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A retrospective observational study of risk factors for postoperative meningitis following resection of meningioma

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Abstract

Objective: This retrospective observational study aimed to explore the risk factors for postoperative meningitis following resection of meningioma.

Methods: A total of 937 patients older than 18 years who underwent meningioma resection at the Department of Neurosurgery of three grade-A general hospitals in Sichuan Province between January 2021 and June 2024 were included. Basic patient information and perioperative variables were evaluated as risk factors for meningitis. Univariate and multivariate analyses were performed to identify the risk factors for postoperative meningitis.

Results: Overall, 47 (5.0%) of the 937 patients were infected with postoperative meningitis. Univariate analysis revealed that albumin level ($<$3.5 mg/dL; $p = 0.017$), preoperative hospitalization (median: 4 days; interquartile range: 2–6 days; $p = 0.034$), tumor location (skull base; $p < 0.001$), surgery duration ($>$3 h; $p < 0.001$), and bleeding volume during operation ($\geq$400 mL; $p < 0.001$) were significantly associated with postoperative meningitis following resection of meningioma. The average postoperative hospital stay in the postoperative meningitis group was 14 days, whereas it was 6 days in the nonpostoperative meningitis group ($p < 0.001$). Furthermore, multivariate analysis showed that tumor location (skull base; $p = 0.004$; odds ratio $= 2.914$; 95% confidence interval: 1.395–6.091), surgery duration ($>$3 h; $p = 0.006$; odds ratio $= 3.024$; 95% confidence interval: 1.370–6.674), and bleeding volume during operation ($p = 0.034$; odds ratio $= 2.057$; 95% confidence interval: 1.056–4.006) were independent risk factors for postoperative meningitis following resection of meningioma.

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Conclusion: Tumor location (skull base), longer surgery duration (>3 h), and higher bleeding volume during operation (≥400 mL) were independent risk factors for postoperative meningitis following resection of meningioma. Moreover, postoperative meningitis was associated with a prolonged hospital stay. These findings can help identify patients with meningioma in need of special intervention to prevent postoperative meningitis and can help surgeons preoperatively identify the risk of postoperative meningitis for meningioma.

Keywords

Meningioma, resection, postoperative meningitis, risk factors, hospital stay

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Introduction

Meningioma is a common benign tumor representing 13%–26% of all intracranial tumors originating from the arachnoid cap cells. It is very common in older adults and females.[1] Meningioma is considered the most common primary brain tumor in the skull. According to the World Health Organization (WHO) classification,[2,3] it can be classified as grades I (benign), II (intermediate), and III (malignant), based on cell type, mitotic activity, cell properties, necrosis, and brain invasion. Among these, grade I has been detected in 90% of all meningioma cases. Grade I shows a variety of histological variations, namely, epithelial, fibrous (fibroblastic), transitional (mixed), sanding, hemangioma, microcystic, secretory, lymphoplasma cell enrichment, and metastatic meningioma. Grade II refers to atypical meningioma that includes clear cells or chordal variations exhibiting a mitotic index of 4 to 19 per 10 high energy fields (HPF), cytosis, high nucleoplasm ratio (small cells), patch-like growth, and spontaneous necrosis without embolization or radiotherapy. Brain invasion meningioma may also be qualified as grade II.[2,3] Grade III meningioma refers to anastomotic meningioma, which includes papillary or rhabdoid morphologic variants, mitotic index of ≥20/10 HPF, and larger areas of spontaneous necrosis.[2,3]

Surgical resection is the preferred treatment; the higher the degree of resection, the lower the likelihood of tumor recurrence.[4] However, surgery may lead to postoperative complications, posing heavy physical and mental burden to the patient.[5] Postoperative meningitis (POM) is a serious complication after neurosurgery, which can prolong the length of hospital stay, increase the cost of hospital stay, cause neurological impairment, and even lead to death.[6] Several studies have reported the risk factors for neurosurgical site infection,[7–10] whereas only a few have focused on the risk factors for POM following meningioma. A study showed that extra-ventricular shunt, preoperative distant site infection, and secondary operation were risk factors for meningitis after craniotomy.[6] In this study, we retrospectively analyzed the risk factors for POM following meningioma resection and examined the incidence of POM and its effect on postoperative hospital stay.

Methods

Patients

We retrospectively analyzed 937 patients who underwent meningioma resection between 1 January 2021 and 31 June 2024 in the Department of Neurosurgery of three tertiary general hospitals in Sichuan Province (West China Hospital of Sichuan University, Deyang People's Hospital, and West China Longquan Hospital, Sichuan University). Inclusion criteria were as follows: (a) patients aged 18–90 years; (b) diagnosis of meningioma (WHO grade I, II, or III) by histology; (c) survival for at least 7 days after surgery; and (d) provision of informed consent. Exclusion criteria were as follows: (a) not the first craniotomy and (b) treated with gamma knife. Overall, 47 (5%) patients developed POM, whereas the remaining 890 were in the non-POM group. The need for ethical approval and informed consent was waived by the Deyang People's Hospital because this was a retrospective observational and anonymous study. We have de-identified all patient details. Our study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013.

Data collection

Clinical data of all patients were obtained from the Information System of three tertiary general hospitals in Sichuan Province and carefully recorded. The following data were collected (Table 1 and Table 2): age at diagnosis, sex, diabetes mellitus status, hypertension status, preoperative blood biochemical index, albumin level, hemoglobin level, red blood cell distribution width–standard deviation, white blood cell count, neutrophil count, lymphocyte count, neutrophils lymphocytes ratio, tumor location (skull base or nonskull base),[11] WHO classification, tumor size, preoperative hospitalization days, postoperative hospitalization days, surgery duration (h), bleeding volume during operation (mL), American Society of Anesthesiologists score, blood transfusion during operation, and subcutaneous drainage after operation.

Table 1. Patient characteristics.

Variables	n (%) or median (range)
Age	53 (18–87)
Sex	
Male	266 (28.4%)
Female	671 (71.6%)
Hypertension	
Yes	233 (24.9%)
No	704 (75.1%)
Diabetes mellitus	
Yes	107 (11.4%)
No	830 (88.6%)
Albumin level (mg/dL)	
<3.5	61 (6.5%)
≥ 3.5	876 (93.5%)
HGB (g/L)	132 (73–199)
RDW–SD (fL)	44.2 (13.3–73.9)
WBC (10^9/L)	5.80 (2.48–15.83)
Neutrophils (10^9/L)	3.34 (0.86–14.58)
Lymphocytes (10^9/L)	1.72 (0.45–7.85)
NLR	1.94 (0.52–27.51)
Tumor location	
Nonskull base	506 (54.0%)
Skull base	431 (46.0%)
WHO grade	
I	823 (87.8%)
II	102 (10.9%)
III	12 (1.3%)
Tumor size (cm)	
≤ 3	323 (34.5%)
>3	614 (65.5%)

Non-normally distributed numerical variables are represented as median and range.
HGB: hemoglobin; RDW–SD: red blood cell distribution width–standard deviation; WBC: white blood cell; NLR: neutrophils lymphocytes ratio; WHO: World Health Organization.
Nonskull base: falx/parasagittal, convexity, cerebellar convexity, and intraventricular.
Skull base: middle fossa, cerebellopontine angle, olfactory groove/planum shenoidale, foramen magnum, orbital/anterior clinoid, tentorium, and tuberculum sellae, petroclival, sphenoid wing, parasellar/cavernous sinus.

Treatment strategy

All patients underwent craniotomy and meningioma resection under a microscope. During the operation, electrophysiological

Table 2. Univariate analysis of the association between each risk factor and postoperative meningitis.

	Postoperative meningitis		
	n (%) or median (IQR)		
Variables	Yes (n = 47)	No (n = 890)	p-value
Age	54 (46–62)	53 (46–62)	0.793[a]
Sex			0.909[b]
Male	13 (4.9%)	253 (95.1%)	
Female	34 (5.1%)	637 (94.9%)	
Hypertension			0.423[b]
Yes	14 (6.0%)	219 (94.0%)	
No	33 (4.7%)	671 (95.3%)	
Diabetes mellitus			0.863[b]
Yes	5 (4.7%)	102 (95.3%)	
No	42 (5.1%)	788 (94.9%)	
Albumin level (mg/dL)			0.017[b]
$<$3.5	7 (11.5%)	54 (88.5%)	
$\geq$3.5	40 (4.6%)	836 (95.4%)	
HGB (g/L)	132 (122–140)	132 (123–142)	0.450[a]
RDW–SD (fL)	44.0 (41.3–46.5)	44.2 (41.9–46.6)	0.742[a]
WBC (10^9/L)	6.15 (4.53–7.46)	5.775 (4.80–6.92)	0.626[a]
Neutrophils (10^9/L)	3.42 (2.60–4.77)	3.335 (2.69–4.22)	0.681[a]
Lymphocytes (10^9/L)	1.76 (1.37–2.07)	1.72 (1.38–2.09)	0.904[a]
NLR	1.93 (1.62–2.43)	1.93 (1.48–2.62)	0.815[a]
Preoperative hospitalization (days)	4 (2–6)	3 (2–6)	0.034[a]
Postoperative hospitalization (days)	14 (11–23)	6 (5–8)	$<$0.001[a]
Tumor location			$<$0.001[b]
Nonskull base	11 (2.2%)	495 (97.8%)	
Skull base	36 (8.4%)	395 (91.6%)	
Tumor size (cm)			0.705[b]
$\leq$3	15 (4.6%)	308 (95.4%)	
$>$3	32 (5.2%)	582 (94.8%)	
WHO grade			0.557[b]
I	40 (4.9%)	783 (95.1%)	
II/III	7 (6.1%)	107 (93.9)	
Surgery duration (h)			$<$0.001[b]
$\leq$3	8 (2.0%)	401 (98.0%)	
$>$3	39 (7.4%)	489 (92.6%)	
Bleeding volume during operation (mL)			$<$0.001[b]
$\geq$400	17 (11.1%)	136 (88.9%)	
$<$400	30 (3.8%)	754 (96.2%)	
ASA score			0.511[b]
0–1	24 (4.6%)	498 (95.4%)	
3–6	23 (5.5%)	392 (94.5%)	
Blood transfusion during the operation			0.148[b]
Yes	8 (8.0%)	92 (92.0%)	
No	39 (4.7%)	798 (95.3%)	
Subcutaneous drainage after operation			0.068[b]
Present	37 (5.9%)	586 (94.1%)	
Absent	10 (3.2%)	304 (96.8%)	

Non-normally distributed numerical variables are represented as median and interquartile range (IQR).
[a]Wilcoxon–Mann–Whitney test; [b]chi-square test.
ASA: American Society of Anesthesiologists; HGB: hemoglobin; RDW–SD: red blood cell distribution width–standard deviation; WBC: white blood cell; NLR: neutrophils lymphocytes ratio; WHO: World Health Organization.

monitoring was performed, prophylactic antibiotics and glucocorticoids were administered, and glucocorticoids were continued until 3 days after the operation.

Definition of POM

The diagnostic criteria for POM were according to the Centers for Disease Control.[12] Patients were required to meet at least one of the following criteria for the diagnosis of meningitis: (a) organisms cultured from cerebrospinal fluid (CSF) and (b) patients exhibiting at least one of the following signs or symptoms with no other recognized cause (fever (>38°C), headache, stiff neck, meningeal signs, cranial nerve signs, or irritability) as well as meeting at least one of the following criteria ((a) increased white cells, elevated protein, and/or decreased glucose in CSF; (b) organisms detected on Gram staining of CSF sample; (c) organisms cultured from blood; (d) positive antigen test of CSF, blood, or urine; (e) diagnostic single antibody titer (IgM); or (f) 4-fold increase in paired sera (IgG) for pathogens).[2] These data were obtained from CSF samples collected by lumbar puncture or lumbar cistern drainage.

Statistical analysis

Patients were divided into meningitis and nonmeningitis groups according to whether meningitis was complicated after surgery, and the basic data collected from patients were classified into categorical and continuous distributions. The chi-square test was used for categorical variables. For continuous variables, the Kolmogorov–Smirnov test was used to identify whether they conformed to the normal distribution. Continuous variables with non-normal distribution were represented by median and interquartile range (IQR) and were analyzed using Wilcoxon–Mann–Whitney test. The risk factors for univariate analysis were screened with a p-value <0.05 as the test level. Significant factors in the univariate analysis were used as covariates in the multivariate analysis, which was performed using a logistic regression model. Wilcoxon–Mann–Whitney test was used to analyze the relationship between POM and postoperative hospital stay. In this analysis, all statistical tests were two-sided, and all statistical analyses were performed using Statistical Products and Services Solution (SPSS) software version 25.0. A p-value of <0.05 was considered to indicate statistical significance. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[13]

Results

Baseline characteristics and clinical features of POM

A total of 937 patients were enrolled in this study, including 266 (28.4%) men and 671 (71.6%) women. The mean age of the patients was 53 (range: 18–87) years. Table 1 shows the basic patient information and preoperative data of hematological biochemical markers. A total of 823 (87.8%) meningiomas were WHO grade I, 10.9% were grade II, and 1.3% were grade III (Table 1). Overall, 47 (5%) patients developed POM, and none of the deaths were related to meningitis.

Risk factors for POM

Univariate analysis (Table 2) revealed that albumin level (<3.5 mg/dL; $p = 0.017$), preoperative hospitalization (median: 4 days; IQR: 2–6 days; $p = 0.034$), tumor location (skull base; $p < 0.001$), surgery duration (>3 h; $p < 0.001$), and bleeding volume during operation (≥400 mL; $p < 0.001$) were significantly associated with POM. Moreover, according to multivariate

Table 3. Multivariate analysis of risk factors associated with POM.

Variable	Odds ratio (95% CI)	p-value
Albumin level (<3.5 mg/dL)	2.194 (0.901–5.343)	0.084
Preoperative hospitalization (days)	0.998 (0.899–1.108)	0.965
Tumor location (skull base)	2.914 (1.395–6.091)	0.004
Surgery duration (>3 h)	3.024 (1.370–6.674)	0.006
Bleeding volume during operation (≥400 mL)	2.057 (1.056–4.006)	0.034

CI: confidence interval; POM: postoperative meningitis.

analysis (Tables 2, 3), tumor location (skull base; $p = 0.004$; OR = 2.914; 95% CI: 1.395–6.091), surgery duration > 3 h ($p = 0.006$; OR = 3.024; 95% CI: 1.370–6.674), and bleeding volume during operation ≥400 mL ($p = 0.034$; OR = 2.057; 95% CI: 1.056–4.006) were independent risk factors for POM.

Association between POM and postoperative hospitalization

There were differences in the length of postoperative hospital stays between the POM and non-POM groups. The median length of postoperative hospitalization for the POM group was 14 days, whereas that for the non-POM group was 6 days.

Pathogens of POM

In this study, CSF samples from 47 patients with POM were examined. All samples cultured for 3 days were negative for bacterial and fungal infections

Discussion

POM can have serious adverse effects on patients' recovery, such as prolonged hospital stay, increased medical burden, and unplanned re-operation.[6,8,9,14–16] In this study, POM significantly prolonged the length of postoperative hospital stay, which is consistent with previous studies.[6,8,9,14–16] Several studies[7–10,14–16] have reported risk factors for meningitis following neurosurgery. However, only a few studies have examined risk factors related to POM after the excision of meningioma.

Meningitis can be divided into aseptic and bacterial types. Previous studies[16–21] have reported a positive CSF culture rate of 0.0%–42.7% in patients with intracranial infection postcraniotomy. However, no bacteria were found in the CSF cultures of patients with meningitis in this study, which may be due to the intraoperative prophylactic administration of antibiotics. In addition, a previous study[18] showed that the positive culture rate significantly decreased after antibiotics therapy for more than 24 h prior to the acquisition of CSF specimens. This increases the difficulty of differentiating postoperative bacterial meningitis from aseptic meningitis.[19] Gupta et al.[22] revealed that appropriate perioperative antibiotic prevention can reduce the incidence of aseptic meningitis. These findings support the possibility that aseptic encephalitis (AM) is a low-grade bacterial encephalitis (BM) caused by staph infection.[22] A survey found significant differences in the use of antibiotics during and after surgery among surgeons performing skull base surgery.[23] According to Wang et al.,[24] elevated body temperature and notable anomalies in CSF cultures in the early postoperative period should not be considered to indicate the need for enhanced antibiotic therapy; instead, craniotomy should be performed with conventional perioperative antibiotic prophylaxis.

In this study, POM was observed in 5% of cases, while the reported incidence of this complication after craniotomy was 1.4%–8.3% in the literature, which might be attributed to different inclusion criteria and diagnostic criteria for meningitis among various studies.[6,8,9,14]

In the present study, tumor location (skull base) was identified as an independent risk factor for POM following meningioma excision. Exposure of the frontal sinus or mastoid air cells during surgery for some tumors located at the cranial base might partly explain the association between tumor location and POM. Zuo et al.[25] reported that tumors at the skull base are a risk factor for postoperative pneumonia. In addition, Shi et al.[26] proposed that the anatomical location of the tumor significantly affects postcraniotomy intracranial infection. Moreover, a previous study suggested that patients with supratentorial and intraventricular tumors are more prone to postcraniotomy intracranial infection.[26]

In the present study, surgery duration (>3 h) was identified as an independent risk factor for POM following resection of meningioma, which was consistent with previous reports.[17,26,27] Shi et al.[26] identified the duration of craniotomy (>7 h) as an independent risk factor for postcraniotomy intracranial infection. Moreover, Patir et al.[27] reported that surgical duration (>4 h) was significantly associated with higher postoperative neurosurgical infection rates. Zhan et al.[17] revealed that surgery duration was an independent risk factor for postoperative central nervous system infection. With the extension of the operation time, there is a greater chance for external bacteria to enter the skull, leading to contamination of the operation area.[16] Golebiowski et al.[28] suggested that contracting the meninges and soft tissues for surgical exposure might lead to reduced perfusion and a time-dependent reduction in local immune defense.

In addition, anesthesia might affect the number and activity of immune cells in the blood as well as the secretion of cytokines.[29] With the prolonged anesthesia time, the immune function of patients can be inhibited during surgery.

Our study also revealed that bleeding volume during operation significantly affected the occurrence of POM following resection of meningioma. Huang et al.[16] reported that an intraoperative bleeding volume of >400 mL increases the risk of POM after the removal of vestibular schwannoma by 2.551 times. The loss of immunoreactive substances in the blood could result in decreased immunity, which might increase the incidence of POM. Furthermore, blood transfusion is often required when the intraoperative blood loss volume is high, which may complicate immune suppression.[30]

Some measures should be considered during surgery to prevent POM. Rinsing with hydrogen peroxide or iodophor is necessary if the frontal sinus or mastoid air cells are exposed during surgery. Hooda et al.[31] noted that preoperative administration of tranexamic acid could significantly reduce intraoperative blood loss in patients with meningioma. A recent study indicated that tranexamic acid can reduce the postoperative infection rate, regardless of blood loss reduction.[32] Ishihara et al.[33] showed that preoperative embolization of meningioma could reduce intraoperative blood loss. Rigorous surgical technique is the most crucial approach to reduce intraoperative bleeding volume and avoid unnecessary prolongation of operative duration. Although several risk factors for POM after the resection of meningioma have been identified, the aseptic technique remains the most important approach to prevent POM.

The present study had some limitations. We failed to detect positive bacterial cultures among patients with meningitis; thus, we could not analyze the distribution of meningitis bacteria.

Conclusion

Tumor location (skull base), surgery duration (>3 h), and bleeding volume during operation (≥400 mL) are independent risk factors for POM following the resection of meningioma. These findings may help the surgical team to identify patients at high risk of POM. Meanwhile, POM was significantly associated with increased length of postoperative hospital stay.

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Author contributions

Yong Gu and Xiaodong Long designed the study and submitted the manuscript. Yuekang Zhang, Mengfei Zeng, and Yangyun Han collected and analyzed the data. Yong Gu drafted the article. Xiaodong Long and Yangyun Han supervised the study. All authors read the final version of the manuscript and approved it for publication.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Disclosures

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