**DOI:** 10.5137/1019-5149.JTN.17866-16.1
Received: 12.04.2016 / Accepted: 31.07.2016
Published Online: 22.08.2016

*Original Investigation*

# Retrospective Analysis of 449 Intracranial Meningioma Patients Operated Between 2007 and 2013 at a Single Institute

Emrah CELTIKCI[1], A. Memduh KAYMAZ[2], Gulsah AKGUL[3], Burak KARAASLAN[2], O. Hakan EMMEZ[2], Alp BORCEK[4]

[1]Yildirim Beyazit University, Yenimahalle Research and Education Hospital, Department of Neurosurgery, Ankara, Turkey
[2]Gazi University, Faculty of Medicine, Department of Neurosurgery, Ankara, Turkey
[3]Yuksek Ihtisas University, Faculty of Medicine, Department of Pathology, Ankara, Turkey
[4]Gazi University, Faculty of Medicine, Department of Neurosurgery, Division of Pediatric Neurosurgery, Ankara, Turkey

Early results of this manuscript was presented as an oral presentation in Turkish Language in April 2015 at the Turkish Neurosurgical Society's 29th Annual Congress, Antalya, Turkey.

## ABSTRACT

**AIM:** Meningioma literature has many large surgical case series, which have been references of text books and neurosurgical practice. Many of those series were published when stereotactic radiosurgery (SRS) was not so common or these series were in terms of World Health Organization (WHO) 2000 classification. In this study, we aimed to make an update to the current literature using WHO 2007 classification system.

**MATERIAL and METHODS:** Four hundred eighty-eight intracranial meningioma patients underwent open surgery in 2007-2013 and 449 of them were included in this study. All pathological specimens were re-evaluated in terms of WHO 2007 classification. All demographical and follow-up records and imaging archives were investigated by using our center's central automation system and National Central Population Management System. If records were not available or not adequate, investigators made phone calls to patients. Pediatric patients were excluded.

**RESULTS:** Three hundred twenty-six female (76.2%) and 123 male (27.4%) patients were analyzed. Their ages ranged from 18 to 84 years (mean=51.6±11.9 years). The most common subtype of meningioma was meningothelial meningioma (51.7%), followed by atypical meningioma (20.3%). WHO Grade I meningiomas had statistically random localization distribution, but WHO Grade II meningiomas were more common in the convexity, parasagittal and middle fossa. Younger age was found to be significantly related with tumor recurrence or progression. Seventy-three (16.2%) patients underwent SRS and 64 (14.2%) patients underwent adjuvant radiotherapy (ART) after surgery. Convexity localization was found to be associated with recurrence, mortality and higher WHO 2007 grade.

**CONCLUSION:** Convexity meningiomas are associated with recurrence, mortality and higher WHO 2007 grade. Convexity meningiomas should be totally resected in order to achieve maximum benefit from surgery,

**KEYWORDS:** Intracranial, Meningioma, Stereotactic radiosurgery, Pathology

**ABBREVIATIONS: ART:** Adjuvant radiotherapy, **CNS:** Central nervous system, **CPA:** Cerebellopontine angle, **ICU:** Intensive care unit, **SRS:** Stereotactic radiosurgery, **VTE:** Venous thromboembolism, **WHO:** World Health Organization.

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**Corresponding author:** Emrah CELTIKCI
**E-mail:** drceltikci@gmail.com

## INTRODUCTION

Meningiomas are neoplasms that originate from arachnoid cap cells. They are one of the most commonly diagnosed primary tumors of the central nervous system (CNS) (3,4,10,11,24,37,42,49). The World Health Organization (WHO) 2007 classification system classifies meningiomas into three grades, I-III, with 16 different variants or subtypes (30,36). Grade III meningiomas show a higher rate of recurrence and mortality compared with Grade I and II meningiomas (19,31,43,47,48).

However, decision making for this disease not only depends on its WHO Grade. Variables including patient characteristics, tumor localization, grade, surgical approach, intraoperative challenges and especially the follow-up period determine outcome. In the literature, there is a female predominance in adulthood meningiomas and a variable ratio of WHO grade II meningiomas (4,8,17,18,23,29,33,46). There is a known relatively high risk of postoperative venous thromboembolism (VTE) (1,6,9,12,20,21,26,28,34). Also there are large series investigating the relationship between age, sex, pathological subtype and location (8,18,42,46, 49). However, there is a lack of large series including multiple variables that can affect the outcome and their intricate relations.

We retrospectively analyzed data of 449 adult intracranial meningioma patients operated between 2007 and 2013 at a tertiary center in Turkey.

## MATERIAL and METHODS

This study includes intracranial meningioma cases that underwent surgery between January 2007 and December 2013 at Gazi University, Faculty of Medicine, Department of Neurosurgery. Patient charts, surgical records and follow-up notes were reviewed and analyzed. Gazi University, Faculty of Medicine, Patient Registry Software and National Population Management Software were used to achieve required data. If there was a need for additional data, telephone calls were made. Data collected at the last follow-up visit were used. Inclusion criteria were 18 years of age or older, no previous surgery for intracranial meningioma, and single meningioma. Patients with inadequate data, younger than 18 years, with previous surgery or stereotactic radiosurgery (SRS), and who had only SRS, multiple meningioma, or any type of neurofibromatosis were excluded from the study due to their possible effects on statistics. We also did not investigate surgical approaches as this study not focused on the effects of surgical approaches.

All patients stayed at intensive care unit (ICU) for at least one night after surgery. If there was no disabling functional loss, all patients were started on oral feeding and mobilization in the first morning after surgery. We used low molecular weight heparin 48 hours after the operation if patient was unable to mobilize well or was bedridden. Also compression stockings were routinely used in every patient until discharge from hospital.

All pathological specimens were re-evaluated by a single pathologist. Pathological classifications referred to the 2007 WHO Classification of Tumors of the Central Nervous System (30).

Parameters were: Age, sex, tumor location, pathological subtype, Simpson grade of surgical excision, tumor recurrence or progression during follow-up, VTE in the follow-up period, adjuvant radiotherapy (ART) during follow-up, SRS during follow-up and survival time.

Tumor locations were classified as parasagittal, convexity, sphenoid, sellar/parasellar, posterior fossa, olfactory groove/ frontobasal, middle fossa/Meckel's Cave, tentorial, peritorcular and intraventricular.

Descriptive data were presented as mean and standard deviation. Fisher's Exact Test, one way variance analysis, and t–test for 2 independent variables were used for group comparisons. Survival was estimated by the Kaplan–Meier method, and the log-rank test was used for comparisons. The institutional ethics committee approved the study and the study protocol.

## RESULTS

### Descriptive Data

Between January 2007 and December 2013, 488 adult patients underwent surgery for intracranial meningioma. Four hundred forty-nine patients' data met the inclusion criteria. Mean follow-up period was 53.42±6.53 months. Mean age was 51.67±11.96 years (min 18, max 84 years). There were 123 (24.6%) male and 326 (65.3%) female. Distribution of localizations and pathological subtypes are summarized in Table I. Three hundred thirty-six (74.8%) patients were WHO Grade 1, 100 (22.3%) patients were grade 2, and 12 (2.7%) patients were grade 3. One patient had sclerosing subtype which is outside the grading system.

Surgical resections were done as follows: 72 (16%) Simpson Grade 1, 277 (61.6%) Simpson Grade 2, and 100 (22.2%) Simpson grade 3 and 4.

VTE was seen in 21 (4.6%) patients and tumor recurrence or progression was seen in 58 (12.9%) patients in follow-up period.

Seventy-three (16.2%) patients underwent SRS and 64 (14.2%) patients underwent ART after surgery. There were 4 patients who underwent both ART and SRS. Three of them were WHO grade 2 atypical meningioma and 1 was WHO grade 3 anaplastic meningioma. All of those 4 patients underwent ART first, then underwent SRS because of tumor progression.

Forty-four (9.7%) patients died until the last follow-up date. Thirteen (29.5%) of those patients were never discharged from hospital after operation. Five of them died because of VTE and the other 8 died from other complications (cardiac and respiratory problems, infection etc.). After discharge, 4 of the remaining 31 patients died because of other malignancies. A patient with transitional meningioma died because of

**Table I:** Distribution of Tumor Locations and Histopathological Subtypes

| Location | Pathology | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Meningothelial | Fibrous | Transitional | Psammomatous | Angiomatous | Microcystic | Secretory | Lymphoplasmacyte – Rich | Metaplastic | Clear cell | Chordoid | Atypical | Rhabdoid | Anaplastic | Sclerosing | Total |
| Parasagittal | 29 | 5 | 6 | 4 | 0 | 1 | 1 | 2 | 0 | 2 | 0 | 18 | 0 | 0 | 0 | 68 |
| Convexity | 49 | 5 | 7 | 7 | 7 | 2 | 4 | 1 | 0 | 3 | 1 | 37 | 1 | 8 | 0 | 132 |
| Sphenoid | 38 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 5 | 0 | 0 | 1 | 49 |
| Sellar/Parasellar | 28 | 0 | 2 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 36 |
| Posterior Fossa | 31 | 1 | 6 | 3 | 1 | 0 | 2 | 0 | 0 | 0 | 3 | 5 | 0 | 1 | 0 | 53 |
| Olfactory Groove/ Frontobasal | 10 | 0 | 1 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 1 | 0 | 20 |
| Middle Fossa/Meckel's Cave | 31 | 0 | 5 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 11 | 1 | 0 | 0 | 53 |
| Tentorial | 11 | 0 | 4 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 23 |
| Peritorcular | 5 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 13 |
| Intraventricular | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| Total | 232 | 12 | 37 | 25 | 14 | 3 | 8 | 4 | 1 | 5 | 4 | 91 | 2 | 10 | 1 | 449 |

colorectal cancer, a patient with meningothelial meningioma died because of myosarcoma, a patient with psammomatous meningioma died because of lung adenocarcinoma, and a patient with lymphoplasmacyte–rich meningioma died because of diffuse large B cell lymphoma. Sixteen of remaining 27 patients died related to neurological deterioration due to recurrence of high grade meningioma. All the remaining 11 patients died because of non-neurological reasons and all of them were elderly (>65 years).

**Group Comparisons**

We found a relationship between WHO Grades and localizations. Results of Fischer's Test demonstrated that Grade 2 and 3 meningiomas were localized more commonly at the convexity ($X^2$=47.27, p=0.009).

There was no correlation between pathological subtypes and sex ($X^2$=12.037, p=0.572), and no correlation between pathological subtypes and Simpson Grade (p=0.256). If we exclude meningiomas located in the convexity or parasagittally, the remaining patients' resection rates are 65.7% for Simpson Grade 2, 33.4% for Simpson Grade 3 & 4 and 0.8% for Simpson Grade 1.

There was no correlation between pathological subtypes and sex ($X^2$ = 12.037, p=0.572) and we found no correlation between age and WHO 2007 grade. On the other hand, the mean age was younger in patients who experienced tumor recurrence or progression during follow up (p=0.025) regardless of tumor grade. Also, the mean age was younger in patients who underwent SRS (p=0.001).

There was a correlation between VTE and sex ($X^2$=4.531, p=0.033). The male gender was found as a risk factor for experiencing VTE. Elderly patients tended to experience VTE in follow-up period (t=-3.012, p=0.003) (Figure 1). We found no statistically significant correlation between VTE and other variables.

When we analyzed all pathological subtypes, the highest tumor recurrence/progression rates were found in anaplastic meningiomas (70%), followed by secretory meningiomas (25%), lymphoplasmacyte–rich meningiomas (25%) and atypical meningiomas (22%). However due to their low patient numbers, it is not possible to do a statistical decision about recurrence rates of secretory and lymphoplasmacyte–rich meningiomas. Among 58 patients who experienced tumor recurrence or progression, 7 patients (12%) were WHO grade 3, 20 patients (34.4%) were WHO grade 2, and 31 patients (53.4%) were WHO grade 1.

Overall and recurrence free survivals were significantly longer in patients with atypical meningioma than those with anaplastic meningioma; 157.1 versus 44.6 months and 121.9 versus 26.3 months (p<0.001). Also convexity localization

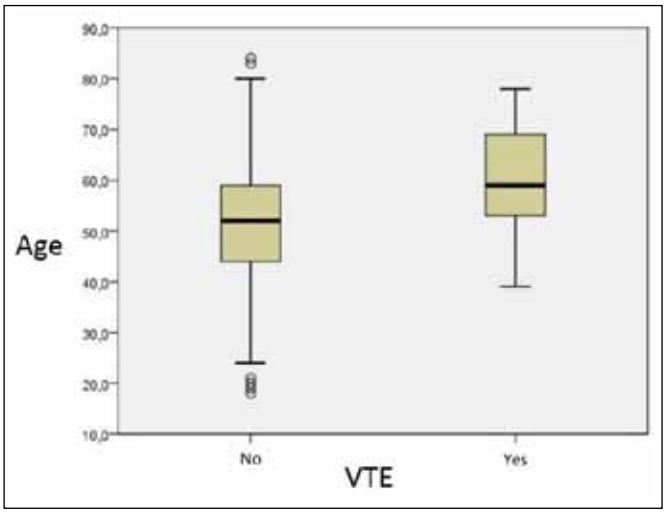


**Figure 1:** Relationship between venous thromboembolism (VTE) and age (t – test for 2 independent variables; t = -3,012, p=0.003).

was found to be related with higher mortality due to higher incidence of higher WHO grades. 18 of 44 patients who died in follow up (40.9%) had convexity meningiomas. Amongst this convexity - mortality group there was 14 Grade 2 or 3 meningiomas.

## ■ DISCUSSION

Our study has similar findings with the literature including female predominance and age distribution (although we excluded the pediatric group)(4,8,17,18,23,35,37,42,46,49). In series of Wang et al. (46), there was a higher female: male ratio in WHO grade 2 and 3 meningiomas, but we found no difference in our series. Our conclusion is, even with pediatric patients or not, this age distribution is a classical characteristic of meningiomas.

VTE is still a risk for patients who underwent intracranial meningioma surgery and clinical incidences range up to 32% (1,6,9,12,20,21,26,28,34). In our series, 4.6% of patients experienced VTE and 5 patients died because of pulmonary embolism. Additionally, we found elderly age and male gender as risk factors for VTE during the follow-up period. In contrast to other series and our series, Hoefnagel et al. investigated the effects of the body mass index (BMI) on thromboembolic complications and found an increased risk in higher weighted patients (23). Effects of BMI on VTE risk is a well-considered study. However, it must be kept in mind if higher BMI patients are also lesser mobilizing ones or not. We concluded that preservation of motor functions and early mobilization after surgery is the key for decreasing VTE rates. Future studies based on calculating mobilization (by the help of new mobile technologies) can be planned to predict individual risk of VTE on meningioma patients.

We found that meningothelial (51.7%) and atypical (20.3%) meningiomas were the most common pathological subtypes of meningiomas. There is an increasing trend to the frequency of Grade 2 meningiomas in literature as well as 26% and 30% (25, 26). Our series has 22.3% Grade 2 patients. Also there are series in which Grade 2 & 3 percentage is approximately 10% (35).

In our series, tumor localization were; parasagittal, convexity, sphenoid, sellar/parasellar, posterior fossa, olfactory groove/frontobasal, middle fossa/Meckel's Cave, tentorial, peritorcular and intraventricular. We classified localizations different than Al-Mefty's classification (15,27). Al-Mefty's classification is much more detailed and more applicable in prospective studies. However, our study is designed as a retrospective study based on clinical notes, surgical records, patients' cards and radiological images. One of the limitations of this study is being a retrospective study, so we tried to summarize and to fit localization classification for our retrospective study. We did not use localization terms as falcotentorium, tuberculum sellae, lateral and middle sphenoid wing, clinoidal, cavernous sinus, sphenoorbital, cerebellar convexity, cerebellopontine angle (CPA), clival and petroclival, temporal bone, foramen magnum, isolated ventricular and pineal region. Instead we used the term "tentorial meningioma" for all tentorium-related meningiomas, "sellar/parasellar" for all sellae and cavernousal meningiomas, "sphenoidal" for all sphenoid-related meningiomas, "posterior fossa" for all cerebellar convexity, foramen magnum and CPA meningiomas and "intraventricular" for all ventricle-related meningiomas. In our series, convexity and parasagittal regions were the most common sites for meningioma growth (44.5%) which is similar with series of Wang et al. and Al-Mefty (15,16,46). Also, non-skull base localizations were found related with higher mortality and higher pathological grade similar with series of Kane et al. (25). Series of Cao et al. implies opposite of this finding, however, as we understand from their manuscript they analyzed just anaplastic subgroup, but not the distribution of other subtypes (7). Our conclusion, which is concordant with findings of Kane et al., is; non-skull base localization is a poor prognostic factor due to higher incidence of grade 2 and 3 meningiomas.

Even though non-skull base localizations are related with poor prognosis, it doesn't mean skull base and posterior fossa meningiomas are surgically easy to deal with. Skull base and posterior fossa are surgically challenging localizations for meningiomas and microsurgical resection of these tumors is frequently associated with new onset of neurological impairment (2,5,13,14,16,22,38-40,41,44,45). There are numerous series in literature, describing surgical approaches to skull base and posterior fossa, explaining challenging parts of those surgeries and neuro-functional results (2,5,14,16,22,38-40,41,44,45). However, many of those series were published when the SRS was not so common (32). In our series, nearly 52.1% of all meningiomas were located in the skull base or posterior fossa. As mentioned in the results section, those locations had relatively higher Simpson grades. As a referral SRS center (Leksell Gamma Knife Model 4C and Perfexion, Elekta), we already performed more than 6000 SRS procedures since 2004. This alternative choice gives chance of intraoperative decision making for total removal of skull base or posterior fossa tumors. Preservation of functional neurological status and decreasing complication rates are very important instead

of total removal of tumors. Our resection rates decrease in skull base, comparing to other localizations. In follow-up period, we performed SRS "where needed". In 249 skull base and posterior fossa patient groups, only 63 patients (25%) underwent SRS (all Simpson grade 2 and higher) and analysis of those patients showed that 24 of them underwent SRS for tumor recurrence or progression in follow-up period (9.6% of all skull base and posterior fossa meningiomas). Remaining patients underwent postoperative adjuvant SRS. In the literature, total removal of basal meningiomas was achieved in 60-87.5% of the patients and 30-56% of the patients suffered complications (2,5,13,14,38-40,45). Our conclusion about SRS is: It is a good choice in meningioma management even post operatively or alone for functional preservation. Additionally, we concluded that SRS is the reason why our series has a relatively higher rate of grade 2 and 3 meningiomas. Convexity meningiomas are much more preferred for surgery by neurosurgeons instead of skull base meningiomas. As convexity is associated with recurrence and higher WHO 2007 grade, that's why we have relatively more grade 2 and 3 meningioma patients.

## CONCLUSION

Convexity meningiomas are associated with recurrence, mortality and higher WHO 2007 grade. To achieve maximum benefit from surgery, convexity meningiomas should be totally resected. Adjuvant therapies like SRS can be beneficial for meningiomas located in the skull base hence total resection of those meningiomas may cause functional loss and they tend to be more benign.

## ACKNOWLEDGMENT

We thank Pinar Celtikci for her help in data collection, and we offer our respect to all our patients for letting us to learn from them.

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