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ORIGINAL ARTICLE

Case Control Study

Factors influencing the surveillance of re-emerging intracranial infections in elective neurosurgical patients: A single-center retrospective study

Jiang-Long Wang, Xi-Wen Wu, Sheng-Nan Wang, Xuan Liu, Bing Xiao, Yu Wang, Jing Yu

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Abstract

BACKGROUND

At present, many studies have reported the risk factors for postoperative intracranial reinfection, including age, sex, time to surgery, duration of postoperative catheterization, emergency procedures, type of disease and cerebrospinal fluid leakage, but the academic community has not reached a unified conclusion.

AIM

To find factors influencing the surveillance of re-emerging intracranial infections in elective neurosurgical patients.

METHODS

Ninety-four patients who underwent elective craniotomy from January 1, 2015 to December 31, 2022 in the Department of Neurosurgery, First Hospital of Jilin University, were included in this study. Of those, 45 patients were enrolled in the infection group, and 49 were enrolled in the control group. The clinical data of the patients were collected and divided into three categories, including preoperative baseline conditions, intraoperative characteristics and postoperative infection prevention. The data were analyzed using SPSS 26.0 software.

RESULTS

There were 23 males and 22 females in the infection group with a mean age of 52.8 ± 15.1 years and 17 males and 32 females in the control group with a mean age of 48.9 ± 15.2 years. The univariate analysis showed that the infection group had higher systolic blood pressures and postoperative temperatures, fewer patients who underwent a supratentorial craniotomy, more patients with a history of

hypertension and higher initial postoperative white blood cell counts than the control group, with statistically significant differences ($P < 0.05$). The multifactorial logistic regression analysis showed that a history of hypertension and a high postoperative body temperature were independent risk factors for postoperative infection in neurosurgical patients.

CONCLUSION

The results obtained in this study indicated that a history of hypertension and a high postoperative body temperature were independent risk factors for postoperative neurological symptoms.

Key Words: Re-emerging infections; Risk factors; Neurosurgery; Elective surgery; Intracranial infections

Core Tip: A postoperative intracranial reinfection not only increases the mortality rate, economic burden and length of hospitalization but may even cause permanent sequelae to the patient. The results obtained in our study indicated that a history of hypertension and a high postoperative body temperature were independent risk factors for postoperative neurologic complications that mostly occur within the first 3 d after surgery. The identified risk factors provide a basis for recommending future prevention strategies.

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INTRODUCTION

Postoperative intracranial reinfection can occur in neurosurgical patients who undergo craniotomy, recover well after surgery and are discharged from the hospital despite having inflammation at the original surgical site, thereby requiring another craniotomy for debridement and treatment. These infections include postoperative meningitis, brain abscess, subdural abscess, epidural abscess and more widespread or diffuse infections such as septic meningitis and ventriculitis, which is one of the common serious complications after neurosurgery. The infected patients often present with severe symptoms such as high cranial pressure, cerebral edema and seizures, and the increasing rate of drug resistance of pathogenic bacteria and the decrease in the rate of positive bacterial cultures make clinical treatment difficult. A postoperative intracranial reinfection not only increases the mortality rate, economic burden and length of hospitalization but may even cause permanent sequelae to the patient.

There are many studies on the risk factors for intracranial infection, including age, sex, duration of surgery, emergency procedures, disease type, cerebrospinal fluid leakage, surgical approach, postoperative temperature, artificial implants and leukocyte level[1,2]. However, there is no unified conclusion on whether these risk factors have an effect on the incidence of postoperative intracranial reinfection, and the value of many risk factors is still unknown[3,4]. In this study, 94 patients with neurosurgical diseases who underwent elective surgery at the First Hospital of Jilin University were enrolled to explore the possible risk factors for the occurrence of postoperative intracranial reinfection. In particular, the effect of postoperative fever on the incidence of postoperative intracranial reinfection was evaluated to provide a theoretical reference for the early prevention and control of postoperative intracranial reinfection. The specific reports are as follows.

MATERIALS AND METHODS

Patient inclusion and exclusion criteria

Inclusion criteria: Infection group: (1) Patients who underwent a craniotomy for the treatment of a neurological tumor, cerebrovascular disease, intracranial hemorrhage, *etc*. recovered well perioperatively and were discharged; and (2) Patients with a late-onset postoperative central nervous system infection who met the following criteria: (a) Patients with unhealed scalp wounds and intermittent subcutaneous sensations, and computed tomography images showed a biconvex intracranial epidural lesion (Figure 1); and (b) Patients who suffered a preoperative scalp infection or subcutaneous rupture that required a repeat craniotomy for debridement treatment but recovered well after surgery and were discharged. Control group: Patients who underwent a craniotomy for the treatment of a neurological tumor, cerebrovascular disease, intracranial hemorrhage, *etc*, recovered well perioperatively and were discharged but did not have a postoperative infection during the same period (from January 1, 2015 to December 31, 2022) following neurosurgery at the First Hospital of Jilin University.

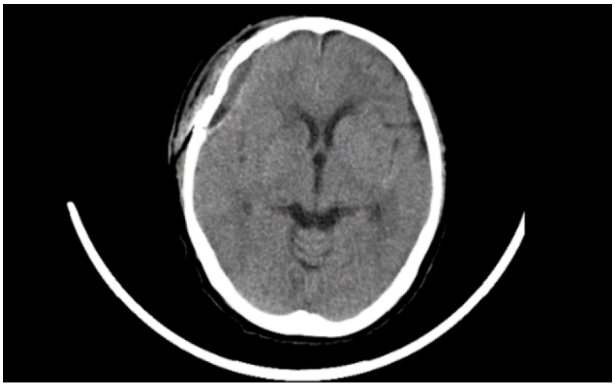

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Figure 1 Computed tomography image of a patient with postoperative reinfection.

Exclusion criteria: (1) Patients with a postoperative diagnosis of septic meningitis, which improved after anti-inflammatory treatment; and (2) Patients with a high suspicion of having an intracranial infection who refused to undergo the debridement procedure.

This study was approved by the Ethics Committee of the First Hospital of Jilin University (Grant No. 2023-293), and informed consent was obtained from all patients or their families.

Data collection

The data of the patients who met the above criteria were collected in the clinical electronic case database in this study and divided into three categories. The first category was preoperative baseline conditions, including age, sex, weight, operation time, operation table, blood pressure and admission white blood cell (WBC) count. The second category was intraoperative characteristics, including surgical access, intraoperative blood transfusion, operation duration and intraoperative implants (cranial mesh plate). The third category consisted of information related to postoperative infection prevention, including postoperative temperature, first postoperative WBC and discharge WBC count.

Methods of analysis

In this study, based on previous literature and routine clinical practice, factors such as age, sex, weight, duration of operation, operation table, blood pressure, operation access, intraoperative blood transfusion, operation duration, intraoperative implants (cranial mesh, artificial dura, *etc*), bone flap return and postoperative body temperature were included. These factors affect the incidence of postoperative intracranial reinfection. A single-factor analysis and a multifactor logistics regression were performed. The risk factors affecting the incidence of postoperative intracranial reinfection were investigated.

Perioperative course of treatment

The patients who met the above criteria were prepared preoperatively, and surgical debridement was performed. After the operation, the specimens that were retrieved from the operative area were sent for pathological examination, and antibiotics were routinely administered to prevent postoperative infection. Patients who suffered a postoperative intracranial reinfection were followed up to observe the postoperative recovery effect.

Statistical methods

SPSS 26.0 software (IBM Corp., Armonk, NY, United States) was used for data analysis. The t test was used for comparisons between groups for data meeting a normal distribution; the Mann-Whitney U test was used for comparisons between groups for data not meeting a normal distribution. The Pearson χ^2 test was used for comparisons among groups for categorical variables. The variables that were statistically significant in the univariate analysis were further included in the logistic regression equation for multivariate analysis to screen patients for risk factors for postoperative intracranial reinfection. $P < 0.05$ indicated that the difference was statistically significant.

RESULTS

Patient data

A total of 94 patients were included in this study. There were 23 males and 22 females in the infected group with a mean age of 52.8 ± 15.1 years and 17 males and 32 females in the control group with a mean age of 48.9 ± 15.2 years.

The postoperative body temperature in the infected group was 38.1 °C (37.7 °C, 38.5°C) with a normal range from 36.9 °C to 39.2 °C. The body temperature in the control group was 37.40 °C (36.8 °C, 37.8 °C) with a normal range from 36.0 °C to 38.5 °C. Forty-one patients in the infected group had a postoperative fever, 36 of which mostly occurred within 3 d

after surgery; 25 patients in the control group had an elevated postoperative body temperature.

All 45 patients in the infected group received artificial implants. In the control group, 43 of 49 patients received artificial implants, while 6 patients did not receive artificial grafts. All 45 patients in the infection group had intraoperative pus accumulation under the bone flap, of which 38 patients were evaluated and the bone flap was returned. Patients with postoperative intracranial reinfection were followed up for 3 years. Among them, 34 patients recovered well without reinfection, and 11 patients were lost to follow-up.

The first postoperative WBC count in the infected group was 13.9 × 10^9/L (11.0 × 10^9/L, 16.6 × 10^9/L) ranging from 3.7-30.4 × 10^9/L. The first postoperative WBC count in the control group was 12.8 × 10^9/L (10.1 × 10^9/L, 15.2 × 10^9/L) ranging from 4.2-22.5 × 10^9/L. The remaining information is detailed in Table 1.

Analysis of factors influencing postoperative intracranial reinfection

The univariate analysis showed that compared with the control group, the infection group had higher systolic blood pressures and postoperative body temperatures (Figure 2), fewer patients who underwent a craniotomy, more patients with a history of hypertension and higher initial postoperative WBC counts, with statistically significant differences ($P < 0.05$). In contrast, age, sex, weight, time to surgery, admission WBC count, discharge WBC count, intraoperative blood loss, intraoperative bleeding volume, surgery duration, artificial implants and bone flap return were not significantly different between the two groups ($P > 0.05$). The indicators that were statistically significant in the univariate analysis were included in the multifactorial logistic regression analysis, which showed that a history of hypertension and a high postoperative temperature were independent factors influencing the incidence of postoperative infection in neurosurgical patients. The remaining information is detailed in Table 2.

DISCUSSION

Neurosurgical craniotomy has a high incidence of postoperative infections due to the difficulty of the procedure and the long hospital stay[5]. Postoperative infections usually manifest as meningitis, brain abscesses, subdural pustules and/or epidural abscesses[6], representing the most common complications in patients undergoing neurosurgical craniotomy[7]. Postoperative intracranial reinfections are highly prevalent during the 3-7 d postoperative period, especially in patients with open craniocerebral trauma, postoperative cerebrospinal fluid leakage, subcutaneous effusion from the incision, ventricular drainage and reoperation for postoperative emergencies. Patients with severe infections complicated by epidural abscesses must undergo debridement again. Related studies have found that the duration of surgery and intraoperative blood transfusion and other indicators have an impact on the incidence of postoperative intracranial reinfection because craniotomy severely damages the protective tissues of the brain. The results of the present study cannot support this view, which may be related to the development of new surgical techniques and improvements in surgical equipment and medical standards, strict perioperative management, timely intraoperative management of bleeding and the patients' nutritional statuses[8].

In the present study, an elevated postoperative body temperature was found to be an independent risk factor for postoperative intracranial reinfection in neurosurgical patients, with most fevers occurring within 3 d after surgery, consistent with the findings of Raviv *et al*[9]. A meta-analysis by Chen *et al*[10] showed that titanium alloy artificial implant material is a risk factor for postoperative infection in neurosurgery patients, which may be related to the body's intolerance to titanium alloy material. In this study, all 45 patients in the infected group received artificial implants, and the increase in their postoperative body temperatures may have been related to the application of artificial implants or differences in patient factors. Therefore, the specific mechanism needs further exploration.

Postoperative fever may also be related to inflammation in the operative area. Measures such as strengthening nutrition, increasing attention, avoiding low protein in the postoperative period and physical therapy of the operative area can be taken to prevent or reduce the risk of infection. Most cases of an elevated postoperative body temperature are associated with an infection, as supported by previous studies[11,12]. Therefore, measures such as bacterial culture should be performed promptly for patients with a postoperative fever to clarify the etiology and provide symptomatic treatment. Until the results of bacterial culture and drug sensitivity are available, it is important to keep track of bacterial resistance, select sensitive drugs for treatment and adjust the medication regimen once the report is available. Luo *et al*[13] found that a postoperative fever could contribute to the early neurological deterioration of patients and that the higher the temperature, the worse their prognosis. The implementation of a more individualized temperature management strategy for neurosurgical patients with an early fever to reduce the peak postoperative body temperature and shorten the duration of fever may help to reduce the risk of postoperative intracranial reinfection.

A meta-analysis showed that the intraoperative use of powdered vancomycin in neurosurgical patients prevented postoperative intracranial reinfection to some degree[14]. Some studies have also shown that the duration of surgery and the time to reoperation have important effects on the incidence of postoperative intracranial reinfection in patients, suggesting that good surgical management practices can effectively reduce the incidence of postoperative infection[15]. Therefore, the prevention of postoperative intracranial reinfection should be based on various aspects, such as strengthening perioperative management and prophylactic application of antibiotics.

In this study, we found that an increased postoperative body temperature was an early warning factor for postoperative intracranial reinfection in neurosurgical patients and can be used as a follow-up tool to prevent postoperative infection in neurosurgical patients. Postoperative temperature should be closely monitored in neurosurgical craniotomy patients, and timely intervention should be implemented to reduce a high temperature and ultimately reduce the risk of postoperative intracranial reinfection.

Table 1 Comparison of clinical data, *n* = 94

Projects	Infection group, *n* = 45	Control group, *n* = 49	Test value	*P* value
Age (mean ± SD)	47.867 ± 15.286	52.816 ± 15.073	1.580[a]	0.118
Male	23 (57.5)	17 (42.5)	2.586[b]	0.108
Weight [kg, M (P_{25}, P_{75})]	65 (58, 75)	64 (57, 68.5)	-1.251[c]	0.211
Time of surgery [mo, M (P_{25}, P_{75})]	7 (4, 10)	7 (3, 9)	-0.951[c]	0.341
First unit	24 (53.3)	24 (49.0)	0.178[b]	0.673
Systolic pressure [mmHG, M (P_{25}, P_{75})]	144 (126, 160)	126 (120, 137)	-3.526[c]	< 0.001
Diastolic pressure [mmHG, M (P_{25}, P_{75})]	80.0 (70.0, 83.0)	80.0 (72.5, 90.0)	-1.345[c]	0.179
History of hypertension	28 (57.1)	8 (17.8)	15.383[b]	< 0.001
Supratentorial craniotomy	32 (71.1)	44 (89.8)	5.290[b]	0.021
Postoperative body temperature [C, M (P_{25}, P_{75})]	38.10 (37.72, 38.50)	37.40 (36.75, 37.80)	-5.471[c]	< 0.001
Admission WBC [10^9, M (P_{25}, P_{75})]	7.98 (6.67, 10.88)	7.52 (5.19, 9.60)	-1.557[c]	0.119
First postoperative WBC [10^9, M (P_{25}, P_{75})]	14.22 (11.08, 16.70)	12.78 (10.13, 15.17)	-2.030[c]	0.042
Discharge WBC [× 10^9/L, M (P_{25}, P_{75})]	8.67 (6.59, 11.30)	8.36 (6.89, 9.91)	-0.701[c]	0.483
Intraoperative blood loss [mL, M (P_{25}, P_{75})]	30 (30, 350)	100 (30, 250)	-0.090[c]	0.929
Intraoperative blood transfusion	12.0 (26.6)	6.0 (12.2)	2.525[b]	0.112
Duration of surgery [h, M (P_{25}, P_{75})]	3.90 (3.00, 5.42)	3.40 (2.45, 5.00)	-1.261	0.207
With artificial implants	45(100)	43(87.8)	3.419 [b]	0.064
Reduction of bone flap	39 (86.7)	47 (95.9)	2.579[b]	0.108

[a]*t* value.
[b]χ^2 value.
[c]*U* value.
Data are *n* (%). M (P_{25}, P_{75}): Median (Interquartile range, Q3-Q1); SD: Standard deviation; WBC: White blood cell count.

Table 2 Multifactorial analysis of patients with postoperative reinfection, *n* = 94

Projects	B value	Standard error	Wald value	OR value	95%CI	*P* value
History of hypertension	1.827	0.630	8.403	6.214	1.807-21.370	0.004
Supratentorial craniotomy	0.679	0.767	0.784	1.972	0.439-8.869	0.367
Postoperative body temperature	2.536	0.598	17.986	0.078	3.913-40.795	< 0.001
First postoperative WBC	0.061	0.061	1.004	1.063	0.943-1.119	0.316

Systolic blood pressure and normal blood pressure were covariates, and systolic blood pressure was included in the multifactorial analysis. CI: Confidence interval; OR: Odds ratio; WBC: White blood cell count.

In this study, it was found that the initial postoperative WBC count was higher in patients with a history of hypertension, and the difference was statistically significant ($P < 0.05$), indicating a higher risk of postoperative intracranial reinfection. Studies on hypertension as a factor influencing the incidence of postoperative intracranial reinfection are scarce, but Saeedinia *et al*[16] and Yao *et al*[17] found a strong association between hypertension and the incidence of postoperative intracranial reinfection. Few studies have reported the relationship between hypertension history and postoperative intracranial bacterial infection, possibly because hypertension patients often have other cardiovascular and cerebrovascular diseases, vascular stenosis, thin vascular walls, malnutrition and other factors. There are few hypotheses regarding this, and AlGamdi *et al*[5] suggested that the higher incidence of postoperative intracranial reinfection in patients may be related to inadequate perfusion of skin and subcutaneous tissues. Therefore, the influence of hypertension history on postoperative intracranial infection needs further study. In the future, we can study the changes in microbial cerebrospinal fluid in patients with intracranial infection after the application of different antihypertensive drugs to further verify our speculation.

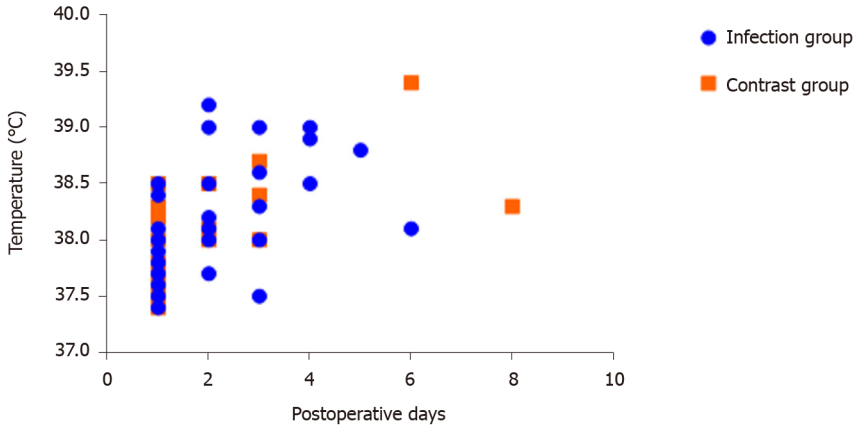

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Figure 2 Scatter plot of postoperative body temperature and postoperative days.

Limitations

This was a single-center retrospective study, and its findings must be validated in a multicenter, large-sample randomized controlled trial. However, our findings are consistent with other studies on postneurosurgical fever and are applicable to a larger population of postneurosurgical patients.

CONCLUSION

The results obtained in this study indicated that a history of hypertension and a high postoperative body temperature were independent risk factors for postoperative neurologic complications that mostly occurred within the first 3 d after surgery. Therefore, clinical staff should pay close attention to patients' postoperative body temperatures after surgery and promptly treat patients with an elevated body temperature. Patients with a history of high blood pressure should also be particularly concerned.

ARTICLE HIGHLIGHTS

Research background

Neurosurgical craniotomy has a high incidence of postoperative infections due to the difficulty of the procedure and the long hospital stay.

Research motivation

There are many studies on the risk factors for intracranial infection. However, there is no unified conclusion on whether these risk factors influence the incidence of postoperative intracranial reinfection, and the value of many risk factors is still unknown.

Research objectives

Ninety-four patients who underwent elective craniotomy from January 1, 2015 to December 31, 2022 in the Department of Neurosurgery, First Hospital of Jilin University, were included in this study. Of those, 45 patients were enrolled in the infection group, and 49 were enrolled in the control group.

Research methods

The clinical data of the patients were collected and divided into three categories, including preoperative baseline conditions, intraoperative characteristics and postoperative infection prevention. The data were analyzed using SPSS 26.0 software.

Research results

A history of hypertension and a high postoperative body temperature were independent risk factors for postoperative neurologic complications.

Research conclusions

The results obtained in this study indicated that a history of hypertension and a high postoperative body temperature were independent risk factors for postoperative neurologic complications that mostly occur within the first 3 d after

surgery.

Research perspectives

Clinical staff should pay close attention to patients' postoperative body temperatures and promptly treat patients with an elevated body temperature. Patients with a history of high blood pressure should also be particularly concerned.

FOOTNOTES

Author contributions: Every author has made substantial contributions to the manuscript; Wang JL drafted the article and contributed to editing and revision; Wang SN downloaded datasets and conducted a bioinformatic analysis; Wu XW and Wang SN provided correction and analysis of statistical methods; Liu X, Wang Y and Xiao B contributed to figures and tables; Yu J substantively edited the manuscript; All authors read and approved the final version of this manuscript.

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