

Olfactory Groove Meningioma: Report of 99 Cases Surgically Treated at the Catholic University School of Medicine, Rome

Roberto Pallini, Eduardo Fernandez, Liverana Lauretti, Francesco Doglietto, Quintino Giorgio D'Alessandris, Nicola Montano, Gabriele Capo, Mario Meglio, Giulio Maira

Key words

- Olfactory groove meningiomas
- Outcome predictors
- Surgical approaches

Abbreviations and Acronyms

CSF: Cerebrospinal fluid
ICU: Intensive care unit
KPS: Karnofsky performance status
OGM: Olfactory groove meningioma
WHO: World Health Organization



Institute of Neurosurgery, Università Cattolica del Sacro Cuore, Rome, Italy

To whom correspondence should be addressed:

Roberto Pallini, M.D., Ph.D.

[E-mail: pallini@rm.unicatt.it]

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INTRODUCTION

Olfactory groove meningiomas (OGMs) account for 8%–13% of all intracranial meningiomas (10, 11). These tumors originate from arachnoidal cells embedded in the midline dural coverings of ethmoid lamina cribrosa and frontosphenoidal suture. OGMs should be distinguished from other midline meningiomas of the anterior cranial fossa, that is, from meningiomas of the planum sphenoidale, which have their dural attachment posterior to the frontosphenoidal suture, and from tuberculum sellae meningiomas, which originate from the dura anterior to the chiasmatic sulcus. This distinction is not a mere anatomical exercise but holds clinical significance. In fact, meningiomas of planum sphenoidale and tuberculum sellae commonly are diagnosed earlier in their clinical course because of visual impairment. These meningiomas are small to medium sized at the time of surgery and can safely be

■ **OBJECTIVE:** We reviewed our series of olfactory groove meningiomas (OGMs) with the aim to relate the surgical approach with outcome and to define clinical and pathologic predictors of prognosis.

■ **METHODS:** Ninety-nine patients who underwent 113 craniotomies at our Institution between 1984 and 2010 were entered this study. The relationship between surgical approach (bifrontal, fronto-orbito-basal, and pterional) and either tumor diameter, extent of tumor resection, complication rate, need of reoperation, and Karnofsky Performance Status (KPS) was analyzed. The impact of age (≤ 70 vs. > 70 years), sex, tumor diameter (< 6 vs. ≥ 6 cm), pre- and postoperative KPS (< 80 vs. ≥ 80), Simpson grade (I-II vs. III-IV), and World Health Organization (WHO) histologic grade (I vs. II-III) on survival was assessed. Kaplan-Meier survival curves were plotted and differences in survival between groups of patients were compared. A multivariate analysis adjusted for age, pre- and postoperative KPS, Simpson grade, tumor diameter, and WHO histologic grade also was performed.

■ **RESULTS:** The fronto-orbito-basal approach ($n = 22$) allowed a significantly greater percentage of Simpson I-II removals than the bifrontal ($n = 70$) and pterional approach ($n = 21$) ($P = 0.0354$ and $P = 0.0485$, respectively). The risk of life-threatening complications trended to be lower in patients operated upon either via the fronto-orbito-basal and via the pterional approach than in those treated via the bifrontal approach. Retraction-related brain swelling did not occur in any case after the fronto-orbito-basal approach ($P = 0.0384$); however, this approach was associated with a greater rate of cerebrospinal fluid leak ($P = 0.0011$). Among prognostic factors, age ≤ 70 years ($P = 0.0044$), tumor diameter < 6 cm ($P = 0.0455$), pre- and postoperative KPS ≥ 80 (both $P < 0.0001$), Simpson grade I-II ($P = 0.0096$), and WHO histologic grade I ($P = 0.0112$) were significantly associated with longer overall survival. Age ($P = 0.0393$) and WHO histologic grade ($P = 0.0418$) emerged as independent prognostic factors for overall survival on multivariate analysis.

■ **CONCLUSION:** In the largest series of OGMs published to date, the bifrontal approach was associated with a greater risk of life-threatening complications compared with the lateral pterional and fronto-orbito-basal approaches. The fronto-orbito-basal approach provided greater chances of total tumor removal than the bifrontal and pterional approaches. Two independent factors for overall survival of patients with OGM were identified, namely age and WHO grade.

approached via a frontotemporal (pterional) route. Conversely, OGMs often reach a large size because of the long clinical phase in which symptoms, such as anosmia and behavioral changes, are underestimated. Therefore, these neoplasms are discovered late in their growth by the onset of epileptic seizures, increased intracranial

pressure, and visual impairment. At this stage, OGMs may involve the whole floor of the anterior cranial fossa, from the crista galli to the tuberculum sellae. The neurosurgeon is then challenged by the need to expose the tumor and its dural attachment under the edematous frontal lobes and to work there for many hours avoiding

retractions that may potentially increase the degree of brain swelling.

The classical bifrontal craniotomy does not allow a safe exposure of large OGMs, as demonstrated by the incidence of life-threatening complications related to brain retraction (1, 5, 11, 18, 21). Alternative surgical routes include the pterional and orbitolateral approaches (1, 2, 11, 15, 17, 19, 21, 23, 24), which expose the posterolateral surface of the tumor from a lateral view, and the fronto-basal-orbital approach (8, 21), in which the tumor is accessed from the underneath exposing its dural attachment first. Here, we report our experience with 99 OGMs and correlate the clinical outcome of the patients with the surgical approach used to remove the tumor. We also define the clinical and pathologic predictors of prognosis in OGMs.

CLINICAL MATERIAL AND METHODS

Patient Population

Ninety-nine consecutive patients with OGMs who had been surgically treated between 1984 and 2010 at the Institute of Neurosurgery, Università Cattolica del Sacro Cuore, Rome, entered this study. There were 35 men (35.4%) and 64 women (64.6%) who ranged in age from 17 to 82 years (median 58, mean 57 years) (Table 1 and Supplementary Table S1). The most frequent complaint was anosmia (59.6%), followed by visual impairment (46.5%), headache (38.4%), and mental changes (35.4); no complaints were present in 4 patients (4%) (Table 2). The tumor was imaged by magnetic resonance in 85 cases and/or by computed tomography in 57 cases; angiography was performed in 7 cases; in 3 cases preoperative embolization was performed. In 80 cases, the tumor was localized to the olfactory groove by reviewing the preoperative radiologic images; in the remaining 19 cases, radiographic reports and surgery notes were used. Ethmoidal invasion was defined as paranasal sinus extension of enhancing tumor through the floor of the anterior cranial fossa. Two patients had undergone previous surgery and were referred at our institution for recurrent tumors (Supplementary Table S1).

The median follow-up was 89 months (range, 2–324 months). All patients were followed up with clinical examination and

Table 1. Basic Demographic Chart in 99 Patients with OGMs

Characteristic	No. patients
Sex, n (%)	
Male	35 (35.4)
Female	64 (64.6)
Age, years	
Median	58
Range	17–82
Preoperative KPS	
Median	80
Range	40–100
Follow-up, months	
Median	89
Range	2–324
OGM, olfactory groove meningioma; KPS, Karnofsky performance status.	

computed tomography/magnetic resonance studies 6 months and 1 year after surgery. In the following 10 years, patients were re-examined at 1- or 2-year intervals. Thereafter, intervals were based on each follow-up result. Tumor recurrence was defined as at least a 20% increase in residual tumor or the appearance of a new lesion with at

Table 2. Presenting Symptoms and Signs in 99 Patients with OGMs

Symptoms and Signs	No. Patients (%)
Anosmia	59 (59.6)
Visual impairment	46 (46.5)
Headache	38 (38.4)
Mental changes	35 (35.4)
Seizures	19 (19.2)
Papilledema	9 (9.1)
Hemiparesis	7 (7.1)
Incontinence	7 (7.1)
Optic atrophy	6 (6.1)
Epistaxis	6 (6.1)
Foster-Kennedy	3 (3.0)
Incidental	4 (4.0)
OGMs, olfactory groove meningiomas.	

least 10 mm in longest diameter on follow-up neuroimaging (4). Surgical mortality was defined as death occurring within 30 days from the date of surgery.

Size and Extension of Tumors

Overall, the mean tumor size was 5.4 cm. Meningioma size was small (≤ 3 cm) in 15 of 99 cases (15.2%), medium (3–6 cm) in 33 of 99 (33.3%), and large (≥ 6 cm) in 51 of 99 (51.5%) of cases (Table 3 and Supplementary Table S2). The mean tumor size was 2.4 cm (range 1.8–3 cm), 4.4 cm (range 3.5–5.5 cm), and 6.9 cm (range 6–9 cm) in small, medium, and large OGMs, respectively. Small OGMs had no locoregional extension. Ethmoidal invasion was present in 4 of 33 cases (12.1%) of medium OGMs and in 7 of 51 cases (13.7%) of large OGMs (Table 3). Optic nerve involvement was present in 12 of 33 (36.4%) and 24 of 51 (47.1%) patients of medium and large OGMs, respectively. Vascular encasement was evident in 2 of 33 (6.1%) and 7 of 51 (13.7%) patients of medium and large OGMs, respectively. In one patient suffering from type II neurofibromatosis, the tumor extended through the middle cranial fossa of one side to the petrous region where it collided with a vestibular schwannoma (14). Hyperostosis of the anterior cranial fossa was found in 28 cases (28.3%).

Table 3. Tumor Size and Growth Patterns of 99 OGMs

Tumor Diameter and Extension	No. Patients (%)
≤ 3 cm	15 (15.2)
Ethmoidal invasion	0 (0)
Optic nerve involvement	0 (0)
ACoA complex involvement	0 (0)
3-6 cm	33 (33.3)
Ethmoidal invasion	4 (12.1)
Optic nerve involvement	12 (36.4)
ACoA complex involvement	2 (6.1)
≥ 6 cm	51 (51.5)
Ethmoidal invasion	7 (13.7)
Optic nerve involvement	24 (47.1)
ACoA complex involvement	7 (13.7)
OGM, olfactory groove meningiomas; ACoA, anterior communicating artery.	

Table 4. Surgical Approaches and Tumor Diameter of 99 OGMs

Surgical Approach*	Tumor Diameter, cm			Total
	≤3 (%)	3–6 (%)	≥6 (%)	
Bifrontal	8 (53.3)	29 (69.0)	33 (58.9)	70 (61.9)
Pterional	7 (46.7)	7 (16.7)	7 (12.5)	21 (18.6)
Fronto-orbital-basal	0 (0)	6 (14.3)	16 (28.6)	22 (19.5)
Total	15	42	56	113

*7 patients underwent 2 operations, 2 patients underwent 3 operations, and 1 patient underwent 4 operations.

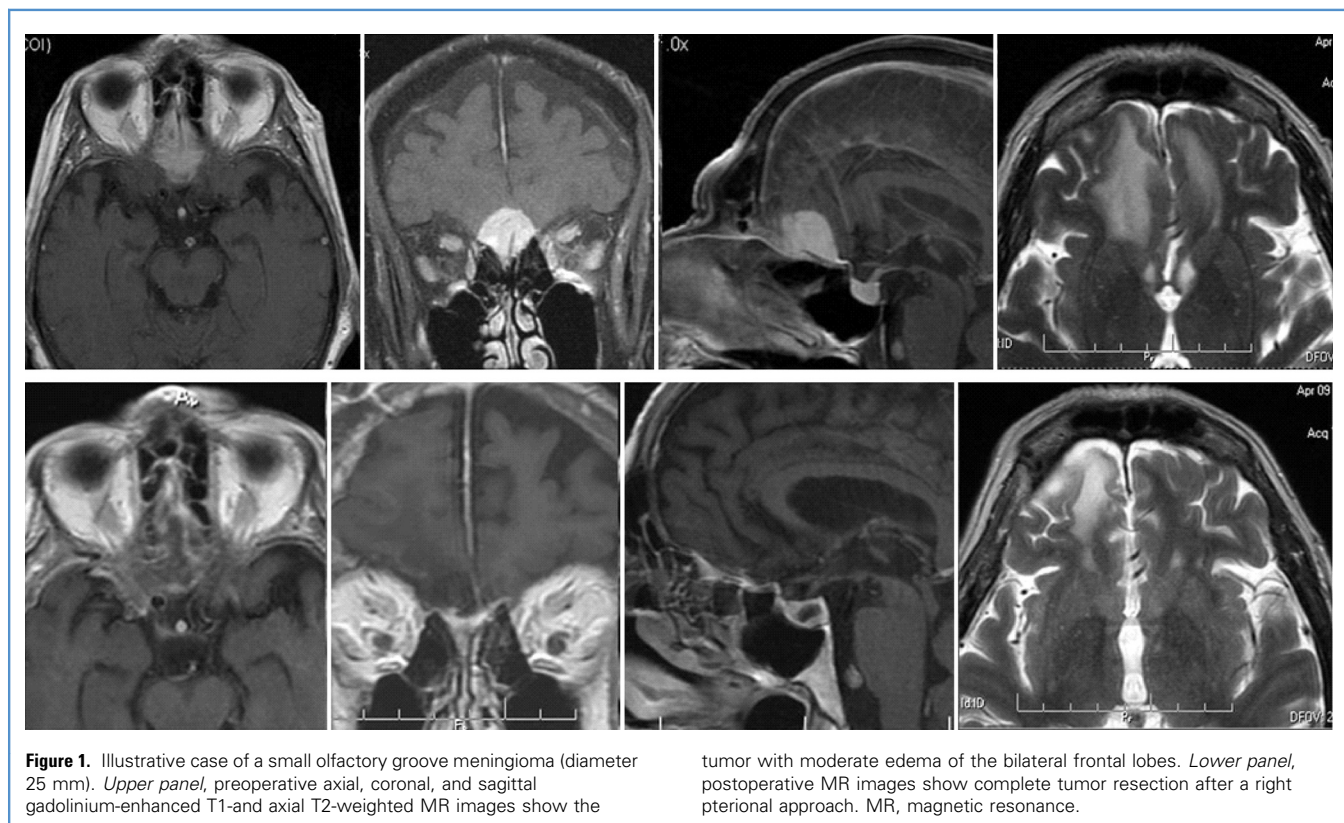
Surgical Approaches

A total of 118 surgical procedures were performed, 113 of which at our institution (Table 4 and Supplementary Table S1). These included bilateral subfrontal approaches (bifrontal approach) in 70 cases (61.9%), frontotemporal approach (pterional approach) in 21 cases (18.6%), and bilateral subfrontal combined with bilateral orbital osteotomy (fronto-orbital-basal approach) in 22 cases (19.5%). In 3 cases, a 2-stage surgery was performed, the first procedure to remove the ethmoid-

nasal extension of the tumor and the second one to remove the intracranial portion. Overall, 14 surgeons were involved in treatment of these tumors.

The bifrontal approach used at our Institution is similar to that described by El Gindi (5). After a bicoronal scalp incision and periosteum dissection, a bifrontal bone flap is lowered up to the orbital rim. The frontal sinus is opened, its posterior wall and mucosa are removed, and the frontonasal duct is closed with muscle. The dura is opened bilaterally; then, the

superior sagittal sinus is sutured at its anterior and cut along with the falx. The nondominant frontal lobe is gently retracted, and tumor resection is carried out mostly from one side. Retraction of the dominant frontal lobe is reduced as much as possible. The pterional approach is performed as described by Yasargil (25) and Tomasello et al. (23). A frontotemporal skin incision is performed, and the skin flap and temporalis muscle are elevated as separate layers taking care to preserve the frontal branches of the facial nerve. A frontotemporal craniotomy is then performed. After the dura is opened, the sylvian fissure is opened widely and the optic-carotid cistern fenestrated to relax the brain and expose the tumor. In the surgical technique used for the fronto-orbital-basal approach, we followed the guidelines described by Sekhar et al. (20). Briefly, after having released the supra-orbital nerves, we performed a bifrontal craniotomy. Then, a bilateral orbitotomy was performed that included 2–2.5 cm of orbital roof crossing the midline just anterior to the crista galli. At the end of procedure, the anterior skull base was reconstructed



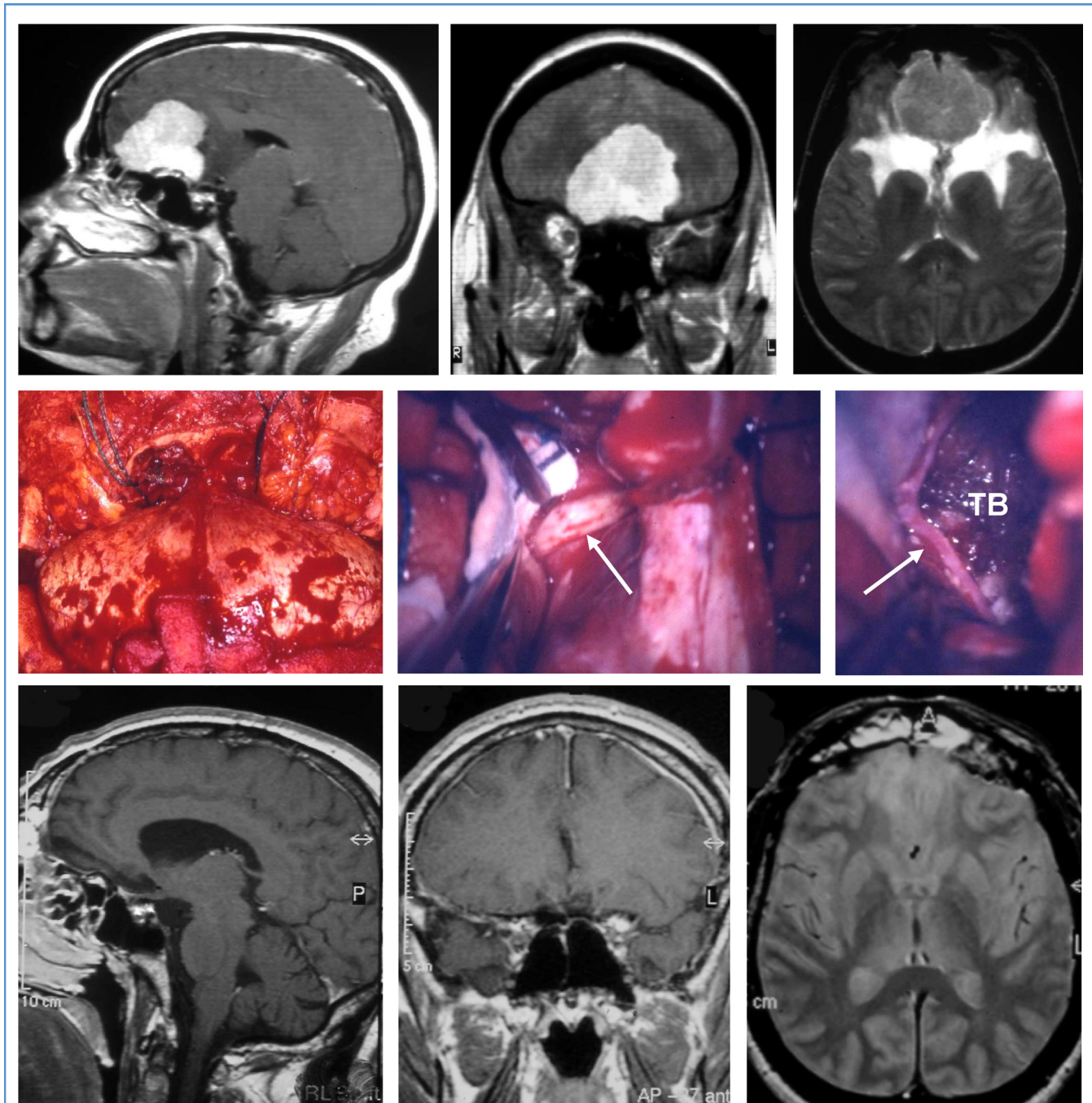


Figure 2. Illustrative case of a medium-sized olfactory groove meningioma (diameter 42 mm). *Upper panel*, preoperative sagittal and coronal Gd-enhanced T1- and axial T2-weighted MR images show the tumor with remarkable edema of the bilateral frontal lobes. *Middle panel*, intraoperative pictures show the fronto-orbito-basal approach (left), release

of the olfactory nerve (arrow) before tumor resection (center), and the tumor bed (TB) at the end of resection (right). *Lower panel*, postoperative sagittal and coronal Gd-enhanced T1- and axial T2-weighted follow-up MR images obtained 13 years after surgery show no tumor recurrence. Gd, gadolinium; MR, magnetic resonance.

with a pedunculated flap of galea and abdominal fat to fill any dead space. In all cases, a subdural catheter is placed at surgery and left for 2–3 days postoperatively to monitor intracranial pressure.

Statistical Analysis

The relationship between surgical approach and either tumor diameter, extent of tumor resection, complication rate, need of reoperation, and

postoperative Karnofsky Performance Status (KPS) was analyzed. The impact of age (≤ 70 vs. > 70 years), tumor diameter (< 6 vs. ≥ 6 cm), preoperative and postoperative KPS (< 80 vs. ≥ 80), Simpson

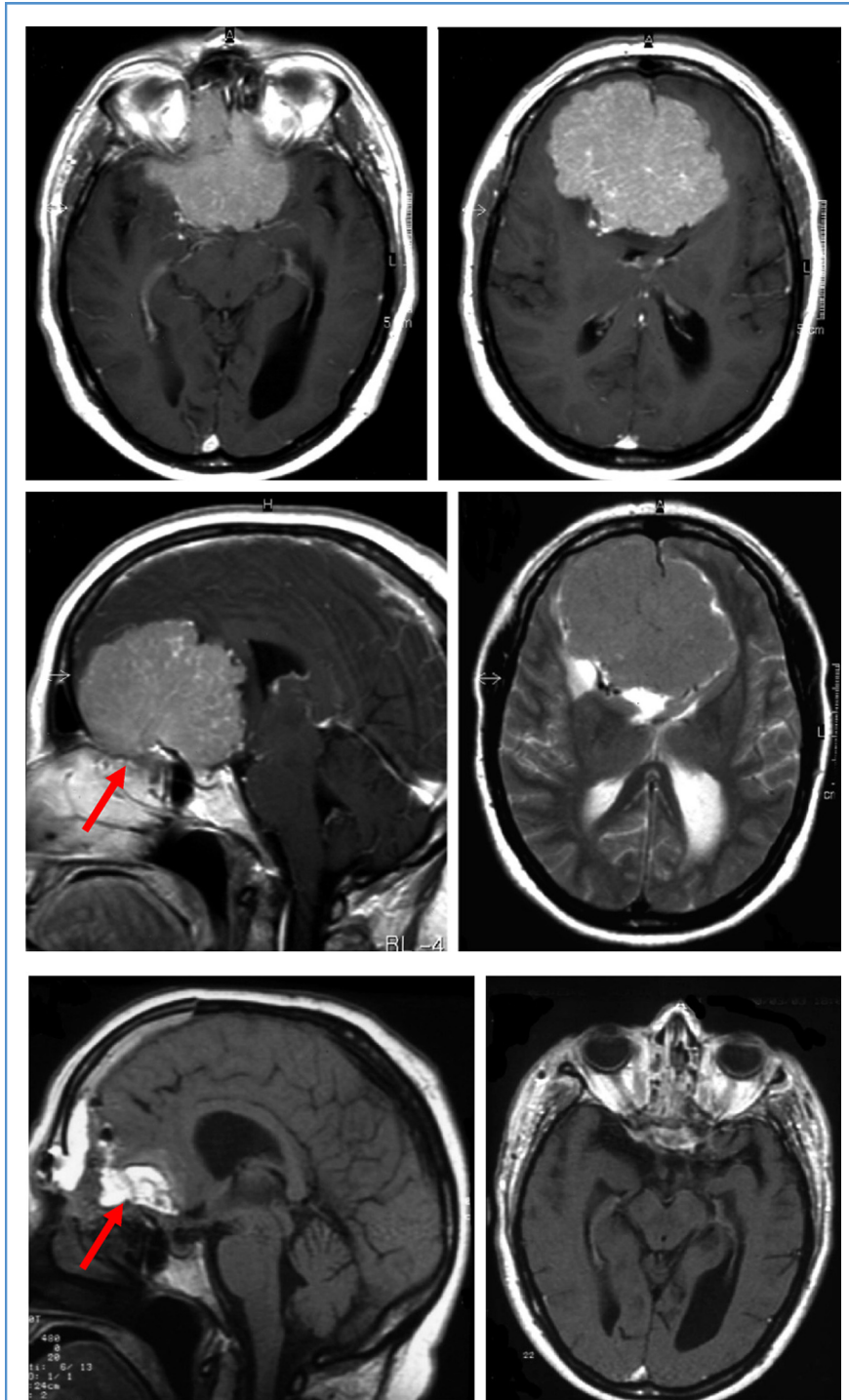


Figure 3. Illustrative case of a large olfactory groove meningioma (diameter 68 mm). *Upper and middle panels*, preoperative axial and sagittal gadolinium-enhanced T1- and axial T2-weighted MR images showing the tumor with brain edema of low degree. The arrow points out an erosion of the ethmoid bone. *Lower panel*, postoperative sagittal and axial unenhanced T1-weighted follow-up MR images obtained 10 years after surgery show no tumor recurrence. The arrow points out the fat graft used for skull base reconstruction. MR, magnetic resonance.

grade (I-II vs. III-IV), and World Health Organization (WHO) histological grade (I vs. II-III) on overall and recurrence-free survival also was assessed. Comparison of categorical variables was performed by χ^2 statistic using the Fisher exact test when appropriate. Differences of postoperative stay in the intensive care unit (ICU) were evaluated by the Mann-Whitney U test. Kaplan-Meier survival curves were plotted, and differences in survival between groups of patients were compared with the log-rank test. Multivariate analysis was performed with the Cox proportional hazards model incorporating the major prognostic factors that included age, preoperative and postoperative KPS, Simpson grade, tumor diameter, and WHO histologic grade. $P < 0.05$ was considered as statistically significant. Statistical analysis was performed by using StatView version 5 software (SAS Institute, Cary, North Carolina, USA).

RESULTS

Surgical Approach and Tumor Size

Of 15 procedures performed in small sized OGMs, 8 used the bifrontal approach and 7 the pterional approach (Table 4 and Figure 1). The fronto-orbito-basal approach was not used in any case to remove small OGMs. Among the 42 medium-sized OGMs, 29 (69.0%) were operated upon via the bifrontal approach, 7 (16.7%) via the pterional approach, and 6 (14.3%) via the fronto-orbito-basal approach (Figure 2). Large OGMs ($n = 56$) were approached through the bifrontal route in 33 cases (58.9%), through the fronto-orbito-basal in 16 (28.6%), and through the pterional in 7 cases (12.5%) (Figures 3 and 4). Of 21 procedures that used the pterional approach, 7 were performed in small OGMs (33.3%), whereas only 8 of 70 (11.4%) and 0 of 22 (0%) of the bifrontal and fronto-orbito-basal approaches, respectively, were used to remove small OGMs ($P = 0.0253$ and $P = 0.0036$, respectively; Fisher exact test) (Table 4). After we excluded WHO grade II-III OGMs ($n = 6$), statistical analysis confirmed that the pterional approach was more frequently used to remove small OGMs than the fronto-orbito-basal approach ($P = 0.0080$, Fisher exact test; Supplementary Table S3).

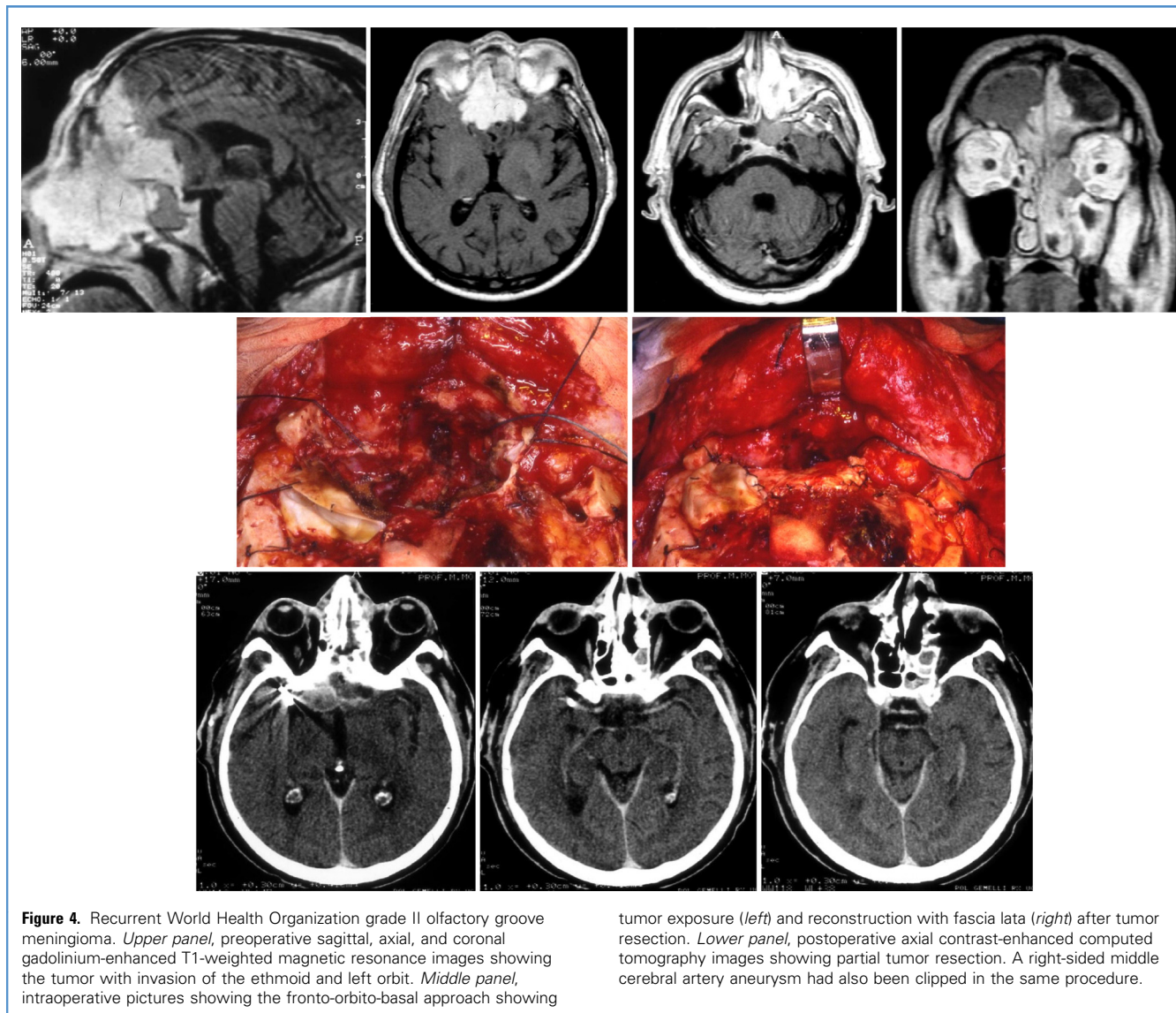


Figure 4. Recurrent World Health Organization grade II olfactory groove meningioma. *Upper panel*, preoperative sagittal, axial, and coronal gadolinium-enhanced T1-weighted magnetic resonance images showing the tumor with invasion of the ethmoid and left orbit. *Middle panel*, intraoperative pictures showing the fronto-orbito-basal approach showing

tumor exposure (*left*) and reconstruction with fascia lata (*right*) after tumor resection. *Lower panel*, postoperative axial contrast-enhanced computed tomography images showing partial tumor resection. A right-sided middle cerebral artery aneurysm had also been clipped in the same procedure.

Surgical Approach and Extent of Resection

Overall, a Simpson's grade I-II resection was achieved in 95 procedures (84.1%), whereas in 18 procedures (15.9%) tumor resection was assessed as Simpson's grade III-IV (Table 5). In 5 cases (4.4%), a Simpson's grade III resection was performed and in 13 cases (11.5%) the tumor was partly removed (Simpson's grade IV). Simpson's grade I-II resection was achieved in 56 of 70 (80%), 22 of 22 (100%), and 17 of 21 (81%) of procedures that used the bifrontal, fronto-orbito-basal, and pterional approach, respectively. Therefore, the fronto-orbito-basal

approach allowed a significantly greater percentage of Simpson I-II removal than the bifrontal and pterional approach ($P = 0.0354$ and $P = 0.0485$, respectively; Fisher exact test). This result was confirmed by analyzing the extent of resection in the group of large OGMs, where Simpson grade I-II resections were more frequently achieved using the fronto-orbito-basal approach compared with the bifrontal and pterional approaches ($P = 0.0410$ and $P = 0.0190$, respectively; Fisher exact test; Supplementary Table S4). Although at lower statistical power, similar results were obtained by including in the analysis only the WHO grade I OGMs (Supplementary

Table S5). Frontobasal hyperostosis was completely removed in 14 cases (50%), whereas in 14 cases (50%) it was either not removed or partly removed.

Surgical Approach and Complications

The complication occurring most frequently was retraction-related brain swelling (14.2%), followed by bleeding (9.7%), deep venous thrombosis and/or pulmonary embolism (8.0%), pneumonia (7.1%), and hydrocephalus (5.3%) (Table 6). Death related to surgery occurred in 4 patients (3.54% of procedures; 4.04% of patients); all of them had large OGMs and were operated on via the

Table 5. Surgical Approaches and Extent of Tumor Resection of 99 OGMs

Surgical Approach*	Simpson Grade		Total
	I–II (%)	III–IV (%)	
Bifrontal	56 (80.0)	14 (20.0)	70
Pterional	17 (81.0)	4 (19.0)	21
Fronto-orbital-basal	22 (100)	0 (0)	22
Total	95 (84.1)	18 (15.9)	113

OGM, olfactory groove meningioma.
*7 patients underwent 2 operations, 2 patients underwent 3 operations, and 1 patient underwent 4 operations.

bifrontal approach. Overall, life-threatening complications, which included retraction-related brain swelling, bleeding, and brain ischemia, accounted for 25.7% of procedures, namely 22 of 70 (31.4%), 5 of 21 (23.8%), and 2 of 22 (9.1%) procedures that used the bifrontal, pterional, and fronto-orbital-basal approach, respectively.

Among life-threatening complications, retraction-related brain swelling occurred after 12 of 70 (17.1%), 4 of 21 (19%), and 0 of 22 (0%) procedures that used the bifrontal, pterional, and fronto-orbital-basal approach, respectively ($P = 0.0384$, Fisher exact test). However, the fronto-orbital-basal approach was associated with a greater probability of cerebrospinal fluid (CSF) leak than the bifrontal and pterional approaches ($P = 0.0011$; Fisher exact test). Postoperative CSF leak was observed in 4 cases operated upon via the fronto-orbital-basal approach; 2 required reoperation, and 2 cases were managed by lumbar drainage. Overall, reoperation was needed after 18 of 113 procedures (15.9%) (Table 7). In 7 cases, a decompressive craniotomy was performed. Six of these patients had been operated upon via the bifrontal approach and one via the fronto-orbital-basal route. Six patients developed communicating hydrocephalus requiring CSF shunt. The fronto-orbital-basal approach resulted in a greater percentage of reoperations for complications compared with the bifrontal and pterional approaches (22.7% vs. 15.7% and 9.2%, respectively). Reoperations after the fronto-orbital-basal approaches included one decompressive craniotomy in

Table 6. Surgical Approaches and Complications of 113 Surgical Procedures* for 99 OGMs

Complication	Surgical Approach*			
	Bifrontal (%) (n = 70)	Pterional (%) (n = 21)	Fronto-orbital-basal (%) (n = 22)	Total (%) (n = 113)
CSF leak	0 (0)	0 (0)	4 (18.2)	4 (3.5)
Meningitis	1 (1.4)	0 (0)	0 (0)	1 (0.9)
Wound infection	2 (2.9)	1 (4.8)	1 (4.5)	4 (3.5)
Bleeding	9 (12.9)	1 (4.8)	1 (4.5)	11 (9.7)
Seizures	1 (1.4)	1 (4.8)	1 (4.5)	3 (2.7)
Retraction-related brain swelling	12 (17.1)	4 (19.0)	0 (0)	16 (14.2)
Brain ischemia	1 (1.4)	0 (0)	1 (4.5)	2 (1.8)
Hydrocephalus	4 (5.7)	1 (4.8)	1 (4.5)	6 (5.3)
DVT/PE	5 (7.1)	2 (9.5)	2 (9.1)	9 (8.0)
Pneumonia	4 (5.7)	2 (9.5)	2 (9.1)	8 (7.1)
Sepsis	3 (4.3)	0 (0)	0 (0)	3 (2.7)
Hypertensive pneumocephalus	0 (0)	0 (0)	1 (4.5)	1 (0.9)
Death	4 (5.7)	0 (0)	0 (0)	4 (3.5)

OGM, olfactory groove meningiomas; CSF, cerebrospinal fluid; DVT, deep venous thrombosis; PE, pulmonary embolism.
*7 patients underwent 2 operations, 2 patients underwent 3 operations, and 1 patient underwent 4 operations.

a patient who had had a stroke as the result of thrombosis of the internal carotid artery homolateral to the parasellar extension of the tumor, one CSF shunt, and 3 procedures of skull base packaging due CSF leak (Table 7 and Supplementary Table S1).

In patients with medium-sized (3–6 cm) OGMs, the postoperative stay in ICU was 5.46 ± 9.13 days (mean \pm SD), 2.67 ± 1.85 days, and 2.93 ± 3.08 days after the

bifrontal, fronto-orbital-basal, and pterional approaches, respectively. In patients with large OGMs (>6 cm), the postoperative stay in ICU was 7.31 ± 11.10 days (mean \pm SD), 2.83 ± 2.04 days, and 3.29 ± 3.68 days after the bifrontal, fronto-orbital-basal, and pterional approaches, respectively. Overall, there was a trend for longer postoperative stay in ICU in patients operated upon via the bifrontal approach

Table 7. Reoperation for Complication of 99 OGMs

Reoperation*	Surgical Approach			
	Bifrontal (%) (n = 70)	Pterional (%) (n = 21)	Fronto-Orbital-Basal (%) (n = 22)	Total (n = 113)
Decompressive craniotomy	6 (8.6)	0 (0)	1 (4.5)	7 (6.2)
Removal of haematoma	6 (8.6)	0 (0)	0 (0)	6 (5.3)
CSF shunt	4 (5.7)	1 (4.8)	1 (4.5)	6 (5.3)
Wound revision	1 (1.4)	1 (4.8)	3 (13.6)	5 (4.4)
Total	11 (15.7)	2 (9.5)	5 (22.7)	18 (15.9)

OGM, olfactory groove meningiomas; CSF, cerebrospinal fluid.
*In 4 cases, 2 different procedures were performed; in 1 case, 3 different procedures were performed.

compared with the fronto-orbito-basal and pterional approaches ($P = \text{NS}$, Mann-Whitney U test).

Outcome

The median preoperative KPS was 80 (range 40–100), 80 (40–100), and 75 (60–90) for the bifrontal, pterional, and fronto-orbito-basal approaches, respectively. Overall, the median KPS at discharge was 80 for the bifrontal and pterional approach and 70 for fronto-orbito-basal approach (Table 8). However, by excluding from the analysis the small-sized OGMs, which were absent in the patient group operated upon via the fronto-orbito-basal approach, the median KPS at discharge was 70 for each of the approaches. At latest follow-up, 64.6% of patients have no evidence of disease, 9.1% of patients are alive with disease, 14.1% are dead for the disease or for disease-related causes, and 12.1% are dead for disease-unrelated causes (Table 9). Overall, the mean survival was 103.4 ± 82.7 months ($\pm\text{SD}$). In WHO grade I OGMs, the 5- and 10-year survival rates were 81.2 (56/69) and 65.3% (32/49), respectively. In WHO grade II-III OGMs, the 5- and 10-year

Table 9. Extent of Resection, Outcome, and Follow-up of 99 OGMs

Extent of Resection at Last Surgery (Simpson Grade)	Outcome				Mean Follow-Up (Range; Months)
	NED (%)	AWD (%)	DD (%)	DUC (%)	
Grade I-II (n = 86)	63 (73.3)	5 (5.8)	8 (9.3)	10 (11.6)	102 (6–298)
Grade III-IV (n = 13)	1 (7.7)	4 (30.8)	6 (46.2)	2 (15.4)	116 (2–324)
Total (n = 99)	64 (64.6)	9 (9.1)	14 (14.1)	12 (12.1)	103 (2–324)

OGMs, olfactory groove meningiomas; NED, not evidence of disease; AWD, alive with disease; DD, dead of disease or disease-related complications; DUC, dead of unrelated causes.
This table includes 2 patients in whom the last surgery was performed at another institution.

survival rates were 60 (3/5) and 25% (1/4), respectively. Tumor recurred in 13 cases (13.1%), which included 10 of 93 (10.8%) WHO grade I and 3 of 6 (50%) WHO grade II-III OGMs. The mean interval for recurrence was 80.1 ± 51.9 months ($\pm\text{SD}$). In WHO grade I OGMs, the mean interval for recurrence was 87.9 ± 56.1 months ($\pm\text{SD}$; median 78, range 12–204 months). In WHO grade II-III OGMs, the mean interval for recurrence was 54 ± 27 months ($\pm\text{SD}$; median 67, range 23–72 months). Of 28 cases with hyperostosis of the anterior cranial fossa, tumor recurrence was noted in 2 of 26 (7.7%) WHO grade I and in 2 of 2 (100%) WHO grade II-III OGMs (Supplementary Figure S1). In both recurring WHO grade I OGMs, hyperostosis of the anterior cranial fossa had been drilled at surgery. In recurring WHO grade II–III OGMs, hyperostosis was removed in one case and left behind in the other case.

Temporal Evolution of Approaches and Surgeon Experience

The surgical approaches were temporally grouped according to the 1984–1990, 1991–2000, and 2001–2010 decades (Table 10). Although the bifrontal approach was used more frequently in the 1980s (81.3% of procedures) and the pterional approach was less frequent in the 1990s (14.6%), there were no significant changes in the use of these approaches over the decades ($P = \text{NS}$, χ^2 test). In the 1980s, the fronto-orbito-basal approach was not used at our institution, whereas it was used in 39 and 10.7% of procedures over the 1990s and 2000s, respectively. During the 1990s and 2000s, there were significant changes in the use of the 3 approaches ($P = 0.0045$; χ^2 test; Table 10). This figure may be related both to historical reasons, because popularity of complex skull base approaches in the 1990s, and to the greater number of large OGMs treated in

Table 8. Surgical Approaches, Tumor Diameter, and Outcomes of 99 OGMs

Surgical Approach* and Tumor Diameter	Median KPS at Discharge
Bifrontal (n = 70)	80
≤ 3 (n = 8)	85
3-6 (n = 29)	80
≥ 6 (n = 33)	70
Pterional (n = 21)	80
≤ 3 (n = 7)	90
3-6 (n = 7)	70
≥ 6 (n = 7)	60
Fronto-orbito-basal (n = 22)	70
≤ 3 (n = 0)	NA
3-6 (n = 6)	75
≥ 6 (n = 16)	70

OGMs, olfactory groove meningiomas; KPS, Karnofsky performance status; NA, not applicable.

*7 patients underwent 2 operations, 2 patients underwent 3 operations, 1 patient underwent 4 operations.

Table 10. Temporal Evolution of the Approaches and Results in 99 OGMs

Decade	No. Procedures	Approach, %			Large OGMs, %	Simpson Grade I-II, %	Life-Threatening Complications, %
		BF	PT	FOB			
1984–1990	16	81.3*	18.8*	0	50 [‡]	62.5 [§]	25
1991–2000	41	46.3* [†]	14.6* [†]	39 [†]	56.1 [‡]	78 [§]	14.6
2001–2010	56	67.9* [†]	21.4* [†]	10.7 [†]	44.6 [‡]	94.6 [§]	25

OGMs, olfactory groove meningiomas; BF, bifrontal; PT, pterional; FOB, fronto-orbito-basal; NS, nonsignificant.

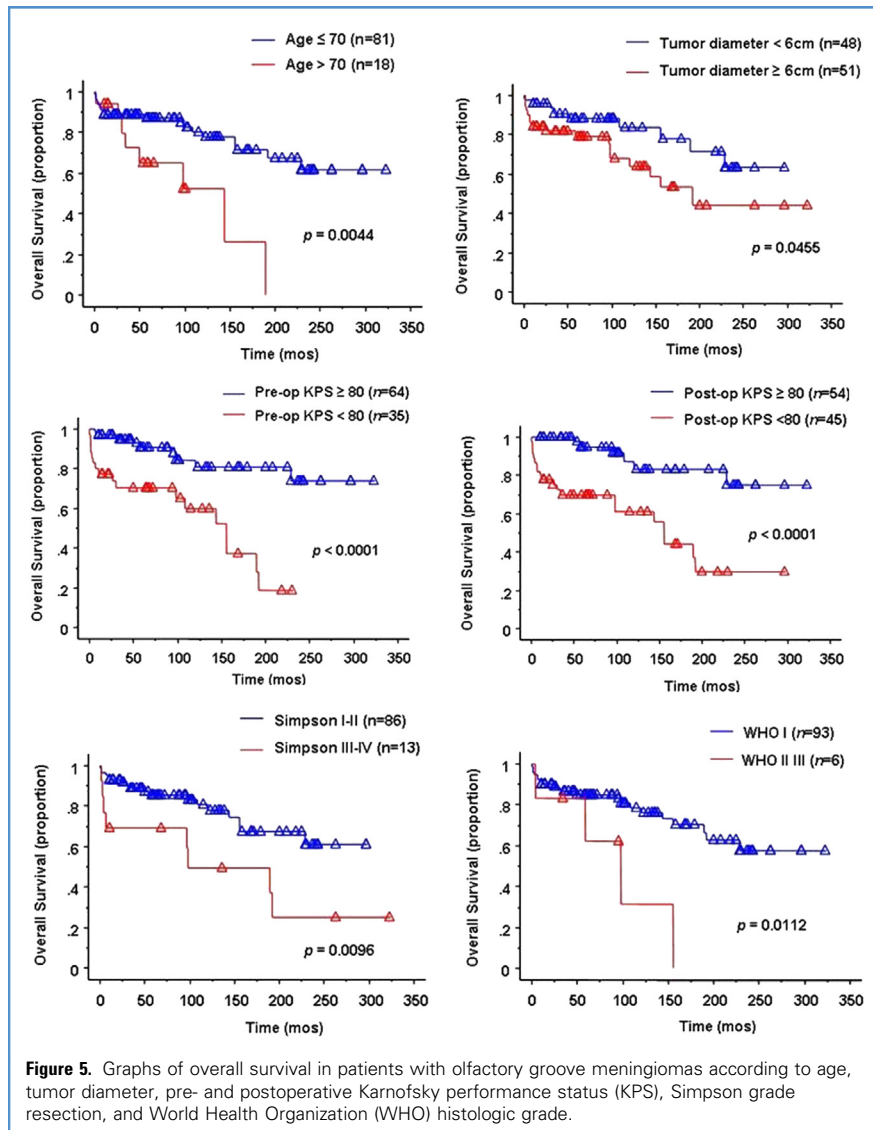
* $P = \text{NS}$ (χ^2 test).

[†] $P = .0045$ (χ^2 test).

[‡] $P = \text{NS}$ (χ^2 test).

[§] $P = .0028$ (1980s vs. 2000s; Fisher exact test); $P = .0257$ (1990s vs. 2000s; Fisher exact test).

^{||} $P = \text{NS}$ (χ^2 test).



the 1990s decade compared with the 2000s (Table 10). A figure that is likely to be related with practice is that the percent of Simpson grade I-II resections was significantly greater in the third decade compared either with the first and with the second decades ($P = 0.0028$ and $P = 0.0257$, respectively; Fisher exact test; Table 10). There were no significant differences in the rate of life-threatening complications among the decades.

To assess the impact of practice on surgical results, the experience of the neurosurgeons ($n = 14$) involved in the treatment of these tumors was arbitrarily categorized into 3 levels, according to the number of

procedures for OGMs they had performed (Supplementary Table S6). Interestingly, the fronto-orbito-basal approach was more frequently used by medium experienced neurosurgeons (5–15 procedures for OGMs) than by neurosurgeons with low (<5 procedures) or high experience (>15 procedures) ($P = 0.0107$, χ^2 test; Supplementary Table S6). There was a trend for the highly experienced surgeons to have lower rates of life-threatening complications ($P = 0.0836$, χ^2 test). To note that the large OGMs were operated upon mainly by surgeons with medium or high experience (Supplementary Table S6).

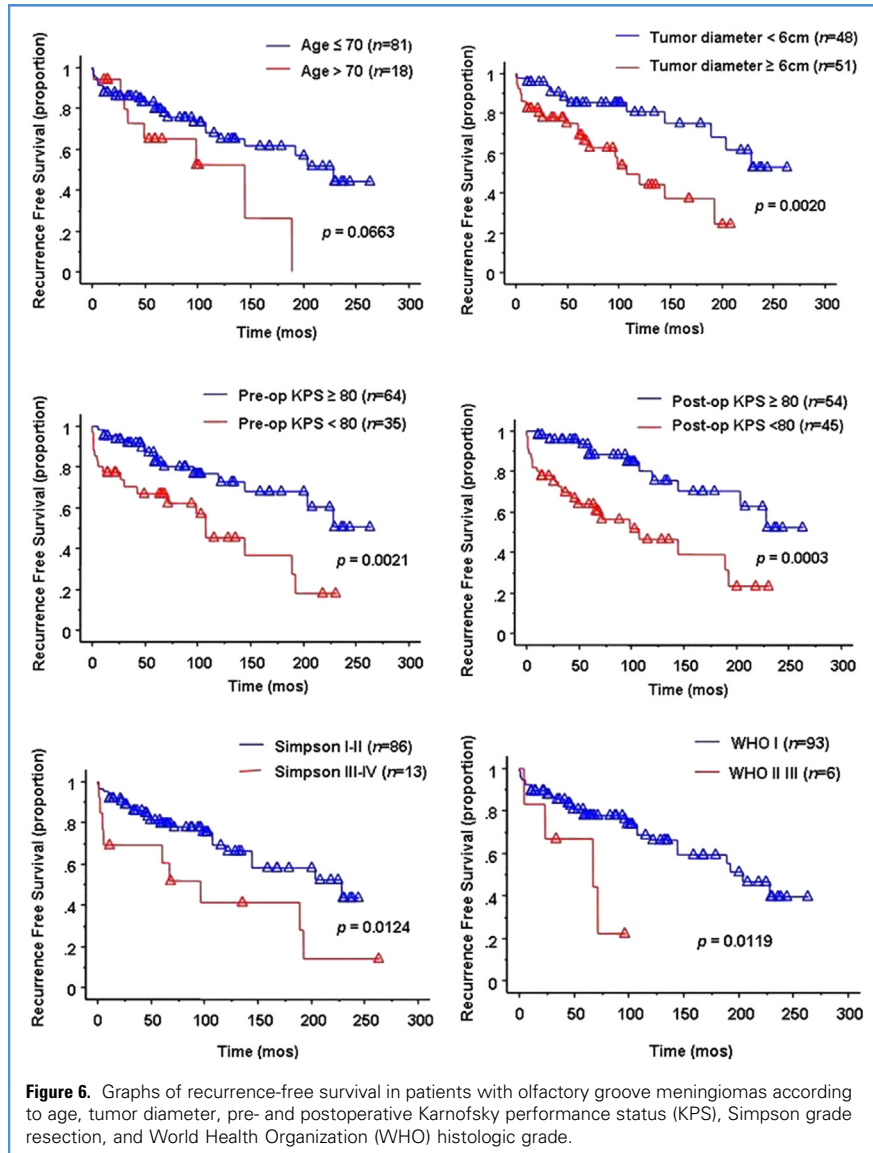
Prognostic Factors for Overall and Recurrence-Free Survival in OGMs

Among potential prognostic factors, age ≤ 70 years ($P = 0.0044$, log-rank test), tumor diameter < 6 cm ($P = 0.0455$, log-rank test), pre- and postoperative KPS ≥ 80 (both $P < 0.0001$, log-rank test), Simpson grade I-II ($P = 0.0096$, log-rank test), and WHO histologic grade I ($P = 0.0112$, log-rank test) were significantly associated with longer overall survival (Figure 5). Sex had no prognostic value on overall survival in our series ($P = 0.9975$). On multivariate analysis, age ($P = 0.0393$) and WHO histologic grade ($P = 0.0418$) emerged as independent prognostic factors for overall survival (Supplementary Table S7). To provide homogenous groups, we plotted overall survival curves after excluding the WHO grade II-III OGM and found that age ≤ 70 years ($P = 0.0014$, log-rank test), pre- and postoperative KPS ≥ 80 (both $P < 0.0001$, log-rank test) and Simpson grade I-II ($P = 0.0437$, log-rank test) were still significantly associated with longer overall survival (Supplementary Figure S2).

Pre- and postoperative KPS ≥ 80 ($P = 0.0021$ and $P = 0.0003$, respectively), tumor diameter ≥ 6 cm ($P = 0.0020$), Simpson grade I-II resection ($P = 0.0124$), and WHO grade I ($P = 0.0119$) predicted longer recurrence-free survival with tumor diameter ≥ 6 cm showing independent value ($P = 0.0429$) and WHO grade trending towards significance ($P = 0.0572$) on multivariate analysis (Figure 6 and Supplementary Table S8). By excluding the WHO grade II-III OGMs, we found that age ≤ 70 years, tumor diameter < 6 cm, and pre- and postoperative KPS ≥ 80 were significantly associated with longer recurrence-free survival ($P = 0.0354$, $P = 0.0067$, $P = 0.0053$, and $P = 0.0004$, respectively; log-rank test) (Supplementary Figure S3).

Surgical Outcome and Prognostic Factors

In the attempt to control for patient and tumor factors that might impact the end points of our analysis on the surgical approaches, i.e., that the fronto-orbito-basal approach achieved greater extent of tumor resection and had less chance for life-threatening complications, we categorized our patients in subgroups that were homogeneous either for age, KPS score,



tumor size, optic nerve/anterior communicating artery involvement, and WHO grade. Relevant findings were as follows. In patients with preoperative KPS <80 ($n = 42$), the chance for Simpson I-II resection was significantly greater when we used the fronto-orbito-basal approach than the bifrontal and pterional approaches ($P = 0.0042$; χ^2 test). Concerning the tumor factors, there was a trend for WHO grade I meningiomas with diameter ≥ 6 cm ($n = 50$) and for WHO grade I meningiomas with optic nerve/anterior communicating artery involvement ($n = 39$) towards a Simpson I-II resection when the fronto-orbito-basal

approach was used ($P = 0.0793$ and $P = 0.0743$, respectively; χ^2 test).

DISCUSSION

This single-center analysis of surgically treated OGMs is limited by the retrospective design with its inherent methodologic deficiencies and by selection bias in determining which approaches were used. It should also be emphasized that this is an institutional and not a single-surgeon series; therefore, case selection and choice of surgical approach reflect the different experience of several surgeons.

Despite this, the large number and long follow-up of OGMs enable comparing results achieved with various surgical strategies and assessing the prognostic value of clinical and pathologic variables.

Major results can be summarized as follows: 1) mortality and life-threatening complications were definitively greater after the bifrontal approach; 2) the fronto-orbito-basal approach allowed a significantly greater percentage of Simpson I-II removal than the bifrontal and pterional approaches; 3) retraction-related brain swelling did not occur in any case operated via the fronto-orbito-basal approach, although the probability for postoperative CSF leak was significantly greater using this approach; and 4) age ≤ 70 years, tumor diameter < 6 cm, pre- and postoperative KPS ≥ 80 , Simpson grade I-II, and WHO grade I were significant prognosticators for longer overall survival with age and WHO grade emerging as independent factors.

Surgical Approaches

Although the first successful surgery for OGMs dates back to the end of the nineteenth century (3), a review of the major neurosurgical series published during the last decades shows that the surgical treatment of OGMs still carries a non-negligible risk of mortality and life-threatening complications and that this risk is greater when the bifrontal approach is used (Tables 11 and 12). Overall, the calculated mortality rate is 5.7%, 0.9%, and 0% after the bifrontal, lateral, and fronto-orbito-basal approaches, respectively (Table 12). Life-threatening complications impact on 19.3%, 3.7%, and 7.4% of cases after the bifrontal, lateral, and fronto-orbito-basal approaches, respectively. These figures are quite likely related to brain retraction, which is minimized using the lateral approaches and the fronto-orbito-basal route.

A question arising from the use of lateral approaches for large OGMs is that there may be blind areas on the opposite side, particularly in cases in which the orbital roofs and the ethmoid lie on different planes along the vertical axis. Despite this, several surgeons have reported excellent results in terms of extent of resection, suggesting that obscured view may not represent a real problem with the use of lateral approaches. In our

Table 11. Literature Review of OGM Neurosurgical Series Published During the Last 2 Decades

Author, Year	No. Cases	Diameter >4-6 cm (%)	Surgical Approach	Simpson Grade I-II (%)	Life-Threatening Complications (%)	Mortality (%)	Recurrence (%)	Mean Follow-up, Months
Rubin et al.*, 1994 (18)	31	73	BF, UF, FL	84	Edema (10) Hemorrhage (10) Stroke (2)	9	7	60
Schaller et al., 1994 (19)	28	NA	FL	96.4	Hemorrhage (3.6)	3.6	NA	NA
Turazzi et al., 1999 (24)	37	86	FL	100	0	3	0	48
Paterniti et al., 1999 (15)	20	NA	FL	100	0	10	0	NA
El Gindi, 2000 (5)	25	NA	BF	NA	Hemorrhage (8)	0	NA	NA
Hentschel and DeMonte, 2003 (8)	13	46	FOB	85	0	0	0	24
Spektor et al., 2005 (21)	80	72.5	BF, UF, FL, FOB	90	Hemorrhage (5.7)	1.3	2.5	70.8
Nakamura et al., 2007 (11)	82	72.5	BF, FL	92.7	Edema (9.8) Hemorrhage (7.3)	4.9	4.9	63.4
Bassiouni et al., 2007 (1)	56	NA	BF, UF, FL	100	Hemorrhage (5.4) Stroke (1.8)	5.4	9.4	67
Romani et al., 2009 (17)	66	37.9	FL	90.9	Hemorrhage (1.5)	0	9.1	45 [†]
Tomasello et al., 2011 (23)	18	100	FL	94.4	0	0	16.7	93.5
Bitter et al., 2013 (2)	61	88.5	FL	98.4	Hemorrhage (3.3)	1.6	5.0	122
Present series	99	51.5	BF, FL, FOB	84.1	Edema (14.2) Hemorrhage (9.7) stroke (1.8)	3.5	10.8	103.4

OGM, olfactory groove meningioma; BF, bifrontal; UF, unilateral frontal. FL, fronto-lateral; NA, not available; FOB, fronto-orbito-basal.

*This article describes 67 meningiomas of anterior cranial fossa including 31 OGMs; data refer to the whole cohort.

†Median follow-up.

series, however, the lateral pterional approach enabled a lower rate of Simpson grade I-II resection compared with the fronto-orbito-basal route. In this context, it is interesting to note that the percentage of Simpson grade I-II removal reported

with the lateral approaches is highly affected by data of single-surgeon series, in which such a degree of tumor resection was achieved in 141 of 149 cases (95%) (17, 19, 23, 24). Including only the institutional series in the analysis, the percentage of

Simpson grade I-II resections achieved with the lateral approaches decreases from 94% to approximately 85%, a figure that is consistent with our results. Therefore, one conclusion may be that the complete resection of OGMs via the lateral approaches is technically feasible in about 94% of cases but this achievement implies a specific experience, an experience that often includes the bifrontal approach as a preliminary step, as demonstrated by Nakamura et al.'s and Turazzi et al.'s series (11, 24).

In recent years, there have been several reports of anterior skull base meningiomas operated upon via endoscopic surgery; however, only a few of deal with the endoscopic transcribiform plate approach for OGMs (for review, see Komotar et al. (9)). In principle, the endoscopic approach to OGMs should avoid brain retraction and provide early tumor devascularization. However, preliminary experience shows that the extent of tumor resection is

Table 12. Meta-analysis of OGM Neurosurgical Series According to Surgical Approaches

Surgical Approach (References)	No. Cases	Diameter >4-6 cm (%)	Simpson Grade I-II (%)	Life-Threatening Complications (%)	Mortality (%)	Recurrence (%)
Bifrontal (1, 5, 11, 21, present series)	212	49.0	88.8	19.3	5.7	8.5
Lateral (1, 2, 11, 15, 17, 19, 21, 23, 24, present series)	321	65.9	94.1	3.7	0.9	5.8
Fronto-orbito-basal (8, 21, present series)	54	64.8	96.3	7.4	0	5.6

OGM, olfactory groove meningioma.

significantly lower than craniotomy. In addition, there are several technical limitations to this approach that include duration of surgery, arterial bleeding control, and difficulty for skull base reconstruction.

Predictors of Prognosis

The present study has allowed definition of survival curves relative to common prognosticators that represent a standard point of reference in modern oncology and that had not been previously reported for patients with OGMs. In their series of patients with OGMs operated upon via the transglabellar/subcranial approach, Pepper et al. (16) used the Kaplan-Meier method to estimate overall and disease-free survival, that were 121.45 and 93.03 months, respectively, and that are consistent with our results. Given the small number of cases, however, the prognostic impact of clinical and pathologic variables was not assessed. In convexity meningiomas, actuarial curves have rigorously been defined by Hasseleid et al. (6), who found that age, sex, WHO grade, and Simpson grade were significantly associated with overall survival. Apart from sex, which we did not find to be predictive in OGMs, estimates like age and WHO grade were common prognosticators for overall survival both in the study by Hasseleid et al. and in our own one. The extent of tumor resection as prognostic factor deserves a separate comment. Several studies have related the Simpson grade resection with survival of meningioma patients; however, heterogeneity of tumor location as well as differences in statistic modeling, including the mere definition of tumor recurrence, generated ambiguous results (6, 7, 12, 13, 22). For example, Oya et al. (13) did not find difference between the recurrence-free survival of patients with WHO I meningiomas treated by Simpson Grade I, II, or III resection. Heald et al. reported that Simpson Grade IV versus Simpson Grade I resected meningiomas were at an increased risk of recurrence or progression, whereas Simpson Grade II versus Simpson Grade I resected tumors were not (7). The study by Ohba et al. (12) on skull base meningiomas showed that the extent of resection (gross total vs. subtotal resection) was associated with progression-free survival on multivariate analysis; however, it did not relate significantly with overall survival. The relevance of Simpson

grade as a prognostic factor of WHO grade I meningiomas has recently been challenged by Sughrue et al. (22), who argued that the benefit of resecting the tumor with dura and underlying bone may be negligible compared with leaving small amounts of tumor.

This result, which conflicts with the common opinion that the Simpson grade of resection represents one main factor for prognosis of meningiomas, has been explained by Hasseleid et al. (6) with the large number of skull base compared with convexity meningiomas included in the Sughrue's series. The concept that in skull base meningiomas the Simpson resection grade may have a lower prognostic value compared with other meningioma locations seems to be confirmed by our study, in which the Simpson grade holds significant value both for overall and recurrence-free survival on univariate statistics but it does not emerge as an independent prognosticator.

Interestingly, reanalyzing the surgical outcome after we controlled for patient and tumor prognosticators showed that patients with a preoperative KPS <80 had significantly more chances for Simpson grade I-II resection when operated on via the fronto-orbito-basal approach. This result demonstrates that in patients with clinically relevant bilateral compression of the frontal lobes adequate exposure and prolonged dissection, both of which are required for total tumor removal, can be performed safely via the fronto-orbito-basal route.

CONCLUSIONS

In this series of OGMs, which is the largest one to our knowledge, the bifrontal approach was associated with a greater risk of mortality and life-threatening complications compared with the lateral pterional and fronto-orbito-basal approaches. Two independent factors for overall survival of OGM patients were identified, namely age and WHO grade. Although its prognostic power is probably caused due to other variables, Simpson grade I-II resection should remain the standard of care for OGMs.

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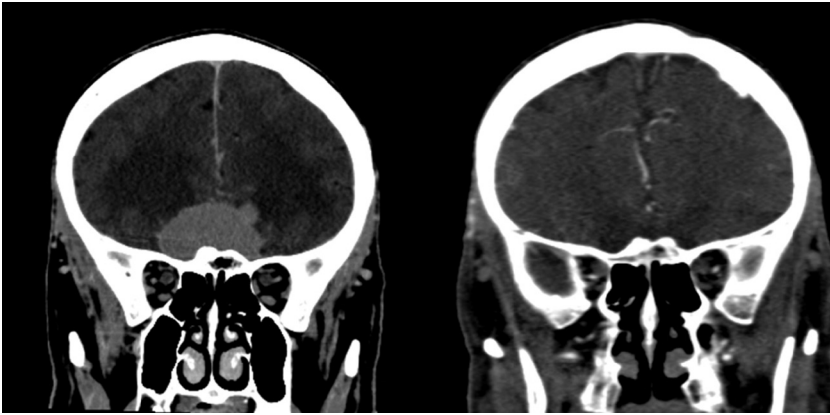
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Supplementary Figure S1. *Left*, preoperative coronal contrast-enhanced CT showing a medium-sized olfactory groove meningioma with a hyperostosis of the right lamina cribrosa. *Right*, postoperative coronal contrast-enhanced CT showing no tumor recurrence with unchanged hyperostosis eight years after surgery. CT, computed tomography.

