## Supra-orbital keyhole removal of anterior fossa and parasellar meningiomas

Manoel Antonio de Paiva-Neto<sup>1</sup>, Oswaldo Inácio de Tella-Jr.<sup>2</sup>

## ABSTRACT

The improvement of surgical techniques as well as the introduction of new surgical instruments promoted the use of keyhole craniotomies in neurosurgery. We evaluated the technical aspects of the supra-orbital keyhole approach considering the indications, limitations, and complications of this approach to treat anterior cranial fossa and parasellar meningiomas. Twenty-four patients (21 females; mean age, 53±8.6 years) operated on between 2002 and 2006 through a supra-orbital eyebrow approach were studied. Maximal tumor diameter ranged from 1.6 to 6 cm. Gross total resection was done in 20 (83.3%). All tumors were histologically benign. Two patients (8%) experienced CSF rinorhea and another two patients suffered transitory diabetes insipidus (8%). One patient experienced transitory hemiparesis. There was one case of meningitis and one mortality. Follow-up ranged between 6 to 66 months (mean 31.5±20.1 months), with no recurrence. The supra-orbital keyhole craniotomy is a useful minimally invasive approach to treat selected anterior fossa and parasellar meningiomas.

Key words: meningioma, supra-orbital craniotomy, olfactory groove, parasellar.

# Minicraniotomia supra-orbitária superciliar no tratamento de meningiomas na fossa craniana anterior e para-selares

## RESUMO

A evolução técnica e a introdução de instrumentais cirúrgicos mais delicados proporcionaram o uso de craniotomias menores no tratamento de patologias intracranianas. Avaliamos os aspectos técnicos da minicraniotomia supra-orbitária superciliar, considerando as indicações, limitações e complicações no tratamento de meningiomas na fossa craniana anterior e para-selares. Vinte e quarto pacientes (21 mulheres; idade média, 53±8,6 anos) operados entre 2002 e 2006 foram estudados. O diâmetro tumoral máximo variou de 1,6 a 6 cm. Ressecção total foi obtida em 20 (83,3%). Todos os tumores eram histologicamente benignos. Dois pacientes (8%) apresentaram fistula liquórica pós-operatória e outros dois diabetes insipido transitórioa (8%). Um paciente evoluiu com hemiparesia transitória. Houve um caso de meningite e um de evolução fatal. O seguimento variou de 6 a 66 meses (média 31,5±20,1 meses), não houve recidiva. A minicraniotomia supra-orbitária superciliar é uma via de abordagem eficaz para o tratamento de meningiomas da fossa craniana anterior e para-selares selecionados.

Palavras-chave: meningioma, craniotomia supra-orbitária, goteira olfatória, para-selar.

Over the last two decades, keyhole surgical approaches have been increasingly used to approach intracranial cranial base lesions promoted by evolution in modern neuroimaging, innovative neurosurgical instrumentation and techniques. One of these approaches, the supra-orbital "eyebrow" keyhole craniotomy requires little brain retraction and affords satisfactory surgical exposure to the frontal fossa and

#### Correspondence

Manoel Antonio de Paiva-Neto Rua Leandro Dupret 847 / 62 04025-013 São Paulo SP - Brasil E-mail: mapnpaiva@ig.com.br

Received 10 March 2009 Received in final form 4 September 2009 Accepted 7 September 2009 <sup>1</sup>MD, MSci, Disciplina de Neurocirurgia Universidade Federal de São Paulo, São Paulo SP, Brazil. Post-Graduation Student, Hospital Professor Edmundo Vasconcelos, São Paulo SP, Brazil; <sup>2</sup>MD, PhD, Disciplina de Neurocirurgia Universidade Federal de São Paulo, São Paulo SP, Brazil. Professor, Hospital Professor Edmundo Vasconcelos, São Paulo SP, Brazil. parasellar area as recently demonstrated by anatomic and clinical studies<sup>1-3</sup>. The minimal scalp and muscle dissection required promote a rapid and less painful recovery compared to standard craniotomies<sup>2,4-8</sup>. The major drawback of the supra-orbital approach is the potential for limited maneuverability given the small bony opening which typically measures 15-20 mm by 25-30 mm<sup>1-4</sup>.

Recently, Brazilian authors have reported their initial experience using this approach to treat intracranial aneurysms and intracranial tumors<sup>9,10</sup>. We have been using the supra-orbital approach for the last 6 years to reach anterior fossa, parasellar tumors and intracranial aneurysms.

Herein we describe our experience and lessons learned using this approach for treatment of anterior cranial fossa and parasellar meningiomas.

#### **METHOD**

#### Patient population and data collection

Between January 2002 and December 2006, 24 patients with olfactory groove (12), anterior clinoid (3) and tuberculum sellae meningioma (9) who underwent a supra-orbital trans-cranial transeyebrow removal were identified. All procedures were performed by two authors (MAPN and OITJ) at UNIFESP-EPM and Hospital Professor Edmundo Vasconcelos. This retrospective study was approved by the Ethic Board of UNIFESP (Process 0808/06). Patients' medical records, clinical visits and imaging studies were reviewed; tumor characteristics, intra and post-operative complications and surgical outcomes of patients were collected. Descriptive statistics were performed and demographic data was given in means ± standard deviation.

#### Supra-orbital "eyebrow" craniotomy

As previously described<sup>1,2</sup>, patients are placed supine in the 3-point headholder and angled 20-60° to the contra lateral side based on the location and projection of tumor to the right or left. All clinoidal meningiomas were approached by the same side of the lesion. For suprasellar tumors 20° has been found to be sufficient, the anterior fossa tumors requires 45 to 60° contralateral rotation. The head is slightly retroflexed as well with the malar eminence prominent staying in the highest point. The skin incision placed within the eyebrow, extends from just medial to the supra-orbital notch laterally and inferiorly until the lateral limit of the eyebrow or beyond, in a skin fold along the frontozygomatic process. Medially, the skin incision remains superficial to avoid injury to the supra-orbital nerve. The skin flap is retracted superiorly with fish hooks to gain supra-orbital exposure. A pericranial flap is then created and incised in a half moon-shaped fashion, then retracted inferiorly along the supra-orbital rim area.

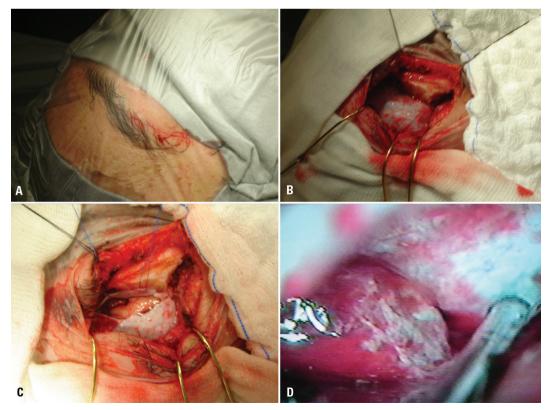


Fig 1. [A] Skin eyebrow incision. [B] Craniotomy size. [C] Picture showing the dural opening. [D] Picture shoing the microscopic visualization of an anterior cranial fossa meningioma before resection.

The temporalis fascia and muscle are released at the superior temporal line and retracted inferiorly and laterally to expose the keyhole below and posterior to the fronto-zygomatic process. A single burr hole is placed below the superior temporal line and posterior to the keyhole with the high sped drill. A free supra-orbital half moonshaped bone flap is made which does not include the orbital rim and measures approximately 15-20 mm by 20-25 mm. The inferior edge of the calvarium is drilled down to provide better exposure to the floor of the frontal fossa. If the frontal sinus has been entered (which rarely occurs), it can be repaired with abdominal fat and the pericranial flap (Fig 1).

The dura is opened in C-shape fashion with its base toward the orbital rim. The operating microscope is brought into use at this point. The olfactory tract is identified and followed back to the ipsilateral optic nerve and carotid cistern. The arachnoid here is opened sharply with egress of CSF and further brain relaxation. A self retaining brain retractor can be placed over the frontal lobe, although in recent cases we usually used the retractor only at the beginning of the case. At this stage procedure continues with the use of operating microscope. Standard microsurgical dissection tumor removal then proceeds with care taken to preserve arachnoids membranes. Following tumor removal, the dura is closed in watertight fashion. The bone flap is re-approximated with titanium plates and screws when available or with nylon stitches. To achieve a better cosmetic result, the superior and inferior edges and medial part of the bone should be placed with minimum distance from the adjacent bone and the bone gaps can be further filled with collagen sponge. The pericranial flap, if not needed for a frontal sinus defect, is placed over the bone flap. The scalp incision is closed with galeal and intradermal stitches.

### Approach selection and surgical goals

For olfactory groove meningiomas we select this approach to tumors that do not invade the frontal or ethmoid sinuses. Also, huge tumors with bilateral optic canal involvement are best approached by other craniotomies<sup>11</sup>. For tuberculum sellae meningiomas we do not use this

Case	Age(y)/Sex	Location of lesion	Diameter(cm)	Extent of resection	Complication
1	56/M	OG	3.3 × 3.6 × 3.2	Gross total	None
2	49/F	OG	$2.5 \times 2.7 \times 3.1$	Gross total	None
3	50/F	OG	$4 \times 3.8 \times 3.6$	Gross total	None
4	54/F	OG	$3.5 \times 3.4 \times 3.7$	Near total	None
5	49/F	OG	$2 \times 2.5 \times 2.7$	Gross total	None
6	68/F	OG	$3.1 \times 2.9 \times 3.2$	Gross total	Meningitis
7	66/M	OG	$6 \times 4.5 \times 5$	Gross total	Death
8	48/F	OG	$3.5 \times 4 \times 3.2$	Gross total	None
9	65/F	OG	$3.5 \times 4 \times 3.2$	Gross total	None
10	62/F	OG	$3.2 \times 3.5 \times 3$	Gross total	None
11	53/F	OG	$3.4 \times 3.6 \times 4$	Gross total	CSF leak
12	52/F	OG	$3.5 \times 2.9 \times 3$	Gross total	None
13	51/F	TS	$2.5 \times 2.5 \times 2$	Gross total	None
14	45/F	TS	$2 \times 2.5 \times 2.3$	Gross total	DI
15	33/F	TS	$1 \times 1.5 \times 1.6$	Gross total	DI
16	51/F	TS	$2 \times 2.5 \times 2.4$	Gross total	None
17	62/F	TS	$3 \times 2.8 \times 2.7$	Gross total	None
18	48/F	TS	$2.7 \times 3 \times 2.6$	Gross total	None
19	56/F	TS	$2 \times 1.8 \times 1.9$	Gross total	CSF leak
20	47/F	TS	$3 \times 2.7 \times 2.6$	Near-total	None
21	56/F	TS	$3 \times 4.2 \times 1.9$	Near-total	None
22	65/M	С	$3.5 \times 3.2 \times 3$	Near-total	PI
23	47/F	С	$2 \times 1.8 \times 2.2$	Gross total	None
24	39/F	С	$2.2 \times 2 \times 2.5$	Gross total	None

OG: olfactory groove; TS: tuberculum sellae; C: clinoidal; DI: diabetes insipidus; PI: perfurant injury.

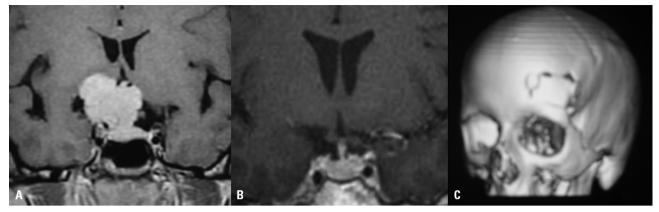


Fig 2. Coronal T1 MR with gadolinium showing a tuberculum sellae meningioma with partial encasement of the right carotid and anterior cerebral arteries [A]. Post operative MRI showing a total resction [B]. Cranial CT sacan after reconstruction showing the craniotomy [C].

approach when there are signs of temporal fossa or gross optic canal extensions and we reserve this approach to clinoid meningiomas that arise at the superior part of anterior clinoid process, pushing the carotid arteries backwards<sup>12</sup>. Although the surgical goal is total tumor removal, in instances of dense tumor adhesions to the optic apparatus, pituitary stalk or Circle-of-Willis structures, tumor remnants are left behind. Similarly, in cases of cavernous sinus invasion, no attempt is made to remove these tumor extensions. Tumor extensions into the optic canal were removed after drilling the roof of the optic canal with great care to avoid opening the sphenoid sinus.

#### **Outcome analysis**

Tumor characteristics including size, location and cavernous sinus invasion were recorded. Clinical notes were reviewed for patient demographics, intra- and post-operative complication rates. Tumor removal rates were defined as: gross total removal according to surgeon's description and if there is no residual tumor seen on the immediate and 3 months post-operative CT/MR images (Simpson I-III), near-total removal if  $\geq$ 90 % of tumor was removed (Simpson IV) or sub-total removal if <90 % of tumor removed (SimpsonV)<sup>13</sup>.

#### RESULTS

Results are summarized in Table. Among 24 patients (12 olfactory groove, 9 tuberculum sella and 3 clinoidal meningioma), there were 21 females and three males. The ages ranged from 33 to 68 years (mean 53±8.6 years). One tumor was between 0 and 2 cm, 17 between 2 and 4 cm and 6 above 4cm of maximal diameter. Of 24 meningiomas, gross total resection was done in 20 (83.3%) and near total in four (16.6%) of cases. The approach was suitable in all but one case with an olfactory groove meningioma, in this case a small part of the tumor (<5%) that was attached to the posterior wall of frontal sinus at the

left side was not visible during a right sided approach and consequently not resected (Fig 3). One patient harboring a tuberculum sellae meningioma presented right cavernous sinus invasion, in this patient all extracavernous tumor was resected (>90%). In two other patients (one with tuberculum sellae and other with clinoidal meningiomas), small parts of the tumor were left behind because adhesions to anterior communicant artery complex. Seventeen patients (70.8%) experienced uneventful recoveries. Several complications occurred. Two patients (8%) experienced CSF rhinorrhea that were treated successfully with external lumbar drainage, another two patients suffered transitory diabetes insipidus (8%). One patient harboring an anterior clinoidal meningioma experienced transitory (two months) left-sided hemi paresis secondary a small perfurant injury. There was one case of meningitis. One patient (4.1%) with a huge olfactory groove meningioma went on to develop hypothalamic dysfunction leading to his demise. Histological examination revealed that all tumors were Grade I meningiomas according World Health Organization (WHO) 2000 classification<sup>14</sup>. The follow-up ranged between 6 to 66 months (mean 31.5±20.1 months), until now there is no recurrence.

#### Illustrative cases

**Case 1** – A 48-year-old woman sought treatment for a 2 month history of a declining peripheral vision in both eyes. Magnetic resonance imaging (MRI) showed a  $2.7 \times 3 \times 2.6$  cm suprasellar tumor with partial encasement of the right carotid and anterior cerebral artery. In January 2005, the tumor was totally removed by a right supra-orbital eyebrow approach. The patient experienced an uneventful post operative recovery and an improvement of her visual symptoms (Fig 2). In her three-year follow-up the patient remains asymptomatic and without tumor recurrence.

**Case 2** – A 54 year-old woman sought treatment for a generalized seizure. Her neurological examination was

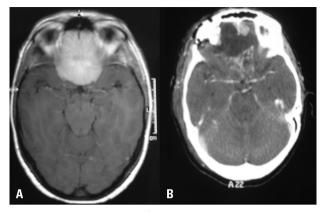


Fig 3. Axial MRI showing an olfactory groove meningioma with anterior extension up to frontal sinus [A]. Post operative CT showing a small remnant on left anterior side [B].

unremarkable and her MRI showed a 3,5x3,4x3,7 cm olfactory groove meningioma with anterior extension to the posterior wall of the frontal sinus. On February 2004, she was submitted to a right supra-orbital eyebrow approach. After the tumor debulking, the falx was cauterized and partially resected to accomplish a contra lateral tumor removal that was considered total during the procedure. The post operative CT showed a small residual tumor in the most anterior and contra lateral frontal base, attached to the anterior falx (Fig 4). The patient experienced an uneventful recovery and has no sign of tumor regrowth in her four year follow-up image.

#### DISCUSSION

With improvements in microsurgical technique, refined instrumentation, surgical navigation and endoscopy, anterior cranial fossa and parasellar tumors traditionally approached by a conventional large fronto-temporal or bifrontal craniotomy are now often accessed through smaller operative corridors<sup>2,15,16</sup>.

In 1900 Krause first demonstrated supra-orbital, subfrontal approach on cadaver, then eight years later he reported the first resection of skull base meningioma through this approach<sup>17</sup>. The initial approach to skull base tumors via supra-orbital route developed in early 20<sup>th</sup> century, but it has not been popular till recent decades<sup>18,19</sup>. The keyhole "eyebrow" supra-orbital craniotomy was reintroduced with "a concept of geometric construction of the surgical approach with a choice of the correct limited craniotomy as a key characteristic for entering a particular intracranial space and for working with a minimum of traumatization"<sup>15</sup>.

Recently, some authors reported two retrospective analyses of patients with anterior cranial fossa meningiomas operated by one surgeon using three different transcranial approaches. They reported that a small frontolateral approach provided best results concerning visual outcomes than the pterional and subfrontal approaches, and similar results regarding rates of total tumor removal<sup>20,21</sup>.

The results of gross total resection of anterior cranial fossa meningiomas reported in the literature, as well as ours (83.3%), obtained after minimally invasive approaches to these tumors have similar results to traditional craniotomy series<sup>20,22-27</sup>. Recently, Reisch and Perneczky reported their experience using the supraorbital eyebrow approach for the treatment of 93 anterior and medial fossa meningiomas. They could remove completely 89.2% of the tumors with minor complications and claimed that temporobasal extensions are the limitations for the approach<sup>2</sup>. These and other authors believe that tumor size is not a limitation for the supraorbital eyebrow approach<sup>1,2</sup>. We believe that limitations of usefulness of this approach are frontal sinus and ethmoid sinus extensions in olfactory groove meningiomas. This approach does not afford access to frontal sinus extensions of the tumor; also cranial base reconstruction after resection of gross ethmoid extensions of the tumor is very difficult. In our series, in one case a small portion of the tumor that was attached to the posterior wall of the frontal sinus was not visualized and then not resected. Probably if we used an endoscopic-assisted technique or neuronavigation, we could have been able to accomplish a total removal. In suprasellar lesions the limitations are temporobasal extensions of the tumor. Also we believe that tumors that grossly invade the optic canal or arise in the inferior part of clinoid process or interdural spaces are best approached by others craniotomies<sup>28,29</sup>. Major adhesions to cranial nerves or vessel are limitations not craniotomy related. Ability to achieve a Simpson Grade I resection after minimally invasive approaches of meningiomas and the real rate of recurrence of these tumors after these approaches is still unclear because of the short follow up of the recent series, including ours<sup>1,2,23</sup>.

The complications reported with this technique are no more than associated with standard craniotomies. The main complication is that of CSF rhinorrhea that was reported to range between 0 to 7%<sup>1,2,22,23</sup> of cases and was observed in two cases in our series, that were successfully treated by lumbar external drainage. Some authors<sup>16</sup> point out that preoperative CT scan should be carefully evaluated for the size and lateral extension of the frontal sinus. We believe that frontal sinus transgression should be aggressively managed with exenteration of the mucosa, watertight dural closure, sinus packing with abdominal fat or a piece of temporal muscle and covered with frontal fascia.

Diabetes insipidus is one of the most commonly reported endocrinological events after removal of suprasellar meningiomas<sup>30</sup>, we observed two cases of transient diabetes insipidus in our series. One patient harboring a clinoidal meningioma experienced a temporary hemipharesy secondary to a small perfurant injury. Another patient died after a severe post operative hypothalamic dysfunction, probably secondary to small perfurant injury during tumor dissection. He harbored the most volumous tumor in our series. Although the size of the lesion does not seem to play an important role in the approach selection of these tumors; as those tumors grow they tend to disrupt arachnoid planes and encase major intracranial vessels and optic nerve<sup>27,31</sup>. Piece by piece resection with careful preservation of arachnoid planes is the most important surgical step for preservation of the microcirculation of the optic nerve and avoidance of other vessels injuries<sup>27</sup>. Arteries supplying the tumor should clearly be differentiated from those supplying the optic system or hypothalamus.

When dense adherences to vascular structures are found, it is safer to leave tumor remnants behind.

In conclusion, the supra-orbital keyhole craniotomy is a useful minimally invasive approach to anterior fossa and suprasellar meningiomas. It allows quick access to the tumor and is minimally invasive with less brain exposure but still affords high rates of tumor removals. It should be considered as part of the neurosurgical armamentarium to manage skull base lesions when indicated and not to replace other well recognized skull base approaches.

#### REFERENCES

- 1. Czirjak S, Szeifert GT. The role of the superciliary approach in the surgical management of intracranial neoplasms. Neurol Res 2006;28:131-137.
- Reisch R, Perneczky A. Ten-year experience with the supraorbital subfrontal approach through an eyebrow skin incision. Neurosurgery 2005;57:242-55.
- Figueiredo EG, Deshmukh V, Nakaji P, et al. An anatomical evaluation of the mini-supraorbital approach and comparison with standard craniotomies. Neurosurgery 2006;59:ONS212-220.
- Perneczky A, Muller-Forell W, Van Lindert E, Fries G. Keyhole concept in neurosurgery: with endoscopic-assissted microneurosurgery and case studies. New York: Thieme, 1999.
- Wiedemayer H, Sandalcioglu IE, Wiedemayer H, Stolke D. The supraorbital keyhole approach via an eyebrow incision for resection of tumors around the sella and the anterior skull base. Minim Invasive Neurosurg 2004;47:221-225.
- Jallo GI, Suk I, Bognar L. A superciliary approach for anterior cranial fossa lesions in children: technical note. J Neurosurg 2005;103:88-93.
- Mitchell P, Vindlacheruvu RR, Mahmood K, Ashpole RD, Grivas A, Mendelow AD. Supraorbital eyebrow minicraniotomy for anterior circulation aneurysms. Surg Neurol 2005;63:47-51.

- Lan Q, Gong Z, Kang D, et al. Microsurgical experience with keyhole operations on intracranial aneurysms. Surg Neurol 2006;66(Suppl 1):S2-S9.
- Fernandes YB, Maitrot D, Kehrli P, Tella OI, Jr., Ramina R, Borges G. Supraorbital eyebrow approach to skull base lesions. Arg Neuropsiguiatr 2002;60:246-250.
- 10. Ponde JM, Prandini MN. [Supraorbital craniotomy to approach the sellar and the parasellar regions]. Arq Neuropsiquiatr 2002;60:661-665.
- Obeid F, Al-Mefty O. Recurrence of olfactory groove meningiomas. Neurosurgery 2003;53:534-543.
- Al-Mefty O, Ayoubi S. Clinoidal meningiomas. Acta Neurochir (Wien) 1991;53 (Suppl): S92-S97.
- Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry 1957;20:22-39.
- 14. Kleihues P, Louis DN, Scheithauer BW, et al. The WHO classification of tumors of the nervous system. J Neuropathol Exp Neurol 2002;61:215-229.
- Fries G, Perneczky A. Endoscope-assisted brain surgery: part 2--analysis of 380 procedures. Neurosurgery 1998;42:226-232.
- Gharabaghi A, Krischek B, Feigl GC, et al. Image-guided craniotomy for frontal sinus preservation during meningioma surgery. Eur J Surg Oncol 2008;34:928-931.
- 17. Krause F. Chirurgie des Gehirns und Rückenmarks nach eigenen Erfahrungen. Berlin: Urban & Schwarzenberg, 1908.
- Landeiro JA, Flores MS, Lopes CA, Lapenta MA, Ribeiro CH. [Subfrontal approach in sellar and suprasellar lesions]. Arq Neuropsiquiatr 2000;58:64-70.
- 19. Delashaw JB, Jr., Tedeschi H, Rhoton AL. Modified supraorbital craniotomy: technical note. Neurosurgery 1992;30:954-956.
- Nakamura M, Roser F, Struck M, Vorkapic P, Samii M. Tuberculum sellae meningiomas: clinical outcome considering different surgical approaches. Neurosurgery 2006;59:1019-1029.
- Nakamura M, Struck M, Roser F, Vorkapic P, Samii M. Olfactory groove meningiomas: clinical outcome and recurrence rates after tumor removal through the frontolateral and bifrontal approach. Neurosurgery 2007;60:844-852.
- 22. Wiedemayer H, Sandalcioglu IE, Stolke D. The supraorbital keyhole approach via an eyebrow incision for resection of tumors around the sella and the anterior skull base. Minim Invasive Neurosurg 2004;47:221-225.
- Shanno G, Maus M, Bilyk J, et al. Image-guided transorbital roof craniotomy via a suprabrow approach: a surgical series of 72 patients. Neurosurgery 2001; 48:559-568.
- Joseph V, Chacko AG. Suprabrow minicraniotomy for suprasellar tumours. Br J Neurosurg 2005;19:33-37.
- Bassiouni H, Asgari S, Stolke D. Olfactory groove meningiomas: functional outcome in a series treated microsurgically. Acta Neurochir (Wien) 2007;149:109-121.
- Colli BO, Carlotti CG, Jr., Assirati JA Jr., et al. Olfactory groove meningiomas: surgical technique and follow-up review. Arq Neuropsiquiatr 2007;65:795-799.
- Goel A, Muzumdar D, Desai KI. Tuberculum sellae meningioma: a report on management on the basis of a surgical experience with 70 patients. Neurosurgery 2002;51:1358-1364.
- Lee JH, Sade B, Park BJ. A surgical technique for the removal of clinoidal meningiomas. Neurosurgery 2006;59:ONS108-114.
- 29. Al-Mefty O. Clinoidal meningiomas. J Neurosurg 1990;73:840-849.
- Fahlbusch R, Schott W. Pterional surgery of meningiomas of the tuberculum sellae and planum sphenoidale: surgical results with special consideration of ophthalmological and endocrinological outcomes. J Neurosurg 2002;96:235-243.
- Margalit NS, Lesser JB, Moche J, Sen C. Meningiomas involving the optic nerve: technical aspects and outcomes for a series of 50 patients. Neurosurgery 2003;53:523-533.