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Original Article

Cerebrospinal fluid cellular and inflammatory profiles in tumor-related postoperative infections: influencing factors and clinical features in oncological patients

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Abstract: Cancer patients undergoing craniocerebral surgery are at risk of secondary intracranial infection, yet differentiating postoperative infection from sterile inflammatory response remains challenging. This study investigated the cerebrospinal fluid (CSF) cellular and inflammatory characteristics, influencing factors, and clinical features of tumor-related postoperative infections. This retrospective study analyzed 170 oncological patients after cranial surgery (36 with intracranial infection, 134 with aseptic inflammation). CSF and blood samples were collected on postoperative days 1-3, 4-5, and 6-7. Assessments included CSF cytology, biochemistry (protein, glucose, chloride), serum markers (white blood cell [WBC] count, C-reactive protein [CRP], procalcitonin [PCT]), CSF culture, and endotoxin detection. Multivariate logistic regression identified risk factors for infection. The infection group showed persistently higher CSF WBC count, neutrophil percentages, and protein levels, and lower glucose levels across all three time points (all $P < 0.01$). Serum CRP and PCT were significantly elevated in the mid-to-late postoperative period (both $P < 0.05$). Independent risk factors included surgery duration > 4 hours (aOR = 3.35, 95% CI 1.39-8.09), external ventricular drainage (EVD) placement (aOR = 2.86, 95% CI 1.21-6.77), and EVD indwelling time > 7 days (aOR = 3.74, 95% CI 1.49-9.41). Patients with ventriculitis had worse prognosis and higher hydrocephalus incidence than those with meningitis alone (both $P < 0.05$). Postoperative intracranial infection in neurotumor patients induces characteristic dynamic changes in CSF and serum inflammatory markers. Regular monitoring facilitates early differentiation from aseptic inflammation, and ventriculitis predicts poorer clinical outcome.

Keywords: Cerebrospinal fluid, intracranial infection, post-tumor surgery, inflammatory markers, risk factors

Introduction

Intracranial complications following neurosurgical tumor resection are critical factors affecting patient prognosis. Among these, postoperative intracranial infection has drawn particular attention due to its high mortality and disability rates [1, 2]. The overall incidence of intracranial infection after neurosurgical tumor resection is approximately 2% to 10%, although this rate may be higher in certain high-risk procedures [3, 4]. Despite continuous improvements in surgical techniques and the perioperative use of prophylactic antibiotics, the risk of infection remains considerable. This is primarily attributed to factors such as surgical disruption of the blood-brain barrier, prolonged operative time, preoperative immunosuppression resulting from tumor mass effect in some patients, and the frequent need for postoperative drainage devices [5, 6]. Clinically, the diagnosis and differentiation of postoperative intracranial infections remain challenging. The core difficulty lies in the substantial similarity between infectious and sterile (chemical) inflammation induced by surgery in terms of early clinical presentation. Both conditions may manifest as fever, headache, altered mental status, or signs of meningeal irritation [7, 8]. Furthermore, both may present overlapping abnormalities in routine cerebrospinal fluid (CSF) analysis, such as elevated white blood cell (WBC) counts. Consequently, reliance on static indicators obtained at a single time point is highly prone to misdiagnosis [9, 10]. The consequences of misdiagnosis are severe. Mistaking an infection

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for aseptic inflammation may delay antimicrobial treatment, potentially leading to sepsis, brain abscess, or even death. Conversely, misidentifying aseptic inflammation as infection results in antibiotic overuse, thereby increasing the risk of drug-resistant bacteria, adverse drug reactions, and healthcare costs [11, 12].

Existing diagnostic criteria, including those from the Centers for Disease Control and Prevention, primarily rely on CSF culture as the "gold standard" [13]. However, CSF culture has limited sensitivity and is time-consuming, often requiring 48 to 72 hours or longer to yield results, which makes it difficult to meet the urgent needs of early clinical decision-making [14, 15]. Therefore, there is an urgent clinical need for a more sensitive dynamic index system that can provide high-value diagnostic clues before microbiological culture results become available. In recent years, although studies have explored the diagnostic value of CSF protein, glucose, lactic acid, and serum inflammatory markers such as C-reactive protein (CRP) and procalcitonin (PCT), the findings have been inconsistent. These inconsistencies may be attributed to differences in study populations, limited sampling time points, and failure to systematically distinguish between infection subtypes (e.g., simple meningitis vs. ventriculitis involving the cerebral ventricles) [16, 17]. This issue is particularly salient in the specialized population of neuro-oncology patients, in whom surgical intervention causes more pronounced disruption to local anatomy and physiology. Moreover, tumor characteristics - such as malignancy grade and the presence of necrosis - may also influence postoperative inflammatory response patterns, further complicating the interpretation of universal markers [18, 19]. Therefore, there is a clear clinical necessity to explore the temporal patterns of CSF cellular and inflammatory marker changes in postoperative neuro-oncology patients, and to clarify their associations with specific clinical factors and prognostic outcomes.

Using a retrospective cohort analysis, we systematically characterized the temporal changes in CSF cytology and inflammatory markers in patients with neuro-oncological tumors who developed intracranial infections following surgery. Our focus was not limited to absolute values at single time points; rather, we examined the differential patterns in CSF leukocyte differential counts, biochemical indicators, and corresponding serum markers between the intracranial infection group and the aseptic inflammation group during three critical postoperative phases: early (days 1-3), middle (days 4-5), and late (days 6-7). We hypothesize that intracranial infection induces a persistent and characteristic CSF response that can be distinguished from the transient response of aseptic inflammation at quantifiable time points. Additionally, the study integrates CSF endotoxin assays and bacterial culture results to further enhance the diagnostic reference framework.

The innovation of this study is multifaceted. First, regarding methodology, we collected dynamic monitoring data from patients at multiple postoperative time points to observe trends in indicator changes rather than relying on isolated values, thereby helping to identify characteristic time windows and rates of change. Second, we conducted a time-series correlation analysis between systemic blood inflammatory markers (CRP, PCT) and local CSF inflammation markers in this population to assess the consistency between systemic and local responses, as well as their diagnostic significance. Third, an in-depth analysis was performed to examine the differential effects of infection types (meningitis vs. ventriculitis) on patterns of indicator changes and clinical outcomes, including the incidence of hydrocephalus and recovery of neurological function. This subgroup analysis is expected to aid in prognosis assessment and stratification of treatment intensity. By elucidating these characteristics and patterns, this study aims to provide empirical evidence for establishing more precise and timely early warning and diagnostic models for postoperative intracranial infections in neuro-oncology patients. Ultimately, this research intends to improve clinical management pathways and outcomes for this patient population.

Research subjects and methods

Research subjects

This study adopted a single-center retrospective cohort design and included adult patients who underwent elective craniotomy for tumor

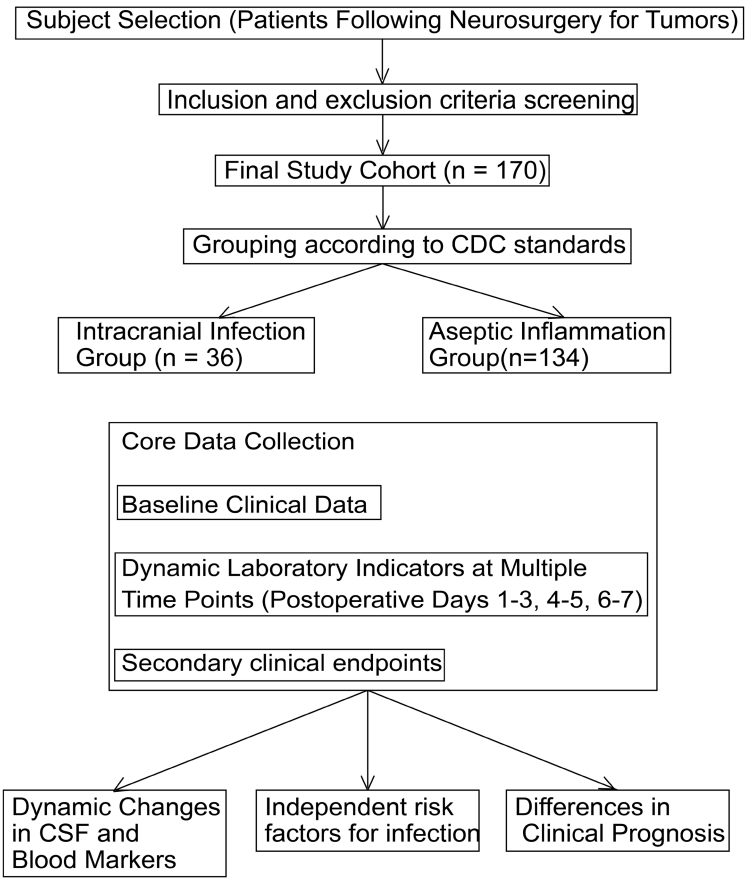

Figure 1. Study flowchart. Note: CDC, Centers for Disease Control and Prevention; CSF, cerebrospinal fluid.

resection in the Department of Neurosurgery of Linyi People's Hospital from January 1, 2020, to December 31, 2024. All surgeries were performed by the same experienced medical team and strictly adhered to standard aseptic techniques and perioperative monitoring protocols. Based on postoperative conditions, patients were divided into an intracranial infection group and an aseptic inflammation group. Group assignment strictly followed the U.S. Centers for Disease Control and Prevention diagnostic criteria for healthcare associated intracranial infections, supplemented by comprehensive clinical assessment. The diagnosis of intracranial infection required meeting at least one of the following criteria: (1) positive bacterial, fungal, or mycobacterial culture of CSF; or (2) presence of fever, meningeal irritation signs, or altered consciousness, accompanied by laboratory evidence including a marked elevation of CSF WBC count, decreased CSF glucose level, and increased CSF protein level, with other non-infectious causes excluded [20]. The aseptic inflammation group consisted of patients who developed infection-like symptoms or mildly elevated CSF cell counts postoperatively but did not meet the above infection criteria, and in whom infection was ruled out. Their symptoms typically resolved as the surgical reaction subsided [21]. All patients with external ventricular drainage (EVD) were managed according to the standardized nursing protocol of the Department of Neurosurgery of the Linyi People's Hospital. The catheter puncture site was disinfected daily with iodophor and covered with sterile dressings. The drainage system was kept sealed, and sampling was performed only under strict aseptic conditions. The drainage device was replaced every 7 days or when signs of blockage were observed. The volume, characteristics, and puncture site condition were recorded daily. Prophylactic antibiotic irrigation was not routinely performed (as shown in **Figure 1**).

Inclusion and exclusion criteria

Inclusion criteria [22, 23]: (1) Age ≥ 18 years; (2) Undergoing first-time craniotomy for primary or metastatic intracranial tumors; (3) Postoperative clinical suspicion of intracranial inflammation or infection, with at least one lumbar puncture or CSF examination via ventriculostomy tube completed for this purpose; (4) Availability of complete perioperative clinical, laboratory, and imaging data.

Exclusion criteria [24, 25]: (1) Diagnosis of central nervous system infection or active systemic infection prior to surgery; (2) Emergency surgery performed due to trauma or non-tumor-related conditions (e.g., aneurysms, vascular malformations); (3) Death from any cause within 72 hours postoperatively, precluding adequate data collection and assessment;

(4) Presence of severe immunodeficiency or hematological diseases that could significantly interfere with the interpretation of inflammatory markers; (5) Severe deficiency of clinical data, rendering reliable group assignment or analysis impossible.

Research plan

Data for this study were obtained from the hospital's electronic medical record system, laboratory information system, and picture archiving and communication system. The extracted content mainly comprised three main parts. First, baseline patient information included demographic characteristics (age, gender), tumor characteristics (pathological type, location, size), and surgical-related variables (operation duration, intraoperative blood loss, use of artificial dura mater repair, placement of external ventricular drainage or lumbar cistern drainage tubes). Second, dynamic monitoring indicators were retrieved from paired blood and CSF test results across three postoperative time windows: days 1-3, days 4-5, and days 6-7. Third, outcome indicators included infection-specific clinical manifestations and final outcomes. All CSF sample collection, processing, and testing were performed in accordance with the hospital's clinical laboratory standard operating procedures. Due to the retrospective nature of this study, the antibiotic treatment plan (including initial selection, timing of adjustments, and dosage) was determined by the clinical attending physician based on each patient's individual condition; no standardized protocol was adopted. Furthermore, the time points for monitoring daily inflammatory indicators in some patients did not perfectly align with the timing of the antibiotic adjustments. Therefore, no quantitative correlation analysis was conducted between inflammatory marker levels and antibiotic efficacy.

Observation indicators

Key indicators: All indicators in this study were based on retrospectively collected clinical laboratory data. Primary laboratory indicators comprised serial blood and CSF test results obtained from patients within standardized postoperative time windows.

(1) Blood sample collection and testing: Blood samples were collected daily between 6:00 and 7:00 AM by ward nurses from the patient's antecubital vein using Vacutainer® vacuum tubes (Becton, Dickinson and Company, 5 mL) with clotting tubes. Immediately after collection, the tubes were gently inverted 5-8 times to mix the sample, and the samples were delivered to the laboratory within 2 hours. Blood inflammatory markers were uniformly measured using the Roche Diagnostics Cobas 8000 fully automated biochemical immunoanalyzer with the manufacturer's original reagents. Test items included serum CRP (measured by immunoturbidimetry) and PCT (measured by chemiluminescence immunoassay). Peripheral blood WBC count was measured using the Sysmex XN-9000 fully automated hematology analyzer with its corresponding reagents, in accordance with the instrument's standardized operating procedures.

(2) CSF sample collection and testing: The collection and processing of CSF samples followed strict aseptic principles. Samples were obtained by lumbar puncture or via a preinstalled external ventricular drainage tube after strict disinfection. CSF was collected in a sterile screw-cap plastic tube (Guangzhou Jet Bio-Filtration Co., Ltd., 3-5 mL) and immediately sent for testing. Routine CSF cytology analysis was performed using the body fluid mode of the Sysmex XN-9000 hematology analyzer. Reported parameters included total CSF WBC count and the percentages of multinucleated cells (predominantly neutrophils) and mononuclear cells (predominantly lymphocytes), derived from cell scatter analysis. CSF biochemical testing (protein, glucose, and chloride concentrations) was performed using the biochemistry module and corresponding reagents of the Roche Cobas 8000 analyzer. All CSF samples underwent concurrent bacterial and fungal culture. Samples were inoculated onto blood agar, chocolate agar, and Sabouraud dextrose agar plates (Komerja), then incubated at 35°C in a 5% CO_2 incubator for at least 5 days, with daily observation. Suspicious colonies were identified using the Bruker MALDI Biotyper® mass spectrometry system [26]. CSF endotoxin and (1,3)-β-D-glucan detection (G test) was performed using a limulus reagent kit (Zhanjiang A&C Biological Company, 0.1 mL). Procedures were strictly conducted in an aseptic environment according to the manufacturer's instructions, with absorbance values read

on an enzyme-linked immunosorbent assay reader for calculation. All CSF samples were sent to the laboratory for testing within 2 hours after collection. Routine cytological and biochemical tests were completed within 4 hours after sample receipt. Bacterial culture samples were immediately inoculated and continuously cultured for 5 days. Endotoxin detection (G test) was completed within 8 hours after sample receipt. The complete time window from sample collection to test completion was recorded.

Secondary indicators: Secondary clinical indicators were obtained through a systematic review of medical records and imaging data. The location of infection foci and classification into ventriculitis or meningitis subtypes were determined by extracting and verifying information from formal radiology reports of cranial computed tomography or magnetic resonance imaging scans performed during the symptomatic period. Imaging equipment primarily comprised Siemens SOMATOM series computed tomography scanners or Skyra series magnetic resonance imaging scanners.

(1) Hydrocephalus incidence: The core feature of hydrocephalus incidence is the occurrence or progressive worsening of pathological enlargement of the cerebral ventricular system after surgery, usually accompanied by clinical manifestations of increased intracranial pressure or the need for surgical intervention. In this retrospective study, the following data collection procedures were performed as outlined below.

Diagnosis confirmation: The primary basis was the patient's postoperative follow-up imaging reports. The diagnostic imaging criteria are: relative to baseline imaging in the early postoperative period (typically within 24-48 hours), clear and progressive enlargement of the frontal horns of the lateral ventricles, the third ventricle, or the entire ventricular system [26, 27]. The imaging report included an explicit radiological diagnosis. Concurrently, clinical records were reviewed to identify evidence of increased intracranial pressure, such as progressive worsening of headache, vomiting, decreased level of consciousness, papilledema, or a lumbar puncture performed due to suspicion of hydrocephalus showing significantly elevated pressure (typically > 25 cm H_2O) [28].

Classification and attribution: Based on imaging findings and potential etiologies, hydrocephalus is categorized into communicating hydrocephalus and non-communicating (obstructive) hydrocephalus. The key determination lies in its correlation with intracranial infection: if hydrocephalus occurs after the diagnosis of intracranial infection, or if it occurs simultaneously with or worsens the imaging manifestations of ventriculitis or meningitis (such as periventricular exudation or ependymal enhancement), it is considered infection-related hydrocephalus. If it precedes evidence of infection or is clearly unrelated to infection (e.g., caused by postoperative hemorrhage or tissue edema obstructing CSF pathways), it is classified as non-infectious hydrocephalus [29]. The specific postoperative date when hydrocephalus was first confirmed by imaging was recorded.

Treatment and outcomes: The treatment methods and outcomes for hydrocephalus were recorded, and whether the patient received invasive treatment was determined. Specific intervention measures included drug therapy (e.g., acetazolamide or mannitol), repeated lumbar puncture for decompression, or definite surgical intervention. Surgical intervention primarily involved ventriculoperitoneal shunt or endoscopic third ventriculostomy. The specific method and timing of the intervention were clearly defined, and postoperative effects were recorded, including imaging evidence of reduced ventricular size compared with preoperative status and symptom relief. For patients who did not receive targeted intervention throughout the hospitalization period, this was also accurately documented. All information was extracted and cross-checked by reviewing medical records, surgical reports, imaging reports, and nursing documents [30].

(2) Glasgow outcome scale (GOS): The GOS was independently evaluated by two attending neurosurgeons. The evaluators were not involved in the data grouping or statistical analysis of this study and were blinded to the patients' group status (infection group vs. aseptic inflammation group). The intraclass correlation coefficient of the scores given by the two evaluators was 0.94 (95% CI 0.89-0.97), indicating good consistency. The final score was calculated as the average of the two evalu-

ators' scores. If the difference between the two scores exceeded 1 point, a third senior physician made the final determination.

Sample size calculation

To assess the statistical reliability of the observed between-group differences and the multivariate analysis results given the current sample size, we conducted a post hoc power analysis. This analysis primarily focused on the key comparisons in the study - namely, the continuous variable of postoperative CSF WBC count and the categorical exposure variables representing significant risk factors identified by multivariate logistic regression (e.g., surgery duration > 4 hours). Using G*Power version 3.1 software, we set a two-tailed test with a type I error probability (α) of 0.05. For comparisons of CSF parameters between the intracranial infection group (n = 36) and the aseptic inflammation group (n = 134) at the primary time points, the statistical power (1-β) exceeded 0.95 when the effect size (Cohen's d) was 0.8 (moderate to large). When the effect size was 0.5 (moderate), the power was approximately 0.75. For the multivariate analysis, using operative time as a binary predictor variable and given the current sample size and observed infection incidence rate, the power exceeded 0.80 for detecting strong associations with odds ratios (ORs) greater than 3.5.

Statistical methods

Statistical analysis methods were selected based on data attributes. Continuous data following a normal distribution are reported as mean ± standard deviation and were compared between groups using the independent-samples t-test. Continuous data not following a normal distribution are expressed as median with interquartile range and were compared between groups using the Mann-Whitney U test. Categorical data are expressed as frequencies and percentages and were compared between groups using the chi-square test. Dynamic changes in laboratory indicators across multiple postoperative time points were analyzed using repeated-measures analysis of variance. Independent risk factors for intracranial infection were first screened using univariate analysis to identify statistically significant variables, which were then included in a multivariate binary logistic regression model for adjustment. All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). A two tailed p value < 0.05 was considered statistically significant.

Ethics statement

This study strictly adhered to medical ethics standards. The research protocol was approved by the Institutional Review Board of Linyi People's Hospital. Given the retrospective nature of the study, all data were derived from anonymized medical records. No additional invasive procedures were performed on patients, and the analysis process posed no risk to patients. Therefore, the Ethics Committee granted an exemption from obtaining patient informed consent. We pledge to maintain strict confidentiality of all collected patient information, which will be used solely for this research. Findings will be published in aggregated form, ensuring that no personally identifiable information is disclosed.

Results

Baseline information

This study included 170 patients. Baseline data (**Table 1**) showed no statistically significant differences between the two groups in terms of age, sex, underlying comorbidities, or tumor characteristics (all $P > 0.05$). However, the intracranial infection group exhibited significantly longer operative times, higher rates of intraoperative CSF leakage, and greater use of EVD compared with the aseptic inflammation group (all $P < 0.05$).

Key laboratory indicators

In the early postoperative period (days 1-3, **Table 2**), CSF WBC count in the intracranial infection group was significantly higher than that in the aseptic inflammation group (mean difference 357.38 × 10^6/L, 95% CI 281.34-433.42, $P < 0.001$). Concurrently, the intracranial infection group exhibited higher CSF neutrophil percentage, CSF protein levels, and serum CRP levels, as well as lower CSF glucose levels (all $P < 0.001$). However, the difference in serum PCT levels between the two groups were not yet statistically significant at this stage ($P = 0.065$).

Table 1. Baseline demographic, clinical, and surgical characteristics of patients

Characteristics	Intracranial infection group (n = 36)	Aseptic inflammation group (n = 134)	Statistical value	*p*	Difference/OR (95% CI)
Demographic characteristics					
Age (years)	52.34 ± 10.27	50.89 ± 11.56	t = 0.71	0.481	1.45 (-2.63, 5.54)
Male, n (%)	21 (58.33)	75 (55.97)	χ^2 = 0.07	0.796	1.10 (0.52, 2.34)
Underlying diseases, n (%)					
Diabetes	7 (19.44)	18 (13.43)	χ^2 = 0.86	0.354	1.56 (0.60, 4.08)
Hypertension	12 (33.33)	41 (30.60)	χ^2 = 0.10	0.749	1.14 (0.52, 2.49)
Preoperative condition					
KPS score	78.61 ± 8.92	80.45 ± 9.37	t = -1.07	0.286	-1.84 (-5.23, 1.56)
Tumor characteristics					
Maximum tumor diameter (cm)	4.23 ± 1.15	3.98 ± 1.24	t = 1.11	0.268	0.25 (-0.20, 0.70)
Malignant tumor*, n (%)	28 (77.78)	92 (68.66)	χ^2 = 1.16	0.281	1.61 (0.68, 3.83)
Lower abdominal area, n (%)	10 (27.78)	25 (18.66)	χ^2 = 1.49	0.223	1.68 (0.73, 3.89)
Surgical-related variables					
Operation duration (hours)	5.82 ± 1.41	4.33 ± 1.28	t = 6.02	< 0.001	1.49 (1.01, 1.98)
Intraoperative blood loss (mL)	450.28 ± 198.67	388.06 ± 176.54	t = 1.86	0.065	62.22 (-3.80, 128.24)
Intraoperative CSF leakage, n (%)	9 (25.00)	15 (11.19)	χ^2 = 4.71	0.030	2.66 (1.06, 6.70)
EVD placement, n (%)	22 (61.11)	35 (26.12)	χ^2 = 17.15	< 0.001	4.52 (2.07, 9.87)
EVD duration (days)	8.45 ± 3.21	5.12 ± 2.89	t = 5.89	< 0.001	3.33 (2.20, 4.46)

Note: Data are presented as mean ± standard deviation, n (%), or OR with 95% CI. Continuous variables were compared using the independent-samples t-test; categorical variables were compared using the chi-square test. KPS, Karnofsky Performance Status; CSF, cerebrospinal fluid; EVD, external ventricular drain; OR, odds ratio; CI, confidence interval. *Malignant tumors refer to World Health Organization grade III-IV gliomas or metastatic tumors. A positive mean difference indicates that the value in the intracranial infection group was higher. A confidence interval that includes 0 suggests that the difference was not statistically significant.

Table 2. Comparison of main laboratory parameters on postoperative days 1-3

Indicators	Intracranial infection group (n = 36)	Aseptic inflammation group (n = 134)	t	*p*	Mean difference (95% CI)
Cerebrospinal fluid parameters					
White blood cell count (× 10^6/L)	485.72 ± 320.15	128.34 ± 85.62	9.47	< 0.001	357.38 (281.34, 433.42)
Neutrophil percentage (%)	78.56 ± 15.23	65.45 ± 18.90	3.91	< 0.001	13.11 (6.49, 19.73)
Protein (mg/dL)	1.52 ± 0.68	0.89 ± 0.41	6.96	< 0.001	0.63 (0.45, 0.81)
Glucose (mmol/L)	2.45 ± 0.87	3.12 ± 0.92	-3.86	< 0.001	-0.67 (-1.01, -0.33)
Blood tests					
Serum CRP (mg/L)	68.45 ± 25.33	52.18 ± 22.47	3.66	< 0.001	16.27 (7.41, 25.13)
Serum PCT (ng/mL)	0.85 ± 0.42	0.71 ± 0.38	1.86	0.065	0.14 (-0.01, 0.29)

Note: Data are presented as mean ± standard deviation. Group comparisons were performed using the independent-samples t-test. CRP, C-reactive protein; PCT, procalcitonin; CI, confidence interval. A negative mean difference indicates a lower value in the intracranial infection group compared with the aseptic inflammation group.

By the mid-postoperative period (days 4-5, **Table 3**), intergroup differences became most pronounced. The intracranial infection group showed a significant increase in CSF WBC count (mean difference 1035.17 × 10^6/L, 95% CI 930.12-1140.22, $P < 0.001$). Furthermore, the intergroup differences in CSF neutrophil percentage, CSF protein levels, serum CRP levels, and serum PCT levels all widened further (all $P < 0.001$). The reduction in CSF glucose levels was also more pronounced in the infection group ($P < 0.001$).

By the late postoperative period (days 6-7, **Table 4**), although all indicators in the intracranial infection group had decreased compared with those in the mid-postoperative phase, the absolute differences from the aseptic inflammation group remained substantial. All comparisons remained highly significant ($P < 0.001$

Table 3. Comparison of main laboratory parameters on postoperative days 4-5

Indicators	Intracranial infection group (n = 36)	Aseptic inflammation group (n = 134)	t	*p*	Mean difference (95% CI)
Cerebrospinal fluid parameters					
White blood cell count (× 10^6/L)	1120.58 ± 502.47	85.41 ± 52.36	18.29	< 0.001	1035.17 (930.12, 1140.22)
Neutrophil percentage (%)	85.23 ± 10.11	58.34 ± 20.12	8.74	< 0.001	26.89 (20.75, 33.03)
Protein (mg/dL)	2.34 ± 0.91	0.72 ± 0.33	14.37	< 0.001	1.62 (1.38, 1.86)
Glucose (mmol/L)	1.88 ± 0.65	3.34 ± 0.88	-9.58	< 0.001	-1.46 (-1.75, -1.17)
Blood tests					
Serum CRP (mg/L)	95.67 ± 31.25	38.45 ± 18.92	13.07	< 0.001	57.22 (48.86, 65.58)
Serum PCT (ng/mL)	2.45 ± 1.12	0.52 ± 0.28	14.82	< 0.001	1.93 (1.68, 2.18)

Note: Data are presented as mean ± standard deviation. Group comparisons were performed using the independent-samples t-test. CRP, C-reactive protein; PCT, procalcitonin; CI, confidence interval. A negative mean difference indicates a lower value in the intracranial infection group compared with the aseptic inflammation group.

Table 4. Comparison of main laboratory parameters on postoperative days 6-7

Indicators	Intracranial infection group (n = 36)	Aseptic inflammation group (n = 134)	t	*p*	Mean difference (95% CI)
Cerebrospinal fluid parameters					
White blood cell count (× 10^6/L)	856.33 ± 401.28	62.15 ± 45.23	16.12	< 0.001	794.18 (699.34, 889.02)
Neutrophil percentage (%)	72.45 ± 18.34	52.89 ± 21.45	5.01	< 0.001	19.56 (11.89, 27.23)
Protein (mg/dL)	1.98 ± 0.78	0.65 ± 0.30	13.92	< 0.001	1.33 (1.14, 1.52)
Glucose (mmol/L)	2.12 ± 0.71	3.45 ± 0.79	-8.83	< 0.001	-1.33 (-1.61, -1.05)
Blood tests					
Serum CRP (mg/L)	78.92 ± 28.74	25.67 ± 12.34	15.32	< 0.001	53.25 (46.52, 59.98)
Serum PCT (ng/mL)	1.56 ± 0.89	0.38 ± 0.21	11.18	< 0.001	1.18 (0.97, 1.39)

Note: Data are presented as mean ± standard deviation. Group comparisons were performed using the independent-samples t-test. CRP, C-reactive protein; PCT, procalcitonin; CI, confidence interval. A negative mean difference indicates a lower value in the intracranial infection group compared with the aseptic inflammation group.

Table 5. Dynamic comparison of peripheral blood white blood cell counts (× 10^9/L, mean ± standard deviation)

Time point	Intracranial infection group (n = 36)	Aseptic inflammation group (n = 134)	t	*p*	Mean difference (95% CI)
Postoperative days 1-3	11.89 ± 3.45	11.23 ± 2.98	2.76	0.006	1.66 (0.49, 2.83)
Postoperative days 4-5	14.56 ± 4.01	9.87 ± 2.45	8.52	< 0.001	4.69 (3.62, 5.76)
Postoperative days 6-7	12.34 ± 3.78	8.95 ± 2.12	6.90	< 0.001	3.39 (2.44, 4.34)

Note: Data are presented as mean ± standard deviation. Group comparisons were performed using the independent-samples t-test. CI, confidence interval.

for all). For example, the mean difference in CSF WBC count remained as high as 794.18 × 10^6/L (95% CI 699.34-889.02). It is worth noting that the cerebrospinal fluid glucose level in the intracranial infection group showed a dynamic pattern of first decreasing and then increasing: it was 2.45 ± 0.87 mmol/L from the 1st to the 3rd day after surgery, dropped to a minimum of 1.88 ± 0.65 mmol/L on the 4th to 5th day, and then rose to 2.12 ± 0.71 mmol/L on the 6th to 7th day. The differences between each time point were statistically significant (post-hoc comparison of repeated measures analysis of variance $P < 0.05$), which is consistent with the clinical process of the local metabolic environment improving after the onset of anti-infection treatment.

The dynamic changes in peripheral blood leukocyte counts (**Tables 5** and **6**) were consistent

Table 6. Repeated-measures ANOVA results for core laboratory indicators

Indicators	Sphericity test (*p*)	Correction method	Group main effect	Time main effect	Group × Time interaction	Post hoc comparison findings
CSF WBC count	< 0.001	Greenhouse-Geisser	F = 142.3 (*P* < 0.001, partial η^2 = 0.459)	F = 38.7 (*P* < 0.001, partial η^2 = 0.187)	F = 56.2 (*P* < 0.001, partial η^2 = 0.251)	Infection group: days 4-5 > days 1-3 > days 6-7; Aseptic group: continuously decreasing
CSF neutrophil percentage	0.002	Greenhouse-Geisser	F = 68.5 (*P* < 0.001, partial η^2 = 0.290)	F = 22.1 (*P* < 0.001, partial η^2 = partial η^2 = 0.116)	F = 31.8 (*P* < 0.001, partial η^2 = 0.159)	Infection group: peak at days 4-5; Aseptic group: early decline
CSF protein	< 0.001	Greenhouse-Geisser	F = 119.6 (*P* < 0.001, partial η^2 = 0.416)	F = 41.3 (*P* < 0.001, partial η^2 = 0.197)	F = 48.9 (*P* < 0.001, partial η^2 = 0.226)	Infection group: days 4-5 > days 1-3 > days 6-7; Aseptic group: continuously decreasing
CSF glucose	0.001	Greenhouse-Geisser	F = 89.4 (P < 0.001, partial η^2 = 0.347)	F = 29.6 (P < 0.001, partial η^2 = 0.150)	F = 37.2 (P < 0.001, partial η^2 = 0.181)	Infection group: lowest at days 4-5; Aseptic group: continuously rising
Serum CRP	0.008	Greenhouse-Geisser	F = 176.5 (P < 0.001, partial η^2 = 0.512)	F = 62.8 (P < 0.001, partial η^2 = 0.272)	F = 71.3 (P < 0.001, partial η^2 = 0.298)	Infection group: peak at days 4-5; Aseptic group: continuously decreasing
Serum PCT	< 0.001	Greenhouse-Geisser	F = 201.3 (P < 0.001, partial η^2 = 0.545)	F = 73.5 (P < 0.001, partial η^2 = 0.304)	F = 85.6 (P < 0.001, partial η^2 = 0.338)	Infection group: peak at days 4-5; Aseptic group: continuously decreasing
Peripheral blood WBC count	0.021	Greenhouse-Geisser	F = 42.6 (P < 0.001, partial η^2 = 0.202)	F = 18.7 (P < 0.001, partial η^2 = 0.100)	F = 33.9 (P < 0.001, partial η^2 = 0.168)	Infection group: peak at days 4-5; Aseptic group: continuously decreasing

Note: Mauchly's test of sphericity was used to assess the sphericity assumption. When the sphericity assumption was violated (P < 0.05), the Greenhouse-Geisser correction was applied for degrees of freedom adjustment. Post hoc multiple comparisons were performed using the Bonferroni correction, with a corrected significance level of α = 0.017. CSF, cerebrospinal fluid; CRP, C-reactive protein; PCT, procalcitonin; WBC, white blood cell; η^2, eta squared; ANOVA, analysis of variance.

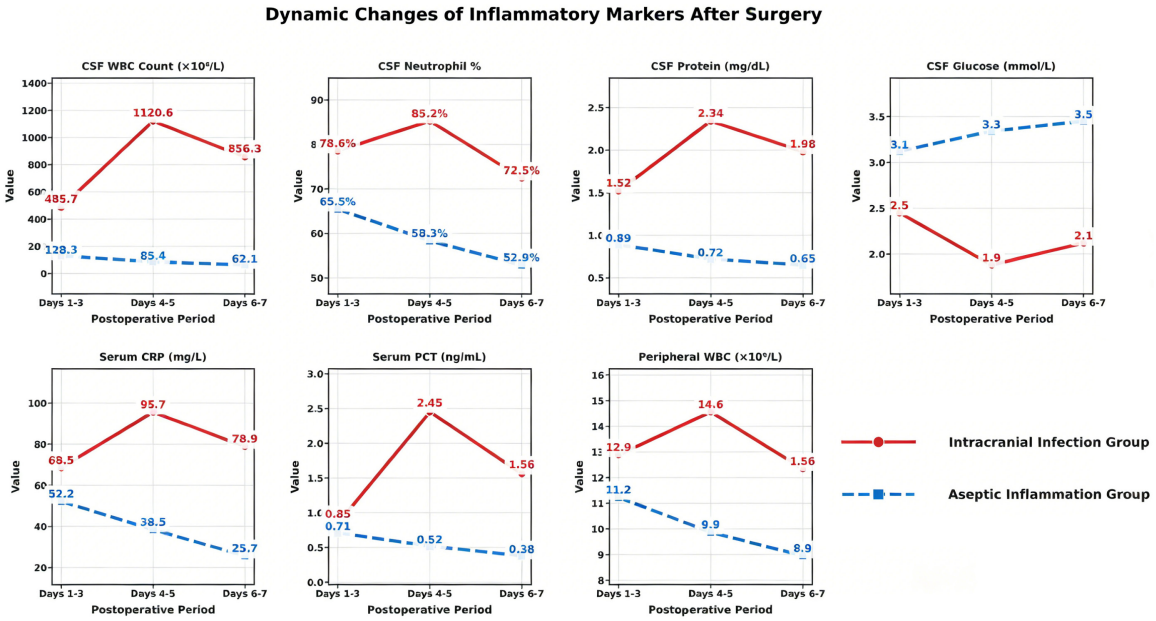

Figure 2. Dynamic changes of inflammatory indicators after surgery. Note: CSF, cerebrospinal fluid; WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin. Data are presented as mean values at each time point.

with the trends observed in inflammatory markers. The intracranial infection group exhibited significantly higher counts at all postoperative time points compared with the aseptic inflammation group (all $P < 0.001$), with the greatest difference observed on days 4-5 (mean difference 4.69 × 10^9/L; 95% CI 3.62-5.76; $P < 0.001$). The dynamic changes in inflammatory markers are shown in **Figure 2**. Among the 36 infected patients, 20 (55.56%) received an initial empirical antibiotic regimen of vancomycin combined with third-generation cephalosporins. Because antibiotic adjustment decisions were influenced by multiple factors (clinical response, drug sensitivity results, liver and kidney function, etc.), and the retrospective data did not fully capture the serial inflammatory marker values before and after each adjustment, this study did not perform a statistical correlation analysis between inflammatory marker levels (e.g., PCT) and antibiotic efficacy.

To comprehensively evaluate the dynamic changes in laboratory indicators after surgery in the two groups, we performed repeated-measures analysis of variance for seven core indicators: CSF WBC count, CSF neutrophil percentage, CSF protein, CSF glucose, serum CRP, serum PCT, and peripheral blood WBC count. As shown in **Table 6**, the *p*-values of Mauchly's test of sphericity for all indicators were < 0.05, indicating that the sphericity assumption was violated. Therefore, the Greenhouse-Geisser method was used for degrees of freedom correction. The analysis revealed that the main effects of group, time, and the group × time interaction effect were highly statistically significant for all indicators (all $P < 0.001$). Specifically, the F-values for the interaction effects were as follows: CSF WBC count, F = 56.2 (partial $\eta^2 = 0.251$); CSF neutrophil percentage, F = 31.8 (partial $\eta^2 = 0.159$); CSF protein, F = 48.9 (partial $\eta^2 = 0.226$); CSF glucose, F = 37.2 (partial $\eta^2 = 0.181$); serum CRP, F = 71.3 (partial $\eta^2 = 0.298$); serum PCT, F = 85.6 (partial $\eta^2 = 0.338$); and peripheral blood WBC count, F = 33.9 (partial $\eta^2 = 0.168$). Post-hoc multiple comparisons with Bonferroni correction further revealed that, in the intracranial infection group, all indicators exhibited a single-peak pattern, reaching their maximum (or minimum) on postoperative days 4-5 and then declining slightly, with differences between each time point remaining statistically significant ($P < 0.017$). In the aseptic inflammation group, most indicators were highest on postoperative days 1-3 and then continuously decreased, with the exception of CSF glucose, which was lowest on days 1-3 and then continuously increased. These results consistently

Table 7. Pathogen detection results and clinical classification in the infected group (n = 36)

Indicators	Number of cases (n)	Percentage (%)	Positive report time (postoperative days)
Positive CSF culture	22	61.11	-
Gram-positive bacteria	14	38.89	-
Staphylococcus epidermidis	9	25.00	5.0 (3-8)
Other coagulasenegative *staphylococci*	4	11.11	5.5 (4-9)
Enterococcus faecium	1	2.78	6.0
Gram-negative bacteria	8	22.22	-
Acinetobacter baumannii	3	8.33	7.0 (5-10)
Klebsiella pneumoniae	3	8.33	4.5 (3-7)
Escherichia coli	2	5.56	5.0 (4-6)
Positive G test (isolated)	6	16.67	-
Clinical classification			
Meningitis	20	55.56	-
Ventriculitis (including concurrent meningitis)	16	44.44	-

Note: CSF, cerebrospinal fluid; G test, (1,3)-β-D-glucan assay. A positive isolated G test was defined as negative bacterial and fungal cultures of CSF with a positive G test result.

Table 8. Comparison of secondary clinical outcome measures

Indicators	Intracranial infection group (n = 36)	Aseptic inflammation group (n = 134)	Statistical value (t/χ^2)	*p*	Difference/OR (95% CI)
Incidence of hydrocephalus n (%)	11 (30.56)	8 (5.97)	$\chi^2 = 19.12$	< 0.001	OR = 6.95 (2.62, 18.45)
GOS score at discharge	3.28 ± 1.12	4.12 ± 0.89	t = -4.68	< 0.001	MD = -0.84 (-1.19, -0.49)
Poor prognosis (GOS 1-3), n (%)	18 (50.00)	22 (16.42)	$\chi^2 = 18.60$	< 0.001	OR = 5.14 (2.34, 11.27)
Length of hospital stay (days)	35.67 ± 10.23	23.45 ± 7.89	t = 7.51	< 0.001	MD = 12.22 (8.96, 15.48)

Note: Data are presented as mean ± standard deviation for continuous variables or as n (%) for categorical variables. Group comparisons were performed using the independent-samples t-test for continuous variables and the chi-square test for categorical variables. GOS, Glasgow Outcome Scale; OR, odds ratio; MD, mean difference; CI, confidence interval. A negative mean difference indicates a lower value in the intracranial infection group compared with the aseptic inflammation group.

demonstrated that inflammatory indicators in the infection group followed a dynamic pattern characterized by a "mid-postoperative peak with sustained elevation", whereas those in the aseptic inflammation group exhibited an evolutionary pattern of "early peak followed by decline". The fundamentally different dynamic trajectories between the two groups (interaction effect $P < 0.001$) provide a powerful dynamic basis for the early differentiation of postoperative infection from aseptic inflammation.

Secondary indicators

In terms of etiology (**Table 7**), among the 36 infected patients, the CSF bacterial culture positivity rate was 61.11% (22 cases). Gram-positive bacteria were predominant, accounting for 14 cases (38.89% of the total intracranial infection group), with coagulase-negative *Staphylococcus* being the most common (9 cases, 25.00%). Gram-negative bacterial infections were observed in 8 cases (22.22%). Additionally, 6 patients (16.67%) had negative CSF cultures but positive Gram staining. Regarding infection types, ventriculitis (including cases with concomitant meningitis) was present in 16 cases (44.44%), whereas pure meningitis occurred in 20 cases (55.56%). Among the 22 patients with positive culture results, the median time to positive report was postoperative day 5 (range: day 3 to day 11). Specifically, 14 cases (63.60%) tested positive on postoperative days 4-5, 6 cases (27.30%) on postoperative days 6-7, and 2 cases (9.10%) after postoperative day 8.

In terms of clinical outcomes (**Table 8**), the incidence of postoperative hydrocephalus in the

Table 9. Comparison of prognostic indicators between the ventriculitis group and the pure meningitis group

Indicators	Ventriculitis group (n = 16)	Pure meningitis group (n = 20)	Statistical value (t/χ^2)	*p*	Difference/OR (95% CI)
GOS score at discharge	2.81 ± 1.05	3.65 ± 0.93	t = -2.57	0.015	MD = -0.84 (-1.51, -0.17)
Poor prognosis (GOS score 1-3), n (%)	11 (68.75)	7 (35.00)	χ^2 = 4.11	0.043	OR = 4.21 (1.05, 16.85)
Incidence of hydrocephalus, n (%)	9 (56.25)	2 (10.00)	χ^2 = 9.06	0.003	OR = 11.57 (2.06, 64.92)
Length of hospital stay (days)	42.19 ± 9.87	30.55 ± 8.46	t = 3.80	< 0.001	MD = 11.64 (5.44, 17.84)

Note: Data are presented as mean ± standard deviation for continuous variables or as n (%) for categorical variables. Group comparisons were performed using the independent-samples t-test for continuous variables and the chi-square test for categorical variables. GOS, Glasgow Outcome Scale; MD, mean difference; OR, odds ratio; CI, confidence interval. A negative mean difference indicates a lower value in the ventriculitis group compared with the pure meningitis group.

Table 10. Univariate logistic regression analysis of risk factors for intracranial infection

Variables	β	Standard error	Wald χ^2	**p**value	OR (95% CI)
Age (per 10-year increase)	0.15	0.20	0.56	0.455	1.16 (0.78, 1.72)
Male (vs. female)	0.09	0.37	0.06	0.806	1.10 (0.53, 2.27)
Diabetes (yes vs. no)	0.44	0.47	0.88	0.349	1.55 (0.62, 3.90)
Operative duration (> 4 hours vs. ≤ 4 hours)	1.79	0.38	22.18	< 0.001	5.99 (2.85, 12.60)
Intraoperative blood loss (> 400 mL vs. ≤ 400 mL)	0.61	0.35	3.04	0.081	1.84 (0.93, 3.65)
Intraoperative CSF leakage (yes vs. no)	0.98	0.45	4.74	0.029	2.66 (1.10, 6.44)
EVD placement (yes vs. no)	1.51	0.37	16.63	< 0.001	4.52 (2.19, 9.33)
EVD indwelling time (> 7 days vs. ≤ 7 days)	1.82	0.39	21.78	< 0.001	6.17 (2.88, 13.22)

Note: CSF, cerebrospinal fluid; EVD, external ventricular drainage; OR, odds ratio; CI, confidence interval. Variables with P < 0.1 in univariate analysis (operative duration > 4 hours, intraoperative blood loss > 400 mL, intraoperative CSF leakage, EVD placement, and EVD indwelling time > 7 days) were entered into the multivariate logistic regression model.

intracranial infection group was as high as 30.56% (11 cases), which was significantly higher than that in the aseptic inflammation group (5.97%, 8 cases; OR = 6.95, 95% CI 2.62-18.45, *P* < 0.001). Neurological function recovery at discharge was also significantly worse in the infection group, with a mean GOS score of 3.28 ± 1.12, compared with 4.12 ± 0.89 in the aseptic group (mean difference -0.84, 95% CI -1.19 to -0.49, *P* < 0.001). The proportion of patients with poor prognosis (GOS score 1-3) in the infection group reached 50.00% (18 cases), which was much higher than that in the aseptic group (16.42%, 22 cases; OR = 5.14, 95% CI 2.34-11.27, *P* < 0.001). Furthermore, the mean hospital stay in the infection group was significantly prolonged at 35.67 ± 10.23 days, which was 12.22 days longer than that in the aseptic group (23.45 ± 7.89 days; 95% CI 8.96-15.48, *P* < 0.001).

Within the intracranial infection group, patients were further divided into the ventriculitis group (16 cases, 44.44%) and the pure meningitis group (20 cases, 55.56%). Statistical comparisons (**Table 9**) revealed that the GOS score at discharge in the ventriculitis group was significantly lower than that in the pure meningitis group (2.81 ± 1.05 vs. 3.65 ± 0.93; mean difference -0.84, 95% CI -1.51 to -0.17, *P* = 0.015). The proportion of patients with poor prognosis (GOS score 1-3) was also higher in the ventriculitis group (68.75% vs. 35.00%; OR = 4.21, 95% CI 1.05-16.85, *P* = 0.043). Furthermore, the incidence of hydrocephalus in the ventriculitis group was significantly higher than that in the pure meningitis group (56.25% vs. 10.00%; OR = 11.57, 95% CI 2.06-64.92, *P* = 0.003), and the length of hospital stay was significantly longer (42.19 ± 9.87 days vs. 30.55 ± 8.46 days; mean difference 11.64 days, 95% CI 5.44-17.84, *P* < 0.001). These results confirm that patients with ventriculitis have a significantly worse prognosis than those with pure meningitis.

Logistic regression analysis

Univariate logistic regression analysis (**Table 10**) revealed that several surgical factors were

Table 11. Multivariate logistic regression analysis of independent risk factors for intracranial infection

Variables	β	Standard error	Wald χ^2	*p*value	Adjusted OR (95% CI)
Operative duration (> 4 hours vs. ≤ 4 hours)	1.21	0.45	7.23	0.007	3.35 (1.39, 8.09)
EVD placement (yes vs. no)	1.05	0.44	5.70	0.017	2.86 (1.21, 6.77)
EVD indwelling time (> 7 days vs. ≤ 7 days)	1.32	0.47	7.89	0.005	3.74 (1.49, 9.41)
Intraoperative CSF leakage (yes vs. no)	0.71	0.50	2.02	0.155	2.03 (0.76, 5.41)
Intraoperative blood loss (> 400 mL vs. ≤ 400 mL)	0.67	0.40	2.80	0.094	1.95 (0.89, 4.27)

Note: CSF, cerebrospinal fluid; EVD, external ventricular drainage; OR, odds ratio; CI, confidence interval. Variables with $P < 0.1$ in univariate analysis were entered into the multivariate logistic regression model for adjustment. Intraoperative blood loss was not retained as an independent risk factor in the final model because the association was not statistically significant after adjustment for operative duration and EVD placement. The result is shown here for completeness.

significantly associated with infection risk. Variables with $P < 0.1$ in the univariate analysis - specifically, operative duration, intraoperative CSF leakage, EVD placement, and EVD indwelling time - were all entered into the multivariate model for adjustment. Multivariate logistic regression analysis (**Table 11**) showed that operative duration exceeding 4 hours, placement of an EVD device during surgery, and EVD indwelling time greater than 7 days remained independent risk factors for intracranial infection after adjustment for other variables. The adjusted OR values for these factors were 3.35, 2.86, and 3.74, respectively. Intraoperative CSF leakage did not retain independent significance in the multivariate model (adjusted OR = 2.03, 95% CI 0.76-5.41, $P = 0.155$). Intraoperative blood loss (> 400 mL vs. ≤ 400 mL) was also included in the multivariate model but did not reach statistical significance after adjustment (adjusted OR = 1.95, 95% CI 0.89-4.27, $P = 0.094$), indicating that it is not an independent risk factor for intracranial infection.

Subgroup analysis based on prognosis

To further investigate factors associated with clinical outcomes, patients in the intracranial infection group were stratified by prognosis based on GOS scores at discharge: patients with GOS scores of 4-5 were classified as the good prognosis group (n = 21), and those with GOS scores of 1-3 as the poor prognosis group (n = 15).

As shown in **Table 12**, during the peak inflammatory period (postoperative days 4-5), there were no significant differences in the various indicators between the two groups of patients (all $P > 0.05$). At the post-treatment stage (postoperative days 6-7), indicators in patients with good prognosis decreased significantly compared with the peak period (decrease rate 47.62 ± 11.28%-74.28 ± 9.56%), whereas indicators in patients with poor prognosis remained at high levels or even increased further, with significant differences between the groups (all $P < 0.001$). The incidence of hydrocephalus in the good prognosis group was also significantly lower than that in the poor prognosis group (9.52% vs. 60.00%, $P < 0.001$).

Antibiotic use

Among the 36 patients with intracranial infections, initial anti-infection therapy primarily consisted of combination regimens (28 cases, 77.78%), with vancomycin combined with third-generation cephalosporins being the most commonly used empirical regimen (20 cases, 55.56%). A total of 19 patients (52.78%) adjusted their antibiotic regimen based on CSF culture and drug susceptibility testing results. Among these, 12 cases (33.33%) achieved step-down therapy, while 7 cases (19.44%) required escalation or modification of the regimen due to detected resistance. The mean total duration of antibiotic therapy was 18.56 ± 6.43 days, with a median duration of 17.00 days.

Efficacy assessment revealed that after standardized anti-infection treatment, 28 cases (77.78%) achieved clinical cure, whereas 3 cases (8.33%) died due to infection. Following treatment, CSF WBC count decreased from 985.42 ± 468.33 × 10^6/L to 145.67 ± 89.23 × 10^6/L (mean difference 839.75 × 10^6/L, 95%

Table 12. Comparison of dynamic changes in inflammatory markers by prognosis in the infection group

Indicators	Good prognosis group (n = 21)	Poor prognosis group (n = 15)	Statistical value (t/χ^2)	*p*	Difference/OR (95% CI)
Peak inflammatory period (postoperative days 4-5)					
CSF WBC count (× 10^6/L)	1105.43 ± 489.27	1141.67 ± 526.89	t = 0.21	0.833	MD = -36.24 (-352.17, 279.69)
CSF protein (mg/dL)	2.31 ± 0.88	2.38 ± 0.96	t = 0.23	0.818	MD = -0.07 (-0.67, 0.53)
Serum CRP (mg/L)	94.21 ± 30.56	97.83 ± 32.41	t = 0.34	0.734	MD = -3.62 (-24.68, 17.44)
Serum PCT (ng/mL)	2.41 ± 1.09	2.51 ± 1.17	t = 0.27	0.793	MD = -0.10 (-0.85, 0.65)
Post-treatment stage (postoperative days 6-7)					
CSF WBC count (× 10^6/L)	425.31 ± 201.46	1258.22 ± 478.34	t = 6.89	< 0.001	MD = -832.91 (-1083.62, -582.20)
CSF protein (mg/dL)	1.21 ± 0.42	2.67 ± 0.89	t = 5.98	< 0.001	MD = -1.46 (-2.04, -0.88)
Serum CRP (mg/L)	35.24 ± 12.33	117.65 ± 31.28	t = 10.41	< 0.001	MD = -82.41 (-100.78, -64.04)
Serum PCT (ng/mL)	0.62 ± 0.27	2.41 ± 0.98	t = 7.48	< 0.001	MD = -1.79 (-2.27, -1.31)
Decline rate (from days 4-5 to days 6-7)					
CSF WBC count decrease (%)	61.53 ± 12.37	-10.21 ± 15.46	t = 15.24	< 0.001	MD = 71.74 (62.96, 80.52)
CSF protein decrease (%)	47.62 ± 11.28	-12.19 ± 13.44	t = 14.52	< 0.001	MD = 59.81 (52.08, 67.54)
Serum CRP decrease (%)	62.57 ± 10.89	-20.31 ± 18.27	t = 16.29	< 0.001	MD = 82.88 (73.11, 92.65)
Serum PCT decrease (%)	74.28 ± 9.56	3.98 ± 12.33	t = 18.97	< 0.001	MD = 70.30 (63.61, 76.99)
Prognostic outcome					
Hydrocephalus incidence, n (%)	2 (9.52)	9 (60.00)	χ^2 = 11.33	< 0.001	OR = 14.25 (2.53, 80.37)

Note: Data are presented as mean ± standard deviation for continuous variables or as n (%) for categorical variables. Group comparisons were performed using the independent-samples t-test for continuous variables and the chi-square test for categorical variables. CSF, cerebrospinal fluid; CRP, C-reactive protein; PCT, procalcitonin; WBC, white blood cell; MD, mean difference; OR, odds ratio; CI, confidence interval. A negative mean difference indicates a lower value in the good prognosis group compared with the poor prognosis group. A negative decline rate indicates an increase from the peak period to the post-treatment stage.

Table 13. Antibiotic use and efficacy in the intracranial infection group

Indicators	Value
Initial empirical antibiotic regimen	
Monotherapy, n (%)	8 (22.22)
Combined treatment, n (%)	28 (77.78)
Vancomycin + third-generation cephalosporins, n (%)	20 (55.56)
Vancomycin + piperacillin/tazobactam, n (%)	6 (16.67)
Meropenem monotherapy, n (%)	2 (5.56)
Adjustment based on drug susceptibility testing	
Regimen adjusted, n (%)	19 (52.78)
Step-down treatment, n (%)	12 (33.33)
Escalation or modification, n (%)	7 (19.44)
Total duration of antibiotic therapy (days)	
Mean ± SD	18.56 ± 6.43
Median (IQR)	17.00 (14.00, 23.00)
Efficacy assessment	
Clinical cure*, n (%)	28 (77.78)
Infection-related death, n (%)	3 (8.33)
Changes in inflammatory indicators after treatment	
Pre-treatment CSF WBC count (× 10^6/L)	985.42 ± 468.33
Post-treatment CSF WBC count (× 10^6/L)	145.67 ± 89.23
Pre- to post-treatment difference (95% CI)	839.75 (712.46, 967.04)
Pre-treatment serum PCT (ng/mL)	2.21 ± 1.08
Post-treatment serum PCT (ng/mL)	0.45 ± 0.27
Pre- to post-treatment difference (95% CI)	1.76 (1.41, 2.11)

Note: Data are presented as mean ± standard deviation for continuous variables or as n (%) for categorical variables. CSF, cerebrospinal fluid; PCT, procalcitonin; WBC, white blood cell; SD, standard deviation; IQR, interquartile range; CI, confidence interval. *Clinical cure was defined as resolution of clinical symptoms, normalization of CSF routine and biochemical parameters, two consecutive negative pathogen detection results, and absence of new neurological complications.

CI 712.46-967.04), and serum PCT decreased from 2.21 ± 1.08 ng/mL to 0.45 ± 0.27 ng/mL (mean difference 1.76 ng/mL, 95% CI 1.41-2.11). These results (**Table 13**) indicate that standardized anti-infection treatment can effectively control intracranial infections; however, some patients still experience poor prognosis, underscoring the importance of early diagnosis and timely adjustment of treatment regimens.

Receiver operating characteristic analysis

Receiver operating characteristic analysis (**Table 14** and **Figure 3**) revealed that all inflammatory markers demonstrated good diagnostic value for intracranial infection on postoperative days 4-5. Among them, CSF WBC count exhibited the highest diagnostic efficacy (AUC = 0.942, 95% CI 0.905-0.979), with an optimal cut-off value of 320.50 × 10^6/L, at which sensitivity was 89.1% and specificity was 86.4%. Serum PCT also demonstrated excellent diagnostic value (AUC = 0.923, 95% CI 0.884-0.962), with an optimal cut-off value of 1.25 ng/mL, yielding a sensitivity of 86.1% and a specificity was 88.9%. CSF neutrophil percentage (AUC = 0.891) and serum CRP (AUC = 0.902) also showed high diagnostic accuracy. The diagnostic efficacy of CSF glucose was relatively low (AUC = 0.733).

After incorporating CSF WBC count and serum PCT into a logistic regression model, the AUC of the combined diagnostic model increased to 0.968 (95% CI 0.946-0.990), with a sensitivity of 91.7% and a specificity of 90.5%, which was significantly better than that of any single indicator (all $P < 0.05$). These results indicate that CSF WBC count and serum PCT are ideal markers for diagnosing intracranial infection following neurosurgery for tumors, and their

Table 14. ROC analysis results for diagnosing intracranial infection based on inflammatory markers on postoperative days 4-5

Detection indicators	AUC	Standard error	*p*	95% CI	Optimal cut-off value	Sensitivity (%)	Specificity (%)
CSF indicators							
CSF WBC count (× 10^6/L)	0.942	0.019	< 0.001	0.905-0.979	320.50	89.1	86.4
CSF neutrophil percentage (%)	0.891	0.027	< 0.001	0.838-0.944	72.50	83.3	84.2
CSF protein (mg/dL)	0.876	0.030	< 0.001	0.817-0.935	1.45	80.6	82.5
CSF glucose (mmol/L)	0.733	0.045	< 0.001	0.645-0.821	2.35	75.0	68.9
Blood indicators							
Serum CRP (mg/L)	0.902	0.023	< 0.001	0.857-0.947	68.50	86.1	85.3
Serum PCT (ng/mL)	0.923	0.020	< 0.001	0.884-0.962	1.25	86.1	88.9
Combined diagnosis							
CSF WBC count + serum PCT	0.968	0.011	< 0.001	0.946-0.990	0.76*	91.7	90.5

Note: ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; CSF, cerebrospinal fluid; CRP, C-reactive protein; PCT, procalcitonin; WBC, white blood cell. The optimal cut-off value was determined based on the maximum Youden index. *The cut-off value for combined diagnosis represents the predicted probability derived from the logistic regression model. ROC curve comparisons were performed using the DeLong method.

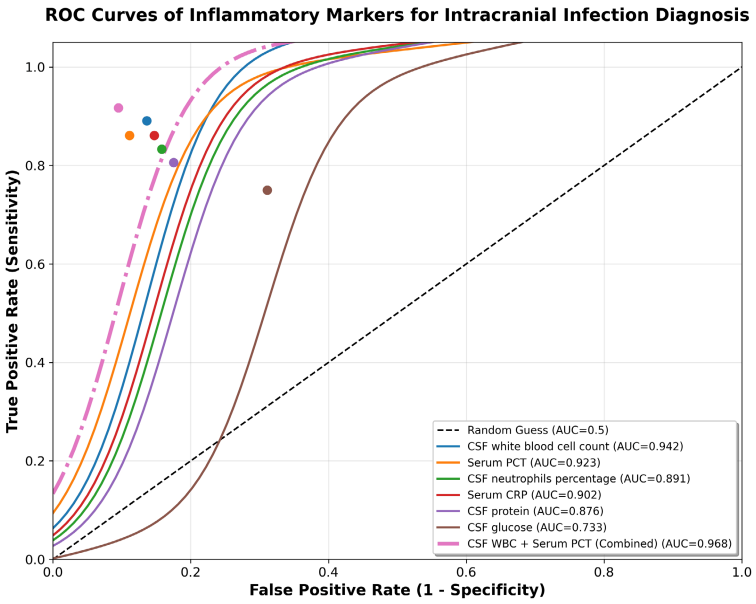

Figure 3. ROC curves of inflammatory markers for diagnosing intracranial infection. Note: ROC, receiver operating characteristic; AUC, area under the curve; CSF, cerebrospinal fluid; WBC, white blood cell; PCT, procalcitonin; CRP, C-reactive protein. The diagonal dashed line represents random guess (AUC = 0.5). ROC curve comparisons were performed using the DeLong method.

combined application can further improve diagnostic accuracy.

Discussion

Postoperative intracranial infection following tumor surgery represents a highly challenging complication in neurosurgery. The difficulty in diagnosing and differentiating it from sterile postoperative inflammation constitutes a critical bottleneck in clinical decision-making. This study conducted a systematic analysis of CSF cell counts and inflammatory markers in 170 patients after neurosurgical tumor resection to examine their progressive evolution patterns. By deeply exploring the influencing factors and clinical outcomes, it aimed to address this clinical challenge. The data showed that in infected patients, CSF presented a characteristic triad: a significant increase in neutrophils (the predominant WBC type), increased protein content, and decreased glucose levels. These indicators reached their peaks or lowest point on postoperative days 4-5 and showed a clear temporal evolution trend. Systemic inflammatory markers in the blood (especially CRP and PCT) increased synchronously in the middle and late stages of infection (postoperative days 4-7), suggesting that the infection had progressed from a local to a systemic inflammatory response. Multivariate analysis identified that surgery lasting more than 4 hours, placement of an EVD device, and

EVD indwelling time exceeding 7 days were independent risk factors for postoperative intracranial infection. Infection, especially when combined with ventriculitis, was closely related to a higher incidence of hydrocephalus and a worse neurological prognosis.

Interpreting the results within the context of existing research provides a greater understanding of their significance and novelty. Regarding CSF cytological characteristics, this study found that the mean postoperative CSF WBC count in the intracranial infection group reached 485.72 × 10^6/L within the early postoperative period (1-3 days), significantly higher than that in the aseptic inflammation group. This finding is consistent with multiple prior studies describing postoperative bacterial meningitis. For instance, Zhang et al. [31] reported a median CSF WBC count of 1478 × 10^6/L and a median polymorphonuclear cell percentage of 84.1% in the intracranial infection group during their investigation of central nervous system infections following glioma surgery. A 2022 study on intracranial infections following brain tumor resection further confirmed that the WBC in the CSF of infected patients increased significantly [32]. Collectively, these data validate that a marked increase in CSF WBCs, particularly the neutrophil proportion, serves as a strong indicator of intracranial infection [33]. However, this study further revealed through dynamic monitoring at three consecutive time points that this change is not static. On the 4th to 5th days after the operation, the WBC in the intracranial infection group rose to 1120.58 × 10^6/L, whereas that in the sterile inflammation group rapidly decreased to 85.41 × 10^6/L. This difference in magnitude and trend helps distinguish persistent infectious inflammation from the self-limiting surgical trauma response in clinical practice, and the “high protein, low glucose” pattern of CSF observed in the infection group is also a classic manifestation of bacterial meningitis. Our data (peak protein level of 2.34 mg/dL and trough glucose level of 1.88 mmol/L in the intracranial infection group) are consistent with published reports [34]. It is speculated that this may be related to the changes in blood-brain barrier permeability caused by surgical trauma and inflammatory responses, as well as the accelerated consumption of glucose by pathogenic bacteria and inflammatory cells [35, 36]. In the present study, CSF glucose in the infection group reached its nadir in the mid-postoperative period and gradually recovered in the late phase, reflecting the combined effects of reduced bacterial burden, resolution of inflammation, and restoration of blood-brain barrier function following antibiotic intervention. This dynamic pattern offers a potential quantitative indicator for clinically assessing treatment response. However, this study did not directly detect markers of blood-brain barrier integrity (such as the ratio of CSF albumin to serum albumin), and this mechanistic inference still requires further verification through prospective studies. It is worth noting that in the group with sterile inflammation, there may also be a transient and mild increase in CSF protein and a slight decrease in glucose in the early postoperative period. This further indicates that the use of individual biochemical indicators for differential diagnosis has limitations. Therefore, a comprehensive interpretation incorporating trends in cell counts may be more valuable than relying on a single threshold (e.g., glucose < 2.2 mmol/L).

In exploring inflammatory markers, this study simultaneously analyzed both CSF-specific and systemic blood indicators. The significant increase in serum CRP and PCT in the later stage of intracranial infection corresponds to the intense inflammatory response in the CSF. This is consistent with the conclusion of a 2025 study on the combined diagnostic value of cell index, CSF PCT, and interleukin-6, which suggested that PCT has unique value in diagnosing Gram-negative bacterial infections [37]. However, that study primarily focused on novel CSF biomarkers. In contrast, this study emphasizes the practical value of dynamically monitoring readily available conventional serum biomarkers (CRP, PCT). Although serum PCT may not be as sensitive as CSF PCT in detecting local infections, the significant increase observed in the intracranial infection group on postoperative days 4-5 (2.45 ng/mL vs. 0.52 ng/mL in the sterile inflammation group) strongly suggests that it can be used as an auxiliary indicator for assessing the systemic inflammatory response and the severity of the condition. This observation supports the use of blood-based markers for infection screening and monitoring in resource-constrained set-

tings or when frequent lumbar punctures are impractical. Although the study did not set a clear diagnostic threshold for CSF WBC, through dynamic analysis it was found that the CSF WBC count in the infection group was 1120.58 × 10^6/L on postoperative days 4-5, whereas the median CSF WBC count in the aseptic inflammation group was only 85.41 × 10^6/L, and there was no overlap between the two groups. This observation suggests that when the CSF WBC count remains higher than 500 × 10^6/L and the neutrophil proportion is > 80% on postoperative days 4-5, it has a high suggestive value for intracranial infection. However, due to the limitations of the retrospective design and the existence of individual differences, this study cannot provide a single cutoff value that has been externally validated. In the future, prospective, multicenter studies combined with receiver operating characteristic curve analysis are needed to determine the optimal diagnostic cutoff value for the postoperative population of neuro-oncology patients.

Based on the independent risk factors identified in this study, we propose the following operative prevention strategy framework: (1) Control of surgical duration: For complex tumor resection surgeries with an estimated duration exceeding 4 hours, it is recommended to conduct a multidisciplinary assessment before the surgery, optimize the configuration of the surgical team and the preparation of equipment, adopt a phased strategy during the operation, and conduct short-term reviews after key steps are completed to avoid unnecessary operational delays. For surgeries that exceed the time limit, postoperative enhanced monitoring for infection (such as daily monitoring of serum CRP/PCT changes starting from postoperative day 2) can be considered. (2) Optimization of EVD management: Strictly follow the "early removal" principle. It is recommended to closely assess the necessity of drainage after surgery and aim to remove the EVD within 7 days. For patients who require prolonged drainage (e.g., due to persistent intracranial hypertension or CSF leakage), it is recommended to replace the catheter on days 5-7 and collect the catheter tip for bacterial culture; strictly assess the drainage tube opening and surrounding skin daily, and cover with sterile dressings to avoid retrograde infection; before removal, routinely collect CSF specimens for examination and confirm that there are no obvious signs of infection prior to removal. (3) Risk stratification monitoring: For patients who simultaneously meet the criteria of surgical duration > 4 hours and EVD retention time > 7 days, it is recommended to upgrade the monitoring plan, including: regularly collecting CSF and blood specimens for dynamic detection on the 3rd, 5th, and 7th days after surgery; increasing the frequency of clinical observation of infection-related indicators (such as measuring body temperature every 4 hours and assessing level of consciousness daily); and once any suspicious signs appear, initiating empirical anti-infective treatment as soon as possible and completing pathogen testing.

The above strategies are proposed based on the risk factor analysis in this study, but their feasibility and effectiveness need to be further verified in clinical practice.

The risk factor analysis results of this study support the prevailing epidemiological understanding of postoperative infections in neurosurgery and provide more specific quantitative evidence. Surgery lasting more than 4 hours was identified as an independent risk factor (adjusted OR = 3.35). This is consistent with the conclusion of a large-scale retrospective study conducted by Zhang et al. [38] in 2025, which clearly stated that the prolongation of the operation time is an important risk factor for postoperative infection. The mechanism may be related to increased surgical trauma, prolonged tissue exposure, and immunosuppression due to extended anesthesia duration [39, 40]. This study confirmed that the placement of an EVD tube (adjusted OR = 2.86) and the duration of drainage tube insertion exceeding 7 days (adjusted OR = 3.74) were independent risk factors. This is consistent with the conclusion of a recent systematic review and meta-analysis in 2025, which also confirmed that the duration of the catheter insertion is the most critical risk factor for EVD-related infections [41]. Our data further quantifies the potential risk threshold of "7 days", providing direct evidence for developing EVD management strategies in clinical practice, such as early removal or replacement. Unlike some studies, intraoperative CSF leakage did not maintain independent significance after multivariable analysis in this study. This may sug-

gest that its risk is largely mediated indirectly through factors such as more complex surgery (reflected in longer operative times) or subsequent interventions requiring EVD placement. The independent risk factors identified in this study (surgery duration > 4 hours, EVD insertion and its duration > 7 days) are highly consistent with the risk factors reported in the National Surgical Quality Improvement Program (NSQIP) neurosurgery module. NSQIP data show that those with surgery duration exceeding the 75th percentile have a 2-3 times increased risk of infection, while the risk of EVD-related infection can increase by 4-5 times. The adjusted OR for surgery duration > 4 hours in this study was 3.35 (95% CI 1.39-8.09), and the adjusted OR for EVD insertion > 7 days was 3.74 (95% CI 1.49-9.41), which are basically consistent with the effect size of the NSQIP model. It should be noted that the above conclusion is applicable only to the tumor patient group. Whether it can be extended to non-tumor patients undergoing brain surgery still requires further verification. However, general models such as NSQIP are mostly constructed based on multi-specialty surgical populations, and although their predictive factors have reference value, their specific predictive efficacy for neuro-oncology patients has not been fully verified. This regression analysis based on a single-center specialized population provides preliminary evidence for establishing a more precise risk stratification model for such patients. Future research should further incorporate the risk factors of this study into existing prediction frameworks and evaluate their incremental predictive value through external validation.

Regarding etiology and clinical outcomes, this study found that Gram-positive bacteria (particularly coagulase-negative staphylococci) predominated in the intracranial infection group (38.89%), consistent with numerous reports indicating that postoperative infections in neurosurgery are mainly caused by skin flora such as Staphylococcus epidermidis. However, a 2022 study on postoperative infections following brain tumor surgery found that the detection rate of Gram-negative bacteria was higher (66.13%) [32]. This difference may stem from differences in epidemiological characteristics, prophylactic antibiotic strategies, and tumor type composition across medical centers [42, 43]. In this study, 44.44% of infected patients were diagnosed with ventriculitis, a critical clinical subtype. Ventriculitis indicates that the infection has breached the pia mater barrier and invaded the core pathways of CSF circulation, making treatment more challenging and the prognosis poorer [44, 45]. This study confirmed that the incidence of hydrocephalus (30.56%) and the proportion of patients with poor prognosis (GOS score 1-3, 50.00%) were significantly higher in the intracranial infection group, especially among those with ventriculitis. This is consistent with trends observed in other studies, which show that intracranial infections prolong hospital stays and increase mortality [46]. Therefore, early recognition of ventriculitis - such as via imaging demonstrating ventricular wall enhancement or ependymitis - is critical for initiating more intensive treatment and assessing prognosis.

Regarding the cost-effectiveness issue of inflammation indicator testing, although this study did not conduct a formal economic evaluation, a preliminary analysis can be conducted from the perspective of clinical decision-making. In this study, the serum PCT test showed significant differences between the infection group and the inflammation group (mean difference of 1.93 ng/mL from the 4th to 5th day after surgery, 95% CI 1.68-2.18), and its dynamic change trend was highly synchronous with the CSF indicators. Although the PCT test (single cost approximately 100-150 yuan RMB) is more expensive than the routine blood routine test (about 20 yuan), considering that the missed diagnosis or delayed treatment of intracranial infection may lead to prolonged hospital stay (in this study, the infection group had an average extension of 12.22 days, 95% CI 8.96-15.48), the upgrade of antibiotics, secondary surgery, and even death, its potential economic burden far exceeds the cost of the test itself. Therefore, for high-risk patients with surgery duration > 4 hours or EVD retention > 7 days, routine combined detection of serum PCT on the 4th-5th day after surgery may have a higher cost-effectiveness ratio. In addition, CRP, as a cheaper inflammation marker (single cost approximately 30 yuan), also has significant differentiation value in the postoperative middle and late stages (mean difference of 57.22 mg/L from the 4th to 5th day, 95% CI 48.86-65.58), and can be used as an alterna-

tive option for grassroots medical institutions. Future research should conduct a formal health economics evaluation, integrating indicators such as detection costs, treatment expenses, hospital stay days, and long-term prognosis, to provide more sufficient evidence-based basis for clinical promotion.

This study observed that the CSF WBC, neutrophil percentage, and protein level in the infection group significantly increased at each time point after surgery, and reached their peaks in the middle stage. This dynamic evolution is consistent with the typical pathological process of bacterial meningitis: after the pathogen invades the subarachnoid space, it activates innate immunity through Toll-like receptors, induces the release of chemokines (such as IL-8, CXCL1), and recruits neutrophils to cross the blood-brain barrier into the CSF [47]. At the same time, inflammatory mediators increase vascular permeability, resulting in a large amount of plasma protein seeping into the CSF, further exacerbating the increase in protein levels [47]. Similar to this study, a previous study has also reported that the CSF protein level in the infection group reaches its peak on the 4th - 5th day after surgery, and then gradually decreases with the control of inflammation [48]. In the sterile inflammatory group, CSF indicators increase slightly in the early postoperative period and then rapidly decrease, which is speculated to be related to the transient opening of the blood-brain barrier caused by surgical trauma and local tissue repair, rather than the continuous inflammation cascade amplification caused by persistent infection.

In terms of serum inflammation markers, this study found that CRP and PCT in the infection group were significantly higher than those in the sterile inflammatory group in the middle and late postoperative periods (4-7 days). CRP is produced by liver cells in response to IL-6 stimulation, and its increase reflects a systemic inflammatory response [49]; PCT has high specificity for bacterial infection and usually does not increase in viral infections or sterile inflammation [50]. Previous studies have shown that continuous elevation of PCT for more than 72 hours after surgery indicates bacterial infection rather than surgical stress response [51]. The phenomenon of significantly higher PCT in the infection group compared to the inflammation group in the later stage of the infection, as observed in this study, further supports its use as an auxiliary indicator for differentiating bacterial intracranial infection.

Regarding risk factors, this study found that surgery duration > 4 hours, EVD retention, and EVD retention time > 7 days are independent risk factors. Extended surgery time means an increase in tissue exposure time, more infection opportunities, and also a prolonged duration of postoperative immunosuppression [52]. The mechanism of EVD-related infections mainly involves the formation of biofilms on the surface of the catheter: bacteria (especially coagulase-negative staphylococci) adhere to the inner wall of the catheter and secrete extracellular polysaccharide matrices, forming a biofilm barrier that enables the bacteria to evade immune clearance and antibiotic killing [53]. In the infection group of this study, the detection rate of coagulase-negative staphylococci was the highest (25.00%), which was highly consistent with this mechanism. A retention time of more than 7 days significantly increased the maturation of the biofilm and the risk of infection, which was consistent with the conclusion of previous studies that the risk of EVD infection increased exponentially over time [54]. Of note, intraoperative blood loss showed a marginal association in univariate analysis but lost significance after multivariate adjustment (adjusted OR = 1.95, P = 0.094), likely reflecting collinearity with prolonged operative duration and EVD placement, rather than an independent risk factor.

To summarize, the innovation and value of this study lies across multiple dimensions. First, methodologically, we used a rigorous multi-time-point dynamic monitoring protocol (postoperative days 1-3, 4-5, and 6-7). This method can not only capture the “slope” and “peak time” of the indicator changes, but also overcome the inherent limitations of single-time detection in differentiating infection from sterile inflammation, providing basic data for establishing a diagnostic model based on the trend of changes; and by conducting longitudinal correlation analysis between classic CSF cytology and biochemical indicators, serum systemic inflammatory markers, clear clinical risk factors and outcomes, a multi-dimensional

assessment framework from local to systemic, and from etiology to prognosis has been established; finally, at the clinical transformation level, it further strengthened the core position of two intervention measures, namely the control of surgical duration and the reasonable removal of EVD tubes, in infection prevention. Concurrently, the dynamic CSF marker profiles we describe provide clinicians with useful guidance for empirical diagnosis and assessment of treatment response while awaiting microbiological results.

Based on the risk factors identified in this study and the specific inflammatory kinetic characteristics following infection, subsequent studies might further explore perioperative immune "preconditioning" for high-risk patients through immunomodulatory strategies (e.g., targeting specific inflammatory pathways), thereby providing new insights into preventing postoperative infections [55]. Based on the findings of this study, we propose the following design framework for a multi-center validation study: Study Design: Multi-center, prospective cohort study, involving at least 5 tertiary grade A hospitals' neurosurgery departments. The expected sample size is no less than 500 cases (with an estimated 80-100 cases in the infection group), to ensure the statistical power for subgroup analysis and model validation. Inclusion Criteria: Consistent with this study, patients undergoing elective craniotomy for tumor resection are included, and paired blood and CSF samples are continuously collected before surgery and on the 1st, 3rd, 5th, and 7th days after surgery. Core Indicators: In addition to the conventional CSF and blood indicators involved in this study, supplementary markers such as the ratio of CSF albumin to serum albumin, CSF lactate, IL-6, and IL-10 are uniformly included to comprehensively evaluate the integrity of the blood-brain barrier and the local immune status. Dynamic Monitoring Strategy: Establish a unified dynamic monitoring pathway for postoperative inflammatory indicators, set "a decrease rate of $\geq$ 50% in indicators from the 5th to 7th day after treatment" as the initial threshold for determining treatment effectiveness, and verify its sensitivity and specificity in multi-center practice. Prediction Model Construction: Based on the multi-center data, integrate dynamic inflammatory indicators with clinical risk factors (operation duration, EVD indwelling time, etc.), construct a visual nomogram prediction model, and evaluate its clinical practical value through internal and external validation. Quality Control: Standardize laboratory testing standards and blood/CSF collection procedures across centers, and establish a data safety monitoring committee to ensure data quality and consistency. The proposal of this plan aims to provide a specific path for the clinical translation of the study conclusions and lay the foundation for conducting higher evidence-level studies in the future. This study did not collect indicators related to the patients' preoperative immune function status (such as peripheral blood lymphocyte count, serum albumin level, neutrophil/lymphocyte ratio, etc.), and thus could not rule out the confounding influence of preoperative immune deficiency on the risk of infection occurrence. Cancer patients often have varying degrees of immune suppression due to the disease itself, malnutrition, or preoperative radiotherapy and chemotherapy, which may independently increase the risk of infection beyond the surgical factors. Future prospective studies should systematically assess the patients' immune status before surgery and incorporate it into a multivariate model for correction.

Limitation

As a retrospective analysis, this study has inherent limitations. For instance, the relatively small sample size (especially with only 36 cases in the intracranial infection group) may limit the ability to identify weakly correlated risk factors and limit further subgroup analyses based on pathogen type or tumor pathology. Moreover, no prospective comparisons were made with promising new markers, such as CSF lactate and interleukin-6. Although the sample size is sufficient to detect significant inter-group differences and strong risk associations in the primary outcome indicators, it may not be able to detect subtle differences or weak associations (such as OR < 2.0), and the relatively small number of intracranial infection cases further restricts the statistical power of more complex subgroup analyses (such as comparisons between different pathogens or between subtypes of ventriculitis and meningitis). Nevertheless, the multi-time-point dynamic data, detailed clinical characterization, and

group comparisons based on strict diagnostic criteria provided in this study provide valuable preliminary evidence for understanding CSF characteristics of intracranial infections following neuro-oncological surgery. They also establish essential parameter estimates and a data springboard for future larger prospective studies. This study did not systematically evaluate indicators of blood-brain barrier integrity (such as the ratio of CSF albumin to serum albumin), thus there is a lack of direct evidence to support the mechanistic inferences regarding the transport of inflammatory markers across the blood-brain barrier, which is one of the main limitations of this research. This study only included patients undergoing neuro-oncology surgeries and did not establish a control group for non-tumor cranial surgeries. Therefore, it was impossible to clearly distinguish the independent effects of tumor factors and surgical factors on infection. Cancer patients may have higher susceptibility to infection due to long-term immunosuppression, preoperative radiotherapy and chemotherapy history, or changes in the local immune microenvironment caused by the tumor itself. However, the design of this study cannot directly compare this. Future research should include non-cancer cranial surgery patients as controls to more accurately assess the specific role of tumor factors in postoperative infection. Furthermore, this study failed to analyze the correlation between different levels of inflammatory indicators (such as PCT > 2 ng/mL vs. ≤ 2 ng/mL) and the efficacy of antibiotics, nor did it systematically report the dynamic changes of inflammatory indicators during antibiotic treatment and their association with efficacy. This is mainly due to the lack of a unified time point and standardized evaluation process for antibiotic adjustment decisions in the retrospective data, making it impossible to conduct reliable subgroup analysis. Future prospective studies should design fixed monitoring plans (such as daily measurement of PCT, CRP, and CSF indicators) and combine clear indications for antibiotic adjustment to evaluate the clinical value of treatment guidance strategies based on inflammatory markers in postoperative intracranial infections of neuro-oncology.

Conclusions

This study on postoperative intracranial infections in patients with neuro-oncological tumors has revealed characteristic dynamic changes in CSF and inflammatory markers: infected patients show a significant increase in WBCs, predominant neutrophils, elevated protein levels, and decreased glucose levels. These indicators (except glucose, which reaches its nadir on days 4-5) peak on the 4th to 5th day after surgery and differ from the manifestations of sterile inflammatory responses. At the same time, the levels of serum CRP and PCT also increase synchronously. The study confirmed that a surgical duration exceeding 4 hours and the retention of an EVD tube for more than 7 days are independent risk factors for infection. Infection (especially when combined with ventriculitis) significantly increases the risk of hydrocephalus and leads to poor neurological function recovery. Through multi-time-point dynamic monitoring, the evolution of infection-related inflammation can be clearly depicted, providing a key time window for early identification. Therefore, for high-risk patients, sequential monitoring of CSF and blood indicators after surgery, and strict control of the duration of surgery and the duration of drainage tube placement, still have important clinical value for early detection of infection and for improving prognosis. Future efforts may combine dynamic indicators with risk factors to develop prognostic frameworks, while leveraging multi-omics technologies to deeply examine the local immune microenvironment, thereby advancing precision prevention and treatment.

Disclosure of conflict of interest

None.

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