poor prognosis group was significantly higher than that of the good prognosis group. Furthermore, the ROC curve of the participants showed that the QSOFA score could predict prognosis in terms of the neurological function of patients with

stage II TBM (AUC, 0.766; 95% CI 0.680–0853), with sensitivity of 75.0% and specificity of 73.5% when the cutoff value was 2 points. Therefore, its clinical application is valuable. When the QSOFA score is ≥ 2, indicating a serious condition, personalized medical decisions should be made to prevent a poor prognosis. Some studies have added specific indicators, such as age and lactate level, to the QSOFA score, thus enhancing the efficacy of the QSOFA score to evaluate prognosis of certain diseases with a significantly improved predictive efficacy[24,26]. This approach also provides novel insights for our future research.

Through multivariate analysis, we found that peripheral nerve dysfunction was an independent risk factor for poor prognosis in patients with stage II TBM. Patients with TBM might show a series of pathophysiological changes, such as exudate accumulation, cerebral infarction, hydrocephalus, and tuberculoma, which can spread downward, involve all segments of the spinal cord, and show corresponding peripheral nerve dysfunction. In our study, 62.5% of the patients in the poor prognosis group had symptoms of peripheral nerve dysfunction, such as limb myodynamia, abnormal sensation, and dysuria. These complications seriously affect the quality of life of patients as well as represent the main causes of disability. A previous prospective study also reported that the presence of peripheral nerve dysfunction upon admission indicated severe condition and was a risk factor for poor prognosis[27]. The peripheral nervous system is a complex motor and sensory neural network. At present, the treatment of TBM is mainly based on early, full-course, combined, and regular anti-tuberculosis treatment. One study stated that high-dose steroid treatment is effective for treating TBM involving the spinal cord[28]; however, another study suggested that this treatment cannot reduce the incidence of neurological sequelae[29]. In short, in clinical practice, patients must undergo a comprehensive evaluation, and timely and accurate medical decisions need to be made for early relief of nerve compression factors. Recovery of neurological function is a long-term, slow, and long-lasting process, requiring the development of personalized neurological rehabilitation plans for patients, so as to gradually and persistently promote the recovery of motor and sensory functions, thereby reducing disability rates and improving neurological prognosis.

Previous studies have shown that hydrocephalus is directly related to poor prognosis[30–32]. Our research also obtained similar findings. Hydrocephalus is caused by TB inflammation in the tentorial fissure, cerebellum, and basal cistern, resulting in a large number of viscous secretions and, consequently, in obstruction of the fourth ventricle or cerebral aqueduct[30]. Hydrocephalus can cause a continuous increase in intracranial pressure, thereby compressing the nerves and brain parenchyma at the base of the skull. When the ventricles shift and cause cerebral hernia, it can lead to coma and death[33]. During this study, seven patients who died had hydrocephalus on CT or MRI scans. Focusing attention on the management of hydrocephalus and controlling intracranial pressure are essential for reducing mortality. In our study, anti-TB drugs, dehydration drugs, and hormonal drugs were used as routine treatments for hydrocephalus. Mild-to-moderate hydrocephalus can be effectively relieved through drug treatment; however, when patients are resistant to drug treatment, surgical intervention should be performed as soon as possible[31]. At present, the most recognized surgical methods are ventriculo-peritoneal shunt and endoscopic third ventriculostomy. During this study, two patients underwent ventriculo-peritoneal shunt, but the prognosis was poOR possibly because of the severity of the brain parenchymal involvement. However, whether ventriculo-peritoneal shunt can improve the outcomes of such patients is still unknown. In clinical practice, it is necessary to closely monitor the vital signs, consciousness, pupils, and other changes. When patients experience symptoms such as worsening headache, projectile vomiting, papilledema, and change in the level of consciousness, vigilance regarding the possibility of intracranial hypertension is necessary, and patients who are at high risk should be identified as soon as possible and receive targeted treatment in a timely manner to prevent cerebral hernia.

According to the univariate analysis, a significant decrease was noted in the absolute value of neutrophils in the poor prognosis group, and this may have been related to the immune response[19]. When humans contract TBM, neutrophils, which are natural immune cells, are activated, and they migrate from the peripheral blood to the focus of infection and use their bactericidal mechanism to engulf bacteria and prevent it from spreading. Subsequently, neutrophil apoptosis occurs, and the neutrophils are recognized and cleared by macrophages. A high neutrophil count may result in a good immune response and compensatory function of the host[7]. A low neutrophil count indicates that the disease has progressed. Although the absolute value of neutrophils has not been proven to be an independent risk factor affecting the prognosis, patients with low neutrophil counts should receive careful attention in clinical practice. A low absolute value of neutrophils may indicate poor immune function, thus making the patients more susceptible to infection with *Mycobacterium tuberculosis*[34]. Therefore, it is necessary for healthcare teams to collaborate and optimize the prognosis of these patients by developing reasonable medication, dietary, and exercise plans; providing guidance regarding how to change unhealthy lifestyle habits; providing vaccines; and strengthening relevant health education to help treat and prevent TBM[35].

The prognosis of stage II TBM has important clinical significance, but very few related studies are available. Therefore, our study is of significance, in that we performed a detailed and comprehensive assessment of the neurological sequelae and risk factors of TBM and provided novel insights and evidence. However, this study has some limitations. First, this study was a retrospective analysis; therefore, it may have been affected by incomplete clinical data collection. Second, this study only analyzed the patients who visited within 19 months, the sample size was small, and the results may have led to some errors. Additionally, although the study was conducted at a single center in one region, patients from all over the country visit our hospital; therefore, the results were representative of our national population. Further prospective studies with larger sample sizes should be conducted at multiple centers to verify the experimental results.

Conclusions

The risk factors for poor neurological outcomes of patients with stage II TBM are complex, and the ability to identify these factors needs to be strengthened. Furthermore, it is necessary to initiate aggressive, scientific, and effective interventions early in the disease course to enhance patient adherence, improve treatment efficacy,

reduce the incidence of adverse outcomes, and prevent disease progression and adverse outcomes. A high QSOFA score, peripheral neurological dysfunction, and hydrocephalus are independent risk factors for the poor prognosis of patients with stage II TBM. Low absolute neutrophil count, high diastolic blood pressure, change in the level of consciousness, and low GCS score may be important risk factors; therefore, patients with these risk factors should be given high priority. The QSOFA score can be used as a quick and simple evaluation tool for predicting the short-term neurological prognosis of patients with stage II TBM.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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References

1. Huang, M. et al. A study of risk factors for tuberculous meningitis among patients with tuberculosis in China: An analysis of data between 2012 and 2019. *Front. Public Health* **10**, 1040071 (2022).
2. Wang, M. G. et al. Treatment outcomes of tuberculous meningitis in adults: A systematic review and meta-analysis. *BMC Pulm. Med.* **19**, 200 (2019).
3. Thwaites, G. E., van Toorn, R. & Schoeman, J. Tuberculous meningitis: More questions, still too few answers. *Lancet Neurol.* **12**, 999–1010 (2013).
4. Ma, X. P., Li, J. M., Zhou, D. & Yang, R. Direct economic burden of patients with tuberculous meningitis in western China. *Acta Neurol. Scand.* **144**, 535–545 (2021).
5. Zhang, J., Hu, X. Y., Ye, H., Fan, X. Q. & Lai, D. M. Construction and application of tuberculosis medical and nursing integration cooperation model. *Public Health Nurs.* **40**, 97–104 (2023).
6. Wasay, M. et al. Cerebral infarction and tuberculoma in central nervous system tuberculosis: Frequency and prognostic implications. *J. Neurol. Neurosurg. Psychiatry* **85**, 1260–1264 (2014).
7. Li, K. et al. Clinical features, long-term clinical outcomes, and prognostic factors of tuberculous meningitis in West China: A multivariate analysis of 154 adults. *Expert Rev. Anti Infect. Ther.* **15**, 629–635 (2017).
8. Gu, J. et al. Prognostic factors of tuberculous meningitis: A single-center study. *Int. J. Clin. Exp. Med.* **8**, 4487–4493 (2015).
9. Merkler, A. E. et al. Neurological complications after tuberculous meningitis in a multi-state cohort in the United States. *J. Neurol. Sci.* **375**, 460–463 (2017).
10. Wen, L. et al. Clinical features, outcomes and prognostic factors of tuberculous meningitis in adults worldwide: Systematic review and meta-analysis. *J. Neurol.* **266**, 3009–3021 (2019).
11. Pehlivanoglu, F., Yasar, K. K. & Sengoz, G. Prognostic factors of neurological sequel in adult patients with tuberculous meningitis. *Neurosciences (Riyadh)* **15**, 262–267 (2010).
12. Stadelman, A. M. et al. Treatment outcomes in adult tuberculous meningitis: A systematic review and meta-analysis. *Open Forum Infect. Dis.* https://doi.org/10.1093/ofid/ofaa257 (2020).
13. Sheu, J. J., Yuan, R. Y. & Yang, C. C. Predictors for outcome and treatment delay in patients with tuberculous meningitis. *Am. J. Med. Sci.* **338**, 134–139 (2009).
14. Arshad, A. et al. Analysis of tuberculosis meningitis pathogenesis, diagnosis, and treatment. *J. Clin. Med.* **9**, 2962 (2020).
15. Marais, S. et al. Tuberculous meningitis: A uniform case definition for use in clinical research. *Lancet Infect. Dis.* **10**, 803–812 (2010).
16. Philip, N., William, T. & John, D. V. Diagnosis of tuberculous meningitis: Challenges and promises. *Malays. J. Pathol.* **37**, 1–9 (2015).
17. Quinn, T. J., Dawson, J., Walters, M. R. & Lees, K. R. Reliability of the modified Rankin scale: A systematic review. *Stroke* **40**, 3393–3395 (2009).
18. Dodd, P. J. et al. The global burden of tuberculous meningitis in adults: A modelling study. *PLoS Glob. Public Health* **1**, e0000069 (2021).
19. Raberahona, M., Rakotoarivelo, R. A., Razafinambinintsoa, T., Andrianasolo, R. L. & Randria, M. J. Clinical features and outcome in adult cases of tuberculous meningitis in tertiary care hospital in Antananarivo Madagascar. *BioMed. Res Int.* **2017**, 9316589 (2017).
20. Woldeamanuel, Y. W. & Girma, B. A 43-year systematic review and meta-analysis: Case-fatality and risk of death among adults with tuberculous meningitis in Africa. *J. Neurol.* **261**, 851–865 (2014).
21. Soria, J. et al. Mortality in hospitalized patients with tuberculous meningitis. *BMC Infect. Dis.* **19**, 9 (2019).
22. Cantier, M. et al. Functional outcomes in adults with tuberculous meningitis admitted to the ICU: A multicenter cohort study. *Crit. Care* **22**, 1 (2018).
23. Lu, C. H., Chang, W. N. & Chang, H. W. The prognostic factors of adult tuberculous meningitis. *Infection* **29**, 299–304 (2001).
24. Liu, Z. et al. Prognostic accuracy of the serum lactate level, the SOFA score and the qSOFA score for mortality among adults with Sepsis. *Scand. J. Trauma Resusc. Emerg. Med.* **27**, 51 (2019).
25. Singer, M. et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* **315**, 801–810 (2016).
26. Spagnolello, O. et al. qSOFA as a new community-acquired pneumonia severity score in the emergency setting. *Emerg. Med. J.* **38**, 906–912 (2021).
27. Kalita, J., Misra, U. K. & Ranjan, P. Predictors of long-term neurological sequelae of tuberculous meningitis: A multivariate analysis. *Eur. J. Neurol.* **14**, 33–37 (2007).
28. Garg, R. K., Malhotra, H. S. & Gupta, R. Spinal cord involvement in tuberculous meningitis. *Spinal Cord.* **53**, 649–657 (2015).
29. Seddon, J. A., Tugume, L., Solomons, R., Prasad, K. & Bahr, N. C. The current global situation for tuberculous meningitis: Epidemiology, diagnostics, treatment and outcomes. *Wellcome Open Res.* **4**, 167. https://doi.org/10.12688/wellcomeopenres.15535.1 (2019).
30. Singh, A. K. et al. Paradoxical reaction in tuberculous meningitis: Presentation, predictors and impact on prognosis: Presentation. *BMC Infect. Dis.* **16**, 306 (2016).
31. Huang, H. J. et al. Old age and hydrocephalus are associated with poor prognosis in patients with tuberculous meningitis: A retrospective study in a Chinese adult population. *Medicine* **96**, e7370 (2017).
32. Raut, T. et al. Hydrocephalus in tuberculous meningitis: Incidence, its predictive factors and impact on the prognosis. *J. Infect.* **66**, 330–337 (2013).
33. Figaji, A. A. & Fieggen, A. G. The neurosurgical and acute care management of tuberculous meningitis: Evidence and current practice. *Tuberculosis (Edinb)* **90**, 393–400 (2010).

34. Pranianto, L. AA woman with tuberculous meningitis (TBM) confirmed COVID-19 in the intensive care unit: A nursing case study. *J Kesehatan LLDikti Wilayah 1 (JUKES)* **2**, 1–7 (2022).
35. Erdem, H. et al. Hamsi scoring in the prediction of unfavorable outcomes from tuberculous meningitis: Results of Haydarpasa-II study. *J. Neurol.* **262**, 890–898 (2015).

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Author contributions
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Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
The study was performed in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of West China Hospital of Sichuan University (ethical code no. 2018 – 598). Due to the retrospective nature of the study, the Ethics Committee of West China Hospital of Sichuan University waived the need of obtaining informed consent' in the manuscript.

Consent for publication
Not applicable.

Additional information
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