Petroclival meningiomas: long-term outcomes of multimodal treatments and management strategies based on 30 years of experience at a single institution

Jin Wook Kim, MD,1 Hee-Won Jung, MD,2 Yong Hwy Kim, MD,1 Chul-Kee Park, MD,1 Hyun-Tai Chung, PhD,1 Sun Ha Paek, MD,1 Dong Gyu Kim, MD,1 and Sang Hyung Lee, MD2

1Department of Neurosurgery, Seoul National University Hospital; and 2Department of Neurosurgery, Seoul Metropolitan Government–Seoul National University Boramae Medical Center, Seoul, Korea

OBJECTIVE A thorough investigation of the long-term outcomes and chronological changes of multimodal treatments for petroclival meningiomas is required to establish optimal management strategies. The authors retrospectively reviewed the long-term clinical outcomes of patients with petroclival meningioma according to various treatments, including various surgical approaches, and they suggest treatment strategies based on 30 years of experience at a single institution.

METHODS Ninety-two patients with petroclival meningiomas were treated surgically at the authors’ institution from 1986 to 2015. Patient demographics, overall survival, local tumor control rates, and functional outcomes according to multimodal treatments, as well as chronological change in management strategies, were evaluated. The mean clinical and radiological follow-up periods were 121 months (range 1–368 months) and 105 months (range 1–348 months), respectively.

RESULTS A posterior transpetrosal approach was most frequently selected and was followed in 44 patients (48%); a simple retrosigmoid approach, undertaken in 30 patients, was the second most common. The initial extent of resection and following adjuvant treatment modality were classified into 3 subgroups: gross-total resection (GTR) only in 13 patients; non-GTR treatment followed by adjuvant radiosurgery or radiation therapy (non-GTR+RS/RT) in 56 patients; and non-GTR without adjuvant treatment (non-GTR only) in 23 patients. The overall progression-free survival rate was 85.8% at 5 years and 81.2% at 10 years. Progression or recurrence rates according to each subgroup were 7.7%, 12.5%, and 30.4%, respectively.

CONCLUSIONS The authors’ preferred multimodal treatment strategy, that of planned incomplete resection and subsequent adjuvant radiosurgery, is a feasible option for the management of patients with large petroclival meningiomas, considering both local tumor control and postoperative quality of life.

https://thejns.org/doi/abs/10.3171/2019.2.JNS182604

KEYWORDS petroclival meningioma; long-term outcome; surgery; surgical approach; oncology
strong adherence to or invasion of the brainstem or the cavernous sinus, extension to multiple cranial fossae, and the difficulty involved in exposing this region.\textsuperscript{3,6,17} Moreover, aggressive extirpation is often closely associated with considerable surgery-induced morbidity but rarely with mortality. A meta-analysis summarizing the surgical outcomes of 1000 patients with petroclival meningiomas revealed the impregnable characteristics of this unique tumor. The meta-analysis reported a gross-total resection (GTR) rate of 49\%, 34\% (range 20\%–79\%) of patients experienced CN deficits in the early postoperative period, and 1.5\% of the patients died within a year of surgery.\textsuperscript{6}

Historically, at the beginning of the neurosurgical era, petroclival meningiomas were considered inoperable and unresectable.\textsuperscript{6} The earliest reported surgical mortality rate exceeded 50\%.\textsuperscript{3,11,24} Since that time, major advances in skull base surgery have been made and have included improvements in surgical instrumentation and techniques, neurophysiological monitoring, advanced neuroimaging, and an understanding of the natural history.\textsuperscript{9} Major advances in various adjuvant modalities, such as stereotactic radiosurgery (SRS) or radiation therapy (RT), enhance the multimodal management of petroclival meningiomas. Nevertheless, the optimal management strategy for petroclival meningiomas remains a matter of debate.

Some authors still insist that aggressive resection using various skull base surgical techniques may guarantee more favorable functional outcomes and a higher local tumor control than incomplete resection of petroclival meningiomas.\textsuperscript{2,11,13} By contrast, a more conservative approach involving planned subtotal resection (STR) followed by adjuvant treatments, such as radiosurgery (RS) or RT, which is guided by relief of mass effects and preservation of neurological functions, has been proposed by other authors.\textsuperscript{5,11,21,23,27}

Although many studies of long-term outcomes according to various management strategies for petroclival meningiomas have been reported, the optimal management strategies remain unclear. Furthermore, the scarcity and heterogeneity of these meningiomas have complicated attempts to classify them and analyze clinical outcomes according to management.\textsuperscript{2} The aim of the present retrospective study was to investigate the long-term outcomes of patients with petroclival meningioma according to their various treatments and to reflect on our management strategies based on our 30 years of experience.

Methods

Because similar meningiomas of various origins can be found in the petroclival region, a clear definition is necessary. A petroclival meningioma is defined as the mass that emanates at or medial to the skull base foramina of CNs V–XI and encompasses the upper two-thirds of the clivus at the petroclival junction medial to CN V.\textsuperscript{1} To analyze the clinical outcomes of patients with a petroclival meningioma accurately, our present study was confined to petroclival, clival, or sphenopetral clival meningiomas. Patients with other meningiomas, including petrosal or cerebellopontine angle or tentorial meningiomas, were excluded from this study.

From 1986 to 2015, a total of 92 patients with a petroclival meningioma underwent resection at Seoul National University Hospital. The patients’ clinical, radiological, surgical, and histopathological records obtained from our electronic database were closely reviewed according to the guidelines of the Institutional Review Board of Seoul National University Hospital. Tumor size was measured as the maximum diameter on preoperative MR images and was classified as small (< 1 cm), medium (1 cm ≤ diameter < 2.5 cm), large (2.5 cm ≤ diameter < 4.5 cm), and giant (≥ 4.5 cm), as previously described.\textsuperscript{17,21}

We analyzed the extent of resection using two independent parameters based on recorded intraoperative findings and postoperative MR images. The extent of resection was categorized into 3 subgroups by a review of the surgical records and postoperative radiological images: GTR, STR, and partial resection (PR). GTR was defined as 100\% macroscopic resection of the tumor and confirmed on postoperative images. STR was defined as a resected tumor volume ≥ 90\% and PR as that of < 90\%.

Various surgical approaches with some sorts of modifications have been used over 30 years. These approaches are largely classified as follows: standard retrosigmoid approach, orbitozygomatic approach, combined suprasellar and infratentorial approach, and transpetrosal approach. The transpetrosal approach was subdivided into anterior and posterior petrosal approaches. The posterior petrosal approach included presigmoid-retrolabyrinthine, translabyrinthine, transcochlear, and transtotic approaches. Functional outcomes of the patients, including their scores on the Karnofsky Performance Scale (KPS) and their neurological outcomes, including CN neuropathy, were evaluated during the follow-up period. The KPS scores and CN outcomes at the most recent follow-up were categorized as: favorable, if the assessment was improved or unchanged; or unfavorable, if it had worsened.

We compared the progression-free surgical outcomes across the various treatment strategies. The period of local tumor control was defined as the time between initial surgery and the date of local tumor recurrence based on radiological findings. Actuarial progression-free survival was analyzed using the Kaplan-Meier method and a log-rank test according to the subgroups. The association between the functional outcomes and each surgical approach was evaluated using a chi-square test (or a Fisher exact test when appropriate); p < 0.05 was accepted as significant, and IBM SPSS Statistics for Windows (version 21.0; IBM Corp.) was used for all analyses.

Results

Patient Characteristics

The patients included 22 males and 70 females with a mean age of 48 years (range 15–74 years). The mean tumor size was 4.4 cm (range 2.0–8.0 cm). Forty-four patients (47.8\%) harbored giant tumors (≥ 4.5 cm), and 47 patients (51.1\%) had large tumors (2.5 cm ≤ diameter < 4.5 cm). Only 1 patient had a medium-sized tumor of 2 cm. There was no surgical case with a small petroclival meningioma < 1 cm. Eighty-five patients (92.4\%) underwent the resection within 1 year of initial diagnosis. The remaining 7 pa-
patients (7.6%) were observed until their symptoms and signs were aggravated. The mean observational duration was 32 months (range 13–66 months).

The mean preoperative KPS score was 85 (range 60–100). About one-third of patients reported headache at their initial presentation, followed by hearing disturbance, facial numbness and pain, gait disturbance, and dizziness. The mean clinical and radiological follow-up periods were 121 months (range 1–368 months) and 105 months (range 1–348 months), respectively. The patient characteristics and detailed clinical information are shown in Table 1.

**Surgical Considerations**

A posterior transpetrosal approach was selected most frequently and used for 44 patients (48%). Among posterior transpetrosal approaches, a presigmoid-retrolabyrinthine approach was most common, followed by transcochlear, transotic, and translabyrinthine approaches. A simple retrosigmoid approach was used in 30 patients (33%), combined with a supratentorial or infratentorial approach in 8 patients (9%) and an orbitozygomatic approach in only 3 patients.

GTR was achieved in only 13 patients (14%), STR in 42 (46%), and PR in 37 (40%). Radical resection of > 90% of tumor volume was achieved in 55 patients (60%).

Pathology was reported as WHO grade I benign meningioma in 87 patients (95%), 3 tumors were reported as WHO grade II, and 2 as WHO grade III. Among the 87 WHO grade I meningiomas, the meningothelial subtype was most common, followed by transitional and secretory types.

**Overall Clinical Outcomes**

**Treatment Group and Tumor Control**

All 92 patients were categorized into 3 subgroups according to the initial extent of resection and following adjuvant treatments. Thirteen patients (14%) were in the GTR and observation group (GTR only), and 56 patients (61%) were in a group with non-GTR followed by adjuvant treatments such as RT or RS (non-GTR+RT/RS). Among 56 patients, 48 patients underwent Gamma Knife radiosurgery (GKRS), and the other 8 patients were treated with radiation therapy. There were 23 patients (25%) in the remaining group with non-GTR without adjuvant treatment (non-GTR-only subgroup). A schematic detailing each subgroup is shown in Fig. 1.

During the follow-up period, overall progression or recurrence was detected in 15 patients (16%). According to the subgroup, the progression or recurrence rate was 12.5% (7 of 56 patients) in the non-GTR+RS/RT subgroup, 30.4% in the non-GTR-only subgroup, and 15.4% in the GTR and observation group.

Details of the surgical approaches, the extent of removal, and pathological subtypes are shown in Table 2.
(7 of 23 patients) in the non-GTR-only subgroup, and 7.7% (1 of 13 patients) in the GTR-only subgroup (Fig. 1). Overall progression-free survival of all patients was 85.8% at 5 years and 81.2% at 10 years (Fig. 2 left), and it was significantly different according to the treatment subgroups (log-rank test, p = 0.05). In the non-GTR-only group, progression-free survival was 80.4% at 5 years and 63.5% at 10 years. No progression was found in either the GTR group or non-GTR+RS/RT group after 5 years (Fig. 2 right).

Additional treatments after recurrence were second surgery in 4 patients, GKRS in 7 patients, and RT in 2 patients. Two patients were lost to follow-up after recurrence.

Functional Outcome and Complications

The mean preoperative and postoperative KPS scores were 85 (range 60–70) and 79 (range 0–100), respectively. At their most recent clinical follow-up, 15 patients (16%) were improved, the condition was stationary in 40 (44%), and 37 (40%) had aggravated KPS status. For postoperative cranial neuropathies, favorable outcomes (improved or stationary) were found in 51 patients (55.4%), and unfavorable outcomes were found in 41 patients (44.6%). The most common immediately postoperative newly developed or aggravated CN deficit was CN VII neuropathy.

Surgically related major morbidity was detected in 9 patients (9.8%). Brainstem infarction was found in 2 patients, postoperative hemiparesis in 3, and postoperative hemorrhagic complication in 4. Surgery-related mortality occurred in 2 patients (2.2%). One patient had delayed hemorrhagic infection. Another patient died because of a cerebral infarction after a second surgery.

Other postoperative surgical complications were postoperative hemorrhage (5 patients, 5.5%), infection (8 patients, 8.7%), CSF leakage (13 patients, 14.1%), and pneumonia (3 patients, 3.2%). Detailed surgical mortality and morbidity are shown in Table 3.

Comparison of Clinical Outcome According to Each Subgroup

Extent of Resection According to Surgical Approach

Comparing the extent of resection according to the surgical approach, there were significant differences (p = 0.023). In particular, when comparing a simple retrosigmoid approach with a transpetrosal approach, the simple retrosigmoid approach showed a lower GTR rate with only 6.7% (2 of 30 patients), and a higher PR rate with 66.7% (20 of 30 patients; p = 0.001, Table 4).

With respect to postoperative complications, 11 (84.6%) of the 13 cases of CSF leakage occurred in transpetrosal approaches (5 in retrolabyrinthine approaches, 3 in transcoclear, 2 in translabyrinthine, and 1 in a transotic approach). Immediately postoperative newly developed or aggravated CN neuropathies according to the surgical approaches are shown in Table 4.
Comparing the GTR (13 patients) and non-GTR (79 patients) groups, we found a relatively higher favorable outcome in the non-GTR group in both postoperative KPS and CN neuropathies (63% and 43%) than in those of the GTR group (38% and 23%). However, there was no significant difference according to subgroup (p = 0.091 and p = 0.174, respectively).

Discussion

Resection of petroclival meningioma remains a formidable challenge for most neurosurgeons. Although many recent reports have demonstrated a marked evolution in the microsurgical management of petroclival meningiomas, most still reveal a low rate of complete resection and considerable surgically related morbidity as demonstrated by a meta-analysis.6

In a brief summary of long-term outcomes of multimodal treatments for 92 patients with a petroclival meningioma during a 30-year period, the overall GTR rate was only 14%; STR was 46% and PR was 40%. However, after incomplete resection, adjuvant treatments such as RT or RS for the residual tumor achieved as good a tumor control rate as that of complete resection (Fig. 2 right). Furthermore, with respect to postoperative functional outcomes including KPS score and CN neuropathies, those in the non-GTR group tended to have a relatively higher favorable outcome, although it was not significantly different. The overall rates of surgery-related major morbidity and mortality were 9.8% and 2.2%, respectively. These results reconfirm the impregnable characteristics of this unique tumor.

Nevertheless, many authors have emphasized the utility of total resection for the cure of petroclival meningioma.4,22,25 It was considered that patients with complete resection ultimately showed more favorable outcomes for both tumor control and functional status than patients with incomplete resection, despite transient neurological deterioration during early postoperative periods.2 For this reason, complete resection appears to be advantageous for various skull base approaches, such as the transpetrosal approach, which have the advantages of shortening the distance to the tumor, broadening the surgical field, and minimizing brain retraction, although they require more extensive and time-consuming bone work than conventional approaches.2,19,20 Almefty et al. concluded that various skull base approaches to true petroclival meningiomas not only facilitate an improved chance of complete resection, but also lessen the risk of morbidity, including CN neuropathies.2 Furthermore, it is clear that modern cranial base exposure, resection techniques, and cranial base repair techniques have allowed the safe resection of a greater

<table>
<thead>
<tr>
<th>Variable</th>
<th>Anterior Petrosal Approach (n = 7)</th>
<th>Posterior Petrosal Approach (n = 44)</th>
<th>Combined Supratentorial/Infratentorial Approach (n = 8)</th>
<th>Retrosigmoid Approach (n = 30)</th>
<th>Orbitozygomatic Approach (n = 3)</th>
<th>Total (n = 92)</th>
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<tr>
<td>Extent of resection</td>
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<td>2</td>
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<tr>
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<td>2</td>
<td>27</td>
<td>2</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>PR</td>
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<td>10</td>
<td>4</td>
<td>20</td>
<td>0</td>
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<tr>
<td>Complications*</td>
<td>CSF leakage†</td>
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<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Diplopia</td>
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<td>7</td>
<td>4</td>
<td>4</td>
<td>3</td>
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<tr>
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<tr>
<td></td>
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<td>16</td>
<td>4</td>
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</tr>
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<td></td>
<td>Low CNs</td>
<td>0</td>
<td>8</td>
<td>2</td>
<td>6</td>
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* Immediately postoperative newly developed or aggravated CN neuropathies.
† Among 13 patients, 2 patients had additional surgery for CSF leakage.
proportion of complex cranial base tumors than past techniques. However, there are also issues that should not be overlooked. The surgical management outcomes of 259 patients with a petroclival meningioma have been reported. To our knowledge, this is the largest surgical series at a single institution. The authors achieved a 52.5% GTR rate and 93% radical resection rate (Simpson grades I–IV), with preferred skull base approaches (235 patients) including presigmoid-retrolabyrinthine transpetrosal (130 patients, 50.2%), anterior transpetrosal-transtentorial (93 patients, 25.9%), and far lateral (12 patients) approaches. Together with these successful surgical outcomes, they also reported surgical complication rates such as postoperative infection (17%) and CSF leakage (5.8%), and 56 patients (23%) with KPS scores < 70 (unable to perform normal activity) at the most recent follow-up. Moreover, they found that postoperative neurological recovery from major surgical morbidity, such as CN neuropathies or motor weakness, was not straightforward.

By contrast, there is a recent trend to minimize such extensive approaches in favor of less aggressive surgical strategies. The frequency of these strategies is gradually increasing, not only in the management of petroclival meningioma, but for most brain tumors, especially those that are benign. The attempt of aggressive extirpation in itself is inevitably associated with a high expense of morbidity and deterioration of quality of life, which are not easily acceptable in this modern era.

Similarly, some authors recommend staged operations using safe and simple approaches. In particular, in the case of a large sphenopetrosal meningioma, an infratentorial tumor initially removed via a retrosigmoid approach followed by the removal of the remaining supratentorial tumor via a frontotemporal approach appears to be a good option. Greater understanding and expansion of the feasibility of adjuvant treatment modalities, such as SRS or other advanced radiation therapy, have an important influence on these trends.

A notable finding in the present study was the verification of historical changes of our management strategies for petroclival meningiomas and identification of these conceptual changes that were actually reflected in treatment strategies and clinical outcomes. A comparison of early-period (1986–2000) and recent-period (2001–2015) outcomes, despite the arbitrary separation, demonstrates several major changes. First, regarding the surgical approach and the extent of resection in the initial surgical management, the application of a simple retrosigmoid approach has gradually increased, although a presigmoid posterior petrosal approach has been most commonly used in the past 30 years. Along with these changes, the GTR rate has greatly decreased and the proportion of incomplete resections, including STR and PR, has increased. Consequently, surgically related major morbidity and mortality rates of the more recent period are lower than those of the earlier period. Complications such as CSF leakage and postoperative aggravated CN deficit show more favorable outcomes in the more recent period. All but two surgically related mortalities occurred in the earlier period. These results reflect the historical changes of our management policy for petroclival meningiomas toward less aggressive and safer treatments. Progression-free survival rates in patients who received incomplete resection followed by RT or RS were similar to those in patients who received complete resection.

Another consideration when choosing the management strategy for petroclival meningiomas is whether an adjuvant treatment modality should be applied and, if so, which type should be chosen and at what point it should be delivered. The present study demonstrated that the tumor progression rate was much lower in patients who received incomplete resection followed by RT or RS than it was in patients who did not receive adjuvant treatment. Thus, we usually recommend early adjuvant treatment for a definite residual lesion if the patient’s clinical and neurological condition is stable, rather than waiting for it to progress.

We have reported radiosurgical outcomes as primary and secondary treatment options for petroclival meningiomas. That study demonstrated a high tumor control rate (the actuarial progression-free survival after GKRS was 94.7% at 5 years and 88.9% at 10 years) and favorable CN outcomes (91%) after GKRS. We have preferred SRS to a conventional RT since the introduction of GKRS in our hospital in late 1998. The effectiveness of this adjuvant treatment appears to be important for the chronological change in our treatment strategies for petroclival meningiomas. Detailed historical changes are shown in Table 5 and Fig. 3. Based on the aforementioned clinical outcomes and our experience over 30 years, we prefer a multimodal treatment strategy for large petroclival meningiomas, such as a planned STR using a simple surgical approach with maximal safety followed by SRS.

In his review, Seifert provided a clear overview of the historical changes in management strategies for petroclival meningiomas based on his personal experience over a period of 20 years. He also noted chronologically significant changes of management strategy and emphasized the necessity of multimodal treatments for patients with petroclival meningioma. He concluded that one of the highest priorities in the management strategy for petroclival meningiomas is the patient’s quality of life, as well as more thoughtful decision-making using comprehensive consideration of tumor-related factors, such as surgical approach and extent of resection according to size, location, and extension.

We recognize several inherent limitations of the present study. Given the rarity and heterogeneity of petroclival meningiomas, it is not practical to gather meaningful numbers of cases in a short period. The chronological changes of management strategy over 30 years are both a strength and a weakness of this retrospective study. We do not argue that our management strategy of planned STR followed by SRS is the only or indeed the best option for the treatment of petroclival meningiomas. Even with the same surgical approach, the details would naturally change over 30 years. Descriptions of the RT technique and the selection criteria for adjuvant treatment (RT vs SRS) would not be identical from one time to the next or from patient to patient. Moreover, the influence of bias in interpreting our results is an important consideration that may limit the generalizability of our conclusions. Nevertheless, we believe that the evolution of our approaches can contribute to establishing optimal management strategies for patients with petroclival meningiomas.
Conclusions

We investigated the long-term clinical outcomes of patients with petroclival meningioma according to various treatments and chronological change of management strategies based on 30 years of experience at a single institution. Our preferred multimodal treatment strategy with planned incomplete resection followed by adjuvant RS is a feasible option for the management of patients with large petro-

clival meningiomas, considering both local tumor control and postoperative quality of life.

References


### TABLE 5. Summary of detailed chronological changes of the surgical approach and extent of resection

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<tr>
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<tr>
<td><strong>Surgical approach, no. (%)</strong></td>
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<tr>
<td>Anterior petrosal approach</td>
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<td>1</td>
<td>7 (7%)</td>
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<tr>
<td>Posterior petrosal approach</td>
<td>27</td>
<td>17</td>
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<tr>
<td>Retrolabyrinthine</td>
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<td>Transotic</td>
<td>5</td>
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<tr>
<td>Combined superior &amp; inferior approach</td>
<td>8</td>
<td>0</td>
<td>8 (9%)</td>
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<tr>
<td>Retrosigmoid approach</td>
<td>6</td>
<td>24</td>
<td>30 (33%)</td>
</tr>
<tr>
<td>Orbitozygomatic approach</td>
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<td>3 (3%)</td>
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<tr>
<td><strong>Extent of resection, no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTR</td>
<td>11</td>
<td>2</td>
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<td>42 (46%)</td>
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<td>PR</td>
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<td>23</td>
<td>37 (40%)</td>
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<tr>
<td><strong>Surgery-related major complication, no. (yr)</strong></td>
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<td></td>
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<tr>
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<td></td>
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<tr>
<td>Delayed hemorrhage &amp; infection</td>
<td>1 (1997)</td>
<td></td>
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<tr>
<td>Major morbidity</td>
<td>5</td>
<td>4</td>
<td>9</td>
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<tr>
<td>CSF leakage</td>
<td>10</td>
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![Installation of GKS](image)

FIG. 3. Chronological changes of management strategies over 30 years. Since the introduction of GKS (GKS) in late 1998, we have preferred a multimodal treatment strategy for petroclival meningiomas using a simple surgical approach with maximal safety followed by SRS. Figure is available in color online only.
meningioma subtotal resection: a volumetric study. *Oper Neurosurg (Hagerstown)* 14:215–223, 2018


Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions
Conception and design: Lee, JW Kim, Jung. Acquisition of data: JW Kim, YH Kim, Park, Chung, Paek, DG Kim. Analysis and interpretation of data: JW Kim, Jung, YH Kim, Park, Chung. Drafting the article: JW Kim. Reviewed submitted version of manuscript: Lee. Approved the final version of the manuscript on behalf of all authors: Lee. Study supervision: Lee, Jung, Chung.

Correspondence
Sang Hyung Lee: SMG-SNU Boramae Medical Center, Seoul National University College of Medicine, Seoul, Republic of Korea. nslee@snu.ac.kr.