



Research article

Risk factors for postoperative pneumonia in patients with posterior fossa meningioma after microsurgery



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ABSTRACT

Objectives: Postoperative pneumonia (POP) is one of the common complications associated with mortality and morbidity. Even so, it has received little intensive research after microsurgical removal for posterior fossa meningioma (PFM). In this study, we aimed to identify perioperative factors for POP after PFM microsurgery to risk-stratify patients and improve clinical outcomes.

Patients and methods: We retrospectively review on all patients who underwent microsurgical resection ($n = 321$) for PFM from January 2016 to December 2018. To identify the risk factors for POP, we performed univariate and multivariate analyses successively.

Results: 44 (13.7%) patients were diagnosed as POP. In accordance with univariate analysis, postoperative Glasgow Coma Scale (GCS) score (<13 ; $p < 0.001$), tumor size ($\geq 3\text{cm}$; $p < 0.001$), procedure duration ($\geq 3\text{ h}$; $p < 0.001$), tumor located in anterior or lateral of brainstem ($p < 0.001$), estimated blood loss (EBL; $> 1000\text{ml}$; $p = 0.001$) and brainstem shift ($p < 0.001$) were associated with POP. By multivariate analysis, the first four were independent risk factors for POP. The study also revealed that POP brought about extended duration of postoperative hospitalization.

Conclusion: The incidence of POP following PFM microsurgery was significantly high (13.7%). Apart from tumor size ($\geq 3\text{cm}$) and procedure duration ($\geq 3\text{ h}$), GCS score (<13) and tumor located in anterior or lateral of brainstem were independent risk factors for POP. Efforts to reduce the duration of surgery, especially among the large tumors located in anterior or lateral of brainstem, may reduce POP rate and hospitalization stay.

1. Introduction

Meningioma is a common tumor in the central nervous system. Approximately 10% of intracranial meningiomas occur in the posterior fossa [1, 2]. These tumors usually are involved in adjacent structures, including the cranial nerves, brainstem, and basilar artery [3, 4, 5]. Although specially anatomical locations determine that microsurgery is challenging, it is one of the elementary standard options for the treatment of PFM because of its effectiveness at present [6]. The incidence of postoperative complications is considerable despite of rapid improvements in surgical techniques and intraoperative monitoring in the past decades. Postoperative pneumonia (POP) remains one of the most common complications after surgery [7]. Compared with other postoperative complications, POP, although it is well known, receives rare attention and few studies have investigated which perioperative factors are explanatory risk factors for POP following PFM microsurgery.

It has been reported that POP can observably increase hospitalization stay and costs, and even increase the risk of asthma, bronchiectasis and chronic obstructive pulmonary disease in future [8, 9]. The incidence of POP can be availably decreased by multidisciplinary team efforts, including oral care and respiratory rehabilitation programs [10, 11]. In consideration of well-being and decreasing the costs of patients, it is imperative to identify risk factors so that we can prevent patients from POP as far as possible. In our study, we retrospectively analyzed the risk factors related to POP after PFM microsurgical resection in our medical institution.

2. Materials and methods

2.1. Patient population and diagnostic criteria of POP

We screened all patients ($n = 321$) with postoperatively pathological diagnosis of meningioma from all patients with lesions located in the

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posterior fossa at West China Hospital of Sichuan University from January 2016 to December 2018. Patients who survived less than 2 days postoperatively or developed pulmonary infection preoperatively were excluded. All extracts of perioperative information of PFM patients were from the medical records. The study was approved by biological and medical ethics committee of West China hospital.

POP was defined as an acute infection of unilateral or bilateral lungs following an operation. Patients were diagnosed as having POP (Figure 1) if the chest imaging examination (X-ray or CT) revealed new or progressive infiltration (atelectasis or vasogenic edema were excluded) and at least one of the following criteria were fulfilled: (1) new and/or progressive symptoms, including coughing, expectoration, fever or hypothermia no other recognized cause and presence of positive laboratory findings (e.g. elevation of C-reactive protein, serum procalcitonin, and leukocyte count); (2) auscultation examination founding lung consolidation signs and/or moist rale; (3) pathogen isolation from blood, sputum, transbronchial lavage, transbronchial brushes; (4) pneumonia was proven histopathologically [12, 13].

2.2. Data collection

The following information of the patients was collected: sex, age, absence of diabetes mellitus or not, smoking history (ever or never), history of hypertension, body mass index (BMI), preoperative serum albumin, neutrophil lymphocyte ratio (NLR), hemoglobin concentration, preoperative chest radiology, size of tumor, positional relationship between tumor and brainstem, hydrocephalus, presence/absence of brainstem shift (defined as the brainstem midline shift), history of microsurgery resection and stereotactic radiosurgery for PFM, the duration of preoperative hospitalization, procedure duration, and estimated

blood loss (EBL), pathological grade of tumor, postoperative minimum GCS score before diagnosis as pulmonary infection. Size of tumor was calculated as the tumor equivalent diameter $(D1 \times D2 \times D3)^{1/3}$ in T1 weighted magnetic resonance imaging (MRI) with gadolinium in axial. Preoperative chest radiography revealed any positive pulmonary manifestations, including nodular opacities, pulmonary bullous and emphysema and/or chronic bronchitis, which was categorized as an abnormality, and the rest were categorized as normality. We also extracted postoperative information, such as the absence of POP or not, pathogens of POP and the duration of postoperative hospitalization.

2.3. Positional relationship between tumor and brainstem (meningioma location)

According to the positional relationship between tumor and brainstem in sagittal view of MRI, we classified PFM into three groups: ① anterior brainstem PFM; ② lateral brainstem PFM; ③ posterior brainstem PFM. Anterior brainstem PFM included petroclival meningioma, clivus meningioma, ventral foramen magnum meningioma, pineal meningioma was also included in anterior brainstem PFM because of similar postoperative outcomes; lateral brainstem PFM included cerebellopontine angle meningioma, jugular foramen meningioma; posterior brainstem PFM included other tentorial meningioma, torcular herophili meningioma, dorsal foramen magnum meningioma, cerebellum convex meningioma.

2.4. Perioperative management

All patients received prophylactic antibiotic management half an hour before skin incision. The antibiotic used for prevention was

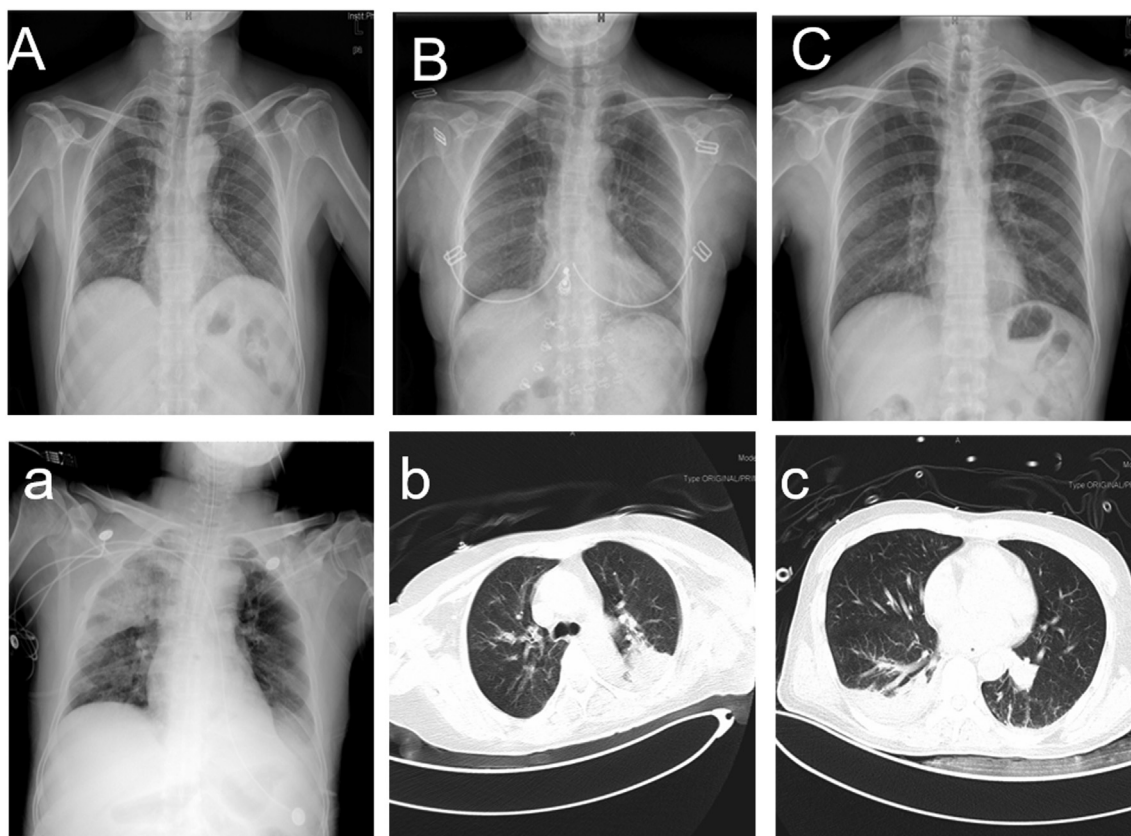


Figure 1. The first row of digital X-ray chest radiographs shows normal lung images of three patients before neurosurgeries (A, B, C). The second row is the post-operative chest images of the corresponding patients. On the 5th day after the operation, multiple flaky shadows were seen on the anterior X-ray chest radiograph of both lungs, and the right lung was more obvious (a). Chest CTs showed the lung consolidation of the left upper lobe (b) and the right upper lobe (c), with pleural effusion.

cefazolin or clindamycin if patients were allergic to cefazolin. All patients was given a dose (40mg) of methylprednisolone within 1 h before surgery to reduce intracranial pressure. One dose of methylprednisolone was used daily for 7–10 days after operation. For each patient, depending on tumor size, tumor location and surgeon's experience, surgical approaches were individually selected to expose and remove the tumors. During tumor resection, patients were in intraoperative neurophysiological monitoring. Eighty-one percent of the operations were performed by two experienced professors (prof. Zhang and prof. Hui). All patients diagnosed with postoperative pneumonia were given empiric antibiotics firstly, and the medication was adjusted according to sputum culture results and therapeutic effect.

2.5. Statistical analysis

Continuous variables (age, NRL) were analyzed by the Wilcoxon-Mann-Whitney test after tests of normality had not demonstrated the Gaussian distribution. Continuous data were expressed as the median and inter-quartile range (IQR). And we used the Pearson chi-squared test or Fisher's exact test to analyze the association between POP and other risk factors. Then we performed multivariate logistic regression analysis by selecting significant factors as covariates in the univariate analysis. Also, we used multivariable logistic regression to decide odds ratios (ORs) for predictors. Moreover, the Wilcoxon-Mann-Whitney test was done to analyze the association between POP and duration of postoperative hospitalization. All statistical analyses were carried out with the SPSS software, version 24.0. Difference was considered statistically significant if the two-sided p value of <0.05.

3. Results

3.1. Baseline characteristics

A total of 44 POP cases (13.7%) were noted in 321 patients following PFM resection in our study. The median age of patients was 52 (IQR 47–61) years. There were 211 females (65.7%) and 110 males (34.3%) with a female predomination. The median BMI was 23.53 (IQR 21.48–25.49) kg/m². 298 patients (92.8%) had WHO grade I tumor, 20 (6.2%) had WHO grade II tumor, and 3 (1.0%) had WHO grade III tumor. 29.6% of PFMs were identified as anterior brainstem PFMs, 29.0% lateral brainstem PFMs, and the rest posterior brainstem PFMs. 53 patients

(16.5%) presented with preoperative hydrocephalus and 121 patients (37.7%) with brainstem shift. We summarized general conditions of patients in Table 1. No patient died of POP in these 44 people. However, one of the patients with a ventral foramen magnum meningioma died of postoperative bleeding on the ninth postoperative day. Another patient with a large petroclival meningioma (d = 4.8cm) died of severe dysfunction of brainstem.

3.2. Risk factors for POP

In line with univariate analysis, there was an evidently association between POP and GCS score (<13; p < 0.001), tumor size (≥3cm; p < 0.001), procedure duration (≥3 h; p < 0.001), tumor located in anterior or lateral of brainstem (p < 0.001), EBL (>1000ml; p = 0.001) and brainstem shift (p < 0.001) (Table 2). Multivariate analysis was carried out to determine which factors were most predictive for POP and the eventual result showed that only tumor size (≥3cm; OR = 3.437, 95% CI: 1.225–9.644; p = 0.019), GCS score (<13; OR = 4.235, 95% CI: 1.314–13.647; p = 0.016), procedure duration (≥3 h; OR = 9.540, 95% CI: 2.153–42.271; p = 0.003), and tumor located in anterior or lateral of brainstem (OR = 7.122, 95% CI: 1.940–26.152; p = 0.003) were independent risk factors related to POP (Table 3).

3.3. Association between POP and duration of postoperative hospitalization

The two patients who died as previously mentioned was excluded when we researched the association between POP and duration of postoperative hospitalization. The median of postoperative hospitalization duration for patients who developed POP vs. those who did not develop POP was 10 (range 6–53) vs 6 (range 2–18) days, respectively (p < 0.001).

3.4. Pathogen

Among the 44 cases of POP, 26 cases (59.1%) were positive for sputum culture, among which the top three causative pathogens were Klebsiella pneumoniae (9 cases), Acinetobacter baumannii (6 cases), and Candida (2 cases).

Table 1. Patient demographics.

Variables	n (%) or median (IQR)
Age (years)	52 (47–61)
Sex	
Male	110 (34.3%)
Female	211 (65.7%)
Smoker	127 (39.6%)
BMI (kg/m ²)	23.53 (21.48–25.49)
Meningioma location	
Anterior brainstem PFM	95 (29.6%)
Lateral brainstem PFM	93 (29.0%)
Posterior brainstem PFM	133 (41.4%)
Pathological grade	
WHO grade I	298 (92.8%)
WHO grade II	20 (6.2%)
WHO grade III	3 (1.0%)
Tumor characteristics	
Size (≥3cm)	178 (55.5%)
Hydrocephalus	53 (16.5%)
Brainstem shift	121 (37.7%)

BMI, Body mass index, IQR, Interquartile range, WHO, World Health Organization, PFM, Posterior fossa meningioma.

Table 2. Univariate analysis of POP risk factors.

Variables	POP (n = 44)	No POP (n = 277)	P value
Sex			0.318 ^a
Male	18	92	
Female	26	185	
Age (years)	54 (IQR 47–64)	52 (IQR 46–60)	0.210 ^b
History of smoking			0.161 ^a
Yes	8	30	
No	36	247	
Diabetes mellitus			0.722 ^a
Yes	4	34	
No	40	243	
Chest Radiology			0.353 ^a
Abnormality	10	47	
Normality	34	230	
BMI (kg/m ²)			0.217 ^a
<18.5 or >28	7	27	
≥18.5 and ≤28	37	250	
Hypertensive disease			0.285 ^a
Yes	15	73	
No	29	204	
Albumin value (mg/dl)			0.529 ^a
<3.5	9	46	
≥3.5	35	231	
Anemia			0.545 ^a
Present	5	38	
Absent	39	239	
Neutrophil lymphocyte ratio	2 (IQR 1.7–2.8)	1.9 (IQR 1.4–2.5)	0.179 ^b
Tumor size (cm)			<0.001 ^a
≥3	38	140	
<3	6	137	
Meningioma location			<0.001 ^a
Anterior or Lateral brainstem PFM	41	147	
Posterior brainstem PFM	3	130	
Meningioma grade			0.397 ^a
WHO grade I	5	18	
WHO grade II, III	39	259	
Glasgow Coma Scale (GCS)			<0.001 ^a
<13	10	15	
≥13	34	262	
Hydrocephalus			0.103 ^a
Present	11	42	
Absent	33	235	
Brainstem shift			<0.001 ^a
Present	34	87	
Absent	10	190	
History of microsurgery for the tumor			0.827 ^a
Yes	4	19	
No	40	258	
Previous radiosurgery for the tumor			0.793 ^a
Yes	2	7	
No	42	270	
Estimated blood loss (ml)			0.001 ^a
≥1000	5	4	
<1000	39	273	
Procedure duration (hours)			<0.001 ^a
≥3	42	131	
<3	2	146	

BMI, Body mass index; IQR Interquartile range; POP, Postoperative pneumonia; PFM, Posterior fossa meningioma; WHO, World Health Organization.

^a Chi-square test.

^b Wilcoxon–Mann–Whitney test.

Table 3. Multivariate analysis of POP risk factors.

Variables	Odds ratio (95% CI)	p-value
Tumor size	3.437 (1.225–9.644)	0.019
Glasgow Coma Scale (<13)	4.235 (1.314–13.647)	0.016
Procedure duration (\geq 3h)	9.540 (2.153–42.271)	0.003
Tumor located in anterior or lateral brainstem	7.122 (1.940–26.152)	0.003
Estimated blood loss (\geq 1200ml)	1.319 (0.289–6.015)	0.721
Brainstem shift	2.013 (0.787–5.149)	0.144

CI, confidence interval; POP, Postoperative pneumonia.

4. Discussion

POP is a frequent postoperative complication, which is controllable and preventable at the same time [14]. Given that it can significantly increase hospitalization duration and costs [8], prevention of such complication is indispensable. However, there is little concentrated research on the risk factors of POP after PFM microsurgery until now. The main objective of this study was to determine independent risk factors for POP in patients with PFM after operations.

4.1. Incidence of POP

In our study of 321 PFM patients, the incidence of POP was 13.7%, which was similar to another previous study of our center [11]. In the reports of Michael et al. and Orin Bloch et al., the incidences of POP in meningiomas were about 1.3% [7, 15], which was obviously lower than ours. This inconformity could be attributed to the following several aspects. First, the subjects are not identical, that is, they included all patients with meningiomas, and ours are limited to posterior fossa meningiomas. From this perspective, our result was near to that of Cai et al. (7.1%), in which patients were diagnosed with infratentorial brain tumors [8]. Second, approximately 58.6% of the patients were diagnosed with PFMs located in front or lateral of the brainstem in our study. Hence, the majority of patients were high-risk patients with POP already in our study.

The above suggests that there may be a significant difference in the incidence of POP between supratentorial meningiomas and infratentorial meningiomas after surgery. However, further studies are necessary to confirm this hypothesis.

4.2. Risk factors for POP

As for procedure duration, the longer surgical duration, the higher the risk of postoperative vomiting, which may increase the rate of postoperative aspiration pneumonia in patients with posterior fossa lesions, especially those with postoperative coma and impaired swallowing function [16, 17, 18]. Furthermore, longer surgical duration also means longer intubation time, which can increase the risk of POP [8].

Concerning tumor size, it was considered to be one of the independent risk factors for POP [11]. Larger tumors usually mean longer operative times and more susceptible to damage to adjacent structures, including cranial nerves and brainstem. In clinical practice, tumor size is usually an important factor influencing a surgical decision. Our findings further underscore the importance of taking tumor size into account when considering surgical interventions.

Our analysis revealed that lower GCS score after operation was an independent risk factor for POP, which was consistent with the previous literature [19, 20]. On the one hand, this may be related to the inhibition of coma-induced gag reflexes leading to aspiration pneumonia. On the other hand, we usually perform mechanical ventilation on such patients, which may injure the airway and increase the possibility of ventilator-associated pneumonia [21, 22]. However, another literature suggests that the GCS score (<15) does not increase the incidence of

postoperative pneumonia [23]. The following two points may account for this inconformity. First, the research subjects are different. The posterior fossa meningioma is anatomically close to the brainstem and the posterior cranial nerve, which is prone to cause intraoperative damage resulting in impaired airway reflex. Second, different GCS segments may also be one of the reasons. Proper nursing care with continuous observation and, if necessary, gastric tube placement can help reduce the risk of aspiration [24].

Our study also showed that the tumor located in anterior or lateral of the brainstem increased the risk of POP. A study of 259 patients with petroclival meningiomas, which are located in front of or lateral of brainstem, had shown that the incidence of POP was significantly high [25]. Another prospective study of 800 patients focusing on factors influencing deferred extubation after infratentorial craniotomy suggested that tumor-induced brainstem shift may account for delayed extubation, which subsequently increased the risk of POP [8]. The particularity of tumor location increases the complexity of the surgical procedure, making the prolongation of the operation inevitable and increasing the risk of damaging these structures during operation. As a result, patients may subsequently develop complications such as disturbance of consciousness, dysphagia, aspiration and these postoperative complications can increase the incidence of POP, including postoperative ventilator-associated pneumonia due to re-tracheal intubation or delayed extubation [11, 26].

Taemin et al. reported EBL was an explanatory risk factor for POP in a series of 464 patients with meningioma after craniotomy, which was inconsistent with ours [15]. The discrepancy between our studies may be accounted for the following factors. First of all, inconsistent baselines of enrollment as before noted may lead to ultimately different outcomes. Second, different cutoffs of EBL may be one of the reasons. In addition, the difference in estimating EBL in practice may also play an important role in the inconsistency.

4.3. The relationship between POP and postoperative hospitalization

Our analysis also revealed that prolonged duration of postoperative hospitalization was in connection with POP after PFM removal, which was consistent with the former findings. In addition, more hospitalization costs were also related to the extension of hospitalization [8, 15].

This study has limitations. First, this was a retrospective study, which is limited by methodological bias. The variables assessed were limited to those available in the medical records. More prospective studies are needed to develop our findings. Second, as a single-center study, it has the disadvantages of selective bias and there are differences in the medical details, including surgical skills among different medical centers. Therefore, our findings require confirmations from other medical team studies with larger sample sizes and better research designs.

5. Conclusion

Compared with supratentorial meningioma, posterior fossa meningioma has a significantly higher incidence of POP. Apart from larger tumor and longer procedure duration, GCS score (<13) and tumor

located in anterior or lateral of brainstem were also recognized as the independent risk factors for POP after PFM microsurgery. Moreover, POP was in connection with a prolonged duration of postoperative hospitalization. Therefore, by identifying high-risk patients, shortening the duration of surgery may be beneficial for reducing the incidence of POP, especially in patients with large tumors located in anterior or lateral of brainstem.

Declarations

Author contribution statement

Y. Zhang: Conceived and designed the experiments.
 Y. Deng: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.
 C. Wang: Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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