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CLINICAL ARTICLE - BRAIN TUMORS

Surgical management of medium and large petroclival meningiomas: a single institution's experience of 199 cases with long-term follow-up

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Abstract
Background Petroclival meningiomas (PCMs) were once regarded as 'inoperable' due to their complex anatomy and limited surgical exposure. This study aimed to evaluate the long-term outcomes of surgically treated PCMs larger than 2 cm.
Methods A series of 199 consecutive patients (137 females, 68.8 %) with PCMs larger than 2 cm from between 1993 and 2003 were included. The clinical charts, radiographs, and follow-ups were evaluated.
Results Gross total resection (GTR) was achieved in 111 (55.8 %) patients, subtotal resection (STR) in 65, and partial resection (PR) in 23. Cranial nerve dysfunctions were the most common complications and occurred in 133 (66.8 %) cases. The surgical mortality was 2.0 %. The Karnofsky Performance Scale (KPS) scores significantly decreased 1 month after the operations (preoperative KPS = 76.8 and postoperative KPS = 64.8; $p = 0.011$, Paired-samples t test). Long-term follow-ups were obtained in 142 patients, the follow-up duration was 171.6 months, and the most recent KPS was 83.2. Permanent morbidities remained in 24 patients (18.9 %). Multivariate analysis revealed that brainstem edema and tumors larger than 4 cm in diameter were independent risk factors in terms of outcomes (KPS < 80). The recurrence/progression rates were 14.5, 31.8, and 53.3 % for the GTR, STR, and PR cases, respectively ($p = 0.002$, Pearson χ^2 test). Gamma Knife radiosurgery for the remnants exhibited good tumor control.
Conclusions Favorable outcomes and low mortality were achieved with the microsurgical management of medium and large PCMs; however, the rates of cranial nerves dysfunction remained high. Radically aggressive resection might not be judicious in terms of postoperative morbidity. The preoperative evaluations and intraoperative findings were informative regarding the outcomes. The low follow-up rate likely compromised our findings, and additional consecutive studies were required.

Keywords Meningioma · Microsurgery · Petroclival region · Radiosurgery · Skull base

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Introduction

Petroclival meningiomas (PCMs) are defined as tumors that arise from the zone anteromedial to the internal acoustic canal (IAC) and attach to the lateral sites along the petroclival borderline. PCMs were once regarded as 'inoperable' and were associated with high morbidity and mortality due to their complex anatomy and the difficulty of exposing the tumor. With the development of multiple techniques, the surgical management of PCMs has achieved vast advancements over the past decades. The mortality rate has decreased greatly to less than 3 %; however, surgical morbidity remains high [3, 10, 32, 42]. PCMs smaller than 2.5 cm account for approximately 20 % of all PCMs [32, 42, 46] and have been reported to have

favorable surgical outcomes [46, 56], but the medium-to-large counterparts are more challenging [29, 32, 42, 66]. While radiosurgery has become an increasingly important strategy, surgery remains critical for medium-to-large PCMs [3, 10, 14, 19, 22, 25, 26, 32, 42, 59, 61]. Due to the indolent biology and low growth rate of benign PCMs, the follow-up durations of previous studies have not been sufficient to define the lifelong outcome [42]. Moreover, the extent of surgical resection and outcome have been reported to be affected by factors that include tumor size, brainstem edema, and vital artery encasement, but these factors vary widely across previous studies, and no unanimous risk parameter has been identified to aid individual treatment or predict neurological decline [9, 29, 32, 59]. Therefore, the present study aimed to summarize a surgical experience and to evaluate the long-term outcomes of medium (>2 cm) and large PCMs at a single institution. Adverse factors that predict poor outcome are investigated to benefit clinical strategic decisions.

Patients and methods

Patient population and radiographs

The data of 199 consecutive cases with medium and large PCMs who underwent surgical management between June 1993 and May 2003, which were the first 10 years following the establishment of the skull base division of neurosurgery at our institute, were reviewed. Clinical charts, neuroimaging, operation records, and follow-up data were obtained. The neurological assessments included cranial nerve (CNs) dysfunction, hemiparesis, and Karnofsky Performance Scale (KPS) scores for the neurological status on admission, at 1 month after surgery, and at follow-up visits. The Beijing Tiantan Hospital Research Ethics Committee approved the study. At the most recent follow-up, the MOS 36-item short-form health survey (SF-36) was collected to evaluate quality of life, and the SF-36 was a standardized, self-reported evaluation [38, 69], which was independent of researchers.

Tumor size was sorted according to the maximal diameter. Peritumoral brainstem edema and the space between the tumor and brainstem were classified into three types (Fig. 1): type 1 referred to the appearance of space between the tumor and the brainstem with no peritumoral brainstem edema, type 2 referred to a lack of space but without peritumoral brainstem edema, and type 3 referred to a lack of space with peritumoral brainstem edema. The encasements of vital the arteries (i.e., the vertebral artery, basilar artery, internal cerebral artery, and posterior cerebral artery) were classified as no encasement, mild (involving several arteries), and severe (involving all arteries) encasement based on radiographs.

Surgical management and follow-up

The surgical approach selection was based on the tumor features, the patient's age and co-morbidities, and the surgeon's preference. The presigmoid approach was used in cases in which the tumor was low and limited to below the IAC with broad attachment to the posterior petrous surface and partial extension into the middle fossa. The subtemporal transtentorial approach was used when the tumor's lower limit was above and medial to the IAC. Extended middle fossa approaches (including zygoectomy and the transpetrosal approach) were used when the tumor extended anterior-superiorly to the sellar region and inferiorly to the mid-clivus. The retrosigmoid approach was used when broad attachment to the posterior petrosal surface without middle fossa invasion was present. In the early group of patients with tumors of the giant basement that reached the jugular foramen, the far lateral approach was used. However, the far lateral approach was replaced with the presigmoid approach in the later group.

Radical removal (Simpson grade I/II) was attempted in all patients except those presenting with en plaque growth pattern with wide dural attachment, invasion into other regions (i.e., intrasellar region and contralateral petrous apex), strong adhesion to neurovascular structures (i.e., brainstem, CNs, and vital arteries), obscure tumor boundary, and/or hard consistency, that usually would not guarantee one-stage radical removal. Surgical strategy was overdetermined and radical removal of those lesions might be counterbalanced by the risks of neurological deficits. The degree of tumor resection was assessed based on postoperative contrasted magnetic resonance imaging (MRI) scans that were independently conducted by two neuroradiologists (Figs. 2, 3, 4, and 5): gross total resection (GTR) (Simpson grade I/II); subtotal resection (STR) (Simpson grade III/IV, with 90–99 % excision of the lesion); and partial resection (PR) (Simpson grade IV, with below 90 % excision of the lesion). The follow-up data were obtained at clinic visits in the majority of cases, and questionnaires and phone calls were also used for some patients. Recurrence was defined as in situ regrowth of tumor after GTR (Simpson grade I/II); and progression was defined as regrowth of residual tumor after STR or PR (Simpson grade III/IV) that was identified if the increase of the maximal residual tumor diameter exceeded 2 mm. Recurrence and progression were identified based on contrast MRI, and we grouped them together (recurrence/progression, R/P) throughout the study rather than intentionally dividing them, because both were the endpoint events of the R/P-free survival analysis.

Statistical analysis

Statistical analysis was performed with SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Independent-samples t test and one-way ANOVA were used to compare KPS scores between variables. Pearson χ^2 test was used for the univariate

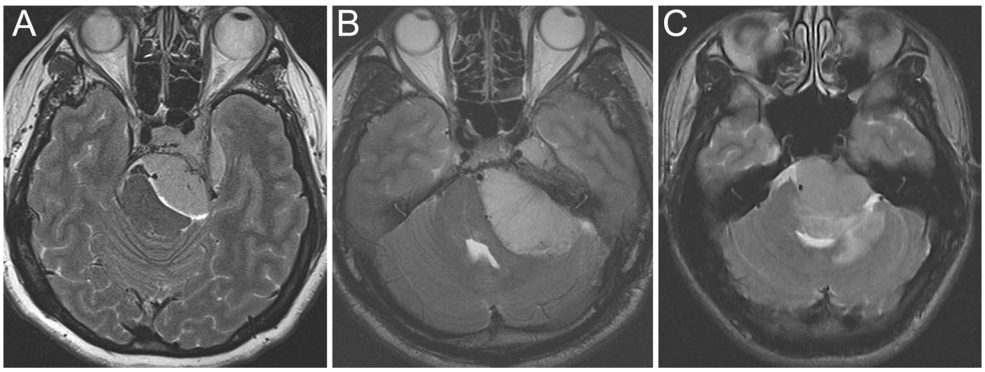


Fig. 1 Classification of the interface between the tumor and brainstem. Type 1 (**a**) refers to the appearance of space between the tumor and the brainstem without no peritumoral brainstem edema; type 2 (**b**) refers to the lack of a space but without peritumoral brainstem edema; type 3 (**c**) refers to a lack of space and the presence of peritumoral brainstem edema

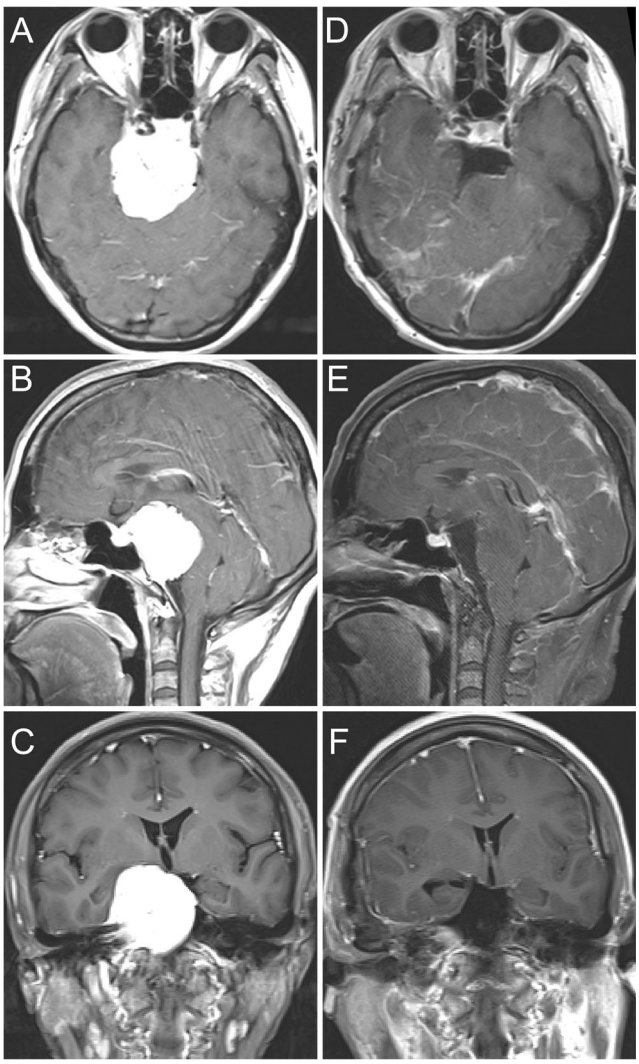


Fig. 2 Case illustration (case 1). A 44-year-old female presented with headache, facial numbness, ataxia, motor and walking deficits, and preoperative KPS score of 70. Preoperative axial (**a**), sagittal (**b**), and coronal (**c**) T1-weighted MRI scans with contrast enhancement revealed a right petroclival meningioma. The presigmoid approach was utilized. Postoperative axial (**d**), sagittal (**e**), and coronal (**f**) T1-weighted MRI scans with contrast enhancement indicated gross total resection. She suffered mild dysfunction of cranial nerves VI and VII but exhibited remarkable improvement during the follow-up duration of 102 months. Her most recent KPS score was 90

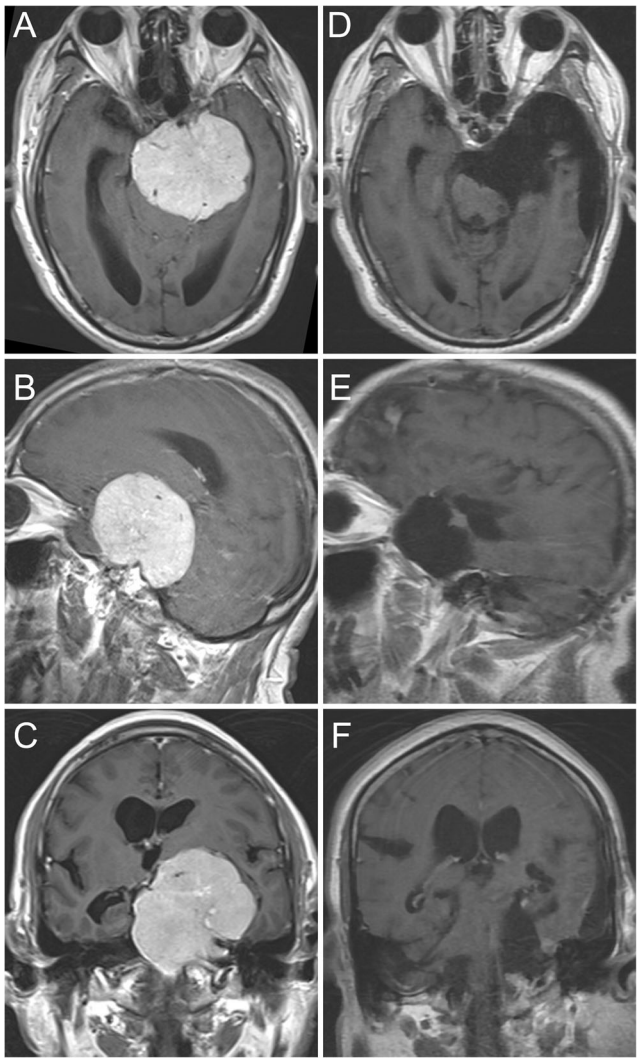


Fig. 3 Case illustration (case 2). A 64-year-old male presented with headache, vertigo, deficits in cranial nerves VIII-X deficits, and a preoperative KPS score of 80. Preoperative axial (**a**), sagittal (**b**), and coronal (**c**) T1-weighted MRI scans with contrast enhancement revealed a huge left petroclival meningioma. An extended middle fossa approach was utilized, and complete resection was achieved as indicated on the postoperative axial (**d**), sagittal (**e**), and coronal (**f**) T1-weighted MRI scans. He experienced severe surgical morbidities that required tracheotomy and mechanical ventilation. The immediate postoperative KPS score was 30 and improved to 70 at a recent evaluation. He currently lives independently and has not experienced recurrence

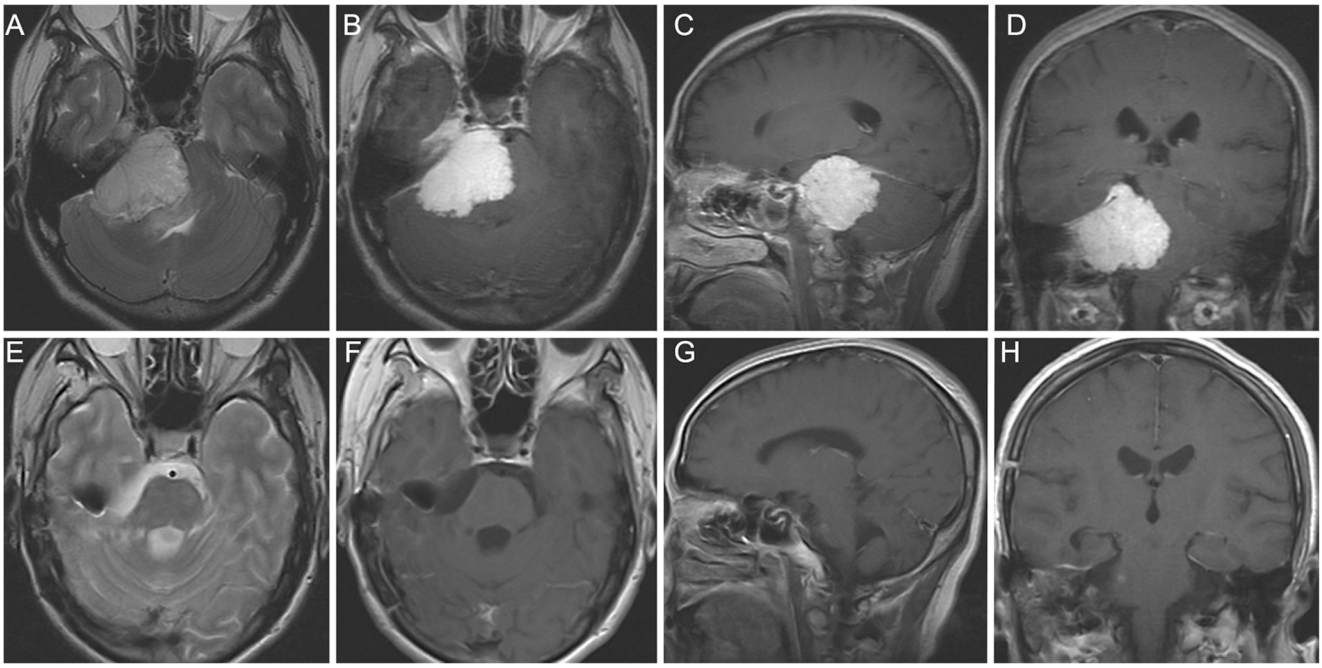


Fig. 4 Case illustration (case 3). A 44-year-old female presented with motor deficits, abnormal gait, and ataxia for 36 months. The preoperative KPS score was 60. Preoperative axial T2-weighted (**a**), axial (**b**), sagittal (**c**), and coronal (**d**) T1-weighted MRI scans detected a right petroclival meningioma. She underwent surgery with the presigmoid approach and experienced complications of palsy in cranial nerves V, VI, and VII that improved during the postoperative period. Postoperative axial T2-weighted (**e**), axial (**f**), sagittal (**g**), and coronal (**h**) T1-weighted MRI scans revealed the complete removal of the lesion. At a recent evaluation, she participated in normal activities and had a KPS score of 90

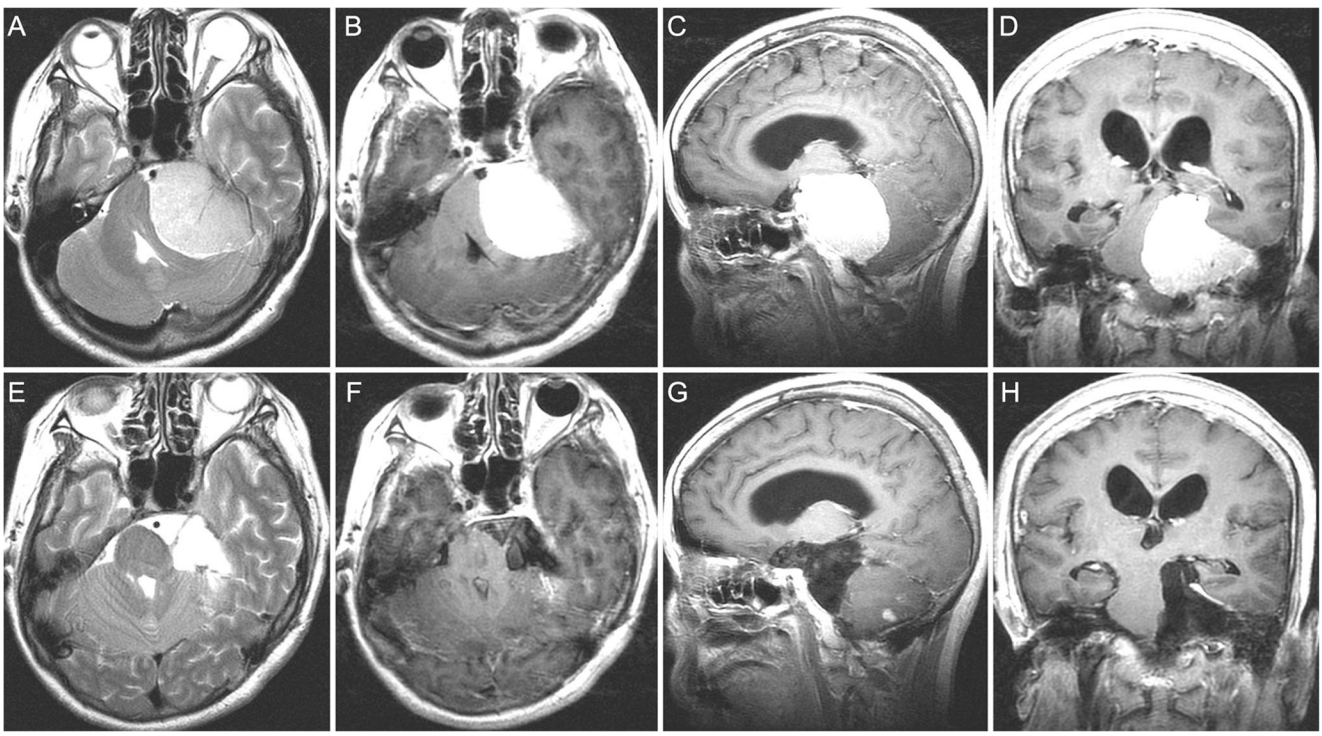


Fig. 5 Case illustration (case 4). A 56-year-old female presented with facial numbness and palsy, abnormal gait, ataxia, and lower cranial nerve deficits for 24 months. Preoperative axial T2-weighted (**a**), axial (**b**), sagittal (**c**), and coronal (**d**) T1-weighted MRI scans revealed a left petroclival meningioma. She had a preoperative KPS of 60 and underwent surgery with the presigmoid approach to remove the lesion. Removal was confirmed by postoperative MRI scans (**e**–**h**). She underwent postoperative radiotherapy and lived independently with a KPS score of 80

analysis of each potential outcome variable. Paired-samples *t* test was used to compare pre- and post-operative KPS scores. Adverse predictors for poor outcome (KPS < 80) were evaluated by multivariate binary logistic regression analysis. Difference was considered significant when the error probability was less than 0.05.

Results

Patient demographics and lesion features

The series enrolled 62 males (31.2 %) and 137 females (68.8 %) with an average age of 46.3 years (range, 15–68 years). Twenty-five (12.6 %) cases had prior surgeries or radiosurgery. Preoperatively, 135 (68 %) cases developed neurological deficits, including cranial nerve (CNs) dysfunction in 115 cases (58 %) and hemiparesis in 42 cases (21 %; Table 1). The mean preoperative KPS was 76.8 (Tables 2 and 3). The presigmoid approach ($n = 108$, 54.3 %) was predominant followed by the subtemporal transtentorial ($n = 36$, 18.1 %), retrosigmoid ($n = 23$, 11.6 %), and extended middle fossa ($n = 20$, 10.1 %), and far lateral approaches ($n = 12$, 6.0 %).

Medium (2–4 cm), large (4–6 cm), and giant (>6 cm) PCMs were present in 35, 133, and 31 patients, respectively. The mean lesion size was 4.7 cm. Data regarding peritumoral brainstem edema and vital artery encasement are detailed in Table 4. Fifty-five cases (27.6 %) developed cavernous sinus invasion. The tumor consistencies were soft (suckable) in 43 (21.6 %) cases and firm (unsuckable) in 156 cases (78.4 %), and 31 (16 %) of the tumors in the latter group were very tough. The pathology subtypes included meningiothelial ($n = 136$), transitional ($n = 38$), fibrous ($n = 17$), and angiomatous ($n = 8$), all of which were WHO grade I.

Table 1 Preoperative symptoms and surgical morbidity

Deficits	Preoperative (%)	Surgical morbidity at 1 month (%)	Permanent surgical morbidity
Overall	199	199	127
No. of patients with deficits	115 (57.8)	133 (66.8)	24 (18.9)
CN II	7 (3.5)	3 (1.5)	0
CN III	24 (12.1)	33 (16.6)	11 (8.7)
CN IV	5 (2.5)	30 (15.1)	9 (7.1)
CN VI	12 (6.0)	25 (12.6)	10 (7.9)
Oculomotor deficit	30 (15.1)	42 (21.1)	15 (11.8)
CN V	–	–	–
Facial numbness	40 (20.1)	36 (18.1)	4 (3.1)
Weak corneal reflex	55 (27.6)	61 (30.7)	6 (5.5)
CN VII	15 (7.5)	27 (13.6)	5 (3.9)
CN VIII	20 (10.1)	10 (5.0)	2 (1.6)
CN IX–XII	14 (7.0)	12 (6.0)	1 (0.8)
Hemiparesis	42 (21.1)	46 (23.1)	7 (5.5)
Ataxia	54 (27.1)	59 (29.6)	8 (6.3)
Aphasia	0	7 (3.5)	2 (1.6)
Hydrocephalus	19 (9.5)	7 (3.5)	0
Subdural hydroma	–	5 (2.5)	0
Intracranial infection	–	5 (2.5)	0
Intracranial hematoma	–	1 (0.5)	0
Severe brain swelling	–	4 (2.0)	0
Subcutaneous FC	–	10 (5.0)	0
Symptomatic DVT	–	2 (1.0)	0
GI hemorrhage	–	6 (3.0)	0
Tracheotomy	–	28 (14.1)	0
Pneumonia	–	7 (3.5)	0
Surgical site infection	–	3 (1.5)	0

CN cranial nerves, *DVT* deep venous thrombosis, *FC* fluid collection, *GI* gastrointestinal

Table 2 Pre- and postoperative KPS scores

	Preoperative (%)	At 1 month after surgery (%)	At recent follow-up (%)	*p* value
No. of patients	199	199	127	
Mean of KPS score	76.8	64.8	83.2	
No. of patients with KPS of 80–100	91 (45.7)	80 (40.2)	78 (61.4)	0.001*
No. of patients with KPS of 50–70	107 (53.8)	109 (54.8)	48 (37.8)	
No. of patients with KPS of 0–40	1 (0.5)	10 (5.0)	1 (0.8)	

*$p < 0.05$ and Pearson χ^2 test

Surgical mortality and morbidity

Four patients (2.0 %) died due to surgical mortality (GTR, $n = 1$; STR, $n = 2$; and PR, $n = 1$). One died from a brainstem injury, one died due to meningitis following cerebrospinal fluid (CSF) leakage, one died due to severe pneumonia and gastrointestinal hemorrhage, and the last patient died due to respiratory failure. The morbidities at 1 month after the operations are listed in Table 1. CNs dysfunctions were the most common complication ($n = 133$, 66.8 %) and were notable immediately after the operation. These dysfunctions included the oculomotor nerves (CNs III, IV, and VI) in 42, the facial nerve in 27, the trigeminal nerve in 36, hearing dysfunction in ten, lower CNs deficits in 12, hemiparesis in 46, and ataxia in 59 patients. CSF leakage occurred in four cases, one of whom required a repair operation, two recovered following lumber drainage, and the leakage in one patient led to lethal intracranial meningitis. Tracheotomies were performed in 28 cases due to of postoperative unconsciousness or gagging and swallowing dysfunction. Additional complications included subcutaneous fluid collection ($n = 10$), hydrocephalus ($n = 7$), and aphasia ($n = 7$), et al. and are detailed in Table 1. Removal of the bone flap was performed in four cases due to postoperative refractory brain swelling. Permanent morbidities remained in 24 patients (18.9 %) and included hemiparesis ($n = 7$), ataxia ($n = 8$), oculomotor deficit ($n = 15$), facial numbness ($n = 4$), and facial palsy ($n = 5$) (Table 1).

Surgical outcomes

GTR was achieved in 111 (55.8 %) cases, STR in 65 cases (32.7 %), and PR in 23 cases (11.6 %). The reasons for the non-total resections included disappearance of the dissection plane, infiltration of the CNs, brainstem, or vessels, and the tumor characteristics (i.e., a hard consistency or extensive regional involvement). At 1 month after surgery in all patients, the KPS scores significantly decreased (mean of 64.8, $p = 0.011$, paired-samples *t* test) due to surgical morbidities (Tables 2 and 3).

At the most recent evaluation, complete long-term follow-up data were available for 142 (71.4 %) cases with an average follow-up duration of 171.6 months (123.6–242.4 months). The total mortality (including four surgical mortalities) at 1 month, 5, 10, 15, and 20 years was 4, 4, 4, 16, and 20 patients, respectively, including eight patients dying of old age, seven patients dying of unrelated disease (heart disease in three patients, hypertensive intracerebral hematoma in one, kidney failure in one, ovarian cancer in one, and breast cancer in one), and one patient died of R/P years after surgery. The cumulative mortality rate at 1 month, 5, 10, 15, and 20 years was 3, 3, 3, 14, and 29 %, respectively (life-table statistics) (Fig. 6). In the remaining 127 cases, the KPS scores also decreased significantly 1 month after surgery but then recovered during the follow-up (recent KPS of 83.2, $p = 0.008$, paired-samples *t* test). Although a higher mean KPS was

Table 3 Clinical data categorized by preoperative KPS score

Preop KPS score	Overall	Group I: < 70	Group II: 70	Group III: 80–100	*p*
No. of patients	199	17	91	91	
Mean of preop KPS	76.8	54.7	70.0	87.7	0.012*†
Mean of postop KPS	64.8	42.9	60.8	73.0	0.016*†
GTR and STR (%)	162 (81.4)	11 (64.7)	75 (82.4)	76 (83.5)	0.177‡
Postop CNs deficits (%)	133 (66.8)	16 (94.1)	60 (65.9)	57 (62.6)	0.039*
Postop hemiparesis (%)	46 (23.1)	11 (64.7)	24 (26.4)	11 (12.1)	<0.001*‡

CNs cranial nerves, *GTR* gross total resection, *postop* postoperative, *preop* preoperative, *STR* subtotal resection

*$p < 0.05$

† One-way ANOVA

‡ Pearson χ^2 test

Table 4 Predictors of KPS score at 1 month after surgery

Variables	No. of patients	Mean of KPS	*p*
Surgery/RT history			0.012*†
No	174 (87.4)	66.1	
Yes	25 (12.6)	56.0	
Age, yrs			0.011*†
<60	171 (85.9)	66.6	
≥60	28 (14.1)	53.9	
Preoperative CNs deficits			0.030*†
Yes	115 (57.8)	60.3	
No	84 (42.2)	71.0	
Tumor size, cm			0.023*‡
2–<4	35 (17.6)	77.1	
4–<6	133 (66.8)	63.2	
≥6	31 (15.6)	51.4	
Tumor consistency			0.001*†
Soft	43 (21.6)	76.3	
Firm	156 (78.4)	61.7	
Vital artery encasement			0.027*‡
No	19 (9.5)	77.4	
Mild	153 (76.9)	65.1	
Severe	27 (13.6)	54.4	
Cavernous sinus involvement			0.169†
Yes	55 (27.6)	61.8	
No	144 (72.4)	66.0	
Tumor-Brainstem interface			<0.001*‡
SAS existence	23 (11.6)	80.7	
No SAS w/o brainstem edema	114 (57.3)	67.5	
No SAS with brainstem edema	62 (31.2)	54.0	
Surgical approach			0.31‡
Presigmoid	108 (54.3)	63.3	
Subtemporal transtentorial	36 (18.1)	64.2	
Extended middle fossa	20 (10.1)	62.0	
Retrosigmoid	23 (11.6)	72.2	
Far lateral	12 (6.0)	70.7	

CN cranial nerve, *GTR* gross total resection, *RT* radiotherapy, *SAS* subarachnoid space, *STR* subtotal resection, *w/o* without

*$p < 0.05$

† Independent-samples *t* test

‡ One-way ANOVA

observed in the long-term follow-up, there was no significant difference between the preoperative and follow-up KPS scores (76.8 vs. 83.2, $p = 0.390$, paired-samples *t* test) (Table 2).

Significantly more patients lived independently after than before surgery (KPS 80–100, 61.4 vs. 45.7 %, $p = 0.001$, Pearson χ^2 test; Table 2). The patients with higher KPS scores 80–100 exhibited higher degrees of tumor resection, a lower incidence of postoperative complications, and better recent KPS score compared with the patients with lower KPS scores. Statistical analysis demonstrated that surgery/radiotherapy history, age older than 60 years, increased tumor size, firm consistency, vital artery encasement, and peritumoral edema and disappearance of the tumor–brainstem interface were risk factors for poor KPS score (Table 4), postoperative hemiparesis (Fig. 7; Pearson χ^2 test), and CNs deficits (Fig. 8; Pearson χ^2 test). However, neither the involvement of the cavernous sinus nor the different surgical approaches influenced the outcomes. Multivariate binary logistic regression analysis revealed that only peritumoral brainstem edema

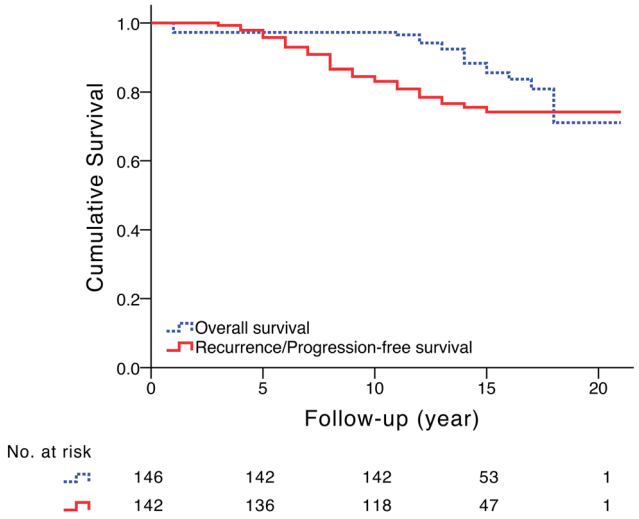


Fig. 6 Overall survival and R/P-free survival by Life Tables analysis. The overall survival at 1 month, 5, 10, 15, and 20 years was 97, 97, 97, 86, and 71 %, respectively. The R/P-free survival at 1 month, 5, 10, 15, and 20 years was 100, 96, 83, 74, and 74 %, respectively

(odds ratio [OR] 4.91, 95 % confidence interval [CI] 1.43–6.93, $p=0.010$) and a tumor size larger than 4 cm in diameter (OR 2.89, 95 % CI 1.09–5.03, $p=0.014$) were independent risk factors for outcome (KPS < 80).

R/P and Gamma Knife radiosurgery

Symptomatic or radiographic R/P was confirmed in 34 patients (34/142; 23.9 %, 95 % CI including continuity correction: 17.4–32.0 %) (Table 5). The cumulative R/P rate (patient number of R/P) at 1 month, 5, 10, 15, and 20 years was 0 % ($n=0$), 4 % ($n=6$), 17 % ($n=24$), 26 % ($n=34$), and 26 % ($n=34$), respectively (life-table statistics) (Fig. 6). The tumor R/P rates significantly increased as the extent of resection decreased. The R/P rates were 14.5, 31.8, and 53.3 % in the GTR, STR and PR patients, respectively ($p=0.002$, Pearson χ^2 test). The overall R/P rate in patients without Gamma Knife radiosurgery (GKR) was 21.8 % (24/110). For the patients with STR or PR, the patients who received GKR exhibited decreased R/P (10/32, 31.3 %) compared with the patients who did not receive GKR (12/27, 44.4 %); however, this difference was not statistically significant ($s=0.296$, Pearson χ^2 test) and thus only indicated a trend toward a lower R/P rate after GKR. Regarding recurrent/progressive tumor less than 3 cm in diameter, GKR was performed in 23 patients, and 15 patients presented with regrowth control, whereas the remaining patients exhibited continued regrowth. Among those with tumors larger than 3 cm, reoperations were performed in seven with favorable tumor growth control. Four patients chose observation due to concerns about the surgical risks, and one of these patients died of R/P. One case developed rapid and aggressive growth 4 years after GKR; however, pathology did not confirm malignant transformation.

Quality of life based on SF-36

We did not send the questionnaires on the SF-36 to patients lost to follow-up ($n=53$) or with confirmed mortality ($n=20$), and finally at the recent follow-up, the questionnaires were collected in 102 (80.3 %) out of 126 patients. In the SF-36 survey for quality of life, the scores of each items were as follows: physical functioning (69.9 ± 14.2), role-physical (61.3 ± 23.2), bodily pain (76.2 ± 15.1), general health (66.8 ± 15.8), vitality (79.7 ± 11.3), social functioning (77.8 ± 13.8), role-emotional (56.5 ± 27.7), and mental health (77.6 ± 12.2). Compared to the excellent study by Mathiesen et al. [38], we did not have the mean values for the general population in China or preoperative SF-36 scores as the baseline to evaluate the changes of recent SF-36 scores.

Sensitivity analysis

A comparison was performed to determine whether significant baseline differences between the followed patients and those lost to follow-up may affect mortality and R/P, but we did not detect any significant imbalance (Table 6).

Sensitivity analyses were performed where all patients ($n=53$) who discontinued the study prematurely without confirmed R/P or mortality were censored as of 12/31/2014, irrespective of their actual date of last follow-up [7, 23]. It was assumed that those lost to follow-up were alive and R/P-free. With these extremely conservative assumptions, a lower boundary was placed on the reported estimates. The adjusted overall mortality was 10.1 % (20/199 patients) (95 % CI including continuity correction: 6.4–15.3 %) and the adjusted R/P rate was 17.4 % (34/195 patients) (95 % CI including continuity correction: 12.5–23.7 %). In the sensitivity analysis, the adjusted R/P rate did not decrease significantly compared to that in 142 patients (17.4 vs. 23.9 %; χ^2 value = 2.161, $p=0.142$, Pearson χ^2 test), neither did the adjusted mortality rate (10.1 vs. 13.7 %; χ^2 value = 1.094, $p=0.296$, Pearson χ^2 test). Furthermore, both insignificant changes were illustrated by the Kaplan–Meier analyses (Fig. 9). Consequently, R/P rates of GTR, STR, and PR were adjusted to be 10.9 % (12/110), 22.2 % (14/63), and 36.4 % (8/22), respectively, but the difference remained significant (χ^2 value = 9.733, $p=0.008$, Pearson χ^2 test) that indicated effectiveness of GTR similar to the result in Table 5.

Discussion

Treatment policies had evolved with the ever-growing knowledge about the management of PCMs, but surgical resection is justified for medium to large PCMs. After reviewing 199 PCM cases in our series with follow-up durations of at least 10 years, we made the following observations: (1) the quality

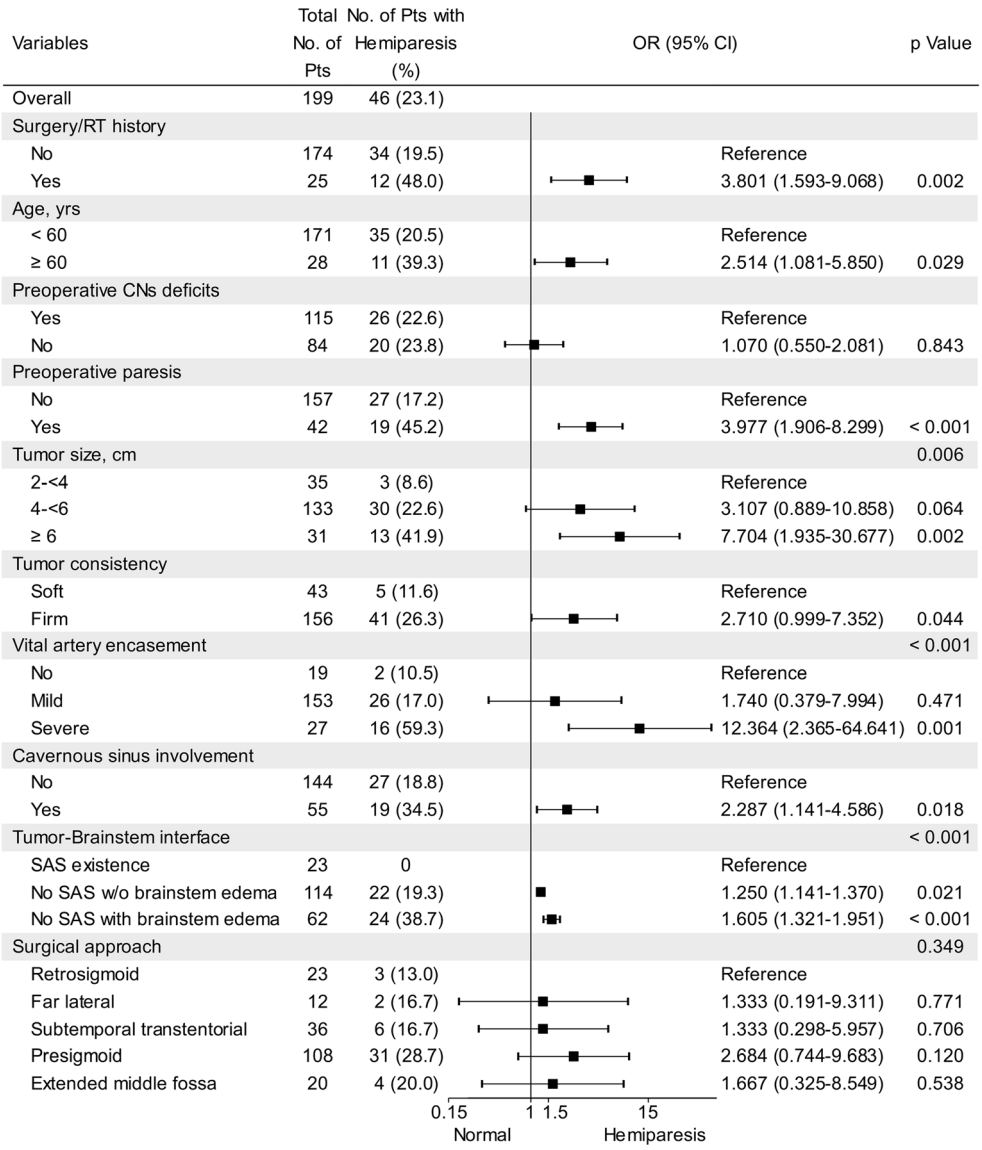


Fig. 7 Odds ratios for postoperative hemiparesis in the prespecified subgroups. The statistical analyses were performed with the Pearson χ^2 test. The *black square* indicates the odds ratios. The *error bars* represent the 95 % CIs. *CI* confidence interval, *OR* odds ratio, *RT* radiotherapy, *SAS* subarachnoid space, *w/o* without

of life declined at 1 month after surgery but gradually improved during the follow-up, and the surgical morbidities diminished over the postoperative course; (2) peritumoral brainstem edema and tumor sizes larger than 4 cm independently predicted poor outcome; and (3) a decreased extent of resection was associated with an increased risk of tumor R/P that could be reduced by GKR. These results suggest the following: (1) early surgery is recommended soon after the diagnosis and GTR should be attempted in most selected patients due to the high regrowth rate of residuals; (2) most surgical morbidities were transient and acceptable, which verifies the feasibility of radical resection; and (3) because of the validity of GKR for residual tumor control, non-total resection plus GKR was the second-most optimal choice for patients with adverse factors. The reliability and representativeness of these results and their implications and relevance for PCMs are discussed below.

Perioperative quality of life

Favorable outcomes could be achieved in patients with PCMs via surgical treatment, and significantly more patients lived independently after surgery compared with preoperatively (KPS 80–100, 61.4 vs. 45.7 %). However, the decreased quality of life due to surgical complications at 1 month after the operations was concerning and has also been reported in previous studies [1, 2, 30, 42]; for example, Natarajan et al. [42] reported a decrease in KPS scores from 78 immediately preoperatively to 62 postoperatively. In our series, ten (5 %) patients' KPS scores decreased dramatically immediately after the operation, and four (2.0 % in total) of these patients died from surgical mortality. The commonly reported causes of mortality include meningitis following cerebrospinal fluid leakage, injury to the brainstem, and pneumonia [1, 22, 32, 42, 66]. These findings reminded us that postoperative

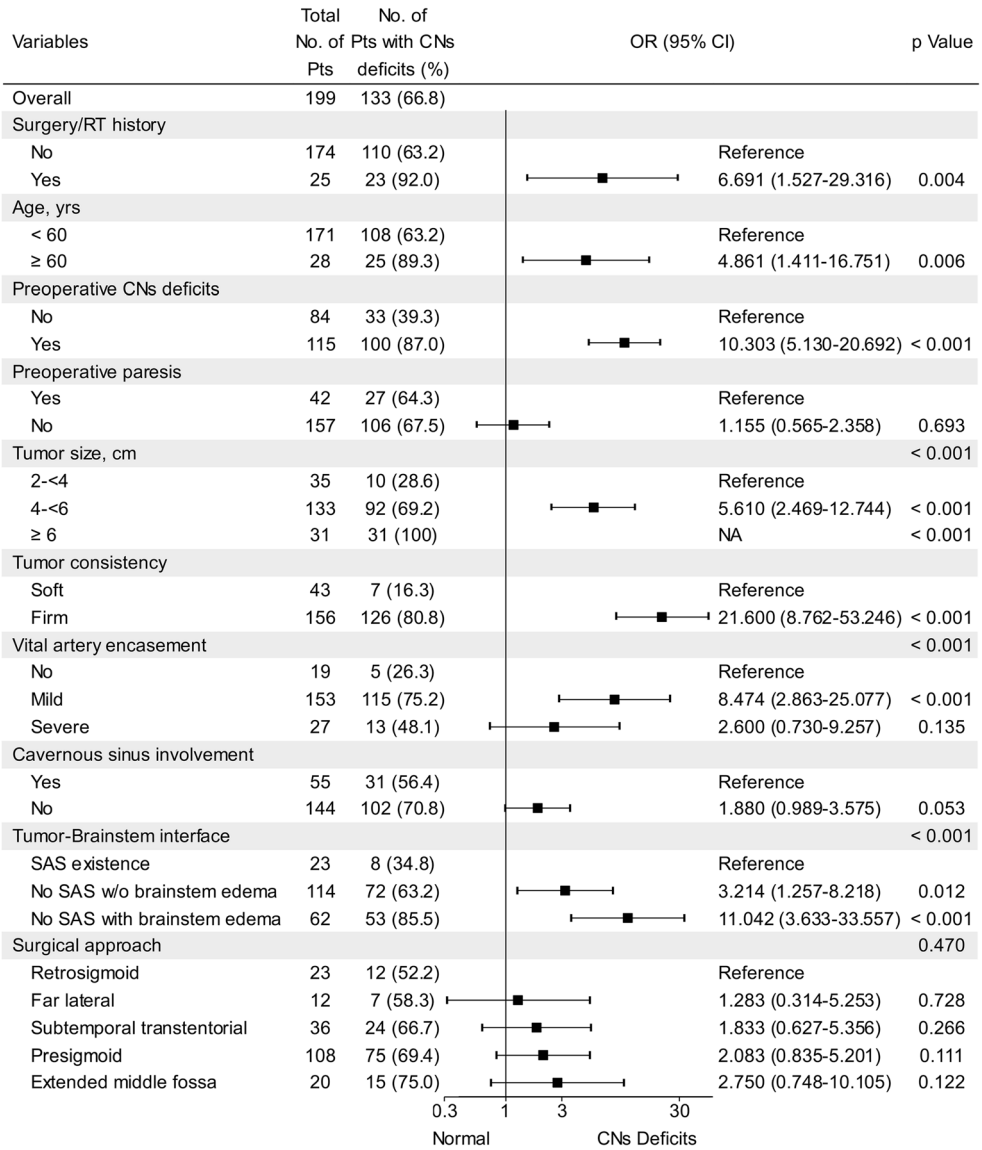


Fig. 8 Odds ratios for postoperative cranial nerve deficits in the prespecified subgroups. The statistical analyses were performed with the Pearson χ^2 test. The *black squares* indicate the odds ratios. The *error bars* represent the 95 % CIs. *CI* confidence interval, *OR* odds ratio, *RT* radiotherapy, *SAS* subarachnoid space, *w/o* without

management is also extremely important in addition to the surgical procedure itself.

Based on our study (Table 3), the preoperative KPS scores were very informative and reliable for assessing the quality of life and neurological deficits at 1 month after surgery. The patients with KPS scores of 80–100 experienced greater extents of tumor resection, a lower incidence of postoperative morbidity, and higher postoperative KPS scores, which implied a better quality of life compared with the patients with lower KPS scores. In contrast, the patients with KPS scores 70 or less had greater chances of developing neurological deficits and hemiparesis because the preoperative neuropathies implied infiltration of the perineurium and damage to several nerve tracts or neurons from the lesions; the second hit from surgery led immediately to neurological decompensation, which meant that no appropriate numbers of nerve tracts or neurons were available to maintain normal neurological function [9, 32]. Although a previous study reported favorable outcomes for patients with KPS scores of 40 or more, the only case in the present study with a KPS of 40 died postoperatively due to a severe brainstem injury [42].

With the advancement of surgical techniques related to the skull base, the outcomes of PCMs are no longer as pessimistic as has been reported previously [6, 28, 71]. However, it is judicious to select patients with KPS scores less than 70 for surgical intervention and to provide these patients additional care. Preoperative evaluation and individualized perioperative management are critical to avoid postoperative morbidities in poor surgical candidates with undesirable conditions. Postoperative proactive physical rehabilitation might be essential for recovery from neuropathies and subsequent improvements in the quality of life.

Table 5 R/P and GKR for tumor control over the long-term follow-up

Extent of resection	Total	No. of patients with R/P (%)	Patients receiving GKR		Patients not receiving GKR		Without GKS versus GKS	
			Total	No. of R/P (%)	Total	No. of R/P (%)	OR (95%CI)	*p*
GTR	83	12 (14.5)	0	–	83	12 (14.5)	–	–
STR	44	14 (31.8)	22	5 (22.7)	22	9 (40.9)	2.354 (0.635–8.725)	0.195†
PR	15	8 (53.3)	10	5 (50.0)	5	3 (60.0)	1.500 (0.170–13.225)	0.714†
STR & PR	59	22 (37.3)	32	10 (31.3)	27	12 (44.4)	1.760 (0.607–5.107)	0.296†
Overall	142	34 (23.9)	32	10 (31.3)	110	24 (21.8)	0.614 (0.256–1.471)	0.271†
p value		0.002*†						

CI confidence interval, *GKS* Gamma Knife surgery, *GTR* gross total resection, *OR* odds ratio, *PR* partial resection, *R/P* recurrence/progression, *STR* subtotal resection

*Comparison of R/P rate between GTR, STR, and PR (p value < 0.05)

† Pearson χ^2 test

Prior surgery or radiosurgery

Prior treatments are often encountered in referral centers [4, 8, 15, 30, 56], but few studies have considered them a risk to total resection. Difficulties in tumor exposure and resection increase due to the proliferation of the arachnoid membrane and adherence to adjacent structures following radiation or repeated operations [32, 61]. Natarajan et al. [42] observed a decrease in the GTR rate from 36.7 % in primary cases to 13.3 % in previously treated cases. Furthermore, the patients with previous treatments experience significantly worse outcomes, including postoperative CNs palsy and hemiparesis, than those without previous treatments; Little et al. [32] concluded that the risk of CNs deficits ($p < 0.001$) and paresis/ataxia ($p = 0.001$) increase with prior resection. Although GKR has been widely considered to be a safe and effective approach for PCMs [20, 26, 47, 48], long-term follow-ups should be continued due to the potential for persistent, insidious growth or possible malignant changes in biological behavior triggered by radiation [11, 35]. Therefore, initial

Table 6 Patients demographics and baseline information

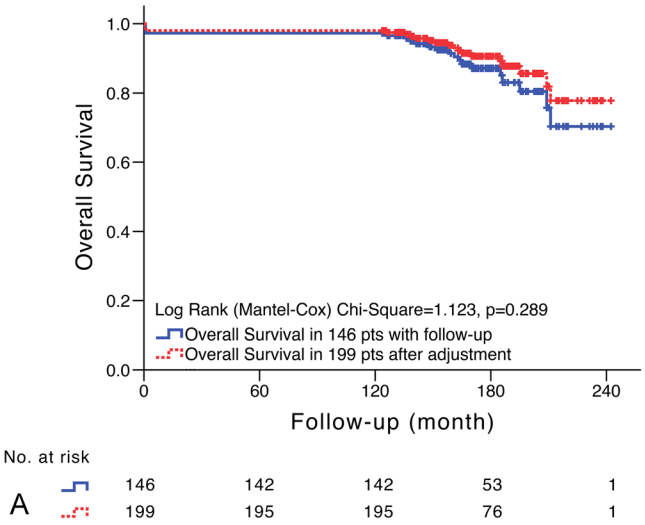
Variates	Patients with follow-up ($n = 142$)	Patients lost to follow-up ($n = 53$)	χ^2/t	*p*
Female, %	98 (69.0)	36 (67.9)	0.021	0.884†
Age, years	46.5 ± 10.1	44.8 ± 11.3	1.001	0.318‡
Previous treatment, %	17 (12.0)	6 (11.3)	0.016	0.900†
Preoperative CN deficit, %	83 (58.5)	28 (52.8)	0.497	0.481†
Preoperative hemiparesis, %	29 (20.4)	10 (18.9)	0.058	0.809†
Tumor size, cm	4.7 ± 1.1	4.6 ± 1.1	0.754	0.452‡
Cavernous sinus involvement, %	39 (27.5)	13 (24.5)	0.170	0.680†
Mean of preoperative KPS	76.5 ± 11.1	79.4 ± 12.0	−1.616	0.108‡
Mean of KPS at discharge	65.9 ± 14.3	66.8 ± 14.1	−0.382	0.703‡
Postoperative CNs deficits, %	97 (68.3)	32 (60.4)	1.085	0.298†
Postoperative hemiparesis, %	33 (23.2)	9 (17.0)	0.894	0.344†
Gross total resection, %	83 (58.5)	27 (50.9)	0.907	0.635†
Subtotal resection, %	44 (31.0)	19 (35.8)		
Partial resection, %	15 (10.6)	7 (13.2)		
Mortality during follow-up, %	16 (11.3)	–		
Recurrence/progression, %	34 (23.9)	–		

Excluding four surgical mortalities

CNs cranial nerves

† Pearson χ^2 test

‡ Independent-samples *t* test



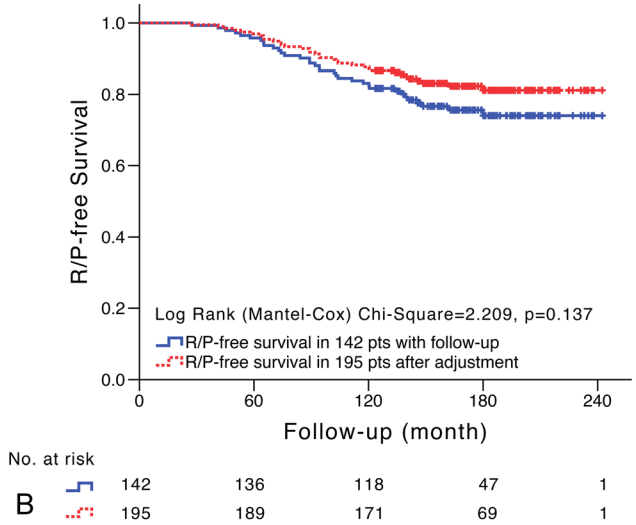


Fig. 9 Kaplan–Meier analysis of overall survival and R/P-free survival. **a** Kaplan–Meier analysis illustrated the overall survival before and after including 53 patients who were lost to follow-up and the change after the adjustment was not significant ($p = 0.289$). **b** Kaplan–Meier analysis illustrated the R/P-free survival before and after the adjustment and this insignificant change ($p = 0.137$) led to the improvement of R/P-free survival over long-term follow-up phase. *R/P* recurrence/progression

operations with the goal of maximal removal that are conducted soon after diagnosis for surgical candidates are significantly important in terms of the outcomes that they should be advocated.

Tumor features and radiographic variables

Vital artery encasement, peritumoral edema of the brainstem, a firm tumor consistency, and tumor adhesion to neurovascular structures (e.g., the basilar artery) have been identified as risk factors for unfavorable outcomes [3, 8, 16, 22, 24, 32, 63, 71]. We only confirmed brainstem edema and lesion size as independent risk factors by multivariate regression. Brainstem edema was always associated with the suspicion of an absent subarachnoid space and the feeding artery from the brainstem and adhesion of the tumor to the brainstem lead to extreme difficulties in total removal and to clinical deterioration [24, 56]. Carvalho et al. [9] demonstrated that only peritumoral edema significantly influences the long-term results. As recommended by Seifert [56], we favored non-total resection and decompression of the brainstem while leaving the tumor rim, and this strategy was more reasonable to prevent impairment of the corticospinal tract.

PCMs with maximal tumor diameters < 2 cm were excluded from the present study because small PCMs can cause asymptomatic or minimal symptoms, and there were limited neuroimaging facility resources in China for screening this subset of patients during the study period. Therefore, the tumors had generally grown into medium- or large-sized lesions when the majority of patients came to the clinic. Another reason is that our initial policy (before 1998) for small PCMs was observation or radiosurgery, but not surgical resection. The present study revealed that a tumor larger than 4 cm in diameter was an independent risk factor for a poor outcome. The tumor size paralleled the incidence of postoperative neurological deficits, including injury to the CNs. This finding might be associated with the significant mass effect of large lesion volumes because such large tumors shift and compressed the surrounding neurovascular structures and increase the possibility of neuropathy [29, 32, 59]. Moreover, tumor size also influences the degree of resection [29, 32]. A previous study supported large lesion size as a risk factor and demonstrated trends toward a decreased GTR rate and an increased surgical morbidity rate as the lesion size increased (>4 cm) [32]. Although Carvalho et al. [9] did not observe tumor size to be an adverse predictor for outcome, the downward extension of the tumor was a risk factor. These authors suggested early treatment rather than waiting and observation because the latter approach might lead to lesion unceasing growth and the involvement of the PCMs with more skull base regions [21].

Tumors with invasion of the cavernous sinus account for approximately 30–50 % of PCMs [19, 32, 34, 42–44]. Due to the complex structures of the cavernous sinus through which CNs III-VI run, the CNs are susceptible to blunt or sharp dissection during the peeling of tumors. Postoperative CNs dysfunctions are present in up to 72 % of patients [42, 58, 66] and are particularly likely to involve extraocular muscle dysfunction and facial numbness even when the operations are performed by very experienced surgeons. We observed an immediate postoperative CNs dysfunction rate of up to 66 %, although this rate was not directly associated with the

postoperative KPS scores, and this finding is similar to the assertion by Almefty et al. [2] that cavernous sinus involvement has an insignificant effect on KPS. Policies for the management PCMs involving the cavernous sinuses have evolved considerably in the past decades due to satisfactory tumor control with radiosurgery and due to the low growth rate of tumor remnants within the cavernous sinus [13, 25, 26, 32, 33, 42, 44, 50]. Despite the soundness and validity of the radiosurgery modality in tumor control [13, 25, 26, 47, 48, 58], relentless/invasive growth patterns following unsuccessful radiation have been reported in some skull base meningiomas, and treatment failure can occur unpredictably at long intervals [11, 27]. For patients with high expectancies of cosmetic maintenance and those older than 60 years, a balance between the risk of surgical complications and the degree of resection should be kept in mind both preoperatively and intraoperatively [4, 9, 12, 24, 32, 59, 61, 66]. We would choose less-aggressive resection for tumors with cavernous sinus involvement, which is consistent with prior reports [10, 32, 34]. Exceptionally, a soft consistency of the tumor is the only indication for an attempt to safely remove tumors within the cavernous sinus.

Older patients with relatively poor systemic function and decreased neurological compensation suffered a greater probability of co-morbidities and easily succumb to surgical injury. In our series, the patients older than 60 years exhibited significantly lower KPS scores (Table 4) and higher rates of postoperative hemiparesis (Fig. 7) and CNs deficits (Fig. 8) compared with the younger patients, and these findings parallel those of a previous study by Sekhar et al. [61]. Little et al. [32] also reported a mildly higher morbidity rate in older patients (age >/= 65 years). However, no similar findings were reported by Carvalho et al. [9]. We proposed that age is an important factor that should be considered during the selection of the surgical approach and the extent of resection [32, 36, 42]; less traumatic approaches and less aggressive resections are recommended for older patients due to the low possibility of regrowth within their expected lifetimes. A large series of 137 patients provides a case in point; the reported GRT was 21 % in older patients in contrast to 45 % in younger patients [32].

Recurrence and progression

The recurrent/progressive rate of PCMs varied from 0 to 42 % [10, 22, 36, 39], including 5–26 % for GTR and 17.6–42 % for STR with or without radiosurgery [8, 10, 15, 22, 28, 42, 57, 60]. Although it is difficult to compare these results due to differences in follow-up durations and definitions of R/P [8–10, 15, 22, 24, 32, 42, 50], the R/P of PCMs is significantly associated with less extensive resection [2, 10, 32, 36, 42]. Comparably, our study also verified the benefit of radical resection in terms of long-term R/P-free survival. Because radiosurgery has been recognized as an evidence-based treatment for tumor control and to decrease tumor R/P [25, 26, 47, 48, 65], it is regarded as a proactive adjuvant strategy for residual PCMs or as a salvage treatment for unresectable lesions. Due to the slow natural growth of benign PCMs [22, 65, 68] and concerns about radiation injury [11, 27, 37], we recommended GKR only for non-benign lesions and in conditions of definitive R/P.

Surgical approaches

The selection of the surgical approaches should be based on the tumor's size, location, and extension. Additionally, age and preoperative neuropathy should also be considered; however, the neurosurgeons' experiences and preferences have been overwhelming factors [14, 22, 24, 32, 42, 46, 50, 51, 53, 72]. Even for similar cases, the choice of approach has been surgeon-dependent to a certain extent [5]. Some surgeons prefer the retrosigmoid approach for its simplicity, remarkable benefit to brainstem decompression, and lack of the need to remove the petrous bone [8, 15, 40–42, 50, 51, 53, 67]. This approach has been widely used by Couldwell et al. [10] ($n=60$), Goel et al. [16] ($n=28$), Seifert [56] ($n=48$), and Samii et al. [49–54] ($n=24$). In our single-institute experience, the retrosigmoid approach was only performed in the initial cases and was suitable for small tumors in the mid-clivus. The piecemeal removal of PCMs via the space between CNs V-VIII risks injury to the CNs that are posterior to the tumor [4, 14, 24, 42, 46].

Some studies have favored transpetrosal approaches, including the presigmoid approach used in 108 of our patients (54.3 %), due to the improved view of the tumor–brainstem cleavage, reduced retraction of brain tissue and the CNs, and the broader surgical field [2–4, 14, 17, 18, 24, 32, 42, 64], but these approaches are more time-consuming, demanding, and traumatic than the retrosigmoid approach and also required critical training [62]. Because the various approaches have both merits and drawbacks, we do not aim to criticize the retrosigmoid approach based on the limited number of our patients ($n=23$) who underwent this approach nor do we wish to comment on the superiority of the presigmoid approach because the retrosigmoid approach with additional suprameatal exposure can safely and effectively address these tumors [52]. Because none of the approaches have been definitely proven to be superior, it is reasonable that satisfactory resections and outcomes can be anticipated when experienced surgeons utilize their familiar approaches and skillful microsurgical techniques.

Sensitivity analysis

In the absence of a nationwide medical network system in the 1990s, the follow-up rate decreased inevitably during the long-term retrospective follow-up. The mortality or recurrence in patients lost to follow-up was unknown, and we acknowledged that the low follow-up rate indeed compromised the confidence of our results. Our follow-up rate (71.4 %) was comparable to that reported by Little et al. [32] (62.0 %, 85/137 patients), and the R/P rate (23.9 %) was similar to that by Bricolo et al. [8] (23.3 %) and Park et al. [45] (22.4 %). To alleviate potential problems related to incomplete follow-up, we compared the baseline information between patients with or without follow-up (Table 6) and did not find any significant imbalance [55, 70].

Otherwise, if all patients ($n = 53$) lost to follow-up were assumed to suffer R/P or mortality, the adjusted R/P rate increased to 44.6 % (87/195 patients) (95 % CI 37.6–51.9 %) and the mortality rate increased to 36.7 % (73/199 patients) (95 % CI 30.1–43.8 %). Because the number of confirmed mortality ($n = 20$) or R/P ($n = 34$) at the most recent follow-up was lower than the number of patients who were lost to follow-up, both adjusted rates increased significantly (χ^2 value = 33.657, $p < 0.001$; χ^2 value = 39.414, $p < 0.001$; Pearson χ^2 test). Given the benign biologic behavior of low-grade meningiomas, the adjusted R/P rate (44.6 %) was higher than that from most prior studies, including the R/P rate (42.1 %) reported by Jung et al. [22] in 38 cases of non-total resected petroclival meningiomas; Moreover, it (44.6 %) was significantly higher than the pooled R/P rate (11.2 %, 117/1582 patients) based on 40 studies with R/P data, regardless of extent of surgical resection, and meanwhile, higher than the pooled R/P rate of non-total resection (18.0 %, 118/654 patients) based on 35 studies [31]. The adjusted high R/P rate (44.6 %) was speculated to be too high for our series because of WHO grade I in all patients. Compared to previous series, the adjusted mortality rate (36.7 %) was also relatively high for our series, but this high rate (36.7 %) would be convincing if R/P and/or unrelated health problems occurred more frequently. Therefore, we preferred conservative assumptions rather than assuming that all those lost to follow-up suffered mortality or R/P. Based on the aforementioned comparison (Table 6) and sensitivity analyses, we proposed that the influence of patients lost to follow-up on the mortality and recurrences was relatively insignificant but should be stressed.

Limitations of the present study

In our series, the patients came from all parts of our country, and many patients were lost to follow-up due to relocations to other regions and changing telephone numbers over the long period. Additional reasons for patients not returning to our hospital for clinical visit might be the patients' unwillingness to follow a scheduled revisit on the condition of the perception of improvement, uneventful postoperative course, and no progress of symptom in the follow-up phase that could not arouse patients' appeal for return visit. It was commonsensical that patients would return for medical consultation given suspicious R/P or symptom progress, but less likely reject medical consultation due to survival instinct. There was no geographically defined subgroup without patients lost to follow-up. Once again, it should be stressed that the low follow-up rate (71.4 %, 142/199 patients) compromised the confidence of our results. Our results convincingly predicted early surgical outcomes but were powerless regarding the long-term outcomes because it seemed less meaningful to compare long-term neurological outcomes based on preoperative KPS scores. Although the statement that "the overall outcome at follow-up was significantly better with higher preoperative KPS" seems unreliable, other studies have also reported the importance of higher preoperative KPS scores in terms of outcome [32, 42]. Our results might be accepted with some degree of caution, but the importance of preoperative neurological status requires further attention. In the future, we will improve our study design to update our knowledge.

Conclusions

Favorable outcomes for medium or large PCMs can be achieved via surgery with low mortality; however, the rate of CNs dysfunction is still high. Surgeries are preferred and cautious for patients with preoperative KPS scores less than 70. Radically aggressive resection might not be judicious due to postoperative morbidity. Preoperative evaluations (i.e., quality of life and neuroimaging features) and intraoperative findings were very informative regarding the outcomes. An age above 60 years, increased tumor size, firm tumor consistency, vital artery encasement, peritumoral brainstem edema, and prior surgery/radiotherapy history were risk factors that were associated with unfavorable outcomes. GKR exhibited good tumor control regarding the residual lesions. The credibility of our long-term optimistic results is limited by the low follow-up rate. Additional consecutive studies with higher follow-up rates should be performed to verify the accuracy of our findings.

Compliance with ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study (retrospective study), formal consent is not required.

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Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speaker's bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Informed consent Informed consent was obtained from all individual participants included in the study.

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Comment

The authors describe an impressive series of 199 patients with petroclival meningioma larger than 2 cm over a period of 10 years who underwent surgical resection. The results are reasonable with 55 % total resection, 2 % mortality, and 24 % permanent morbidity, mainly cranial nerve disorders. The authors prefer the presigmoid approach for resection of these tumors. While their preferred approach is a very reasonable option, a retrosigmoid craniotomy with suprameatal extension (if needed) can give quick and safe access to these tumors and similar results can be achieved. Large-size tumors and brainstem edema are determinant factors affecting outcome, and careful microsurgical dissection is the key to aim for better clinical results. Nevertheless, the temporary or permanent cranial nerve deficit is most often associated with surgery of these larger tumors even in the best of hands, and strategies to minimize morbidity, including near total resection followed by radio surgery, are commonly agreed upon to achieve better functional results and ultimately a more acceptable quality of life. The authors are to be congratulated for their critical review of their series and reasonable surgical outcome.

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