scientific reports

OPEN

A predictive model for secondary central nervous system infection after craniotomy based on machine learning

Junjie Chen[1,4], Tingting Hu[2,3,4], Jiuxiao Yang[1], Xiao Yang[1], Hui Zhong[1], Zujian Zhang[1], Fei Wang[1] & Xin Li[1]✉

To analyze the risk factors of secondary Central nervous system infections (CNSIs) after craniotomy, and to establish an individualized predictive model for CNSIs risk. The independent risk factors were screened by univariate and multivariate logistic regression analysis. Logistic regression, naive bayes, random forest, light GBM and adaboost algorithms were used to establish predictive models for secondary CNSIs after craniotomy. The predictive model based on the Adaboost algorithm demonstrated superior prediction performance compared to the other four models. Under 5-fold cross validation, the accuracy was 0.80, the precision was 0.69, the recall was 0.85, the F1-score was 0.76, the area under the ROC curve was 0.897,and the average precision was 0.880. The top 5 variables of importance in Adaboost model were operation time, indwelling time of lumbar drainage tube, indwelling lumbar drainage tube during operation, indwelling epidural drainage tube during operation, and GCS score. In addition, Adaboost model with the best prediction performance was used for clinical verification, and the prediction results were compared with the actual occurrence of CNSIs after surgery. The results showed that the accuracy of Adaboost model in predicting CNSIs was 60%, the accuracy of Adaboost model in predicting non-CNSIS was 92%, and the overall prediction accuracy was 76%.

Keywords Craniotomy, Central nervous system infection, Machine learning, Predictive model

Central nervous system infections (CNSIs) are classified into primary and secondary infections, and they represent one of the most severe postoperative complications in neurosurgery. Primary CNSIs are rare in clinical practice[1]. This study primarily focuses on secondary CNSIs following craniotomy. CNSIs can manifest as acute, subacute, or chronic conditions, resulting from the disruption of protective structures such as the scalp, skull, dura mater, and blood-brain barrier due to trauma or surgery, which allows external pathogens to invade the central nervous system[2].These infections can be further categorized based on their location into meningitis, ventriculitis, encephalitis, brain abscess, and subdural or epidural infections[3].

The early clinical manifestations of patients with central nervous system infections (CNSIs) are often nonspecific. For patients suspected of having CNSIs, lumbar puncture is performed to obtain cerebrospinal fluid for etiological examination. A definitive diagnosis of CNSIs can be made if pathogens are cultured from the cerebrospinal fluid. Although cerebrospinal fluid culture is the gold standard for diagnosing CNSIs, in clinical practice, the positive rate of pathogen culture is low, and the culture process is time-consuming. According to research, the positive rate of cerebrospinal fluid culture in meningitis cases is only 5.4–24.3%[4–7], which poses challenges for clinicians in making early diagnoses and implementing timely and effective interventions. Secondary CNSIs following craniotomy may result from the combined effect of one or more contributing factors[8], making isolated studies difficult in clinical practice. In recent years, advances in computer artificial intelligence, particularly in the subfield of machine learning, have enabled significant progress in interdisciplinary applications. Currently, numerous machine learning algorithms have been successfully applied to the development of disease risk prediction models. For instance, Van Niftrik et al.[9] constructed a high-risk patient prediction model using machine learning to identify early postoperative complications in intracranial

[1]People's Hospital of Deyang City, Deyang 618000, Sichuan, China. [2]Medicine and Engineering Interdisciplinary Research Laboratory of Nursing & Materials, West China Hospital, 610041 Chengdu, China. [3]Sichuan University-The Hong Kong Polytechnic University Institute for Disaster Management and Reconstruction, 610041 Chengdu, China. [4]These authorscontributed equally to this work: Junjie Chen and Tingting Hu. ✉email: 389568085@qq.com

tumor cases, achieving an accuracy of 0.70, which outperformed traditional statistical models. Similarly, Nie et al.[10] developed a prediction model for ICU cerebral hemorrhage mortality using a machine learning algorithm, with the random forest algorithm yielding the best sensitivity and specificity, and an area under the ROC curve of 0.819, indicating good predictive performance. To date, most related studies have focused on analyzing the factors influencing CNSIs, and there are no research reports on the application of machine learning to establish predictive models for secondary CNSIs after craniotomy.

Therefore, the purpose of this study is to analyze the factors related to secondary CNSIs following craniotomy and to develop a predictive model based on machine learning algorithms. The goal is to assist clinicians in the early prediction of CNSIs and to enable timely intervention for patients with secondary CNSIs after craniotomy, ultimately improving the prognosis for these patients.

Methods
Participants
This study utilized a retrospective cohort design. A total of 1599 patients who underwent craniotomy at the Affiliated Hospital of North Sichuan Medical College between January 2019 and December 2020 were selected for inclusion. The Synthetic Minority Over-sampling Technique was used to process the data at a 1:2 ratio, categorizing 150 patients with postoperative CNSIs as the case group and 300 patients without CNSIs as the control group. The inclusion criteria for this study were as follows: (1) undergoing craniotomy; (2) surgical incisions classified as Class I or II (Class I incisions are considered clean wounds, Class II incisions are clean-contaminated wounds (some patients had disruption of dural integrity and consequently cerebrospinal fluid leakage)); (3) patients aged 18–80 years; and (4) complete clinical data. The exclusion criteria were as follows: (1) a history of CNSIs before the operation, such as meningitis, encephalitis, or brain abscess; (2) a history of severe medical conditions and poor general health (e.g., cardiac function IV, respiratory failure, renal failure); (3) a diagnosis of cancer; and (4) incomplete medical records.

Predictors and data preprocessing
In the early stage, through literature review, analysis and discussion by members of the research group, a total of 30 influencing factors of this study were determined, mainly including: (1) General clinical data of patients: age, sex, smoking history, drinking history, basic disease history (including hypertension, diabetes history), whether complicated with sinusitis or not. (2) Perioperative status: GCS score, perioperative hormone use, emergency operation, preoperative preparation time, surgical incision classification, ASA classification of anesthesia, endotracheal intubation, indwelling lumbar cistern drainage tube, intraoperative use of microscope, intraoperative implantation of dural patch, intraoperative indwelling epidural drainage tube, intraoperative indwelling number of drainage tube, indwelling ventricular drainage tube, the amount of intraoperative blood loss, operation time, admission to ICU, postoperative albumin content, indwelling time of lumbar cistern drainage tube, indwelling time of epidural drainage tube, incision effusion, cerebrospinal fluid leakage, intracranial gas accumulation, tracheotomy and the number of operations after admission.

Statistical method
SPSS 26.0 was used for statistical analysis, and the counting data were expressed by [n (%)]. The measurement data in accordance with the normal distribution were represented by the mean ± standard deviation $(\bar{x} \pm s)$, and the non-normal distribution data were represented by the median value (quartile spacing). The measurement data obeying normal distribution are compared by independent sample t-test, the measurement data that do not obey normal distribution are compared by nonparametric test, and the counting data are compared by x^2 test and continuity correction x^2 test. Logistic regression analysis was used to determine the independent risk factors of secondary CNSIs after neurosurgical craniotomy.

Construction of predictive model
The data set was randomly split into a training set (80%) and a test set (20%). The training set was used to construct the predictive model, while the test set was employed to evaluate the model's predictive performance. Python 3.9 was utilized to implement five classical machine learning algorithms under 5-fold cross-validation, including Logistic Regression (LR), Naive Bayes (NB), Random Forest (RF), LightGBM (LGBM), and AdaBoost (AB).

Evaluation and validation of the prediction model
The commonly used evaluation metrics for machine learning algorithms—accuracy, precision, recall, F1-score, area under the ROC curve (AUC) and the average precision (AP)—were applied to assess the performance of five risk prediction models for secondary CNSIs after craniotomy. Medical records from 100 patients who underwent craniotomy and met the inclusion and exclusion criteria were collected from the Department of Neurosurgery at the Affiliated Hospital of North Sichuan Medical College in Nanchong between January 1, 2021, and June 30, 2021. The nine indicators listed in Table 3 were gathered for these patients. The model with the best performance was used for prospective clinical validation, where its predictions were compared with the patients' discharge diagnoses, expressed as the accuracy rate (%).

Ethics statement
The experimental protocols were approved by the Ethics Committee of Affiliated Hospital of North Sichuan Medical College (No. 2021ER210-1). Due to the retrospective nature of the study, the Ethics Committee of

Affiliated Hospital of North Sichuan Medical College waived the need for obtaining informed consent. We confirmed that all methods were carried out in accordance with the relevant guidelines.

Results

In this study, a total of 1599 patients were selected, including 150 patients with CNSIs, with an infection rate of 9.38%. A total of 450 patients who met the criteria were included in this study. Among them, 210 (46.7%) were males. 240 (53.3%) female cases. The average age was (56 ± 12.4) years. 128 patients had a history of smoking. 94 patients had a history of alcohol consumption. 176 patients had a history of underlying diseases.

The proportion of pathogens detected in cerebrospinal fluid of patients with CNSIs after craniocerebral surgery

A total of 30 cases of cerebrospinal fluid pathogen culture were positive in postoperative secondary CNSIs patients, and the positive rate of cerebrospinal fluid pathogen culture was 20%. A total of 30 strains of pathogenic bacteria and 15 strains of Gram-positive bacteria were isolated from infected patients, including 4 strains of Enterococcus faecium, 3 strains of Staphylococcus aureus, 2 strains of Staphylococcus cephalus, 1 strain of Staphylococcus epidermidis, 1 strain of Staphylococcus equi, 1 strain of Staphylococcus Koch, 1 strain of Staphylococcus wallichii, 1 strain of Staphylococcus haemolyticus and 1 strain of Streptococcus constellation. There were 15 strains of Gram-negative bacteria, including 7 strains of Klebsiella pneumoniae, 5 strains of Acinetobacter baumannii, 1 strain of Escherichia coli, 1 strain of Serratia marcescens and 1 strain of Enterobacter cloacae (Table 1).

Risk factors analysis of secondary CNSIs after craniotomy

The results of univariate analysis showed gender, alcohol consumption, GCS score, emergency operation, number of operations after admission, operation time, intraoperative blood loss, intraoperative use of microscope, indwelling lumbar cistern drainage tube, indwelling time of lumbar cistern drainage tube, indwelling epidural drainage tube during operation, incision effusion, number of indwelling drainage tube during operation, indwelling ventricular drainage tube, cerebrospinal fluid leakage, tracheotomy, postoperative albumin content, admission to ICU was statistically significant ($P < 0.\ 1$) (Table 2).

Multivariate Logistic regression analysis showed that gender, GCS score, operation time, indwelling lumbar cistern drainage tube, indwelling lumbar cistern drainage tube, indwelling epidural drainage tube, indwelling ventricular drainage tube, times of admission and emergency operation were independent risk factors for secondary CNSIs after craniotomy (Table 3).

Evaluation results of five prediction models for secondary CNSIs after craniotomy

Based on the comprehensive evaluation of performance metrics across the five prediction models, the Adaboost model demonstrates superior performance compared to the other four models. It achieved an accuracy of 0.800, a precision of 0.690, a recall of 0.850, an F1 score of 0.760, an area under the ROC curve (AUC) of 0.897, and an average precision (AP) of 0.880, indicating it has the best predictive capability (Table 4).

Area under ROC curves of five prediction models of secondary CNSIs after craniotomy

The area under the ROC curve of the AB model is 0.897, the area under the ROC curve of the LR model is 0.879, the area under the ROC curve of the RF model is 0.848, the area under the ROC curve of the LGBM model is 0.817, and the area under the ROC curve of the NB model is 0.789 (Fig. 1).

	Pathogenic bacteria	Number of plants ($n = 30$)	Constituent ratio (%)
Gram-positive bacterium	Enterococcus faecium	4	13.33
	Saphylococcus aureus	3	10.00
	Staphylococcus cephalus	2	6.67
	Staphylococcus epidermidis	1	3.33
	Staphylococcus equinus	1	3.33
	Staphylococcus cohnii	1	3.33
	Staphylococcus warneri	1	3.33
	Staphylococcus hemolyticus	1	3.33
	Streptococcus constellatus	1	3.33
Gram-negative bacterium	klebsiella pneumoniae	7	23.33
	Acinetobacter baumannii	5	16.67
	Escherichia coli	1	3.33
	Serratia marcescens	1	3.33
	Enterobacter cloacae	1	3.33

Table 1. Proportion of pathogens detected in cerebrospinal fluid of patients with CNSIs after craniocerebral surgery.

Related influencing factors		Case group	Control group	x²/Z/t	*P*
Gender	Male	82 (54.67%)	128 (42.67%)	5.786	0.016*
	Female	68 (45.33%)	172 (57.33%)		
Smoking	Yes	48 (32%)	80 (26.67%)	1.398	0.237
	No	102 (68%)	220 (73.33%)		
Drink alcohol	Yes	40 (26.67%)	54 (18%)	4.545	0.033*
	No	110 (73.33%)	246 (82%)		
Basic diseases	Yes	57 (38%)	119 (39.67%)	0.117	0.733
	No	93 (62%)	181 (60.33%)		
Emergency operation	Yes	20 (13.33%)	60 (20%)	3.041	0.081*
	No	130 (86.67%)	240 (80%)		
Preoperative sinusitis	Yes	60 (40%)	124 (41.33%)	0.074	0.786
	No	90 (60%)	176 (58.67%)		
Classification of surgical incisions (category)	I	142 (94.67%)	273 (91%)	1.874	0.171
	II	8 (5.33%)	27 (9%)		
Intraoperative use of microscope	Yes	113 (75.33%)	189 (63%)	6.892	0.009*
	No	37 (24.67%)	111 (37%)		
Intraoperative implantation of dura mater patch	Yes	128 (85.33%)	270 (90%)	2.131	0.144
	No	22 (14.67%)	30 (10%)		
Indwelling lumbar cistern drainage tube during operation	Yes	95 (63.33%)	61 (20.33%)	81.638	<0.001*
	No	55 (36.67%)	239 (79.67%)		
Indwelling epidural drainage tube during operation	Yes	141 (94%)	248 (82.67%)	10.961	0.001*
	No	9 (6%)	52 (17.33%)		
Indwelling ventricular drainage tube	Yes	19 (12.67%)	15 (5%)	8.415	0.004*
	No	131 (87.33%)	285 (95%)		
Admission to the ICU	Yes	98 (65.33%)	149 (49.67%)	9.913	0.002*
	No	52 (34.67%)	151 (50.3%)		
Postoperative cerebrospinal fluid leakage	Yes	7 (4.67%)	0 (0%)	11.337	0.001*
	No	143 (95.33%)	300 (100%)		
Postoperative incision effusion	Yes	4 (2.67%)	1 (0.33%)	4.955	0.026*
	No	146 (97.33%)	299 (99.67%)		
Postoperative intracranial gas	Yes	137 (91.33%)	278 (92.67%)	0.248	0.619
	No	13 (8.67%)	22 (7.33%)		
Postoperative tracheal intubation was performed	Yes	105 (70%)	167 (55.67%)	8.593	0.003*
	No	45 (30%)	133 (44.33%)		
Postoperative Tracheotomy	Yes	35 (23.33%)	42 (14%)	6.142	0.013*
	No	115 (76.67%)	258 (86%)		
Steroids were used in the perioperative period	Yes	25 (16.67%)	65 (21.67%)	1.563	0.211
	No	125 (83.33%)	235 (78.33%)		
Age (years)		55 (48, 65)	57 (48.25, 65)	−1.038	0.299
GCS score (score)		15 (10, 15)	15 (13.25, 15)	−2.034	0.042*
ASA grade		3 (2, 3)	2 (2, 3)	−1.332	0.183
Preoperative preparation time (d)		2 (1, 3)	2 (1, 4)	−0.820	0.412
Operation time (h)		4.17 (3.32,5.27)	3.67 (2.57, 4.57)	−3.669	<0.001*
Intraoperative blood loss (ml)		400 (200, 600)	200 (150, 500)	−4.157	<0.001*
Duration of epidural drainage (d)		2 (2, 2)	2 (2, 2)	−1.613	0.107
Lumbar drainage tube indwelling time (d)		4 (0, 9)	0 (0, 0)	−11.883	<0.001*
Number of drainage tubes (root)		1 (1, 1)	1 (1, 1)	−4.621	<0.001*
The number of operations post-admission(number)		1 (1, 1)	1 (1, 1)	−3.322	0.001*
The postoperative albumin concentration (g/L)		29.491 ± 5.362	30.955 ± 4.827	−2.922	0.004*

Table 2. Results of univariate analysis. *Indicates $P < 0.1$.

Precision-Recall curves of five prediction models of secondary CNSIs after craniotomy

The average precision of the LR model is 0.860, the average precision of the NB model is 0.810, the average precision of the RF model is 0.770, the average precision of the LGBM model is 0.820, and the average precision of the AB model is 0.880 (Fig. 2).

Influence factor	β	SE	Wald x^2	OR	*P*	95%CI
Gender	0.861	0.348	6.123	2.365	0.015	1.196–4.675
GCS score (score)	−0.181	0.053	11.803	0.834	0.001	0.753–0.925
Emergency operation	1.352	0.514	6.916	3.864	0.009	1.411–10.583
Operation time (h)	0.200	0.102	3.869	1.221	0.049	1.001–1.490
Indwelling lumbar cistern drainage tube during operation	−1.498	0.358	17.541	0.224	<0.001	0.111–0.451
Indwelling epidural drainage tube during operation	−2.211	0.731	9.149	0.110	0.002	0.026–0.459
Indwelling ventricular drainage tube	−1.286	0.515	6.237	0.277	0.013	0.101–0.758
Lumbar drainage tube indwelling time (d)	0.341	0.061	31.491	1.407	<0.001	1.249–1.585
The number of operations post-admission(number)	1.508	0.723	4.354	4.517	0.037	1.096–18.616

Table 3. Statistical analysis of multi-factor logistic regression for influencing factors of CNSIs.

	Accuracy	Precision	Recall	F1-score	AUC	AP
LR	0.800	0.710	0.610	0.650	0.879	0.860
NB	0.711	0.590	0.670	0.630	0.789	0.810
RF	0.767	0.680	0.700	0.690	0.848	0.770
LGBM	0.744	0.660	0.640	0.650	0.817	0.820
AB	0.800	0.690	0.850	0.760	0.897	0.880

Table 4. Performance evaluation indicators of the five models.

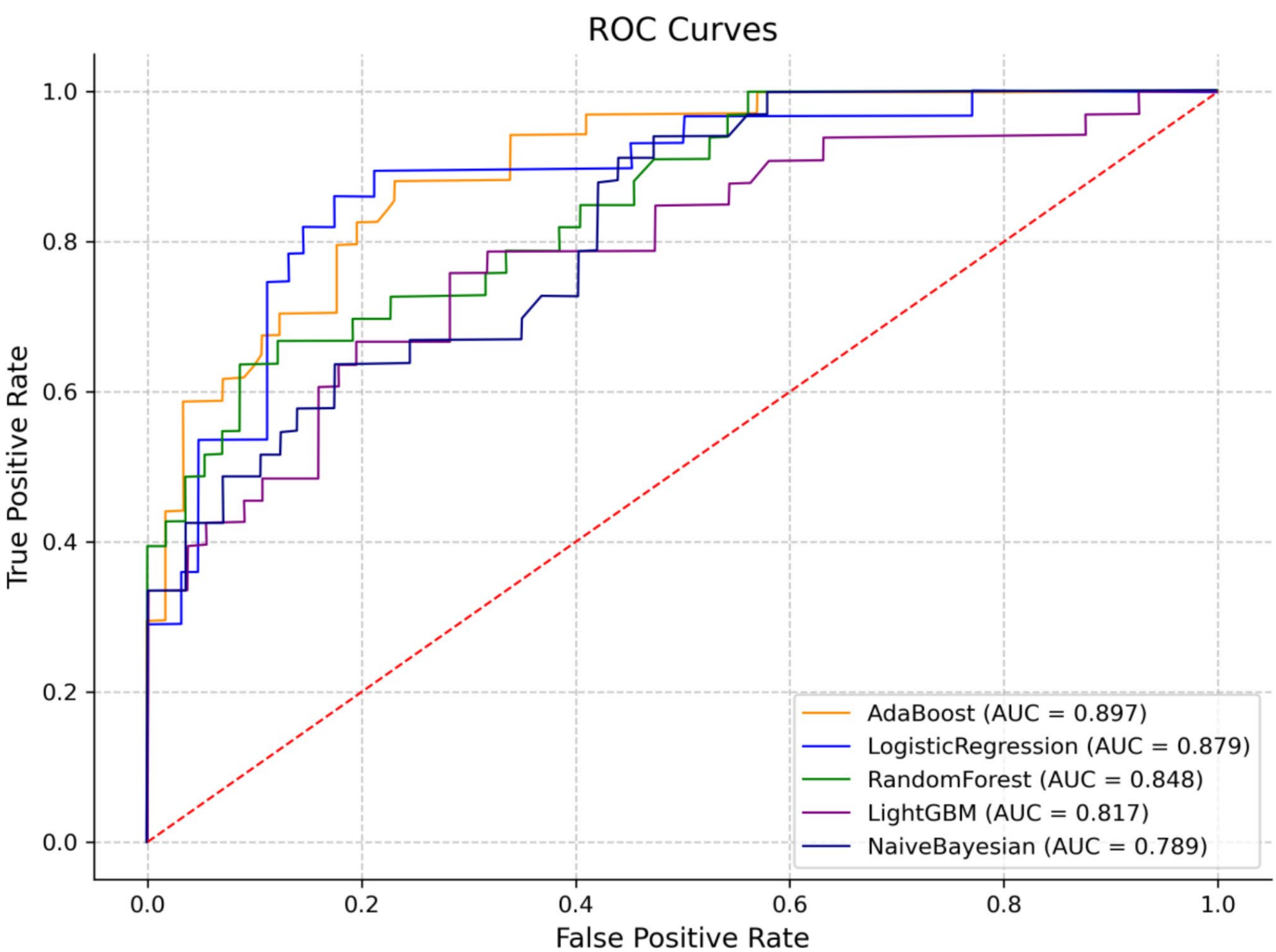

Fig. 1. ROC curves of the 5 machine learning models.

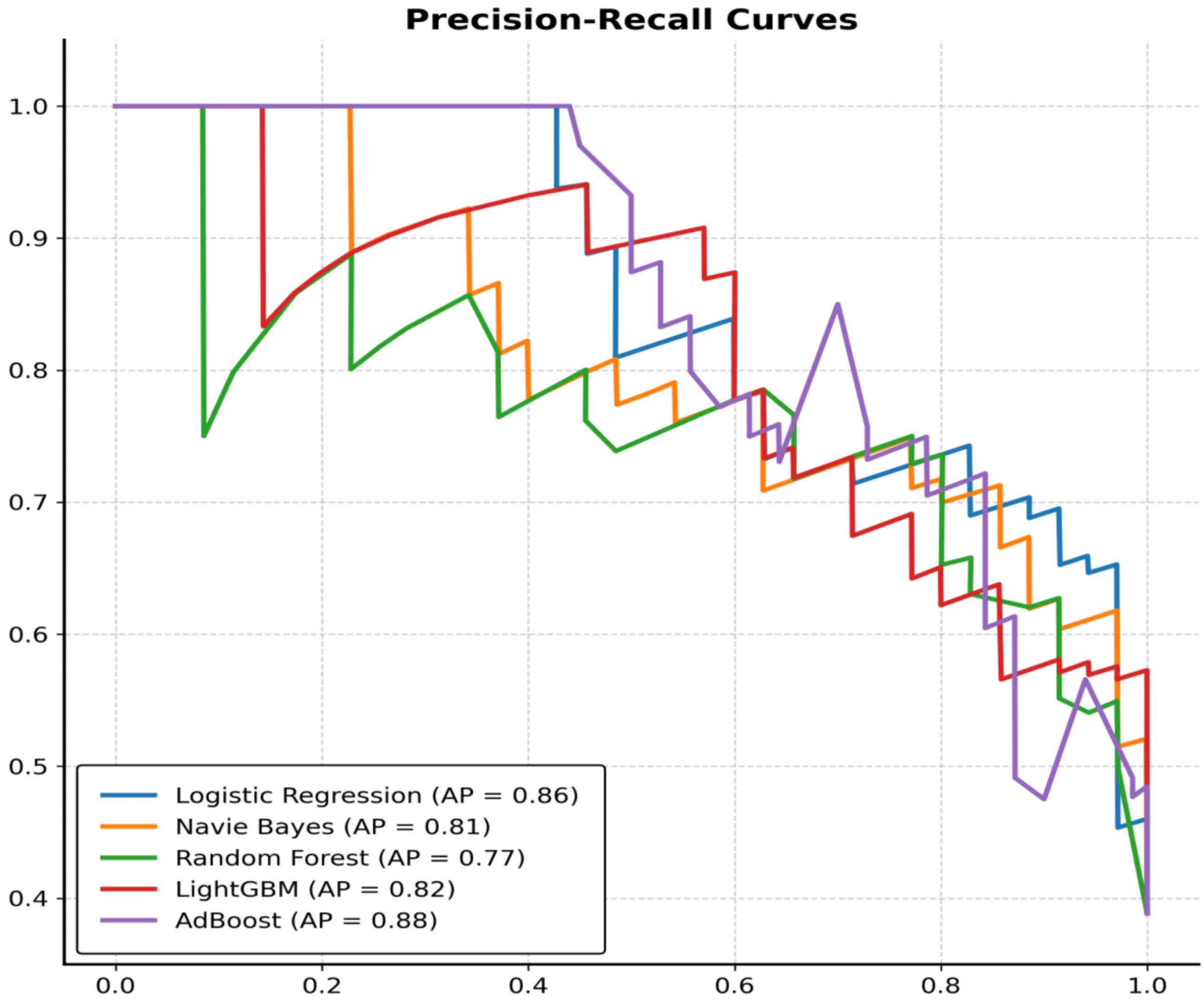

Fig. 2. Precision-Recall curves of the 5 machine learning models.

Importance ranking of variables included in Adaboost prediction model

The top 5 variables of Adaboost model were operation time, indwelling time of lumbar cistern drainage tube, indwelling lumbar cistern drainage tube during operation, indwelling epidural drainage tube during operation and GCS score (Fig. 3).

Clinical validation of secondary CNSIs after craniotomy

The medical records of 100 patients who underwent craniotomy and met the inclusion and exclusion criteria in the Department of Neurosurgery of the affiliated Hospital of North Sichuan Medical College in Nanchong from January 1, 2021 to June 30, 2021 were collected. 9 indexes in Table 3 of the patients were collected, and the best Adaboost prediction model was used to predict whether CNSIs would occur. The results of the prediction model were compared with the discharge diagnosis of the patients.

The results show that the prediction accuracy of Adaboost model for non-occurrence of CNSIs is 92%, for the occurrence of CNSIs is 60%, and the overall prediction accuracy is 76%. It shows that Adaboost prediction model is feasible in judging whether patients with secondary CNSIs after craniotomy (Table 5).

System development results

The system is built on a BS architecture. When deployed on a server, users can directly access the system via a browser. The system framework is developed using Spring Boot, while the data analysis, modeling, and prediction components are implemented using the Hadoop + Spark distributed system. Interface diagram of the early warning system is shown in Fig. 4. Users need to enter the variable values during weaning, leave any missing values blank, and click the Predict button. The result will then be displayed to the user.

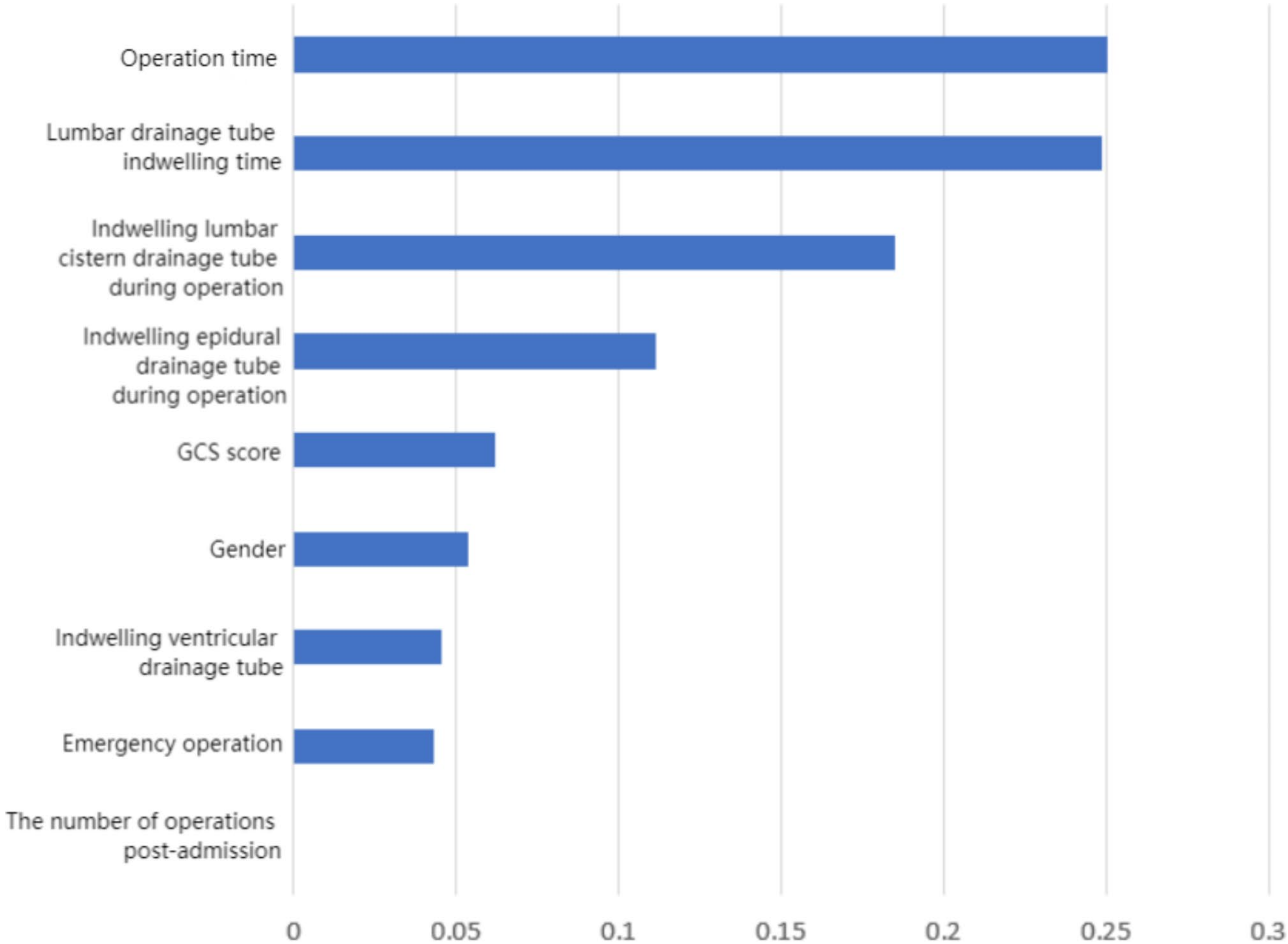

Fig. 3. Importance ranking of predictive model variables Clinical verification of secondary CNSIs model after craniotomy.

Model discrimination result	Actual Infection		
	Uninfected	Infected	Accuracy rate (%)
Uninfected	46	20	92
Infected	4	30	60
Total	50	50	76

Table 5. Adaboost model discrimination and actual infection results.

Discussion

As one of the most common and serious complications following craniocerebral surgery, CNSIs significantly impact the subsequent treatment, prognosis, and quality of life of patients. Under normal physiological conditions, the central nervous system is situated within a completely closed environment, protected by the scalp, skull, meninges, blood-brain barrier, blood-cerebrospinal fluid barrier, and cerebrospinal fluid-brain barrier. Consequently, the incidence of CNSIs is much lower compared to infections in other systems that are directly connected to the external environment, such as the respiratory and urinary systems. However, neurosurgery often requires craniotomy, which partially compromises the protective barriers, allowing the central nervous system to be exposed to the external environment. This exposure increases the likelihood of pathogenic microorganisms entering the brain, thereby elevating the risk of CNSIs. Due to the presence of the blood-brain barrier, conventional antibiotics often struggle to penetrate it effectively, making it difficult to achieve therapeutic drug concentrations within the brain to eradicate the pathogens, thus complicating the clinical management of CNSIs. Some experts and scholars have suggested intrathecal injection as a treatment for CNSIs, but this method requires frequent lumbar puncture or lumbar cisterna drainage. These procedures can themselves lead to retrograde bacterial infection, further increasing the incidence of CNSIs. According to previous studies, the incidence of CNSIs after craniotomy is approximately 4.6–10%[4], and once CNSIs occurs,

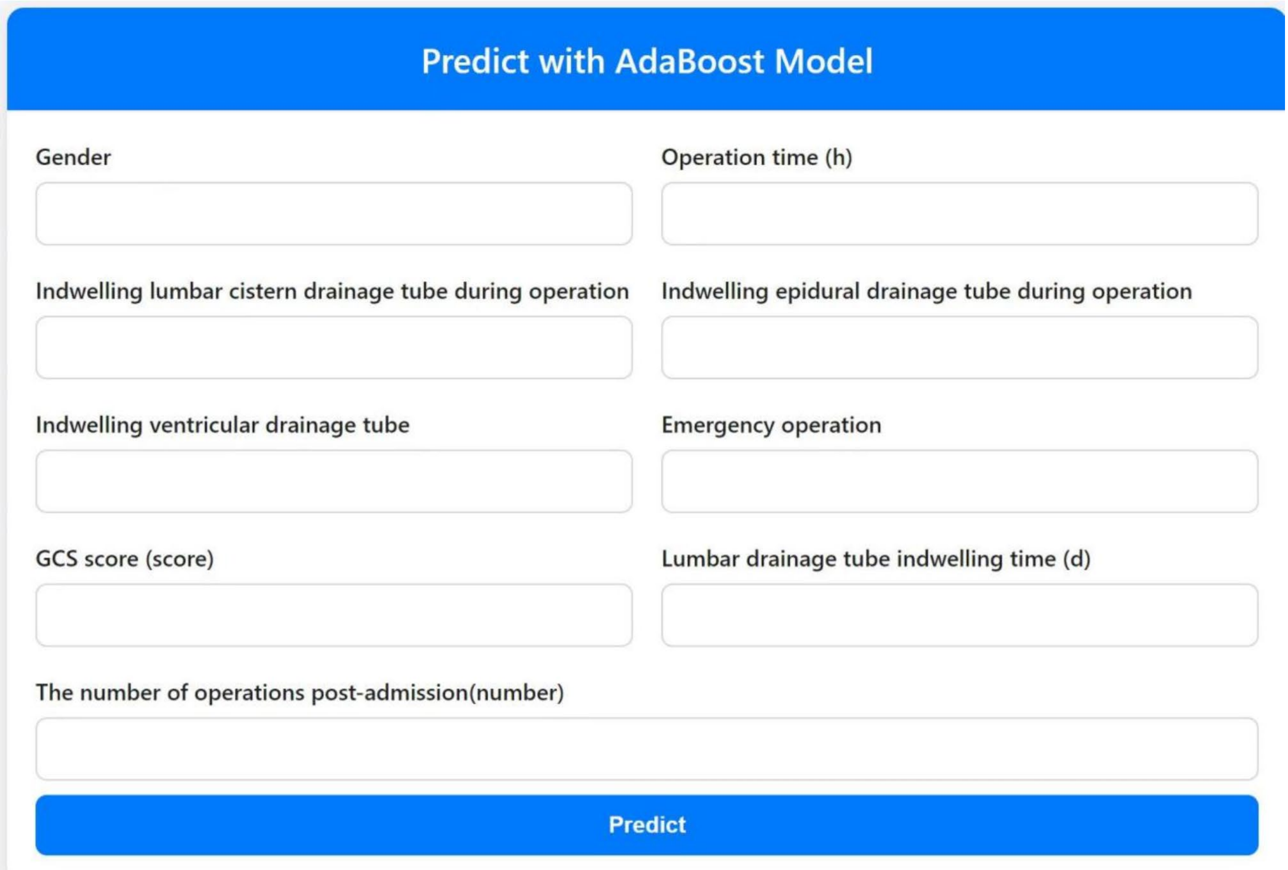

Fig. 4. Interface diagram of the early warning system of secondary CNSIs after craniotomy.

the mortality rate can be as high as 15–30%[5]. In this study, the infection rate of secondary CNSIs after craniotomy was found to be 9.38%, consistent with the results reported in the literature.

CNSIs are associated with high rates of disability and mortality. Once CNSIs occur, they can significantly impact the prognosis and quality of life of patients. Delayed treatment or the emergence of multi-drug resistant bacteria can further endanger patients' lives. Currently, the clinical diagnosis of CNSIs is primarily based on a combination of patients' clinical manifestations, laboratory tests, and imaging data. However, the early clinical signs and laboratory markers of CNSIs often lack specificity, making early diagnosis challenging. By studying the risk factors associated with the occurrence of CNSIs, it is possible to identify and intervene in high-risk populations at an early stage, thereby preventing and controlling the infection. A review of the literature from the past five years, both domestically and internationally, has identified dozens of potential factors that may contribute to the development of CNSIs[11–15]. These factors primarily include the patient's age, underlying comorbidities, duration of surgery, presence of indwelling drainage tubes, duration of tube placement, cerebrospinal fluid leakage, surgical approach, among others. After analysis and discussion, the research group members determined 30 kinds of influencing factors of secondary CNSIs after neurosurgical craniocerebral surgery. Gender, alcohol consumption, GCS score, emergency operation, number of operation after admission, operation time, intraoperative blood loss, intraoperative use of microscope, intraoperative indwelling lumbar cisternal drainage tube, indwelling time of lumbar cisternal drainage tube, intraoperative indwelling epidural drainage tube, incision effusion, number of indwelling drainage tube, indwelling ventricular drainage tube, cerebrospinal fluid leakage, tracheal intubation, tracheotomy were obtained by univariate analysis There were statistically significant differences in albumin content between open surgery and postoperative surgery, and admission to ICU. Further multivariate Logistic regression analysis showed that gender, GCS score, operation time, intraoperative indwelling lumbar cisternal drainage tube, indwelling time of lumbar cisternal drainage tube, intraoperative indwelling epidural drainage tube, indwelling ventricular drainage tube, number of operations after admission and emergency operation were independent risk factors for CNSIs after neurosurgical craniocerebral surgery.

The effects of operation time, indwelling time of lumbar cisternal drainage tube, intraoperative indwelling lumbar cisternal drainage tube, epidural drainage tube, ventricular drainage tube and the number of operations after admission on secondary CNSIs after craniotomy were consistent with the results of previous studies.

Some studies have demonstrated that the duration of surgery is closely related to the incidence of secondary CNSIs after craniotomy[16]. Anudeng et al.[17] found that the infection rate of CNSIs was 6.9% when the operation time was less than 4 h, but it increased to 21.3% when the operation time exceeded 4 h, indicating a positive correlation between operation time and infection rate. In this study, operation time ranked first in importance among variables in the Adaboost model, highlighting its significant impact on postoperative secondary CNSIs. Therefore, it is crucial to perform neurosurgical craniotomies in a sterile laminar flow operating room whenever possible. Surgeons should meticulously sterilize the patient's scalp in the surgical area before the procedure, strictly control the number of personnel in the operating room, limit the frequency of entry and exit, and rigorously adhere to sterile principles during surgery to ensure a successful outcome and minimize the operation time.

Drainage tubes are usually placed during neurosurgery, which mainly include lumbar cidal drainage tubes, ventricular drainage tubes, epidural drainage tubes, subdural drainage tubes and subcutaneous drainage tubes according to different purposes. In our neurosurgical center, patients requiring control of intracranial pressure (ICP) during and after surgery, we place a lumbar drainage catheter preoperatively. The lumbar drainage catheter can be removed when the postoperative intracranial pressure remains stable within normal ranges, and there are no signs of cerebrospinal fluid (CSF) leakage. Ventricular drainage is urgently placed in patients with acute obstructive hydrocephalus or intraventricular hemorrhage to lower intracranial pressure. It is also placed in patients with severe traumatic brain injury to monitor ICP and drain CSF. The ventricular drainage catheter can be considered for removal when the patient's clinical symptoms improve, hydrocephalus resolves or stabilizes, and intracranial pressure returns to normal levels. Long-term lumbar drainage is not only prone to the risk of drainage tube blockage and reflux, but also prone to colonization of external pathogens on the drainage tube, thereby increasing the possibility of retrograde infection. To prevent postoperative epidural hematoma, we routinely place an epidural drainage catheter. The epidural drainage catheter can be removed when postoperative head CT scans show no fluid accumulation in the epidural space and the drainage volume significantly decreases or ceases. Arts et al.[18] believed that the occurrence of CNSIs was closely related to the duration of drainage tube indwelling, which was consistent with the results of this study. Lin et al.[19] considered that indwelling lumbar drainage tube was an independent risk factor for CNSIs. In addition, some studies have suggested that the probability of CNSIs is greatly increased when the external ventricular drainage tube is placed for more than one week, and infection usually occurs on the 3rd to 7th day after surgery. The probability of secondary CNSIs in patients undergoing external ventricular drainage is 10 times that in patients without external ventricular drainage[20–21]. The research results of Omar et al.[22] showed that the distance between the head drainage tube orifice and the surgical incision was closely related to whether the postoperative cerebrospinal fluid leakage occurred. When the subcutaneous tunnel length of the head drainage tube was more than 5 cm, the infection rate of the patients was significantly reduced compared with that of the drainage tube placed in the incision. The results of this study showed that intraoperative lumbar drainage tube, epidural drainage tube and ventricular drainage tube were independent risk factors for secondary CNSIs after craniotomy, which was consistent with the results of previous studies.

Some patients undergoing craniotomy may experience postoperative complications such as re-bleeding in the surgical area, intracranial hypertension that is unresponsive to medication, or severe hydrocephalus. When surgical indications are met, secondary surgery is often required to alleviate symptoms and save the patient's life. Korinek et al.[23] they believed that the initial surgery disrupts the original anatomical structures, leading to potential difficulties in distinguishing these structures during the second operation, which may prolong the operation time. Additionally, performing a re-operation through the original incision within a short period can introduce oozing blood and exudates into the original surgical area, potentially leading to CNSIs.

GCS score, gender, and emergency surgery were new findings of this study, which were rare in previous reports

A lower GCS score indicates a greater degree of consciousness disturbance and a more severe condition, also reflecting the severity of craniocerebral injury. Previous studies have suggested that patients with GCS scores ≤ 8 are 2.53 times more likely to develop CNSIs than those with GCS scores > 8[24]. This increased risk may be related to the pathophysiological characteristics of patients with consciousness disorders. Patients with disturbed consciousness often have elevated brain tissue metabolism and increased oxygen consumption. They are also frequently complicated by intracranial hypertension, which leads to insufficient cerebral blood perfusion. This insufficiency directly impairs the uptake and utilization of glucose and oxygen in brain tissue, further exacerbating brain injury and creating a vicious cycle. Severe brain injury may prolong surgery or necessitate multiple operations, thereby indirectly increasing the likelihood of CNSIs[25].

Currently, there is no consensus on the effect of gender on CNSIs. Some studies suggest that gender[26] is an independent risk factor for secondary CNSIs after craniotomy, which aligns with the findings of this study. However, Guo et al.[27] hold the opposite view. A summary of previous studies suggests that the influence of gender on the occurrence of CNSIs may be related to the following factors: ① It may be associated with unhealthy lifestyle habits more prevalent among men. For example, men are more likely to engage in habits such as smoking and drinking compared to women. Some studies have shown that patients with a long-term smoking history who do not quit smoking before surgery have an increased risk of infection following deep brain surgery[28]. ② Differences in sex hormones and their effects on gene expression and the immune system. Studies have reported differences in the expression of inflammatory cytokines between genders, with leukotrienes playing a significant role in the regulation of immune and inflammatory responses. Testosterone synthesis in men reduces the production of phospholipase-D, leading to lower leukotriene synthesis in men compared to women[29]. The influence of gender on secondary CNSIs after craniotomy requires further investigation through multi-center, prospective large-sample studies to draw definitive conclusions in the future.

Limitations of the study

1. First, the sample size included in this study is small. Expanding the sample size will allow for more robust construction and validation of the prediction model.
2. Stability and reliability of the prediction model, it is necessary to conduct external validation using large, multi-center datasets.
3. There are still limitations in the inclusion of influencing factors. In the early stages, the research team primarily focused on selecting factors that could be intervened upon, and did not consider different diagnostic factors that may lead to craniotomy. In the future, it will be necessary to incorporate more independent risk factors to further improve the prediction model and enhance its predictive performance.

Conclusion

A prediction model for secondary CNSIs after craniotomy was constructed using machine learning, with the Adaboost model demonstrating the best predictive performance and high accuracy. This model can be effectively used to predict secondary CNSIs following craniotomy.

Data availability

The datasets used in the current study are available from the corresponding author upon reasonable request.

Received: 12 May 2024; Accepted: 1 October 2024
Published online: 22 October 2024

References

1. Wang, L. Y. et al. Risk factors for intracranial infection after craniotomy: A case-control study. *Brain Behav.* **10**(7), e01658 (2020).
2. Sneh-Arbib, O. et al. Surgical site infections following craniotomy focusing on possible post-operative acquisition of infection: Prospective cohort study. *Eur. J. Clin. Microbiol. Infect. Dis.* **32**(12), 1511–1516 (2013).
3. Suthar, R. & Sankhyan, N. Bacterial infections of the central nervous system. *Indian J. Pediatr.* **86**(1), 60–69 (2019).
4. Guo, K. et al. Risk factors for postoperative intracranial infections in patients with pituitary adenoma after endoscopic endonasal transsphenoidal surgery: Pneumocephalus deserves further study. *Neurosurg. Focus* **47**(2), E5 (2019).
5. Kim, H. et al. Analysis of the factors affecting graft infection after cranioplasty. *Acta Neurochir. (Wien)* **155**(11), 2171–2176 (2013).
6. Hweidi, I. M. et al. Surgical site infections after craniotomy: A matched health-care cost and length of stay study. *J. Wound Care* **27**(12), 885–890 (2018).
7. Zhang, Y. et al. Clinical application and evaluation of metagenomic next-generation sequencing in suspected adult central nervous system infection. *J. Transl. Med.* **18**(1), 199 (2020).
8. Yao, J. & Liu, D. Logistic regression analysis of risk factors for intracranial infection after multiple traumatic craniotomy and preventive measures. *J. Craniofac. Surg.* **30**(7), 1946–1948 (2019).
9. van Niftrik, C. H. B. et al. Machine learning algorithm identifies patients at high risk for early complications after intracranial tumor surgery: Registry-based cohort study. *Neurosurgery* **85**(4), E756–E764 (2019).
10. Nie, X. et al. Mortality prediction in cerebral hemorrhage patients using machine learning algorithms in intensive care units. *Front. Neurol.* **11**, 610531 (2021).
11. Kim, T. et al. Risk factors of surgical site infections after supratentorial elective surgery: A focus on the efficacy of the wound-drain-tip culture. *Acta Neurochir. (Wien)* **155**(11), 2165–2170 (2013).
12. Xu, Y. et al. Risk factors related to intracranial infections after transsphenoidal pituitary adenomectomy under endoscope. *Ideggyogy. Sz.* **73**(11–12), 399–403 (2020).
13. Yang, Z. J. et al. Prevention of postoperative intracranial infection in patients with cerebrospinal fluid rhinorrhea. *Chin. Med. J. (Engl.)* **124**(24), 4189–92 (2011).
14. Kono, Y. et al. One thousand endoscopic skull base surgical procedures demystifying the infection potential: Incidence and description of postoperative meningitis and brain abscesses. *Infect. Control Hosp. Epidemiol.* **32**(1), 77–83 (2011).
15. Yang, Y. N. et al. The risk of intracranial infection in adults with hydrocephalus after ventriculoperitoneal shunt surgery: A retrospective study. *Int. Wound J.* **17**(3), 722–728 (2020).
16. Lepski, G. et al. Recursive partitioning analysis of factors determining infection after intracranial tumor surgery. *Clin. Neurol. Neurosurg.* **205**, 106599 (2021).
17. Anu Laulajainen-Hongisto, A. et al. Otogenic intracranial abscesses, our experience over the last four decades. *J. Int. Adv. Otol.* **13**(1), 40–46 (2017).
18. Arts, S. et al. Complications of external cerebrospinal fluid drainage in aneurysmal subarachnoid haemorrhage. *Acta Neurochir. (Wien)* **163**(4), 1143–1151 (2021).
19. Lin, C., Zhao, X. & Sun, H. Analysis on the risk factors of intracranial infection secondary to traumatic brain injury. *Chin. J. Traumatol.* **18**(2), 81–83 (2015).
20. Palasz, J. et al. External ventricular drain management in subarachnoid haemorrhage: A systematic review and meta-analysis. *Neurosurg. Rev.* **45**(1), 365–373 (2022).
21. Han, H. et al. The risk factors of intracranial infection in patients with intracerebral hemorrhage undergone hematoma puncture: What should we care. *BMC Infect. Dis.* **20**(1), 949 (2020).
22. Omar, M. A. & Mohd Haspani, M. S. The risk factors of external ventricular drainage-related infection at hospital Kuala Lumpur: An observational study. *Malays. J. Med. Sci.* **17**(3), 48–54 (2010).
23. Korinek, A. M. et al. Risk factors for neurosurgical site infections after craniotomy: A critical reappraisal of antibiotic prophylaxis on 4578 patients. *Br. J. Neurosurg.* **19**(2), 155–162 (2005).
24. Wang, K. P. et al. Meta-analysis of risk factors for intracranial infection after craniocerebral injury in China. *Hebei Med.* **24**(9), 1527–1532 (2018).
25. Ding, C. Y. et al. Predictive factors of postoperative infection-related complications in adult patients with cerebral cavernous malformations. *Sci. Rep.* **10**(1), 863 (2020).
26. Zhang, E. H. et al. The diagnostic value of serum and CSF inflammatory markers and WBC count in intracranial infection after neurosurgery. *Chin. J. Pract. Neurol. Dis.* **22**(4), 374–379 (2019).
27. Shen, J. et al. Application of microarray technology for the detection of intracranial bacterial infection. *Exp. Ther. Med.* **7**(2), 496–500 (2014).
28. Ding, J. R. et al. Detection results of pathogens in cerebrospinal fluid of 6 patients with suspected intracranial infection. *Shandong Med.* **35**, 83–85 (2014).

29. Shaw, T. D. et al. The utility of 16S rRNA gene sequencing on intraoperative specimens from intracranial infections: An 8-year study in a regional UK neurosurgical unit. *Br. J. Neurosurg.* **20**, 1–6 (2021).

Acknowledgements
The authors would like to thank Affiliated Hospital of North Sichuan Medical College for assistance with data collection.

Author contributions
C.J.J. contributed to the data collection and wrote the first draft, and revised the manuscript. H.T.T. contributed to data analysis.Y.J.X. and Y.X. revised and the manuscript. Z.H., Z.Z.J. and W.F. contributed to data collection and coding. L.X. is the principal investigator and contributed to the study idea and design, as well as the subsequent drafts.

Funding
The study was supported by Scientific Research Project of the Sichuan Provincial Health Informatics Society (2023026). The study was supported by The Special Incubation Project of the People's Hospital of Deyang (FHT202308). The study was supported by the Science and Technology Project of Deyang City (2022SCZ140).

Declarations

Competing interests
The authors declare no competing interests.

Additional information
Correspondence and requests for materials should be addressed to X.L.